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Scientific Abstracts

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Airway Management

Airway Management - 1 Endotracheal Intubation in Mucopolysaccharidosis type IVA: A Single Institutional Experience

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Introduction: Mucopolysaccharidosis type IVA (MPS IVA; Morquio Syndrome [OMIM #253000]) is a rare, autosomal recessive lysosomal storage disorder (LSD) that is caused by a deficiency of the enzyme N-acetyl-galactosamine-6-sulfatase - GALNS (1,2). Whilst there is heterogeneity in the context of severity and phenotype, patients with MPS IVA rarely survive past their second decade of life (1-3). The majority of children with MPS IVA cease growing before the age of eight years, are wheelchair-bound by their teenage years and often require multiple anaesthetics for surgical interventions throughout their lifetime (1,3-5). Airway obstruction and respiratory failure remain the leading cause of death in this cohort (1,3,5). Intubation and extubation can be particularly challenging in patients with MPS IVA due to limited mouth opening, short neck length and a reduced range of motion, large tongue, micrognathia, subglottic narrowing, and atlanto-axial instability (due to odontoid hypoplasia and ligamentous laxity). Airway obstruction is often multilevel, with upper airway obstruction caused by adenotonsillar hypertrophy secondary to glycosaminoglycan (GAGs) infiltration (Figure. 1). Commonly, there is also significant tracheal narrowing, deviation and buckling that is pathognomonic for the condition (Figure. 2). Recently, global, consensus based multidisciplinary guidance by Akyol et al (2019) recommend the use of videolaryngoscopy (VL) to aid intubation in all patients with MPS IVA. However, there remains a paucity of reporting of endotracheal intubation grade and technique (including adjuncts) in patients with MPS IVA undergoing anaesthesia.

Methods: A retrospective chart review was undertaken from 2009-2019, at a single institution (highly specialised tertiary referral centre for paediatric inherited metabolic diseases) to ascertain the frequency of surgery, difficulty in endotracheal intubation, as well as the techniques and modality for airway management during anaesthesia.

Results: 16 patients with MPS IVA were identified from our institutional central database, that had undergone anaesthesia. The median age was 13.5 (range: 6-17) years. The mean number of anaesthetics per individual was 6 (range: 4-9). 13/16 patients were either currently or had previous administration of enzyme replacement therapy with elosulfase alfa (Vimizim®). There was an absence of genotype-phenotype correlation, There was ubiquitous presence of both restrictive and obstructive airway disease in all patients, with 11/16 patients having symptoms of obstructed sleep apnoea, 9/16 patients having undergone adenotonsillectomy, 7/16 having macroglossia on clinical examination and 14/16 having evidence of tracheal narrowing on radiological imaging. We ascertained that Cormack-Lehane airway grading varied amongst individuals, with four individuals being grade 1, eight being grade 2 and four being grade 3. VL was the preferred modality for endotracheal intubation in most individuals (12/16), with three cases of failure to secure the airway with conventional, direct laryngoscopy was then successful with VL. Interestingly, in two individuals that had grade 1 and 2b view during direct laryngoscopy, the anaesthesiologist were unable to secure the airway due to severe subglottic stenosis and the patient was ventilated via a laryngeal mask airway as a rescue measure.

Conclusion: Patients with MPS IVA may frequently present for surgery and present a number of challenges to anaesthesiologists in the context of airway management. Even when airway grading appears reasonable at direct laryngoscopy, the presence of subglottic stenosis can preclude successful endotracheal intubation. We thus recommend that patients with MPS IVA should undergo pre-anaesthesia airway imaging and indirect, flexible fibre-optic airway assessment, to allow for dynamic airway assessment, planning and risk stratification. Moreover, anaesthesia for MPS IVA should be undertaken at specialised centres by experienced anaesthesiologists.

