# Title of Abstract
Conversion of labor analgesia for intrapartum cesarean delivery: dural puncture epidural vs combined spinal epidural vs epidural

## Purpose
The conversion of neuraxial labor analgesia to surgical anesthesia via an epidural catheter is frequently used for laboring women requiring a cesarean delivery (CD). The dural puncture epidural (DPE) technique may have an additional advantage over the CSE and traditional epidural techniques when performed using a larger gauge spinal needle allowing for translocation to occur that may improve the rate of conversion. We hypothesized that the DPE technique was associated with increased successful conversion rate of neuraxial analgesia to surgical anesthesia for CD compared to epidural and CSE.

## Methods
This was a multicenter cohort study. Records were retrospectively searched from February 1, 2017 through May 31, 2021 (Institution A) and from September 1, 2021 through September 15, 2022 (Institution B) for all patients with neuraxial labor analgesia and subsequent CD. Failure of conversion was defined as requirement of either a new neuraxial block at time of CD or use of general anesthesia. The type of block (DPE, CSE, epidural), spinal needle gauge, and maternal demographics were collected. The primary outcome was the failure rate of conversion to surgical anesthesia by block type analyzed using a multivariable logistics regression model. Secondary outcomes included rates of failure of surgical conversion by spinal needle gauge and presence of dural puncture analyzed using Chi-square test.

## Results
During the study period, 1479 (A=706, B=773) parturients met inclusion criteria. Labor neuraxial analgesia type distribution for A was 322 (45.6%) DPE, 255 (36.1%) epidural, 129 (18.3%) CSE and B was 57 (7.4%) DPE, 706 (91.3%) epidural, 10 (1.3%). The combined data showed no significant difference in neuraxial labor analgesia conversion failure by block type (p=0.48). However, there was evidence of a significant site by treatment interaction (p=0.03) and thus estimates were reported separately by site. Institution A had 12.7% (90) failed neuraxial conversion for surgical anesthesia, while B had fewer 6.5% (50) failed conversion. Moreover, CSE technique at institution B was associated with increased odds of failure.

## Conclusion
We did not find any significant difference in neuraxial labor analgesia conversion failure for CD between DPE and epidural groups. Given the significant site by treatment interaction, larger sample sizes are required to ascertain our findings and the absence of any clinically meaningful differences.

## References (Max 3)
Table 2 – Results from multivariable logistic regression

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<td></td>
<td>Odds Ratio (95% CI)</td>
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<td>5.79 (1.36, 24.7)</td>
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<td>Combined spinal/epidural</td>
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<tr>
<td>Dural puncture epidural</td>
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<tr>
<td>Spinal needle gauge</td>
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<tr>
<td>No spinal (epidural)</td>
<td>4.79 (0.86, 26.7)</td>
<td>0.199</td>
<td>0.62 (0.30, 1.31)</td>
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<td>27g</td>
<td>1.18 (0.41, 3.38)</td>
<td>0.75 (0.42, 1.32)</td>
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<tr>
<td>25g</td>
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<tr>
<td>No</td>
<td>1.40 (0.57, 3.48)</td>
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*All models are adjusted for age, BMI, gestational age, parity, number of previous CS, date of CS, trained OB anesthesia fellow at time of CS, number of epidural bolus, time from epidural placement to CS, and emergent CS status. For each model, all two-way interactions between the exposure of interest and covariables were assessed. No meaningful two-way interactions were identified. Odds ratios represent the multiplicative increase in odds of failure to convert to anesthesia for CS associated with the given characteristic. Corresponding 95% confidence intervals and p-values are also presented. Missing data was handled using multiple imputation.
Title of Abstract

Treatment of post cesarean delivery lower segment incision pain with topical 5% lidocaine ointment: a clinical audit

Authors

Presenting Author: Luc Saulnier BA (Hons.), MA

Co-Author: Simon Massey MB BCh, MRCP, FRCA, FRCPC – BC Women’s Hospital – Vancouver, BC
Susan Bright MD FRCP – BC Women’s Hospital – Vancouver, BC
Anthony Chau MD MMSc FRCP – BC Women’s Hospital – Vancouver, BC

Purpose

Severe post cesarean delivery (CD) pain is associated with chronic pain, greater opioid use, delayed functional recovery, and postpartum depression.[1] In post-cesarean delivery patients complaining of burning incisional pain unresponsive to opioid analgesia, we have anecdotally observed a decrease in pain scores following use of topical lidocaine 5% ointment. We aimed to evaluate the pain scores before and after the use of topical lidocaine 5% ointment in post-cesarean delivery patients.

Methods

Patients who described their incisional pain as “burning and/or stinging and/or itching” 24h post CD were enrolled in this audit. Patients were then assessed using the Douleurs Neuropathiques 4 (DN4). A score of ≥4 on the DN4 signals the presence of neuropathic pain.[2] Following this, a visual analog scale (VAS) pain score (0=no pain to 10=unbearable pain) was used to rate patients pre-treatment pain. Patients then had a ribbon of 5g of 5% lidocaine ointment applied around the incision with a width of 5-6 cm and allowed to dry. At 1hr after ointment application, patients were asked to rate their pain on using the same VAS score. The primary outcome was the difference in VAS scores before and after treatment analyzed by Wilcoxon signed-rank test. Secondary outcomes were the median DN4 scores and the individual frequency of patients describing their pain as burning, stinging or itching.

Results

20 patients were included in this audit. There was a significant reduction in median VAS scores after lidocaine ointment treatment (6.75 vs. 3.00, p<0.01). The median DN4 was 4.00 (3.00-4.75 [2.00-6.00]). 19/20 (95%) patients reported “burning” pain, 9/20 (45%) reported “stinging” pain, and 3/20 (15%) reported “itching” pain.

Conclusion

Topical 5% lidocaine ointment may be beneficial for patients with pain characteristics that are described as “burning, stinging, and itching”, as this form of atypical pain was reduced by 56%. The commonest pain characteristic was “burning” (95%). From this, a larger randomized control trial is

References (Max 3)


Contact Information

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Name of Supervisor

Simon Massey

Supervisor’s Affiliation
Figure 1. Pre–treatment and post-treatment VAS pain score for 5% lidocaine ointment

Pre-treatment VAS pain median: 6.75 (4.00-7.50 [2.00-9.00]); post-treatment VAS pain median: 3.00 (2.00-5.00 [1.00-8.00])
Title of Abstract
Identifying gaps in care delivery to support patients in pain management after inpatient surgeries: a scoping review

Authors
Janny Xue Chen Ke, Maya de Vos, Katarina Kojic, Mark Hwang, Jill Osborn, Alana Flexman, Heather Stuart, Jason Park, Lindsay Blake, and Daniel I. McIsaac

Purpose
Post-surgical pain is seen in greater than 80% of surgical patients, with most of these patients rating their pain as moderate or severe. Poorly controlled postoperative pain has negative implications on recovery and is a critical risk factor for developing persistent post-surgical pain. However, there is no mechanism to systematically support patients in pain management after discharge from hospital. The aim of this scoping review is to identify the major gaps in care delivery that patients undergoing inpatient non-cardiac surgeries experience in pain management while recovering at home.

Methods
This scoping review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews. Searches were conducted in PubMed MEDLINE, EMBASE, EBSCO CINHAL, Web of Science, and Cochrane Database of Systematic Reviews. Additionally, a grey literature search was conducted. Inclusion criteria were adult patients, non-cardiac surgeries, and included at least one gap in management of postsurgical pain within the first three months of recovery. Exclusion criteria were cardiac surgeries and ambulatory or day surgeries. Articles were screened for inclusion and data was extracted by two independent reviewers. Each identified gap was defined, described, and related to the impact on patients. Gaps identified were grouped together into overarching themes if their definitions were deemed sufficiently similar by consensus amongst the study team.

Results
Of the 4794 results obtained from research databases and grey literature, 35 articles met the inclusion criteria. 51 gaps in the care of postoperative pain management for adult patients undergoing non-cardiac surgery were extracted from the 35 articles, and 5 overarching themes for gaps were identified in: patient and healthcare provider education (n=18); organizational structure and healthcare systems (n =16); individualized management (n = 8); available evidence (n = 4); and population specific challenges (n= 4) including chronic pain/opioid tolerant patients, elderly patients, and patients with malignancy.

Conclusion
This scoping review revealed major gaps during a critical period in postoperative pain management. These gaps represent targets for further research, opportunities to address systemic issues that may contribute to poorly controlled postsurgical pain, and an avenue for improving patient-center care.

References (Max 3)

Contact Information
Name
Maya de Vos

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<th><strong>Supervisor's Affiliation</strong></th>
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<tr>
<td>Department of Anesthesia, Providence Health Care; UBC Faculty of Medicine, Department of Anesthesiology; and Dalhousie University, Department of Anesthesiology</td>
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Title of Abstract
Incidence of general anesthesia for Cesarean delivery before and during the COVID-19 pandemic at BC Women’s Hospital: a retrospective clinical audit

Authors
Maisa Samiee Undergraduate Student – University of British Columbia
Luc Saulnier BA (Hons.), MA, BC Women’s Hospital - Vancouver, BC
Simon Massey MB BCh, MRCP, FRCA, FRCPC – BC Women’s Hospital – Vancouver, BC
Vit Gunka MD FRCPC – BC Women’s Hospital – Vancouver, BC

Purpose
General anesthesia (GA) for Cesarean delivery (CD) is associated with significant maternal complications and poorer neonatal outcomes (1). In reaction to the COVID-19 pandemic, our institution increased our spinal anesthesia (SAB) 0.75% bupivacaine dose to minimize the rate of conversion to GA and to avoid aerosol generation with intubation. We aimed to compare annual incidences of GA before and during COVID at our institution, which has a CD rate of 35-38%.

Methods
Institutional ethics approval was not required for this clinical audit. We retrospectively analyzed data from all 94 GAs for CD between the April 01, 2018 to March 31, 2019 fiscal year (pre-COVID) and all 64 GAs for CD between the April 01, 2021 to March 31, 2022 fiscal year (intra-COVID). The primary outcome was the overall incidence of GA between pre-COVID and intra-COVID time periods. Secondary outcomes were the difference of incidence of GA for elective CD between pre-COVID and intra-COVID, the difference in incidence of all SAB to GA conversions for CD between pre-COVID and intra-COVID, and the difference in average dose of SAB 0.75% bupivacaine between pre-COVID and intra-COVID.

Results
The incidence of GA for all CD decreased from 3.9% in pre-COVID (94/2403) to 2.5% in intra-COVID (64/2535) periods. Incidence of GA for elective CDs decreased from 1.3% to 0.7% during this same time period and the conversion rate for all SAB to GA was reduced from 1.12% to 0.04%. SAB dose increased from 1.58 mL (11.85 mg) to 1.78 mL (13.35 mg) t(33)=-2.81,p=.008 [-.35, -.06]. Furthermore, during COVID-19 we detected a 36% reduction of overall GA for CD, a 46% reduction of GA for elective CD, and a 96% reduction of SAB conversion to GA

Conclusion
The incidence of GA for all CD in our institution before and during COVID-19 was below the 5% SOAP benchmark metric for Center of Excellence certification. Concluding that increasing the SAB bupivacaine dose may have contributed to reducing GA in all categories of CDs during the COVID-19 pandemic.

References (Max 3)

Contact Information
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Name of Supervisor
Dr. Simon Massey

Supervisor’s Affiliation
Figure 1. Incidence of all GA for CD cases, elective CD cases, and cases with conversion to GA from SAB: 2018/2019 compared to 2021/2022.
Abstract-05

Title of Abstract
Time to first recognition of postpartum abnormal sensorimotor deficits following neuraxial anesthesia or analgesia - a retrospective cohort study

Authors
Thomas Yang, BMBS FANZCA.
Wee-Shian Chan, MD FRCP
Anthony Chau, MD MMSc FRCPC

Purpose
Delayed recognition of postpartum peripheral neuropathy may have a negative impact on quality of recovery. Our primary aim was to determine the mean time to first recognition of abnormal sensorimotor deficits in patients diagnosed with postpartum peripheral neuropathy at our institution following neuraxial anesthesia or analgesia. As a secondary aim, we sought to determine the mean time to first ambulation, stratified by mode of delivery.