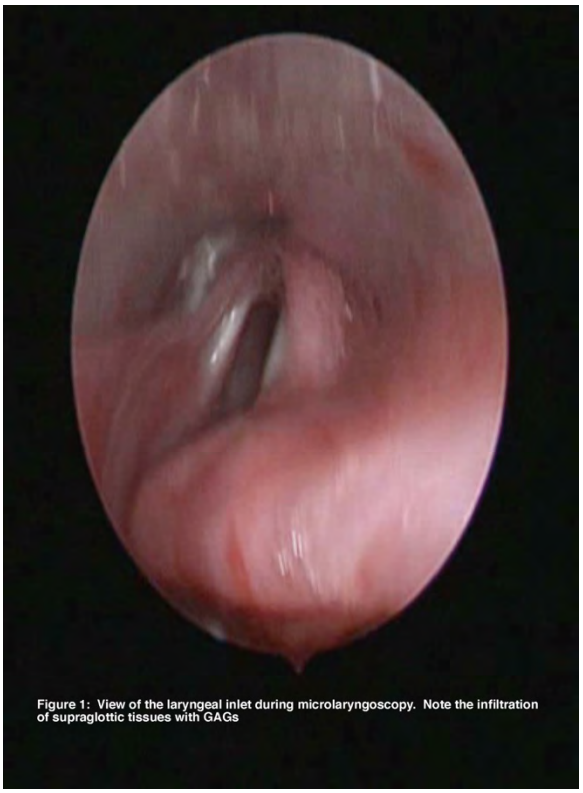
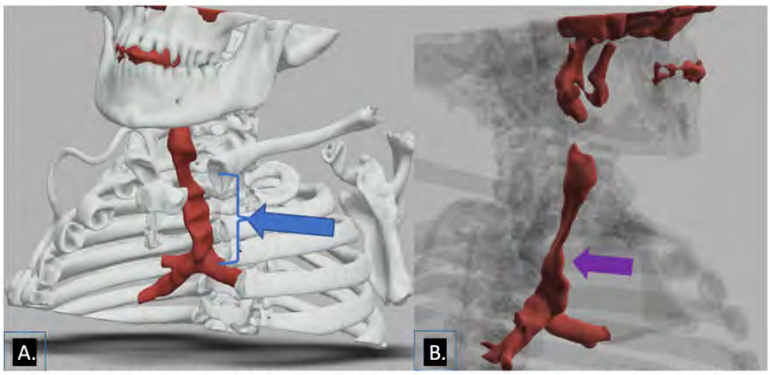


Figure 1: View of the laryngeal inlet during microlaryngoscopy. Note the infiltration of supraglottic tissues with GAGs



Legend: 3D rendered tracheal reconstructions in a patient with severe, end-stage MPS IVA. Note the multi level airway tortuosity, obstruction with narrowing and buckling causing a 'ribbon like' appearance of the trachea (blue arrow)that is a classical hallmark feature of the disease. The narrowest segment (purple arrow) is 2mm and at the level of the tracheal inlet.

Table 2. Airway Grading

Patient	Airway Grade Cormack-Lehane	Intubation Technique
A	Grade 2	Glidescope - ET
B	Grade 1	Conventional, Difficult ET (tortuous trachea) -> LMA
C	Grade 2	Glidescope - ET
D	Grade 2b	Glidescope - ET (tortuous trachea) -> LMA
E	Grade 1	Glidescope - ET
F	Grade 3	Conventional, , Boogie - ET
G	Grade 2	Glidescope - ET (tortuous trachea)
H	Grade 1	Glidescope - ET
I	Grade 2	Glidescope - ET
J	Grade 1	Conventional, ET
K	Grade 2	Glidescope - ET
L	Grade 3	Conventional, , Boogie - ET
M	Grade 2	Glidescope - ET
N	Grade 3	Glidescope - ET
O	Grade 2b	Glidescope + bougie - ET (tortuous trachea)
P	N/A	Glidescope + bougie - ET (tortuous trachea)

Table 1. Baseline Demographics

Patient	Presentation	Age at Diagnosis	Consan-guinity	Sex	Genetics	Age ERT started	OSA	Adeno-tonsillect omy	BIPAP	Tracheal Stenosis	Macro glossia
ERT treated subjects											
A	Difficulty walking	37	No	F	Heterozygous p.(Gly155Arg)	43	No	No	No	Yes	No
B	Gibbus	27	No	M	Homozygous p.(A291T)	112	Yes	Yes (72 , 147)	Yes	Yes	Yes
C	Gibbus	22	N/A	M	Not recognised gene	39	Yes	(41)	No	No	Yes
D	Difficulty walking	18	No	M	Homogenous p.(w141x)	78	Yes	No	Yes	Yes	No
E	Difficulty walking, scoliosis	30	N/A	F	N/A	67	No	No	No	Yes	Yes
F	Chest deformity	43	No	F	Heterozygous p.(arg251Ter)	69	Yes	Yes (121)	No	Yes	No
G	N/A	132	No	M	Homozygous p.(A291T)	78	Yes	Yes (70, 142)	Yes	Yes	No
H	N/A	35	N/A	F	c.423-11_425del14/ c.860C>T	38	Yes	Yes (32, 51, 89)	No	Yes	No
I	Family history, chest deformity	31	No	M	Hetero/I113F, Y240C	183	Yes	Yes (36)	No	Yes	Yes
J	Difficulty walking	131	Yes	F	Homozygous p. (His166Arg)	175	Yes	No	No	Yes	No
K	Gibbus	14	No	M	Heterogenous p. (I113F) and p. (R386H)	43	Yes	Yes (35)	No	No	Yes
L	Difficulty walking	73	No	F	Heterozygous p.(tyr254cys) and p. (Gln311Pro)	108	No	No	No	Yes	No
M	Gibbus, stiff joints	33	Yes	F	Homozygous p.(A291T)	129	No	Yes (121)	No	Yes	Yes
Non ERT treated subjects											
N	Difficulty walking	29	No	M	Homogenous p.(Ser264Asn)	N/A	Yes	No	Yes	Yes	No
O	Growth, skeletal dysplasia	96	N/A	F	Homogenous p. (Gly116Val)	N/A	Yes	Yes (134)	Yes	Yes	Yes
P	Difficulty walking	161	N/A	F	Heterozygous p.901G>T (Gly301Cys)	N/A	No	No	No	Yes	No