Methods
Following institutional ethics approval, patients with postpartum neurologic deficits following neuraxial placements referred for anesthesiology and/or obstetric internal medicine consultation from 2013-2022 were retrospectively identified using an administrative database. Risk factors associated with postpartum neuropathy (e.g. duration of second stage, maternal BMI), anesthetic technique and obstetric outcomes were collected. The primary outcome was mean time to first recognition of neurologic deficit stratified by modes of delivery (vaginal, instrumental, attempted vaginal to unscheduled cesarean and scheduled cesarean), measured from the time of delivery to the time of neurologic deficit first reported to the anesthesiology team by the patient or nursing staff. Secondary outcomes were mean time to ambulation, measured from time of delivery to first observed ambulation.

Results
To date, 50 cases have been reviewed. 44 (88%) patients were diagnosed with peripheral neuropathy. Remaining 6 (12%) patients had full sensory and motor recovery deemed to be related to residual local anesthetic block. The mean (SD) time to first recognition of neurologic deficit for all patients after delivery was 18.0 (13.3) h. When patients with residual local anesthetic block were excluded, the mean (SD) time to first recognition of neurologic deficit was 19.0 (13.9) h. The mean (SD) time to ambulation was 25.4 (13.9) h. When stratified by mode of delivery, women who attempted vaginal delivery and required intrapartum cesarean delivery had the longest mean(SD) time to first recognition of neurologic deficit at 21.5 (16.8) h, and longest mean(SD) time to first ambulation at 30.3 (14.8) h.

Conclusion
Patients at our institution with abnormal neurologic deficits who were subsequently diagnosed with peripheral neuropathy were not recognized until approximately 19 hours post-delivery.

References (Max 3)
Wong CA et al. Obstet Gynecol 2003

Contact Information
Name
Thomas Yang

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Anesthesiology – fellow

Name of Supervisor
Anthony Chau
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Title of Abstract

Association of second stage labor with epidural blood patch placement following dural punctures - a retrospective cohort study.

Authors

Thomas Yang, BMBS FANZCA.
Anthony Chau, MD MMSc FRCPC.

Purpose

Epidural blood patch (EBP) is indicated for patients with moderate to severe postdural puncture headache (PDPH), or those with mild headaches unresponsive to conservative treatment. The heterogeneity in severity of PDPH may be related to the variable losses in cerebrospinal fluid (CSF) volume. Specifically, the degree of CSF loss following a dural puncture may be higher in women who experienced Valsalva, pushing and expulsive efforts during second stage of labor. We sought to investigate the risk of epidural blood patch placement in women who did or did not experience second stage labor.

Methods

Following institutional ethics approval, patients with documented accidental dural puncture with an epidural needle or dural puncture with a spinal needle diagnosed with PDPH following an anesthesia consultation from 2020 to 2022 were identified using an administrative database. Details on the anesthetic technique, labor and delivery course, PDPH severity and outcomes were retrospectively collected. The primary outcome was the association of second stage of labor with epidural blood patch placement analyzed using a multivariable logistic regression model, controlling for dural puncture needle gauge (17G vs. 25G vs. 27G) and BMI. Secondary outcome was the time to first recognition of PDPH and pain score on initial recognition in women who did or did not experience second stage of labor analyzed using Mann-Whitney test.

Results

A total of 46 patients met inclusion criteria for review. 24 (52%) women experienced second stage labor, the remaining women did not: they had either first stage dystocia requiring emergency caesarean delivery or a scheduled cesarean delivery. Women who experienced second stage of labor and developed PDPH had a significantly increased odds of needing an EBP (OR 4.4; 95%CI 1.098 to 19.60, p=0.042). The median pain score on initial recognition of PDPH were similar but the median[IQR] time to first recognition of PDPH significantly earlier in women who underwent second stage of labor (17.5h [12.8-25.9] vs. 29.4h [26.2-81.3], p=0.0003).

Conclusion

In women with accidental dural punctures from an epidural needle or PDPH following dural punctures from a spinal needle, maternal exposure to second stage labor was significantly associated with the need for EBP and earlier recognition of PDPH.

References (Max 3)


Contact Information

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Anesthesiology – fellow

Name of Supervisor

Anthony Chau

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BC Women's Hospital, University of British Columbia

**Supervisor's Email**

**Authorship Statement**

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Title of Abstract

Improving Familiarity Among Operating Room Members Using an Anesthesia Resident-led Intervention

Authors

Émilie Chan, Mario Kovacevic, Michelle Mozel, Susan Lee

Purpose

The aim of this project was to increase familiarity within the OR team members by 25% at the Royal Colombian Hospital over the course of a 9-month period ranging from September 2021 to May 2022.

Methods

Develop method to measure familiarity within the OR. Assess baseline familiarity within the ORs.

Results

OR introductions had an overall positive feedback on improving familiarity within the OR team and is part of the mandated WHO briefing checklist. OR introductions took less than one minute to do thereby not contributing to any delays to the OR workflow.

Conclusion

We learned that collecting data from anesthesia residents and staff is challenging as there is an element of survey fatigue. OR introductions were always initiated by the anesthesia resident, this change is unlikely to be sustained without systematic changes involving both the surgical and nursing.

References (Max 3)


Contact Information

Name

Emilie Chan

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Anesthesiology – resident

Supervisor’s Email

Authorship Statement

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**Title of Abstract**

Neuropathic pain-related pharmacotherapy and the multiple sclerosis prodrome: A population-based matched cohort study

**Authors**

*co-senior authors

**Purpose**

Multiple Sclerosis (MS) is an immune-mediated disorder characterized by the progressive degeneration of the central nervous system. Over 50% of MS patients experience neuropathic pain, and gabapentinoids and/or anticonvulsants are one of the first line of treatment for neuropathic pain. However, little is known on the use of such treatments during the prodromal phase (pre-MS onset). The purpose of this study was to estimate the use of neuropathic pain-related medications in the five years before MS onset, which could shed light on whether neuropathic pain forms part of the MS prodrome.

**Methods**

This was a population-based matched cohort study which utilized linked health administrative data from British Columbia from 1996 to 2013. Individuals with ≥3 MS records (physician and hospital coded ICD-9/10-CA and/or MS disease-modifying drug prescriptions) were defined as cases. The cases’ first demyelinating-disease related claim was defined as the index date. Up to 5 controls from the general population were matched to cases by sex, age, calendar-year, and geographical location at index date. In the five years before index date, cases and controls were compared for whether they had at least one prescription for gabapentanoids with and without other anticonvulsants (as use of both drugs may suggest treatment for epilepsy rather than for neuropathic pain). Sex and age at index date adjusted odds ratios (aOR) and 95% confidence intervals (CIs) were estimated using logistic regression.

**Results**

The cohort was comprised of 4,862 MS cases and 22,649 controls and most were female (72%). In the 5 years before the index date, 15.7% of cases and 6.3% of controls had filled at least one prescription for any anticonvulsants, and 10.2% of cases and 4.4% of controls had filled prescriptions for gabapentinoids in combination to other anticonvulsant prescriptions. Finally, 5.5% of cases and 1.9% of controls had filled a prescription for gabapentinoid not combined with any other anticonvulsants. Statistically, the odds of a filled prescription were higher for cases than controls for any anticonvulsants (aOR = 2.66, 95% CI: 2.42, 2.92), and for gabapentinoids with and without other anticonvulsants (aOR = 3.17, 95% CI: 2.7, 3.71 and aOR = 2.45, 95% CIs: 2.19, 2.74, respectively).

**Conclusion**

Neuropathic pain-related medication use was more common in the five years before MS onset versus the matched general population. Results suggest that neuropathic pain may be part of the MS prodrome, which may provide opportunities for earlier recognition and intervention.

**References (Max 3)**

Access to data provided by the Data Steward(s) is subject to approval but can be requested for research projects through the Data Steward(s) or their designated service providers. All inferences, opinions, and conclusions drawn in this publication are those of the author(s), and do not reflect the opinions or policies of the Data Steward(s).

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<td><strong>Supervisor's Affiliation</strong></td>
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**Authorship Statement**

- I confirm that I have read and meet the authorship criteria as listed above.
Title of Abstract

Characterization of the neurophysiologic differences between phenotypes of traumatic brain injury: An historical cohort study

Authors

Eleen Yang, Eric Chow, Eunicia Ursu, Ryan Hoiland, Mypinder Sekhon, and Donald Griesdale

Purpose

Traumatic brain injury is characterized by different pathoanatomic patterns of injury, which include diffuse axonal injury (DAI) and other phenotypes (contusions, extra-axial collections, subarachnoid and intraventricular hemorrhage). Although radiographically delineated, the physiologic responses to injury have not previously been characterized. The purpose of this project was to compare patients with either isolated DAI, mixed DAI (DAI and other patterns of injury) and non-DAI with respect to intracranial pressure (ICP), mean arterial pressure (MAP), and brain tissue oxygenation (PbtO2).

Methods

This was a single-centre historical cohort study of patients admitted to the ICU at Vancouver General Hospital with a diagnosis of TBI and who underwent invasive multimodal neuromonitoring between September 2014 to November 2022. Admission computed tomography (CT) scans of the head were used to determine following pathoanatomic patterns: isolated DAI (petechial or intraventricular hemorrhage), non-DAI (epidural or subdural hematoma, contusion, and traumatic subarachnoid hemorrhage), or mixed DAI (DAI and one of a non-DAI phenotype). ICP, MAP and PbtO2 were collected using ICM+ Brain Monitoring Software (Cambridge UK). We fitted a linear mixed model (specifying “patient” as a random effect) to estimate the average profiles of PbtO2, ICP and MAP over time. We used a restricted cubic-splines model to plot the non-linear relationship between PbtO2 and MAP.

Results

The 72 patients in the cohort had the following phenotypes of injury: 22 (31%) with isolated-DAI, 21 (29%) with mixed-DAI, and 29 (40%) with no-DAI. The mean (standard deviation) age of the cohort was 36 (15) years, and 56 (78%) were male. The most frequent etiologies of the TBI were motor vehicle collisions in 28 (40%) and falls in 18 (26%). The median [interquartile interval] admission Glasgow Coma Scale Motor was 3 [1 – 4]. The median duration of invasive monitoring was 4 [2.0 – 5.5] days. As seen in the figure, the mean ICP was lower for patients with an isolated-DAI (13 [5]) compared to those with either mixed-DAI (17 [11]) or no-DAI (17 [9]) (P=0.048). There was no difference in MAP or PbtO2 between the phenotypes. MAP increased over time in all phenotypes. Overall, 16 of 72 (22%) patients died in hospital, which was highest amongst those who sustained mixed-DAI (7 of 21 [33%]).

Conclusion

Irrespective of phenotype of injury, all patients had similar trajectories of MAP and PbtO2 over time. ICP was lower in those patients with an isolated-DAI. Our next steps will include examining indices of autoregulation and comparing therapeutic interventions amongst the three phenotypes of injury.

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Figure (if applicable)

- [MAP-PbtO2-ICP-over-time.jpg](#)

Figure legend: Individual light blue lines are a locally weighted scatterplot smoothing (LOWESS) for each individual patient. The dark line is the spline function across all patients with its 95% confidence interval. The $P$-values are referent to No-DAI category.
Creation of a Website for Perioperative Ultrasonography: A Learning Project

Jordan Meyers, Su-Yin MacDonell, Mario Kovacevic

Purpose

Develop an online point of care ultrasound resource for medical students and junior residents, in accordance with the goals outlined in the National Curriculum for Canadian Anesthesiology Residency set out by the Royal College.

Methods

This learning project involved three main components:

1. Review the current and future POCUS standards set out by the Royal College, as well as other ubiquitous POCUS exams.
2. Utilize the I-AIM framework to create a referenceable framework for medical students and junior residents to learn and apply POCUS in a clinical setting.
3. Add Ultrasound subsection and modules to existing www.SPHPOM.com online platform.

Results

Building on the work of Mario Kovacevic and Dr. Su-Yin MacDonell in the creation of www.SPHPOM.com, an Ultrasound tab, was added to the website, which contains a dropdown menu containing seven ultrasound modules including cardiac, lung, airway, DVT, IVC, gastric and FAST ultrasound. Each ultrasound module was organized into the following subheadings according to the I-AIM framework:

1. Background
2. Indication
3. Acquisition
4. Interpretation
5. Medical decision making
6. Pitfalls and modifications
7. Comprehension questions

Conclusion

The Ultrasound tab of www.SPHPOM.com is currently published online, providing learners with a resource for point-of-care ultrasound learning. Learners on their perioperative anesthesia rotation can contribute to the ultrasound website with additional subsections.

References (Max 3)


Contact Information

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Authorship Statement

- I confirm that I have read and meet the authorship criteria as listed above.

Figure (if applicable)

- Meyers UBCResearchDay2023.png

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## Creation of a Website for Perioperative Ultrasonography: A Learning Project

### Abstract

Perioperative ultrasonography (POCUS) is an increasingly utilized field for healthcare professionals, especially in the perioperative and intensive care settings. To address the need for standardized education and training, a learning project was designed to improve understanding and application of POCUS in perioperative settings.

### Learning Project Overview

This learning project is divided into three main components:

1. **Initial Design:**
   - Develop a website with interactive modules and quizzes to enhance learning and retention.
   - Incorporate feedback from users to continuously improve the content.

2. **User Engagement:**
   - Use social media campaigns to promote awareness of POCUS in perioperative settings.
   - Collaborate with medical institutions to integrate POCUS training into their curricula.

3. **Evaluation:**
   - Implement a comprehensive evaluation plan to measure the effectiveness of the learning project.
   - Conduct surveys to gather user feedback and improve the website.

### Needs Assessment

The project was developed with the following goals in mind:

- **Identify Key Topics:**
  - Acute and chronic conditions requiring POCUS
  - Equipment and technique
  - Image interpretation

- **Develop Educational Modules:**
  - Interactive case studies
  - Video tutorials
  - Online quizzes

- **Conduct Pilot Testing:**
  - Collaborate with medical students and residents to refine the modules
  - Gather feedback for iterative improvements

### Authorship Statement

- I confirm that I have read and met the authorship criteria as listed above.

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## References

From Garbage to Green: A Soft Plastic Recycling Initiative in the Anesthesia Department of Royal Columbian Hospital

Moura, Claire*; Narsingani, Karim*; Dhillon, Simrin; Tweedle, Shelley; Lee, Susan
*Equal contributions to the project
**This was a resident led initiative with contributions from all current UBC Anesthesia residents.

Purpose

Climate change is a significant threat to human health, and the Canadian healthcare system is responsible for 4.6% of national carbon emissions. Anesthesia-related activities contribute up to 25% of all operating room waste. It has been shown that 97.5% of Canadian anesthesiologists have a willingness to recycle but only 30.2% currently do so. The purpose of this anesthesia resident-led quality improvement project was to develop a soft plastic recycling program within the anesthesia department at Royal Columbian Hospital, with the goal of increasing daily soft plastic recycling to 1kg.

Methods

A brand-new soft plastic recycling program was created, complete with visual aids in each operating room to help with proper sorting and disposal. To fine-tune its effectiveness, multiple PDSA (Plan-Do-Study-Act) cycles were implemented. Starting with one operating room, the program's success was measured by weighing the daily soft plastic output and assessing any errors. The errors included evaluating the number of hard plastics, glass products, paper products, biohazardous or confidential material being mixed in with the soft plastic waste. After successful results, the program was expanded to all operating rooms with a continued error assessment. Working alongside cleaning staff, a pathway was established for transporting soft plastic waste to the hospital's waste management wing before being collected by a third-party vendor.

Results

Single OR recycling produced a median of 162.5g of daily soft plastic waste. This increased to a daily soft plastic recycling median of 1060g once the program was expanded to all of the operating rooms. There were a total of 80 erroneous objects placed incorrectly in the soft plastics recycling. The most common error identified was the mixing of hard plastics with soft plastics, accounting for 76.24% of all errors. This was followed by glass and paper products accounting for 9.9% and 8.91% of errors, respectively. The remaining 4.95% of errors were biohazardous materials. However, 4 out of the 5 total materials identified as biohazardous were mixed on a single day of measurements indicating a potential measurement error. Throughout our data collection no confidential material containing patient identifiers was mixed in with the soft plastic recycling.

Conclusion

This QI project demonstrated the feasibility and effectiveness of implementing an anesthesia soft plastic recycling program in a hospital setting. Ongoing monitoring and education are essential to sustaining the program's success and ensuring appropriate disposal practices.

References (Max 3)


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### Title of Abstract
Severe intraoperative hyperkalemia after low-dose mannitol in a healthy neurosurgical patient

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### Purpose
To describe a case of severe intraoperative hyperkalemia associated with low-dose mannitol administration in a healthy patient undergoing an elective intracranial neurosurgical procedure

### Methods
Clinical features (Case Review): A 27-year-old male presented for elective neurosurgical repair of a symptomatic Type 1 Chiari malformation. He was generally healthy, with no cardiac or renal comorbidities, and had no surgical or anesthetic history. During the procedure, 0.5 mg/kg (50 grams) of intravenous mannitol was infused over twenty minutes. Shortly after, peaked T-waves were identified on three-lead electrocardiogram. Subsequent arterial blood gas analysis demonstrated severe hyperkalemia with a potassium of 7.1 mmol/L. The patient was treated with calcium, insulin, and furosemide, and his potassium corrected. The case proceeded and the patient recovered uneventfully. Subsequent post-operative laboratory testing of his serum chemistry showed complete resolution of hyperkalemia.

### Results
This case report reviews previous case data of mannitol administration associated with hyperkalemia, commenting on demographics and relevant comorbidities, and also reviews possible mechanisms including its osmotic activity and the corresponding interactions of other electrolytes. Finally the possible implications of mannitol dosing and the implications of ideal versus total body weight calculations are considered.

### Conclusion
Mannitol has previously been reported to cause electrolyte disturbances, including hyperkalemia, particularly when used at higher doses. Mechanisms of this phenomenon remain poorly understood, but this account of severe hyperkalemia in a healthy patient suggests this risk may be independent of dose.

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Authorship Statement

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**Title of Abstract**
Remodeling of Small Airways and Associated Arterial Vasculature is a Hallmark of Idiopathic Pulmonary Fibrosis

**Authors**
Najmeh Assadinia, Andres Moran-MacDonald, Keith Wu, Kohei Ikezoe, Stacey Ledoux1, Joel D Kooper, James C. Hogg, Dragos Vasilescu, Tillie-Louise Hackett

**Purpose**
Idiopathic pulmonary fibrosis (IPF) is the most common and deadliest interstitial lung disease. Micro computed tomography (microCT) studies from our group have shown both the loss and traction of the terminal bronchioles are early features of fibrosis in IPF. However, it is currently unknown whether the associated pulmonary arteries are also remodeled. The goal of this project was to perform structural quantification of terminal bronchioles (TBs) and the terminal bronchiole-associated vessels (TBVs) in IPF lungs and compare the measures with matched controls using microCT imaging.

**Methods**
Explanted lungs from IPF transplant patients (n=8) and age matched controls (n=8) were inflated with air to 10cm of H2O and frozen. 2cm thick slices were taken from apex to base of the lungs and 8 systematic uniform random samples per lung. Samples were scanned with microCT for assessment of TBs and the TBVs, which were then assessed using stereology to analyze the lumen and wall area, length, roughness, and number.

**Results**
We confirmed that the number of TBs per lung was significantly decreased in IPF lungs compared to donor control lungs (p=0.0056). Similarly, the number of TBVs per lung was decreased in IPF lungs compared to control lungs (p=0.0067). Furthermore, there were more TBs without a TBV in IPF lungs compared to control lungs (p=0.0016). Interestingly, the total arterial volume per tissue sample was increased in IPF patients compared to controls (p=0.0028). This was due to the remaining TBVs in IPF lungs being remodeled, with an increased vessel lumen volume (p=0.0162) and wall thickness (p=0.0014) compared to control lungs.

**Conclusion**
Loss of TBs and TBVs is a pathological feature in the IPF lungs. The remaining TBs and TBVs are distended and thickened leading to bronchiectasis and angioectasis, respectively, which increase airway and vessel volumes. Thus, Pulmonary arterial vasculature can be a potential target for IPF therapies.

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Figure (if applicable)

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Figure 1: 3-dimenional segmentation of representative A) control lung and B) IPF Lung showing arterial vasculature (red) and airways (cyan).

Comparison of C) terminal bronchial (TB) lumen volume, D) number of TBs, E) terminal bronchiolo vessel (TBV) lumen volume, and F) number of TBVs between IPF and Control lungs.
Title of Abstract

Efficacy of continuous morphine infusion as a primary analgesic modality in patients undergoing open pyeloplasty: a retrospective chart review

Authors

Ridhima Bhatia, Samantha Pang, Caitlin Gallagher, Kourosh Afshar, Nicholas West, Matthias Görges, Katherine Bailey

Purpose

Pyeloplasty is a common procedure for correction of ureteropelvic junction obstruction and is associated with postoperative pain. A continuous morphine infusion (CMI) is often the primary analgesic modality, though it is associated with side effects such as nausea and vomiting. This retrospective study aimed to characterize postoperative pain in pyeloplasty cases with CMI analgesia to prepare for a prospective study of the Erector Spinae Plane Block (ESPB). ESPB is a safe and effective analgesic technique for pediatric surgery [1,2], which may reduce CMI requirements and side effects.

Methods

This was a quality improvement study, which our research ethics board deemed exempt from review under TCPS2 article 2.5. We conducted a retrospective chart review of 117 patients who underwent pyeloplasty between 2008 and 2021. Patients who were under one year old, underwent a laparoscopic/robotic procedure, did not receive CMI, or had a neurological disorder were excluded. Collected data included demographics, intraoperative opioids, postoperative opioids (CMI, intravenous and oral morphine doses), pain scores, incidence of postoperative nausea and vomiting (PONV) determined by anti-emetic doses, and length of hospital stay. Total postoperative morphine consumption, including CMI, intravenous bolus, and oral doses, was also calculated. We modelled the effect of CMI and total postoperative morphine consumption on postoperative outcomes using linear regression.

Results

Of the 117 pyeloplasty cases, 54 (46%) met our eligibility criteria. These patients (38 males) were median (interquartile range) 49 (23-80) months old, and their procedures lasted 128 (106-140) minutes. These patients received a CMI for 24 (20-45) hours at an average of 15.8 (9.2-18.6) mcg/kg/hr. In total, 26/54 (48%) patients had nausea, and 20/54 (37%) patients had at least one episode of emesis. Age was associated with total postoperative morphine consumption ($\beta=2.860$, SE=1.298, $p=0.032$). Total postoperative morphine consumption significantly predicted the number of episodes of nausea ($\beta=0.004$, SE=0.001, $p=0.002$) (Figure 1) and length of the hospital stay ($\beta=0.001$, SE=0.001, $p=0.002$). Furthermore, the length of the procedure significantly predicted the length of the hospital stay ($\beta=0.007$, SE=0.002, $p=0.006$) and episodes of emesis ($\beta=0.01$, SE=0.006, $p=0.006$).

Conclusion

Our retrospective analysis indicated a significant association between postoperative opioid consumption and the subsequent opioid side effect of PONV and increased length of hospital stay. These data will be used to plan a prospective research study comparing ESPB and CMI on postoperative outcomes.

References (Max 3)


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**Figure (if applicable)**
- [ESPB_APTcharts.jpg](#)

**Figure 1.** Total postoperative morphine consumption is significantly correlated with postoperative (a) nausea $r(52)=0.48$, $p<0.001$ and (b) episodes of emesis, $r(52)=0.28$, $p=0.04$. 
**Title of Abstract**

MINS and Renal Transplant at SPH

**Authors**

Su-Yin MacDonell, Christopher Prabhakar, Serenity Aberdour

**Purpose**

This was a retrospective chart review, examining the incidence of myocardial injury after non cardiac surgery (MINS) in patients having undergone renal transplant at a single institution (St Paul’s Hospital) in Vancouver, Canada. We also sought to determine for this patient population: a) 30 day mortality, new CHF, non fatal MI b) Impact of MINS diagnosis on patient medication management c) Current MINS screening rate at our facility

**Methods**

This was a retrospective chart review of eligible patients' EMRs at SPH from an 18 month period.