Table 1. above illustrates the baseline demographics of the 16 subjects, including age (months) at diagnosis, consanguinity, what the presenting symptom was, the genetic mutation identified, the date when ERT therapy commenced (if applicable). We also record whether the child was diagnosed with obstructive sleep apnoea (OSA), if they had undergone an adenotonsillectomy (age at surgery in months) and the whether the child had been instituted on non-invasive, bilevel ventilation (BIPAP). * All ages are reported in months.

Airway Management - 2 STAT Page RICU: An Analysis of 10 Years of Pages to the Anesthesia Airway Service at A Large Academic Hospital

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Introduction: Anesthesiologists frequently perform urgent and emergent out-of-operating room (OOR) endotracheal intubations. Many large academic hospitals have a dedicated airway team for OOR and non-Emergency Department intubations. Data is lacking on the utilization of this key resource. Knowing trends of timing, location, and urgency of OOR intubation can allow better resource planning and decrease disruptions in patient care. This study analyzes all plain text pages to the airway team pager at a large academic teaching hospital over 10-years' duration to describe timing and content of calls to the OOR intubation team.

Methods: This study included 16,912 pages received by the RICU Consult (OOR Airway Service) pager, staffed by Anesthesia-trained intensivists at Massachusetts General Hospital, between January 1, 2010, and October 31, 2021. Symbolic Natural Language Processing was used to analyze plain text pages for content related to relevance, acuity, and location of intubation request. Airway related pages were further classified into Code Blue, STAT RICU, and non-STAT RICU. Duplicate pages were excluded.

Results: An average of 4 airway pages were received during each 24-hour period. 85.9% (n=14,527) pages contained information relevant to OOR intubation; majority were for non-STAT intubations (41.0%; n=6935), fewer for STAT intubation (29.6%; n=5000) or Code Blue (14.7%; n=2486). Majority of patients requiring intubation were in an ICU (65.6%; n=7903). Other notable acute care locations included cardiac catheterization lab (4.9%; n=594) and the Emergency department for rescue (3.9%; n=473). Chances of receiving an airway page were highest between 11am and 12pm (6.1%; n=728) and gradually decreased to lowest between 3am and 4am (2.8%; n=334). STAT-RICU pages showed less temporal variation compared to non-STAT or Code Blue pages (Fig 1; p-value for trend 0.03). Pages were most frequent during mid-week: Code Blue pages on Tuesday (16.8%) vs. least frequent on Sunday (11.6%); STAT RICU on Wednesday (15.4%) vs. Saturday (12.9%); non-STAT RICU on Tuesday (15.4%) vs. Monday (13.4%) (p 0.01). There was no significant difference in frequency of pages between different months of the year. Year 2020 had the highest proportion of non-STAT RICUs (54.6%) among all airway-related pages (Fig 2; p 0.04), likely related to COVID-19 pandemic.

Conclusion: An average of four airway pages were received each day, most frequently during late morning hours on weekdays. Paging data is a more readily accessible resource compared to individual patient data obtained from Electronic Medical Records. It can build the foundation for further research into costs of providing an OOR intubation service at large academic hospitals and its impact on patients being cared for directly by the anesthesiologists covering the RICU pager.

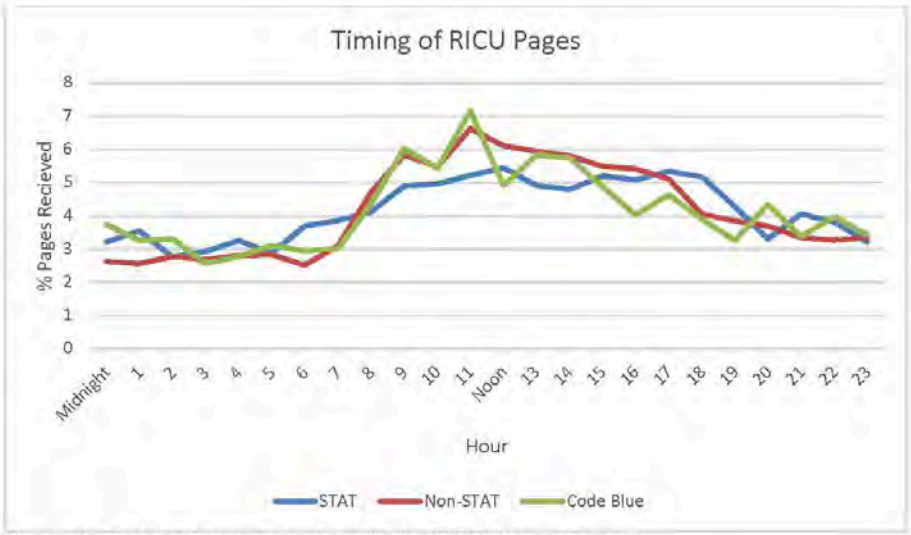

Figure 1: Timing of pages received by the OOR Airway Service

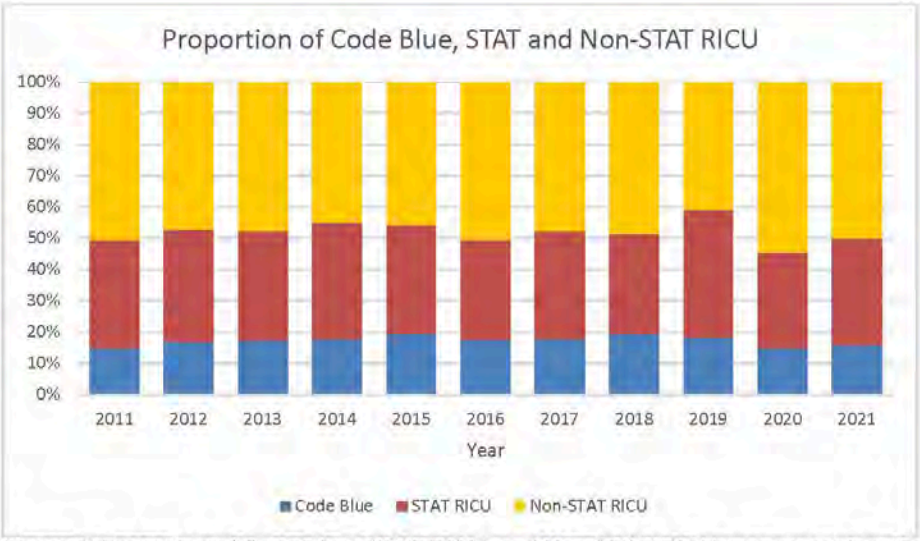

Figure 2: Proportion of Code Blue, STAT RICU, and Non-STAT RICU as a proportion of all airway pages received

Airway Management - 3 Increasing Faculty Competency in Pediatric Fiberoptic Intubation: A Quality Improvement Project

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Introduction: Personnel performing pediatric fiberoptic intubation (FOI) is on the decline due to availability of videolaryngoscopes and the spread of pediatric anesthesia to many non operating room locations where sedation or natural airway is provided. This poses a challenge and potential threat to patient safety when an emergency situation arises or in case of a difficult airway. Continued maintenance of fiberoptic skills is imperative to be proficient. Our hospital cares for complex airway cases in syndromic and non syndromic children. Most faculty take overnight call and serve as a resource for emergency airway support. Previous projects have focused on anesthesia residency training.1 We targeted pediatric anesthesia faculty in this quality improvement (QI) project. The SMART aim was to increase the percentage of faculty completing 5 FOI from 50% to 90% by June 2022 in children.