MINS criteria: diagnostic criteria outlined by the AHA as well as their prognostic criteria for hsTnT

**INCLUSION CRITERIA:** All patients who had renal transplant surgery at SPH from June 2019 to December 31 2021 who were eligible for MINS protocol.

**EXCLUSION CRITERIA:** All other surgical patients. Renal transplant patients not eligible for MINS

MINS diagnosis: confirmed through independent review by Drs Su-Yin MacDonell and Christopher Prabhakar. Dr Serenity Aberdour reviewed individual patient EMRs for 30 day mortality, new CHF, non fatal MI, patient medications.

**Results**

A) Incidence of MINS in SPH renal transplant patients: 75 of 245 patients (approx 30%)
B) 30 day: mortality (in hospital): 0
C) New CHF within 30 days: 0
D) Non-fatal MI/arrest within 30 days: 5
E) Impact on patient management: 6 patients newly started on ASA and/or a statin. Additional 5 patients with MINS were restarted on a previously discontinued ASA and/or statin.
F) ICU/CCU admissions (unplanned): 11 within the entire review period. 6 occurring within 30 days of transplant procedure.
G) Screening rate: 205 met criteria for screening. Of these:
   a. 88/205 were screened with BNP
   b. 140/205 were screened with post op troponin
   c. 69/205 BNP positive were screened with post op troponin
   d. 139/205 properly screened = 67.8% screening rate

**Conclusion**

The incidence of MINS was just over 30%, somewhat higher expected.
Non fatal MI incidence and 30 day mortality was low.
Current screening rate indicates a potential area for quality improvement at our facility.
MINS screening did have an impact of patient medication management.

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Title of Abstract

Interleukin-1 Alpha Counteracts Transforming Growth Factor-β1 and β2 Signaling In Lung Extracellular Matrix Remodeling

Authors

Kauna Usman1,2, May Fouadi1,2, Kingsley Okechukwu1,2, Emmanuel T. Osei1,3, Tillie-Louise Hackett1,2.
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Purpose

The Lung extracellular matrix (ECM) forms an essential scaffold for cells within the lung and also a reservoir for cytokines and growth factors. Repetitive lung injury causes persistent inflammatory immune cell infiltration, the production of growth factors and remodeling of the ECM, leading to lung fibrosis. Interleukin-1 alpha (IL-1α) and transforming growth factor-β (TGF-β) are important in mediating inflammation and ECM production respectively. Our goal was to assess the cross-talk of IL-1α and TGF-β signaling as both are released during lung injury but have only been studied in isolation.

Methods

Primary human lung fibroblasts (PHLF) were seeded (100,000/well), grown to 80% confluence and treated with media control, or 1 ng/ml IL-1α with or without 50 ng/ml TGF-β1 or TGF-β2. PHLF were also treated with media control or 12.5 nM miR-146a mimic with or without 50 ng/ml TGF-β1 or TGF-β2. Using a 3-Dimensional collagen gel model, PHLF were seeded (40,000/well) and weighed at 72 hours following treatment to assess ECM remodeling. Protein samples were extracted after 1, 6 and 72 hours for Western blot and miRNA samples were extracted at 6, 24 and 48 hours for quantitative polymerase chain reaction. The spent media was also collected for enzyme-linked immunosorbent assay.

Results

Stimulation of PHLF with TGF-β1 and TGF-β2 induced collagen I and fibronectin (P < 0.05) but attenuated decorin protein expression, these were inhibited when IL-1α was present (p < 0.05). Treatment of TGF-β1 and TGF-β2 also induced myofibroblast differentiation and the expression of α-smooth muscle actin, which was inhibited by IL-1α (P < 0.05). Further, the presence of IL-1α led to the inhibition of collagen I gel contraction (P < 0.05). Stimulation with IL-1α induced the expression of IL-6, IL-8 and thymic stromal lymphopoietin (P < 0.05), which were not inhibited by TGF-β1 or TGF-β2. IL-1α and not TGF-β1 and TGF-β2 led to the downregulation of IL-1 receptor-associated kinase-1 (IRAK1) and tumor necrosis factor receptor-associated factor-6 (TRAF6) protein expression. IL-1α stimulation led to the up-regulation of miR-146a which may regulate TGF-β induced collagen I and α-SMA synthesis.

Conclusion

Our data show that the inflammatory mediator IL-1α is essential for modulating the remodeling response of TGF-β1 and TGF-β2 and that this crosstalk may be important for balancing tissue repair versus tissue fibrosis. Future work will focus on their dysregulation in lung diseases involving fibrosis.

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Measurement of single cell and spatial multiomics within the brains of rats following fentanyl self-administration.

Rishika Daswani (1,2), Kelly Hrelia (3,4), Beth Whalen (2), Amrit Samra (2), Basak Sahin (2), Catharine Winstanley (3,4), Amrit Singh (1,2)

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The opioid crisis continues to impact Canadian communities, with an increase of 48% in suspected opioid-related overdoses between January 2019 and June 2022. Opioid use leads to permanent changes in brain circuitry including changes in neuronal response and plasticity. The gaps in our understanding of opioid actions within the brain prevent the development of effective therapies. Our goal is to identify molecular changes in various regions of the rat brain using single-cell multiomics and spatially resolved subcellular transcriptomics in response to the self-administration of fentanyl.

We utilized four rats bred on a Long-Evans background (2F/2M) to develop the exposure model. Rats underwent ten 2-hour sessions of continuous access self-administration (SA) of fentanyl (1.5 mcg/kg/infusion) or saline followed by five 2-hour sessions of intermittent access SA. After 15 days of SA, rats underwent two weeks of forced abstinence, where they were tested for cue-induced reinstatement of drug seeking behaviour on days 1, 7, and 14. Animals were euthanized, and the brains were immediately extracted and flash frozen on dry ice. Corresponding blocks from the two hemispheres of the frontal lobe of each brain were used to profile single cell gene expression and single cell chromatin accessibility using 10x Multiome protocol and 1000 RNA targets using NanoString CosMx Spatial Molecular Imager. Analyses were performed using various R-packages; Seurat, Signac, limma and CellChat.

The 10x multiome data consisted of 9,535 nuclei with 25,627 mRNA counts and 124,882 ATAC peaks. The NanoString data consisted of 11,722 cells for the panel of 1000 RNA target molecules. Initial data showed distinct populations of neuronal and nonneuronal cells in the brain, with many cell populations showing a transcriptional response to fentanyl exposure. Eleven cell-types were identified based on expression of marker genes, with Meis2-positive neurons being most abundant. Most cell types consisted of genes that displayed an interaction between drug and sex, suggesting sex-specific cell-specific gene expression in response to fentanyl exposure. We identified many mitochondrial genes that were up regulated in macrophages after fentanyl exposure compared to saline. Macrophages have the greatest number of ligand-receptor interactions with vascular leptomeningeal cells and perineuronal nets.

This study is the first to simultaneously apply single cell multiomics and spatial subcellular transcriptomics to the rat brain following exposure to fentanyl. It provides valuable insights into the molecular mechanisms of opioid-induced changes to brain circuitry.

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Abstract

Title of Abstract

Development and internal validation of a model that incorporates postoperative hypotension to predict troponin level after inpatient non-cardiac surgery

Authors

Ryan Best MD, Su-Yin MacDonell MD MSc FRCP, Sihaoyu (Sherry) Gao, Paula Branco PhD, Zahra Ali, Anusha Kambhampati, Jayalakshmi Iyer, Philip J Devereaux MD PhD FRCP, Alana Flexman MD FRCP, Matthias Görges PhD, Lang Wu PhD, Ron Ree MD FRCP, Charles Lo MD MBA FRCP, Janny Xue Chen Ke MD FRCP

Purpose

Myocardial injury after noncardiac surgery (MINS) affects 15% of patients and is associated with increased 30 day mortality. The postoperative days zero, one, and two account for approximately 40%, 40%, and 10% of MINS, respectively. As MINS is often asymptomatic, identification requires postoperative troponin monitoring. However, existing models have limited performance in identifying high risk patients, are not responsive to postoperative hypotension that is associated with MINS. Our goal was to develop a model that incorporates postoperative hypotension to predict troponin levels.

Methods

We received Research Ethics Board approval. This was a retrospective cohort study of Cerner electronic medical records that included patients aged ≥ 45 years who underwent index inpatient noncardiac surgery from January 2020 to June 2021 at the St. Paul’s Hospital, Vancouver, BC, and had MINS protocol ordered. Patients were excluded if they had no documented vital signs or postoperative troponin, or within 72h postoperatively underwent repeat surgery or were readmitted. We developed a multivariable linear mixed effects model using a priori predictors (percentage duration of mean arterial pressure (MAP) < 75 mm Hg on postoperative days zero to two, age, sex, emergency surgery, Revised Cardiac Risk Index, and postoperative glomerular filtration rate) to predict the respective daily maximum troponin level on days zero to two. Repeated patient-based five-fold cross validation was performed.

Results

The cohort included 847 patients, with a mean age (SD) of 72 (11) years, and 57.5% were male. The most common surgical services were general (31.2%), orthopedic (27.5%), urology (26.6%), and vascular (10.4%), with a median (interquartile range) surgery duration of 114 [72-170.5] minutes and length of stay of 6.19 [3.15, 13.14] days. The mean (standard deviation) for the percentage of duration of MAP < 75 mm Hg on days 0, 1, and 2 were 20 (26), 16 (26), and 13 (25), respectively. There were 7 (0.8%) patients with type one myocardial infarction, and 40 (4.7%) with type two. The median (IQR) for maximum troponin was 20 [12, 37.25] preoperatively and 24 [15, 48] postoperatively, respectively. In terms of model performance, the RMSE was 15.9 and the conditional R-squared was 0.9.

Conclusion

We developed and internally validated a model to predict troponin level that incorporates postoperative hypotension. The model fit the data well but does not have sufficient accuracy for clinical practice. Better data through prospective and frequent sampling may improve model performance.

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Title of Abstract
Evaluation of Opioid Prescribing Practices after Orthopaedic Surgery at St. Paul's Hospital

Authors
Kamola Ismadiyarova (1), Nicola Edwards MSc (1), Donna Rahmatian PharmD (3), Tamara Mihic PharmD (3), Felicia Young PharmD (3), Ainsley Sutherland MD, PhD (1,2)

Affiliations: (1) Providence Health Care Department of Anesthesia; (2) University of British Columbia Department of Anesthesiology, Pharmacology and Therapeutics, (3) Providence Health Care Pharmacy

Purpose
Canada is among the top opioid prescribers worldwide1; however, increasing research demonstrates presence of a large discrepancy between how much is prescribed and used.2 Considering the ongoing opioid crisis in Canada, minimizing opioid prescriptions and reducing community exposure is critical. More accurate opioid prescriptions would spare patients the burden of cost, inconvenience of disposal, and risk of diversion. Through this observational retrospective quality improvement project, we aim to evaluate patients’ actual opioid requirements to develop more tailored discharge prescriptions.

Methods
Orthopaedic surgical patients (n=117) were phoned 1-2 weeks after discharge to be asked about what prescriptions they have received for pain, and how much of it they have used. Other questions inquired about storage and disposal of excess tablets, overall pain control, side effects, and use of multimodal analgesia. Exclusion criteria included opioid usage prior to admission either recreationally or for chronic pain, discharge to an inpatient rehabilitation or nursing facility, and significant post-operative complication(s). Descriptive statistics were used to assess the primary and secondary outcomes. Of note, to analyze amounts of remaining opioids, we compared values of prescribed to consumed opioids, without taking into account whether the prescriptions were filled or partially filled. Amounts were standardized and are presented as morphine milligram equivalents (MME).

Results
Data from 42 patients was used for analysis. Median MME prescribed was 412.5, and median MME consumed 1-2 weeks post-discharge was 142.2. At the time of survey, more than half (22/42) of the patients were not utilizing any opioids. Of those, only 18% (4/22) had finished their prescriptions (one patient required a refill); the rest had median of 185 MME of unused tablets. Of those still taking opioids, 60% (12/20) had 2 types prescribed; 25% (3/12) had finished the 1st opioid and continued the 2nd, while median of 275 MME was left unused among the 50% (6/12) who have either not started or stopped taking one of their opioids. The averages of patient-reported pain levels on the day of survey and on average since discharge were 2.5 and 3.8 on a 10-point scale, respectively. Overall patient satisfaction with pain control was high, with >90% reporting “very satisfied” or “satisfied” ratings.