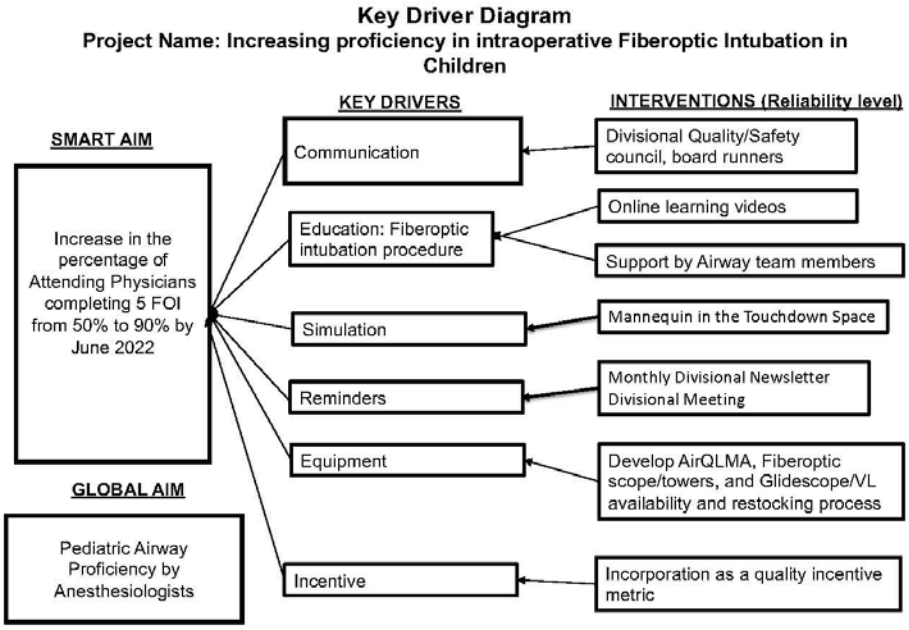
Methods: The project was QI and did not require IRB approval. The Key Driver Diagram is shown in Figure 1. The setting is a large tertiary pediatric center with 60 board certified pediatric anesthesiologists. With approximately 45,000 anesthetics per year, there was ample opportunity for FOI. The FOI was done either for emergency or elective airway securement for procedures requiring anesthesia. Data was tracked in REDCap. The primary outcome was a process measure of percentage of faculty completing the FOI. Analysis was done using the Institute for Healthcare Improvement (IHI) run chart template.2

Results: Baseline data showed only 50% faculty completed ≥ 5 FOI over a year. All faculty participated in this QI project. There were 3 PDSA cycles tested. PDSA#1 involved incorporation of airway proficiency as a quality incentive metric. PDSA#2 was a hands on workshop provided by a core team of 7 faculty from the airway group. This group conducts airway related simulation, education and research. PDSA#3 included a series of airway educational videos created by the airway team on tips and tribulations of airway management. Figure 2 shows that the primary measure, percentage of faculty completing FOI increased over time with a special cause variation as indicated by 8 points above the median.

Conclusion: FOI completion amongst pediatric anesthesia faculty was improved using a QI approach using PDSA methodology. We expect to see a second special cause variation with the median above the goal. The spread and sustain plan will be introduced. Hospitals requiring a similar improvement in their practice can benefit from this QI project.

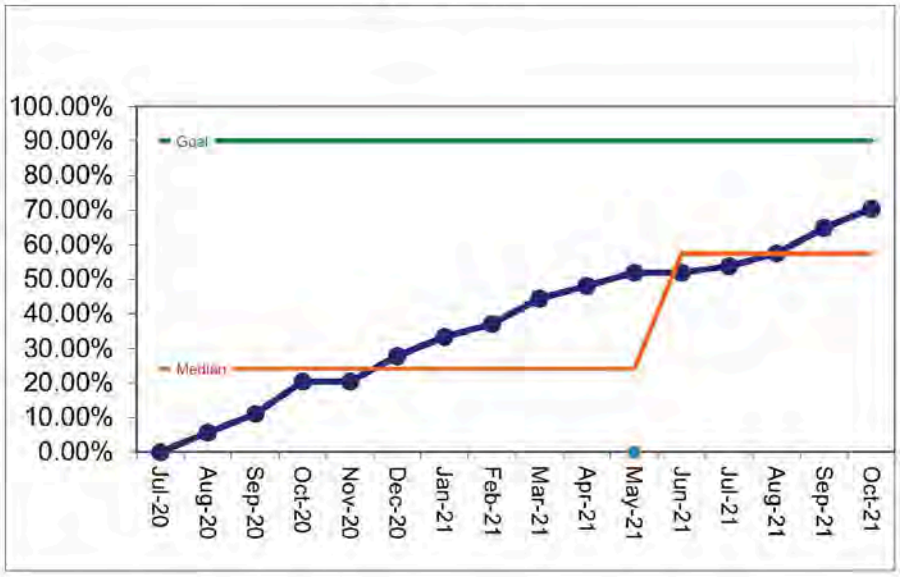
References: 1. M. Wheeler, Andrew G. Roth, Richard M. Dsida, B. Rae, R. Seshadri, Christine L. Sullivan, et al. Teaching Residents Pediatric Fiberoptic Intubation of the Trachea: Traditional Fiberscope with an Eyepiece versusa Video-assisted Technique Using a Fiberscope with an Integrated Camera. Anesthesiology 2004;101:842-846. 2. http://www.ihi.org/resources/Pages/Tools/RunChart.aspx. Accessed Nov 21, 2021

Figure 1: Key Driver Diagram



Key Driver Diagram showing the primary process measure, global aim, key drivers and interventions. The interventions will affect the key drivers and in turn the primary SMART aim as shown by the direction of the arrows.

Figure 2: Run Chart



Legend: This is a Run Chart with months on the x-axis and the percentage of pediatric anesthesia faculty who have completed more than 5 fiberoptic intubations on the y-axis. The blue line indicates the data plotted over time. The red line is the median. The deflection of the red line in May 2021 indicates a special cause variation noted by 8 points above the median. The green line indicates the goal line.

Airway Management - 4 Introducing a New Dimension for Assessing Central Airway Pathology in Mucopolysaccharidosis type-IVA: 3D Reconstruction, 3D Printing and Virtual Endoscopy - Advanced Airway Analytics

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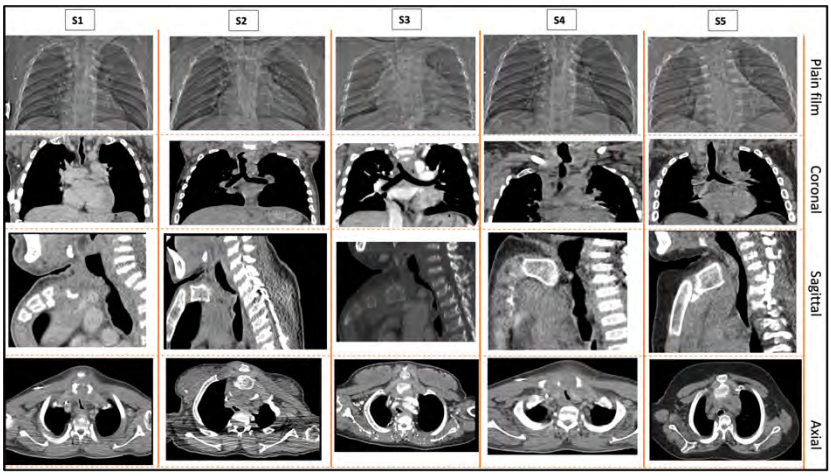
Introduction: Three-dimensional reconstruction (3D-recon), 3D printing and virtual endoscopy (VE) - collectively defined as Advanced Airway Analytics (AAA), have expanded rapidly in the past decade with a broad uptake in healthcare and beyond. There is currently a paucity of investigatory and validation studies within the anaesthetic literature for AAA. The Mucopolysaccharidosis (MPS) are a group of rare, lysosomal-storage-disease that feature profound, central airway pathology. MPS-IVA is characterised by tracheal tortuosity, 'buckling' and narrowing that leads to progressive, multi-level airway obstruction and respiratory failure. Current modalities for imaging the large airways including plain x-ray films, computerised-tomography (CT) and magnetic-resonance-imaging (MRI). The modalities of imaging remain suboptimal for assessing complex airway pathology as they fail to accurately delineate the true character of the aberrations in anatomy and consequently plan for cognisant airway management during anaesthesia.

Methods: Objective: To ascertain how 3D-tracheal reconstruction, 3D prints and VE compare to traditional 2D CT images and fibreoptic airway endoscopy respectively. Methods: Segmentation of CT neck and thorax images were undertaken from five children with MPS type-IVA. This yielded 3D-reconstructions of the airway (saved as stereolithography-STL files) and dynamic VE (MPEG-4 video). 3D-recons were then 3D-printed to create life-size models. The VE were then compared to actual airway endoscopy undertaken during general anaesthesia. AAA was validated qualitatively - by a panel of experts in MPS airway, and quantitatively by assessing limits of agreement between measurements of radial tracheal calibre from CT and 3D modelling; assessing Bland-Altman plots and assessing mean difference and 95% limits of agreement.