Conclusion
Our observations suggest that amounts of opioids prescribed following an orthopaedic procedure tend to exceed patients’ requirements. Further exploration of procedure-specific opioid utilization, and modification of prescribing practices may be beneficial to both patients and community.

References (Max 3)

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<td>British Columbia Department of Anesthesiology, Pharmacology and</td>
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### Title of Abstract

The involvement of glutamate variability in pain sensitivity and other participant characteristics

### Authors

Cassandra Choles, Oscar Ortiz, Jessica Archibald, Lukas Linde, and John Kramer

### Purpose

Pain is a complex and subjective experience. Pain research in humans has largely neglected to acknowledge this variability; however, it could reflect important personal features that are relevant to our understanding of pain. For instance, increased pain sensitivity has been associated with reduced variability in areas like the cingulate cortex, which is involved in the perception of pain [1]. Here, we used proton magnetic resonance spectroscopy (1H-MRS) to investigate resting-state glutamate variability within the cingulate cortex in relation to inter-subject pain sensitivity.

### Methods

Resting glutamate levels were measured at two timepoints (at 3 and 6 minutes) in participants not diagnosed with chronic pain or any other major health conditions, through four 1H-MRS respective scans in the cingulate cortex: the anterior, anterior mid-, posterior mid-, and posterior cingulate cortices. Scores from the Pain Sensitivity Questionnaire and Depression Anxiety Stress Scale (DASS) to quantify perceived pain sensitivity and mental health contributions. For a quantitative measure of pain sensitivity, electroencephalogram activity with a slightly painful laser stimuli were collected. A measure of variability within each cingulate region was calculated via the coefficient of variation from these two timepoints. Variability was explored within and across the four regions, and in relation to sex.

### Results

Preliminary results (N = 30, age range: 18 - 60) demonstrate that glutamate variability did not significantly differ within each of the four cingulate regions across the two timepoints (p > 0.05), or across the regions between sexes, F(3,29) = 1.05, p > 0.05. A trend of reduced variability was observed in the mid-cingulate regions, but did not reach significance. Next steps involve analysing glutamate variability within, and between cingulate regions in relation to pain sensitivity (perceived and quantified), mental health contributions, and sex for the full sample of 50 participants.

### Conclusion

These findings suggest there is limited variation in glutamatergic activity in ‘healthy’ participants at rest, with the current sample size. This provides a basis to expand our population into participants living in chronic pain, to assist more effectively in understanding and diagnosing pain.

### References (Max 3)


### Contact Information

**Name**

Cassandra Choles

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Pharmacology – MSc student

**Name of Supervisor**

Cassandra Choles

**Supervisor’s Affiliation**
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The pleiotropic properties of angiotensin II receptor AT1 blocker losartan on protective endothelial function are mechanosensing-dependent and AT2 receptor-independent.

Elodie Sauge, Pascal Bernatchez

Losartan is an anti-hypertensive angiotensin II (Ang II) receptor type 1 (AT1R) blocker with a long list of therapeutic properties in diseases not linked to hypertension. We showed that losartan activates endothelial function in vivo via the release of vasodilatory nitric oxide (NO), which is typically associated with aerobic exercise and laminar flow. As AT1R blockade has been shown to trigger an Ang II ‘switch’ towards NO-releasing AT2R, we investigate the role of AT2R and laminar flow response-deficient caveolin-1 KO mice on losartan’s effects on endothelial function.

WT and AT2R KO mice were chronically treated for 4 weeks with losartan (0.6 g/l) in drinking water or regular water. Acute stimulations of WT, caveolin-1 (Cav-1) KO and AT2R KO mice were performed with a losartan metabolite, as losartan is a prodrug. The endothelial NO release properties of losartan and its metabolite were evaluated via vasoconstriction and vasorelaxation of mouse aorta rings using dual-wire myograph systems.

Losartan metabolite prevented phenylephrine (PE)-induced contraction by up to 65 % (p < 0.01) in L-NAME and endothelium removal-sensitive fashion in WT mice. Use of transgenic mice revealed that these effects involve the eNOS/caveolin-1 axis and the endothelium-dependent hyperpolarization factor (EDHF), but were independent of AT2R. Similarly, ATR2 KO mice showed that chronic treatment with losartan decreased PE-induced contraction by 52.3 % ATR2 KO (p < 0.05), compared to controls.

Our data show that losartan and its metabolite can activate endothelial function in an AT2R-independent manner. We observed that the effects of losartan metabolite on mouse aortic rings were absent following endothelium denudation and dependent on the caveolin-1 mechanosensing machinery.

Elodie Sauge

Pharmacology – PhD student

Pascal Bernatchez

Pharmacology, HLI

I confirm that I have read and meet the authorship criteria as listed above.
# Title of Abstract

Investigating genetic predictors for variable morphine responses in children

# Authors

Erika N Scott, Janet Zhang, Colin JD Ross, Bruce C Carleton, S Rod Rassekh, Ruth E Grunau, and Catrina M Loucks

# Purpose

Morphine is commonly prescribed for the relief of serious pain in children, but responses vary widely. Several genes have now been associated with morphine response. Therefore, the purpose of this study is to determine whether patients with variable morphine responses (both adverse effects and no pain relief) carry known genetic variants at higher frequencies than other patients of similar ancestries.

# Methods

We aim to ultimately recruit and clinically characterize \( n=40 \) children with adverse effects at low doses and \( n=40 \) children with no pain relief despite high doses of morphine to compare with \( n=180 \) previously-recruited children with typical responses at low doses and \( n=180 \) previously-recruited children with typical response at high doses of morphine, respectively. A systematic review is currently being conducted to identify candidate genetic variants for morphine response. Genome-wide genotyping will be conducted on all patients and minor allele frequencies of candidate genetic variants will be compared between case and control groups.

# Results

To date, we have identified 32 patients with morphine adverse effects (e.g., pruritus, allergic reactions/anaphylaxis, respiratory depression, agitation, hallucinations, prolonged sedation); 3 patients with inadequate pain relief; as well as ~3000 previously-recruited potential control patients. Recruitment and clinical characterization of all patients are ongoing and we will present an update on cohort numbers as well as a comparison of minor allele frequencies for candidate genetic variants identified in our systematic review.

# Conclusion

Investigating genetic variants that contribute to variable morphine responses in children will help to further understand the underlying mechanisms and facilitate the development of predictive tests so that the safest and most effective pain management strategies are used.

# Contact Information

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UBC/BCCHRI

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**Authorship Statement**

- I confirm that I have read and meet the authorship criteria as listed above.
Abstract-23

Title of Abstract
Pediatric Pain Prediction: a study to gather preoperative risk factors and patient-reported outcomes to develop prediction models for significant postoperative pain

Authors
Hana Tak, Samantha Pang, Nicholas West, Neil K Chadha, Randa Ridgway, Heng Gan, Christa Morrison, Matthias Görges

Purpose
Approximately one in five children experience persistent postoperative pain for up to 12 months after surgery [1]. This can be associated with undesired consequences, including poor quality of life, decreased trust in the healthcare system, increased opioid use, and additional use of healthcare resources such as emergency room visits [2,3]. Creating personalized perioperative management plans may be possible by identifying factors that increase postoperative pain risk. Hence, we aim to develop risk prediction tools that identify children at high risk of persistent postoperative pain.

Methods
With research ethics board approval, we plan to recruit 300 parents of children under 13 years and 100 adolescents undergoing surgery, as well as their parents, to complete pre- and post-operative surveys. Surveys are sent automatically via REDCap and augmented with data from the electronic health record. A preoperative survey captures potential risk factors (demographics, parent’s anxiety and chronic pain, the child’s social relationships, anxiety, depression, trauma, catastrophizing, physical activity, and previous surgeries). Postoperative surveys periodically assess the patient’s recovery outcomes up to 90 days after the procedure, including pain levels, medications, mobility, and satisfaction. Exploratory analyses were performed in R, including generating summary statistics and plotting demographics- and procedure-stratified functional recovery and pain progression over time.

Results
Data collection is ongoing: we have enrolled 225/400 participants, of median (interquartile range) 6 (2-11) years old. Orthopedic patients (n=33, 15%) experienced the most pain during their recovery, while general surgery patients (n=39, 17%) had the least pain. However, there was significant variability in patients’ pain experiences across all surgical groups (figure 1a). Most patients suffered from limited mobility after surgery: orthopedic patients throughout their first month of recovery, plastic surgery patients (n=20, 9%) throughout the first two weeks, while most patients in other surgical groups experienced mobility limitations only during the first week (figure 1b). Postoperatively, patients generally used a combination of acetaminophen and ibuprofen after discharge (n=135, 60%), with only orthopedic or general surgery patients taking opioids at home (n=10, 4%).

Conclusion
Preliminary data exploration has identified promising targets for risk prediction modelling. Finalized models for significant postoperative pain or delayed functional recovery will be integrated into a preoperative risk communication tool in a future pilot cohort and evaluated for effectiveness.

References (Max 3)

Contact Information
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Abstract

Matthias Görges

Supervisor’s Affiliation

University: University of British Columbia; Hospital: BC Children’s Hospital

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Figure (if applicable)

- APT_PainPrediction_abstract_figure.png

![Graphs showing average post-operative pain levels and post-operative mobility scores per patient by surgery type.]

Figure 1a. “Average pain” levels reported by each patient on post-operative days 1, 2, 3, 7, 15, 30 and 90, separated by type of surgery received.

Figure 1b. “Mobility” levels reported by each patient on post-operative days 1, 2, 3, 7, 15, 30 and 90, separated by type of surgery received.
Abstract-24

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<th><strong>Title of Abstract</strong></th>
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<td>Defining the Minimal Clinically Important Difference (MICD) of Days Alive and At Home (DAH) within 30 days after inpatient noncardiac surgery: a retrospective population cohort study</td>
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<th><strong>Authors</strong></th>
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<tr>
<td>Ben Chen MD, Daniel I. McIsaac MD MPH FRCPC, David B. MacDonald MD FRCPC, Janny Xue Chen Ke MD FRCPC</td>
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<td>Days alive and at home within 30 days after surgery (DAH30) is a validated patient-centered perioperative outcome. To facilitate research and quality improvement, there is interest in better understanding the Minimal Clinically Important Difference (MCID) of DAH30, which specifies the minimum number of additional days at home after surgery that may be perceived as meaningful and relevant to patients. Our objective was to define the Minimal Clinically Important Difference (MCID) in for Days Alive and At Home within 30 Days (DAH30) for patients undergoing noncardiac inpatient surgery.</td>
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<td>After Research Ethics Board approval, we conducted a secondary analysis of a previously published retrospective population cohort study (1). This study included all patients aged ≥ 45 undergoing their inpatient noncardiac surgery in two tertiary hospitals in Halifax, Canada, from 2013 to 2017. Data was extracted from hospital and provincial health records through Health Data Nova Scotia. DAH30 was calculated by subtracting 30 days by the number of days spent admitted in a hospital (including re-admissions) within 30 days after surgery. Patients who died during the index hospitalization would be assigned a DAH30 of zero. The MICD was evaluated using both distribution-based methods (0.3 standard deviation (SD), 5%, and 10% range of DAH30 (2)) and anchor-based methods (morbidity and ICU).</td>
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<td>The cohort contained 30,619 patients in the cohort, with a mean (SD) age of 66 (11), 50.2% female, and 2.0% mortality. There were 15,477 patients undergoing elective surgeries, and 15,142 nonelective surgeries. The median [interquartile range (IQR)] DAH30 for the overall cohort, elective surgery patients, and nonelective surgery patients were 28 [24 to 29], 28 [27 to 29], and 27 [19 to 29], respectively. The 5% and 10% DAH30 range was 1.5 and 3.0 days for both elective and nonelective surgeries, and the 0.3 SD was 1.4 for elective and 3.0 days for nonelective patients. Amongst elective patients, there were 246 (1.6%) postoperative ICU admissions, with a median DAH30 difference of 11 days. Amongst nonelective patients, there were 578 (3.8%) ICU admissions, and the difference in DAH3 medians for patients with or without ICU admission for patients with or without ICU admission was 19 days.</td>
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<td>We evaluated the MICD in a large population cohort. The MICD values varied widely depending on the method of calculation and whether the surgery was elective.</td>
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<td><strong>Name</strong></td>
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<td>Ben Chen</td>
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**Please choose your affiliation and position**

Anesthesiology – resident
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<tr>
<th>Name of Supervisor</th>
<th>Janny Xue Chen Ke</th>
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<td>Supervisor's Affiliation</td>
<td>PHC anesthesia and UBC</td>
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Abstract

Title of Abstract
Anesthetic practice in a tertiary pediatric hospital and perioperative complications during indirect diode laser photocoagulation therapy for retinopathy of prematurity (ROP)

Authors
Lindy Moxham, Dr. Mei Foong Yeoh, Dr. Simon Whyte, Dr. Katherine Bailey, Dr. Randa Ridgway

Purpose
Treatment for ROP is laser photocoagulation under general anesthesia. Neonatal intubation is associated with significant physiological risk. Humidified high-flow nasal cannula (HHFNC) therapy splints open the airways and enables neonates to breathe spontaneously under total intravenous anesthesia (TIVA), mitigates the risk of intubation and may promote regression ROP (1,2,3). Purpose of this study: 1. Review the anesthetic practice of our institution 2. Review perioperative complication rates 3. Identify any correlation between anesthetic practice and complication rates

Methods
A retrospective chart review of patients at BC Children’s Hospital who received a laser photocoagulation procedure between January 2020 and December 2022 was performed. Data collected included patient demographics, anesthetic techniques, perioperative airway management, intraoperative complications.