Results: 3D-reconstructions offered superior imaging to traditional 2D CT imaging (Figures 1&2). Additionally, VE was found to be comparable to traditional endoscopy and allowed for the demarcation of airway pathology beyond the point of critical airway narrowing, thus providing visualisation of distal structures when traditional rigid or flexible endoscopy would not be possible, or considered safe. Moreover, airway narrowing could be assessed from multiple perspectives, including dynamic airway assessment. There was no significant difference between measurements of tracheal dimensions when assessed by Bland-Altman analysis (bias: 0.03; 95% Limits of Agreement: -0.105-0.173) (Figure 3).

Conclusion: Three-dimensional reconstruction (3D-recon) including 3D-printing and VE are an innovative, non-invasive, malleable and easily accessible technology that our own practice has found to be both safe, reliable and reproducible. VE offers a safe, non-invasive alternative to traditional endoscopy under general anaesthesia, in an otherwise very high-risk patient cohort.

References: 1. Paediatr. Respir. Rev. 2019; 32:55-65 2. Mol. Genet. Metab. Rep. 2019; 20:100487 3. Inherit. Metab. Dis. 2013; 36:211-219 4. J. Clin. Anesth. 2015; 27:508-513.5 5. 3D Print Med. 2020; 6(1):17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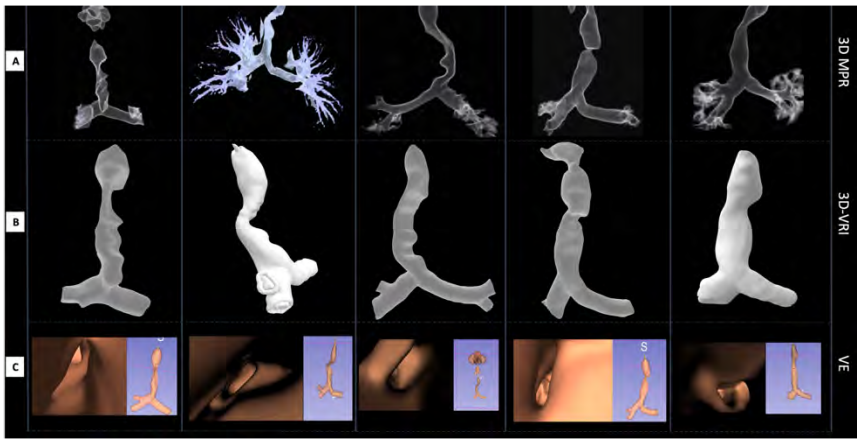
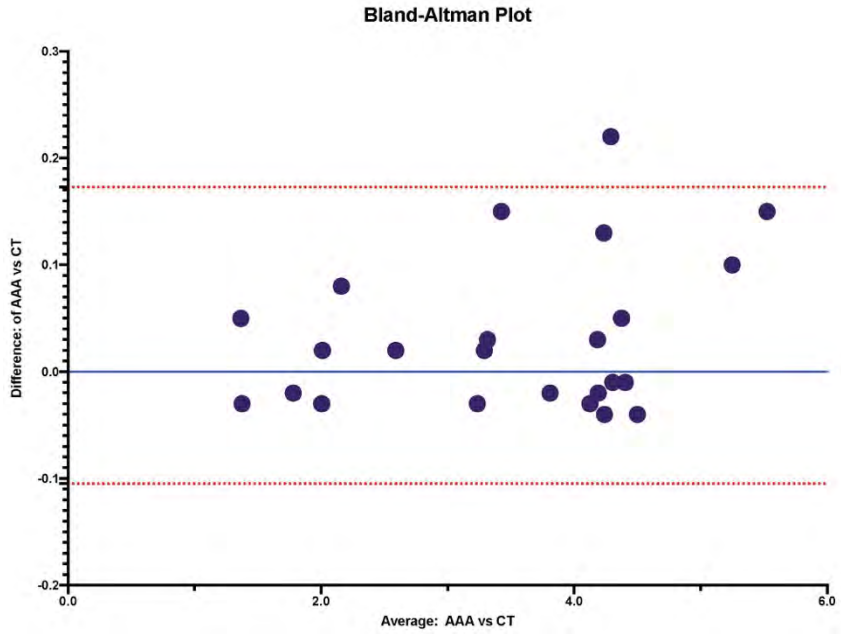

A
B
C
3D MPR
3D-VRI
VE


Bland-Altman Plot
Difference: of AAA vs CT
Average: AAA vs CT
0.3
0.2
0.1
0.0
-0.1
-0.2
0.0
2.0
4.0
6.0

Airway Management - 5 Out-of-Operating Room Emergency Intubation Practice Patterns

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Introduction: The purpose of this research is to evaluate anesthesiologists' approach to emergency out-of-operating room (OR) intubations given various clinical scenarios. Outside of the OR, the critical nature of airway control escalates complications and concerns for patient safety. Emergency airway control prompts providers to cautiously approach intubations and optimize their initial attempts. To better understand emergency intubation strategies, we surveyed anesthesia providers to examine how their approach to emergency intubations outside of the OR alters across clinical scenarios.