Results
24 patients (demographics in Table 1) received 30 laser photocoagulation procedures. For 3 procedures, patients were intubated prior to coming to OR, 8 were planned intubations, 13 were carried out with low flow nasal cannula (LFNC) as the oxygen delivery technique, 4 with HHFNC, 2 with BiPaP and 1 patients’ airway technique was unreported. 15% (2/13) patients in the LFNC group required rescue intubation (Table 2).

Conclusion
56% of procedures were completed successfully without intubation. Rescue intubation in the LFNC patients might have been spared with the utilization of HHFNC. Given the small sample size for conclusions, a prospective study is planned using HHFNC as the technique of choice for ROP surgery.

References (Max 3)

Contact Information
Name
Mei Foong Yeoh

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Name of Supervisor
Dr. Katherine Bailey

Supervisor’s Affiliation
Anesthesiology
**Authorship Statement**

- I confirm that I have read and meet the authorship criteria as listed above.

**Figure (if applicable)**

- [Table-1-2.png](#)

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<th>Mean gestational age, weeks+days</th>
<th>Mean weight, g</th>
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<td>At birth</td>
<td>24+5</td>
<td>746</td>
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<td>Day of Procedure</td>
<td>42+6</td>
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Table 1: Patient demographics

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<th>Airway technique (n)</th>
<th>Lowest recorded oxygen saturation, %</th>
<th>Lowest recorded heart rate, bpm</th>
<th>Apneic events, n (%)</th>
<th>Desaturation events, n (%)</th>
<th>BMV, n (%)</th>
<th>Rescue intubation, n (%)</th>
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<td>LFNC (13)</td>
<td>86</td>
<td>100</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td>1 (8%)</td>
<td>2 (15%)</td>
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<tr>
<td>HHFNC (4)</td>
<td>85</td>
<td>115</td>
<td>1 (25%)</td>
<td>1 (25%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
<td>BiPAP (2)</td>
<td>98</td>
<td>135</td>
<td>0 (0%)</td>
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Table 2: Intraoperative incidences
Abstract

**Title of Abstract**
Of mice and men: co-humanization of mouse muscular dystrophy and cholesterol metabolism via genetic modification and dietary regulation

**Authors**
Zeren Sun, Zoe White, PhD, Pascal Bernatchez, PhD

**Purpose**
Research on muscular dystrophy (MD) has long been hampered by the lack of rodent models that mimic the severity of the human condition. We have shown in MD mice lacking apolipoprotein E (ApoE), which increases plasma total cholesterol (TC) and triglycerides (TG), drastically exacerbated MD severity. However, whether MD muscles show intra-myofiber cholesterol abnormalities in unknown, along with which component of cholesterol metabolism contributes to such exacerbation remains unclear and both are the focus of this investigation.

**Methods**
Muscle extracts from Dysferlin-deficient (Dysf) mice, a mild MD model, were subjected to Western blot for 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) and low-density lipoprotein receptor (LDLR). Filipin stain was used to analyze muscle free cholesterol. Dysf mice were also engineered to express human cholesterol ester transfer protein (CETP)-human apolipoprotein B (ApoB) transgenes, which will humanize their non-high-density lipoprotein cholesterol (non-HDLc)/HDLc ratio, a common marker of cardiovascular risk. The importance of TG to disease exacerbation was studied in Dysf/ApoE double-knockout mice fed a cholesterol-rich (10% fat, 2% cholesterol) or a TG/cholesterol-rich diet (60% fat, 2% cholesterol). Plasma lipoproteins were analyzed. Gait tracking and hanging test were performed to test muscle function. Muscle damage was assessed by masson's trichrome stain.

**Results**
Dysf muscles showed increased expression of HMGCR and LDLR, accompanied by increased free cholesterol accumulation compared to wild-type muscles. Introduction of CETP/ApoB in Dysf mice humanized their non-HDLc/HDLc ratio but did not affect muscle function or morphology. For Dysf/ApoE mice, a cholesterol-rich diet significantly increased plasma TC and non-HDLc and caused ambulatory dysfunction together with severe pathological changes in MD muscle. In contrast, a TG/cholesterol-rich diet further increased plasma TG compared to cholesterol-rich diet group but unexpectedly prevented muscle damage.

**Conclusion**
Humanization of non-HDLc/HDLc ratio via human CETP/ApoB transgene did not exacerbate MD muscle pathology in MD, whereas TG had a protective effect. Therefore, we suggest that TC is the main culprit behind MD exacerbation in Dysf/ApoE mice.

**Contact Information**

**Name**
Zeren Sun

**Please choose your affiliation and position**
Pharmacology – PhD student

**Name of Supervisor**
Pascal Bernatchez

**Supervisor’s Affiliation**
Department of Anesthesiology, Pharmacology & Therapeutics

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**Authorship Statement**

- I confirm that I have read and meet the authorship criteria as listed above.
# Title of Abstract

Identification of pharmacogenetic variants influencing the likelihood of developing methotrexate-induced mucositis in pediatric oncology patients using pathway analyses

## Authors

Xiao Yu Cindy Zhang, Erika N. Scott, Bruce C. Carleton, Colin J. D. Ross, Wyeth W. Wasserman, Catrina M. Loucks

## Purpose

Methotrexate, while an effective, widely used drug in childhood cancer, causes debilitating mucositis — a painful condition in various soft tissues, which often results in the inability to eat and subsequently, malnutrition. In severe cases, open sores lead to life-threatening infections. Supportive care often requires frequent hospitalization, adding to the burden and reducing quality of life for the patients and their caregivers. Our study aims to pinpoint the hidden genetic components that cause some children to have severe mucositis while others tolerate the treatment better.

## Methods

To identify gene pathways that are most likely to impact mucositis risk, we captured genes associated with methotrexate pharmacokinetics/pharmacodynamics from PharmGKB, 14 published pathobiological pathways (e.g., WNT/β-catenin signaling) predicted to underlie mucositis development (2) using MSigDB (3) /Enrichr, and novel pathways based on genes previously associated with mucositis from literature using StringDB. To pinpoint pathways highly enriched for genetic variations associated with mucositis development in methotrexate-treated children, we are using the Joint Association of Genetic variants (JAG) tool (1) to consider raw genome-wide genotyping data collected from 278 children with and without mucositis (CTCAE grade ≥ 2 vs. 0 toxicity) recruited through the Canadian Pharmacogenomics Network for Drug Safety (CPNDS).

## Results

Genotyping and clinical data were collected for mucositis cases (n=86) and controls (n=192) treated with high doses of methotrexate (≥ 1000 mg/m2) across 6 Canadian academic hospitals. After curating and reconciling the identified pathways, 18 non-redundant pathways with a priori evidence for association with treatment-induced mucositis were finalized. These gene sets were subjected to pathway enrichment analysis using JAG, which identified two gene sets—IL6 and WNT/β-catenin signaling (empirical P-values 0.0408 and 0.0476, respectively). Six genes (PRKCD, LRP5, PPARD, CSNK1A1, AGT and PIK3R2) within these two sets achieved significance, suggesting that genetic variation within these genes may drive the observed phenotype of drug-induced mucositis. Next, we will determine if these findings can be validated in a CPNDS-recruited replication cohort and a publicly available GWAS dataset.

## Conclusion

Identifying pathways and genes enriched with genetic variants predictive of clinically-significant mucositis will both enable precision medicine approaches and inform the development of treatments to reduce toxicity and improve patient quality of life.

## References (Max 3)


## Contact Information

Name

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Name of Supervisor
Catrina Loucks

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Figure (if applicable)
- [2-gene-sets-reached-statistical-significance-in-the-null-distribution-of-10000-permutations.png](image-url)
Abstract

Title of Abstract
Age-Dependent Effects of Endothelial Function and Telmisartan

Authors
Evans, A., Sauge, E., and Bernatchez, P.

Purpose
To determine whether aging affects the endothelial function-enhancing properties of telmisartan treatment

Methods
The descending artery was isolated from younger (4.5 months, n = 3) and older (8 months, n = 1) wildtype female mice and sectioned into 1mm segments. Vessel segments were then mounted on a myograph, stretched to a tension of 6.0 mN, and preconstricted twice with 30 mM of high potassium chloride Krebs buffer. Vessels were then constricted with EC90 dose of phenylephrine (10^-6 M) followed by increasing concentrations of acetylcholine. Vessels were then incubated for 30 minutes with 25 µM telmisartan or 0.25% DMSO control and then extent of vessel contractility was measured with increasing concentrations of phenylephrine. Vessels were then preincubated with 25 µM telmisartan or DMSO, as well as L-NAME for 30 minutes. Extent of vessel contractility was then measured with increasing concentrations of phenylephrine, followed by increasing concentrations of SNP.

Results
We found that there was an enhanced vasodilatory response in telmisartan-treated vessels compared to control, with a greater vasodilatory response in older mice compared to younger mice (56.0% decrease in vessel contractility in younger mice vs. 76.0%). Furthermore, this effect had a greater L-NAME reversibility in younger mice compared to older mice (21.9% L-NAME reversibility in younger mice vs. 9.6% in older mice).

Conclusion
Telmisartan-treated vessels show age-dependent effects with respect to their vasodilatory response and L-NAME reversibility. This suggests that age-related changes to the vasculature impact nitric oxide signaling.

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**Title of Abstract**

Mucus Plugged Airways in Asthma are Marked by Prominent Airway Remodeling

**Authors**

Aileen Hsieh (1), Maude Liegeois (2), May Fouadi (1), Clarus Ka-Wing Leung (2), John V. Fahy (2), Tillie Hackett (1)

1. Centre for Heart Lung Innovation, University of British Columbia, Vancouver, British Columbia, Canada
2. Cardiovascular Research Institute, University of California San Francisco, San Francisco, California

**Purpose**

The hallmark features of asthma include mucus cell hyperplasia, mucus accumulation, reticular basement membrane thickening, and increased smooth muscle mass. Recently, airway mucus plugs have been identified as a persistent radiological feature on computed tomography lung scans of patients with moderate to severe asthma and are associated with worse clinical outcomes. To date, the relationship of airway remodeling within mucus-plugged airways in asthmatic subjects has not been investigated.

**Methods**

The study included lungs from 9 fatal asthma cases, 5 non-fatal asthma cases (history of asthma but death from a non-asthma cause), 5 healthy control cases, and 10 Global Initiative for Obstructive Lung Disease (GOLD) 3 and 4 COPD patients who underwent lung transplantation, which served as disease controls for mucus plugs. Lungs were inflated, frozen, and randomly sampled for histology. Two or more airways with and without mucus plugs were assessed per case for a total of 117 airways. The thickness of total airway wall, airway epithelium, reticular basement membrane, and smooth muscle mass were quantified using Euclidean Distance Mapping to assess each wall measurement across the entire airway cross-section.

**Results**

As previously reported in the literature, total airway wall thickness of patients with asthma and COPD was significantly greater compared to age-matched controls (P < 0.05) For the specific airway wall components, asthma patients had a significantly thicker airway epithelium, reticular basement membrane and smooth muscle layer compared to controls, whereas COPD patients had thicker smooth muscle. Interestingly, when the airways within the same patient were sorted into airways with or without mucus plugs, in all asthma patients, mucus-plugged airways had significantly greater remodeling of the reticular basement membrane (Figure 1) and airway epithelium (P < 0.05) compared to non-mucus plugged airways. Further, the airway remodeling in mucus-plugged airways from fatal asthma patients was significantly greater compared to mucus-plugged airways from non-fatal asthma patients (P < 0.05).

**Conclusion**

Airway narrowing heterogeneity is an important feature of fatal asthma episodes. This study demonstrates that airway remodeling is more prominent in mucus-plugged airways in fatal asthma compared to non-fatal and mucus plugs may play a critical role in airway narrowing and collapse in fatal asthma.

**Contact Information**

**Name**

Aileen Hsieh

**Please choose your affiliation and position**

Pharmacology – PhD student

**Name of Supervisor**

Dr. Tillie Hackett

**Supervisor’s Affiliation**

Centre for Heart Lung Innovation, University of British Columbia, Vancouver, British Columbia, Canada
Authorship Statement

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Figure (if applicable)

- Fig1.jpg
Title of Abstract

Age-associated Differences in Non-diseased Lung Fibroblast Inflammatory and Extracellular Matrix Processes

Authors

Kingsley Okechukwu Nwozor, Kauna Usman, Chen Xi Yang, May Al-Fouadi, Aileen Hsieh, Irene H. Heijink, Corry-Anke Brandsma, Tillie-Louise Hackett

Purpose

Ageing is a major risk factor for chronic lung diseases. With ageing, the structure of the lung is remodelled, altering the extracellular matrix. Fibroblasts are the major structural cell within the lung that maintains the extracellular matrix (ECM). However, there is a knowledge gap in the age-associated fibroblast function, in terms of ECM production and organisation, as well as their responses to inflammatory (IL-1α) and remodelling mediators (TGF-β) involved in wound repair. Thus this study aimed to investigate lung fibroblast function in response to IL-1α and TGF-β1 with chronological age

Methods

Primary human lung fibroblasts (PHLFs) were obtained from 12 younger (5 – 49 years) and 20 older (50 – 83 years) with no respiratory disease. For ECM and cytokine production, cells were seeded 100k cells/well in 6 wells plates and cultured till 90% confluent. Cells were serum-deprived overnight and treated with either control media or 1ng/ml IL-1α or 50 ng/ml of TGF-β1 for 72 hrs. Cell-free supernatant was collected for ELISAs, while the cell lysate was collected for western blotting. To evaluate collagen contraction in a 3D environment, 40k cells/well (12 wells plate) were seeded on a pre-cast bovine collagen 1 gel (0.4 mg/ml), treated with either control media or 1ng/ml IL-1α or 50 ng/ml of TGF-β1 for 72 hrs. Gel contraction was quantified by weight. Differences between and within groups were tested using the Mann-Whitney U test, and Wilcoxon ranked test, respectively.

Results

Compared to lung fibroblasts derived from younger donors, fibroblasts derived from older donors had elevated secretion of IL-6 and IL-8. When treated with IL-1α, fibroblasts from younger and older donors expressed elevated levels of IL-6 and IL-8 compared to untreated fibroblasts, but this response was stronger in younger subjects than in older subjects. Following treatment with TGF-β1, younger and older subjects expressed elevated levels of collagen 1 and fibronectin compared to untreated fibroblasts. The fold induction was higher in the older subjects than the younger subjects. In the 3D collagen contraction model, we observed a reduction in the ability of fibroblasts from older subjects to contract collagen I gel, compared to fibroblasts from younger subjects.

Conclusion

Our results suggest that lung fibroblasts from older individuals may have a dampened response to damage signal, and an exaggerated response to remodelling signals from the epithelium. These could lead to aberrant inflammatory response, repair and tissue remodelling.

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Name of Supervisor

Tillie Louise-Hackett

Supervisor’s Affiliation

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### Supervisor's Email

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**Title of Abstract**

Reversal of Early Type 1 Diabetes-Induced Vascular Damage with Angiotensin Receptor Blockers

**Authors**

Christopher Yuen* [1], Zoe White [1], Angela M. Devlin [2], Pascal Bernatchez [1]

[1] Department of Anesthesiology, Pharmacology and Therapeutics, Faculty of Medicine, University of British Columbia
[2] Department of Pediatrics, Faculty of Medicine, University of British Columbia

**Purpose**

Type 1 diabetes (T1D) is an autoimmune disease that causes insulin-producing pancreatic β-cell destruction. Cardiovascular disease is a major complication of diabetes. In addition to their antihypertensive properties, angiotensin II receptor blockers (ARBs) such as losartan, are effective in activating protective, nitric-oxide (NO)-dependent endothelial function. However, it is unknown if they can reverse early changes in vascular homeostasis caused by T1D in order to improve cardiovascular outcomes.

**Methods**

Ins2+/Akita (Akita) mice, heterozygous for an Ins2 variant, were assessed as a model of diabetes and compared to age/sex matched Ins2+/+ mice (controls) at diabetes onset (blood glucose ≥ 16.6mmol/L); 4 weeks post-diabetes onset; 12-weeks post-diabetes onset. Losartan treatment (0.6g/L drinking water) was initiated at 4 weeks post-diabetes onset. Non-invasive mean arterial blood pressure (MABP) and aortic pulse wave velocity (PWV), indicator of aortic stiffness, were measured. Ex vivo wire myography of isolated aortic rings was conducted to determine contributions of the smooth muscle and endothelium on vascular reactivity. Nitric oxide synthase inhibitor L-NAME was used to assess basal NO production. Two-way ANOVA was used to analyze the effect of genotype and losartan treatment. Repeated measures ANOVA was used to analyze between group differences in vascular function.

**Results**

At 4-weeks post diabetes onset, male Akita mice had 70.2% greater PE-induced smooth muscle constriction (p < 0.04), a 24.5% reduction in Ach-induced endothelium NO-dependent vasorelaxation (p < 0.01) and 51.7% greater (490.4cm/s vs 319.3cm/s) in PWV compared to control mice. At 12-weeks post diabetes onset, male Akita mice had 16.2% greater MABP (p < 0.01), 241.1% greater PWV (p < 0.01), 16.2% greater PE constriction, and a 20.2% reduction (p < 0.01) in Ach relaxation. Losartan reduced MABP in Akita (22.8%) and control (23.5%) mice, reduced PE contractility in Akita (71.1%) and control (46.1%) mice (p < 0.01). Losartan lowered PWV in male Akita mice to control levels (362.2cm/s vs 393.3cm/s). Losartan also attenuated the impaired Ach-induced vasodilation, suggesting rescue of endothelial protective properties.

**Conclusion**

Early intervention with losartan prevents aortic stiffness while rescuing endothelial protective properties by increasing NO production, which may be an effective treatment option to reduce long term risk for T1D associated cardiovascular complications.

**Contact Information**

**Name**

Christopher Yuen

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**Name of Supervisor**

Pascal Bernatchez

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<table>
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<tr>
<th>Department of Anesthesiology, Pharmacology and Therapeutics, Center for Heart Lung Innovation</th>
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Title of Abstract

Resolving the Pathobiology of Vascular Remodeling in COPD using High-resolution MicroCT Imaging

Authors


Purpose

Vascular abnormalities in vessel structure and function have been observed in all stages of COPD but the mechanism remains unknown. The goal of this study was to use high-resolution microCT imaging to investigate microstructural changes in the small airways and associated arterial vasculature and determine if the number of terminal bronchioles (TB) and terminal bronchiole associated vessels (TBV) are reduced and remodeled in mild to very severe COPD. These findings will improve the understanding of vascular disease in COPD and how early vascular changes may contribute to reduced lung function.

Methods

Explanted lungs from donor controls (n=8), ex-smokers (n=8), mild/moderate COPD (n=8), and very-severe COPD patients (n=8) undergoing transplantation were inflated to 10CM H2O and fixed. A total of 256 unbiased, systematic uniform random (SUR) samples (n=8 per lung) were scanned with microCT and assessed using stereology for total alveolar surface area, total vessel volume, terminal bronchiole and TB-associated vessel counts, and cross-sectional lumen and wall area.

Results

Compared to control lungs, the mean number of terminal bronchioles (TB) per mL of lung in patients with very-severe COPD decreased by 57% (p<0.005) and the number of TB-associated vessels (TBV) decreased by 45% (p<0.005). The number of TBs and TBVs was reduced even in regions of the lung with normal alveolar surface area in mild/moderate COPD versus control (p<0.01). In the remaining TBs and TBVs in very-severe COPD lungs, the mean lumen area was decreased by 31% in TBs (p<0.001) and 36% in TBVs (p<0.01) versus control lungs. Additionally, TBs and TBVs had an increase in mean wall area percent versus control lungs by 40% (p<0.001) and 20% (p<0.001), respectively. When comparing the total vessel volume with control, the vessel volume was decreased by 28% in ex-smokers (p=0.05), 43% in mild/moderate COPD (p<0.01), and 54% in very-severe COPD (p<0.005) patients.

Conclusion

Early loss of small airways and the associated pulmonary vasculature is a feature of COPD. In very-severe COPD, remaining TBs and TBVs are remodeled with lumen narrowing and wall thickening. When assessed by disease severity, there is a gradual decline in vessel volume compared to control lungs.

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Abstract-32

Authorship Statement

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Title of Abstract

Blood based biomarkers of brain injury: re-application of a prognostic tool for the diagnosis of impaired oxygen diffusion into the brain

Authors

Ryan L. Hoiland, Connor A. Howe, Sophie Stukas, Travis Gibbons, Tison Schoenthal, Sonny Thiara, Jennifer Cooper, Denise Foster, Rebecca Grey, Peter Gooderham, Donald E. Griesdale, Cheryl L. Wellington, Philip N. Ainslie, Mypinder S. Sekhon

Purpose

Determining if an anesthetized and/or critically ill patient is suffering cerebral tissue hypoxia mediated secondary brain injury is imperative to tailoring their clinical care. However, cerebral tissue hypoxia may arise due to a multitude of pathophysiologic factors that manifest as impairments in convective and/or diffusive cerebral oxygen delivery but are as of yet detectable at the bedside. We aimed to determine the utility of blood-based biomarkers of brain injury as a method to detect impairments in the diffusion of oxygen from the cerebral vasculature into the brain (i.e. O2 diffusion).

Methods

Radial artery and internal jugular vein blood gas and brain injury biomarker analyses were performed in 12 healthy controls and 14 comatose post-cardiac arrest patients with a hypoxic-ischemic brain. We measured cerebral blood flow (controls & HIBI patients) and brain tissue oxygen tension (PbtO2; HIBI only) prior to, and during, a ~10 mmHg reduction in arterial carbon dioxide tension (i.e., hypcapnia). The functionality of O2 diffusion was defined as the slope of the relationship between the hypcapnia induced change in cerebral oxygen extraction fraction (O2EF) and cerebral blood flow (ΔO2EF% ∙ ΔmL-1 ∙ min-1). The mean±standard deviation for O2 diffusion in the controls was used to calculate O2 diffusion Z-scores for controls and patients. A Z-score > 1.65, indicating an O2 diffusion that would be worse than 95% of a control population, was considered impaired O2 diffusion.

Results

O2 diffusion was impaired in HIBI patients with cerebral tissue hypoxia (PbtO2 < 20 mmHg; -0.19 [-0.26 – -0.11] % ∙ mL-1 ∙ min-1; P=0.01), but not patients without cerebral tissue hypoxia (PbtO2 > 20 mmHg; -0.57 [-1.40 – -0.36] % ∙ mL-1 ∙ min-1; P=0.99) when compared to controls (-0.60 [-0.75 – -0.39] % ∙ mL-1 ∙ min-1). The serum concentration of Neurofilament-light predicted impairments in O2 diffusion (Z-score > 1.65) in HIBI patients with a sensitivity of 75% and specificity of 100% (receiver operator curve characteristic analysis area under the curve = 0.92; P=0.001).

Conclusion

Blood-based biomarkers of brain injury hold promise as a tool for the bedside diagnosis of impairments in the diffusion of oxygen from the cerebral vasculature into the brain. This may help inform patient care and help guide the implementation of treatments that aim to avoid cerebral tissue hypoxia.

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**Authorship Statement**

- I confirm that I have read and meet the authorship criteria as listed above.
## Title of Abstract

Age and sex differences in pharmacodynamic endpoints during the induction of anesthesia with propofol in children

## Authors

Bianca Vizcaino, Rachel Bates, Lindy Moxham, Matthias Görges, Simon Whyte

## Purpose

Propofol is a widely utilized general anesthetic. However, its narrow therapeutic index means there is only a small difference between the dose needed for loss of consciousness (LOC) and apnea [1]. There is also considerable interindividual variation in dosing requirements. Propofol is gaining popularity for procedural sedation outside of the operating room, creating significant risks that non-anesthesiologists may not be able to recognize or rescue from. This study aims to generate evidence for more tailored propofol dosing recommendations in children by accounting for age and sex.

## Methods

In this REB-approved, prospective, non-randomized, single-cohort study, families of eligible children ages 3-18y undergoing planned propofol induction of anesthesia with the intent to induce apnea provided informed consent for study participation. This study aims to recruit children stratified by age category (3-5, 6-10, 11-18y) and sex groups using groups of 60 participants in each group. Induction was achieved using a fixed rate (1500 mcg/kg/min) propofol infusion. Times to four pharmacodynamic endpoints include loss of eyelash reflex (LOER), tolerance of nasal cannula (NC), bispectral index (BIS) < 60, and apnea (absence of end-tidal CO2 for 20 seconds) were recorded, and corresponding propofol doses derived. The therapeutic index was defined as the dose difference between LOC and apnea endpoints. Analysis of propofol doses required to reach these endpoints was performed using R.

## Results

To date, 327 out of 360 participants have been recruited. Preliminary results suggest that while propofol doses for LOER and NC are similar between age groups, older patients (11-18y) require a smaller weight-adjusted dose than the younger two groups of patients (3-10y) to reach apnea (Figure 1A). The youngest patients (3-5y) require a higher weight-adjusted dose to achieve BIS < 60; however, n is lower, and BIS is not validated in younger children (Figure 1A). Although the therapeutic index between LOER and apnea is similar between the younger two age groups, the oldest group’s is significantly smaller (Figure 1B). While propofol doses for LOER, NC, and BIS are similar between sexes, females require a significantly smaller propofol dose to reach apnea (Figure 1C) and have a significantly smaller therapeutic index for propofol between LOC and apnea (Figure 1D).

## Conclusion

The oldest (11-18y) and female groups require a smaller propofol dose to reach apnea and have a smaller therapeutic index, indicating that increased vigilance should be used for these patients to increase safety of propofol administration.

## References (Max 3)


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Abstract

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Authorship Statement

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Figure (if applicable)

- Abstract_agex_figure.png

A

B

C

D

Pharmacodynamic Endpoint

Pharmacodynamic Endpoint

Age Group

3 to 5
6 to 10
11 to 18

Significance codes: 0 ≤ p < 0.001, ***; 0.001 ≤ p < 0.01, **; 0.01 ≤ p < 0.05, *; p > 0.05, unmarked.

A. Median doses required to reach endpoints, stratified by age. Error bars represent 2.5th and 97.5th percentile.
B. Median doses required to reach endpoints, stratified by sex. Error bars represent 2.5th and 97.5th percentile.

C. Therapeutic Index, stratified by age.

D. Therapeutic Index, stratified by sex.
**Title of Abstract**

A Transcriptomic Approach to Understanding Pain Signals in the Spinal Cord and Brain

**Authors**

Ryan Loke, John L.K. Kramer

**Purpose**

Pain is a major cause of disability and leads to an estimated $40 billion in annual healthcare costs in Canada. Understanding the underlying mechanisms that contribute to pain signaling remains an immense challenge. Gene expression analysis using transcriptomics can further our understanding of pain signaling pathways by detecting broad changes in gene expression in key pain signaling regions like the spinal dorsal horn. The goal of this study is to use transcriptomics to identify brain regions with similar expression profiles as the dorsal horn and verify these results with animal models.

**Methods**

Human RNA isoform transcriptomic data was obtained from the Human Protein Atlas. Paired T-tests and the R package “DESeq2” was used to assess differential gene expression between the dorsal and ventral horn of the spinal cord. Genes were also filtered pre-analysis for minimum expression levels and minimum log fold change expression values to reduce statistical noise during Benjamini-Hochberg false discovery rate correction. This “genetic fingerprint” was cross referenced to the Allen Brain Atlas using ENRICHR to identify specific brain regions with similar upregulated expression profiles as the dorsal horn. Identified brain regions will be verified for activity in mice models using recording electrodes implanted in desired areas to monitor activity during a painful stimulus.

**Results**

Preliminary differential analysis identified 604 genes upregulated in the dorsal horn. This genetic fingerprint has been mapped to the Bed Nucleus of the Stria Terminalis, which is located in the basal forebrain and is referred to as the extended amygdala. This small group of nuclei has previously been found to play an important role in behavioral responses and has been implicated for a functional role in many limbic functions, however, it has not been directly implicated for a role in pain. Currently, finalization of differential analysis needs to be completed to confirm our results before verification of identified brain regions through in vivo recordings in animal models can take place.

**Conclusion**

Gene expression analysis provides an alternate avenue to understanding pain signaling pathways from the spinal cord to the brain through broad changes in expression levels. This may help researchers create therapeutic interventions and identify brain regions that can be targeted for pain management.

**References (Max 3)**

1) Lebow, M. A., & Chen, A. (2016). Overshadowed by the amygdala: The bed nucleus of the stria terminalis emerges as key to psychiatric disorders. Molecular Psychiatry, 21(4), 450–463. [https://doi.org/10.1038/mp.2016.1](https://doi.org/10.1038/mp.2016.1)


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Ryan Loke

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Abstract

**Title of Abstract**

Differences in pharmacodynamic endpoints with propofol anesthesia in children based on self-reported ancestry

**Authors**

Rachel Bates, Bianca Vizcaino, Lindy Moxham, Matthias Görges, Simon Whyte

**Purpose**

Propofol is an intravenous anesthetic agent with a narrow therapeutic index, such that the dose difference needed to induce loss of consciousness and apnea is small. It is also highly variable between patients [1]. Genetic ancestry and its links to variations in allele frequency may play a role in determining pharmacodynamic (PD) endpoints of propofol anesthesia [2]. This study examines relationships between self-reported ancestry and variability in induction PD endpoints, with the potential goal of individualizing pediatric propofol dosing.

**Methods**

In this REB-approved, single cohort, non-randomized study, pediatric patients aged 3-18y underwent propofol induction of anesthesia. With informed consent and assent, we asked families to self-report their ancestral origin based on the Canadian Census categories. During induction, we administered propofol at a constant rate of 1,500 mcg/kg/min to a maximum of 10 mg/kg or until the patient reached apnea (defined as the absence of end-tidal CO2 for 20 seconds). We captured four pharmacodynamic endpoints: loss of eyelash reflex (LOER), tolerance of nasal cannulae (TONC), bispectral (BIS) index < 60 for 30 sec. and apnea. We collected buccal swabs for future genome-wide association analysis. Using R statistical software, descriptive and inferential statistical analysis of weight-adjusted propofol doses were undertaken with Census categories.

**Results**

Data from 292 children (136 females, median (IQR) age 8.4 [5.2 - 13.2] years) were available. Sixty-five participants did not reach apnea at the maximum propofol dose, and 103 had no valid BIS measurement. Overall, we observed no effect by Census category but considerable variability in participants who identified as White (see Figure 1). The distribution of self-reported ancestry in the study sample was significantly different from the Metro Vancouver pediatric population, with fewer-than-expected numbers in several Census categories. An overrepresentation of White participants was observed at 53.6% of our sample when compared with the study population of 43.1% [3]. As such, further meaningful statistical analysis is limited by small sub-sample sizes.

**Conclusion**

Self-reported ancestry may not significantly contribute to PD variability during propofol induction. However, power to detect such differences is limited by small sample sizes in some Census groups. Planned genetic analysis of ancestry will allow us to further investigate sample variability.

**References (Max 3)**


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Figure (if applicable)

- ancestry_final_plot_boxplot.png
Abstract

Characterizing age-related changes in endothelial nitric oxide synthase (eNOS) localization and the caveolin-1-eNOS interaction in mouse pulmonary arteries

Authors

John Lim, Ivan Robert Nabi, Pascal Bernatchez

Purpose

Age-associated dysregulation of vascular nitric oxide (NO) production adversely affects the vasodilatory response and contributes to atherosclerosis and hypertension (1). eNOS is typically localized to either the Golgi body or plasma membrane lipid rafts rich in caveolin-1 (Cav1) (2), the main negative regulator of eNOS activity. It is, however, unclear how Cav1 and eNOS localization changes with age.

Methods

Wild type mice were grouped into two age groups – ‘young’ mice below 3 months of age, and ‘old mice’ above 10 months of age. Mice were euthanized and perfused, and their pulmonary arteries were dissected and cut longitudinally to expose the endothelial layer face-up. These whole-mount pulmonary artery were doubly labelled for eNOS and Cav1, as well as GM130, a Golgi marker, and imaged by confocal microscopy. After background correction, eNOS expression, eNOS proportion within the PM and the Golgi, Golgi length and width, and Cav1-eNOS co-localization were quantified. To compensate for inter-sample variability, at least eight images containing ten cells each were analyzed for each pulmonary artery. The experiment was repeated five times per age group to facilitate statistical analysis by unpaired T-test.

Results

Golgi bodies in older vessels were around the same size (p = 0.11) and length (p = 0.51) as in younger vessels. However, Golgi bodies shrunk in width (p < 0.0001), and the ratio of Golgi length to width increased with age (p < 0.0001), showing that the Golgi is flattening in older mice. Strikingly, eNOS expression decreased in older vessels (p = 0.001), but only outside of the Golgi (p < 0.0001). As a result of the decline of the PM and cytosolic eNOS populations, the proportion of eNOS in the Golgi was elevated in the vessels of older mice (p < 0.0001).

Endothelial eNOS expression decreased in older vessels (p = 0.02), consistent with the observed decrease in Fig. 3-1. The Manders’ co-localization coefficient (M1) of Cav1 and eNOS significantly decreased in older vessels compared to younger vessels (p = 0.03). Cav1 expression increased, but not significantly (p = 0.12).

Conclusion

These findings show age-related changes in eNOS expression and localization within the pulmonary artery – decreased eNOS expression and Cav1 co-localization, and a shift in eNOS expression towards the Golgi – which have implications for therapeutics targeting vascular eNOS NO production.

References (Max 3)

These findings show age-related changes in eNOS expression and localization within the pulmonary artery – decreased eNOS expression and Cav1 co-localization, and a shift in eNOS expression towards the Golgi – which have implications for therapeutics targeting vascular eNOS NO production.

Contact Information

Name

John Lim

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<th>Pascal Bernatchez</th>
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<td>Department of Anesthesiology, Pharmacology and Therapeutics, UBC</td>
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| Figure (if applicable)      |                   |
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Table 2 – Results from multivariable logistic regression*

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* All models are adjusted for age, BMI, gestational age, parity, number of previous CS, date of CS, trained OB anesthesia fellow at time of CS, number of epidural bolus, time from epidural placement to CS, and emergent CS status. For each model, all two-way interactions between the exposure of interest and covariables were assessed. No meaningful two-way interactions were identified. Odds ratios represent the multiplicative increase in odds of failure to convert to anesthesia for CS associated with the given characteristic. Corresponding 95% confidence intervals and p-values are also presented. Missing data was handled using multiple imputation.