Methods: An online survey was distributed via REDCap to anesthesiologists at the University of Chicago Medical Center. Demographics collected include years of anesthesia experience, comfortability of emergency airway management, and the number of out-of-OR intubations performed. We asked respondents to consider out-of-OR emergency intubations in four clinical scenarios regarding a combination of (1) the patient's airway exam (favorable or unfavorable) and (2) the patient's hemodynamic condition (stable or unstable) (Figure 1). For each scenario, respondents were asked questions regarding typical initial intubation strategy (direct laryngoscopy, video laryngoscopy, fiberoptic bronchoscopy), how often or percentage of time they induce general anesthesia, and how often they used neuromuscular blocking agents (NMBAs). Survey data was analyzed descriptively to determine the current out-of-OR emergency intubation practice patterns.

Results: Respondents (n=65) ranged in clinical experiences from less than five years (43%, 28) to more than 16 years of practice (23%, 15), and many were fellowship-trained (48%, 31). Majority of the participants were either comfortable (28%, 18) or very comfortable (40%, 26) with emergency airway management outside the OR and had performed more than 15 emergency intubations in the past five years (82%, 53). Direct laryngoscopy was the primary intubation strategy in scenarios 1 (69%, 45) and 2 (62%, 40). Video laryngoscopy was the primary strategy in scenarios 3 (63%, 41) and 4 (58%, 38). Nearly half of providers almost never or rarely use general anesthesia in scenarios 2 and 3 (48%, 31), and majority of providers in scenario 4 (86%, 56) almost never or rarely use general anesthesia. The frequency of NMBAs use decreases as the clinical scenarios increase in complexity. Majority of respondents often or always use NMBAs in scenario 1 (66%, 43), while the majority of respondents in scenario 3 (54%, 35) and scenario 4 (68%, 44) almost never or rarely use NMBAs in emergency intubations settings.

Conclusion: As clinical scenarios increase in airway and hemodynamic complexity for emergency intubations out-of-OR, the need for more dynamic airway visualization increases while the use of general anesthesia and neuromuscular blocking agents decreases. The described practice patterns may affect patient outcomes and quality improvement strategies regarding emergency intubations outside the OR.

Table 1. Demographic characteristics of the respondents.

Variable	Number	Percentage
Years of Anesthesia experience (including residency)		
0-5	28	43
6-10	15	23
11-15	7	11
16-20	3	4.6
>20	12	18
Fellowship Training		
Yes	31	48
No	34	52
Comfortability with out-of-OR emergency airway management		
Not at all	3	4.6
Somewhat comfortable	18	28
Comfortable	18	28
Very comfortable	26	40
Number of emergency intubations performed (within 5 years)		
1-5	1	1.5
6-10	5	7.7
10-15	6	9.2
>15	53	82

Figure 1. Clinical Scenarios. Scenarios 1 and 4 ask respondents to consider a clinical situation where both the airway exam and hemodynamics are favorable or not, respectively. Scenario 2 is denoted with an "H" for only hemodynamic instability. Scenario 3 is denoted with an "A" for only an unfavorable airway exam.

Table 2. Intubation Strategy.

	Scenario 1	Scenario 2-H	Scenario 3-A	Scenario 4
Direct Laryngoscopy	45 (69%)	40 (62%)	3 (4.6%)	4 (6.2%)
Video Laryngoscopy	20 (31%)	24 (37%)	41 (63%)	38 (58%)
Fiberoptic Bronchoscopy	-	1 (1.5%)	20 (31%)	22 (34%)
Other	-	-	1 (1.5%)	1 (1.5%)

Table 3. Frequency of General Anesthetic Use.

	Scenario 1	Scenario 2-H	Scenario 3-A	Scenario 4
Almost Never (<1%)	3 (4.6%)	12 (18%)	11 (17%)	33 (51%)
Rarely (1-10%)	2 (3.1%)	19 (29%)	20 (31%)	23 (35%)
Sometimes (11-50%)	19 (29%)	24 (37%)	24 (37%)	8 (12%)
Often (51-90%)	27 (42%)	6 (9.2%)	9 (14%)	-
Almost Always (91-100%)	14 (22%)	4 (6.2%)	1 (1.5%)	1 (1.5%)

Table 4. Frequency of Neuromuscular Blockade Use.

	Scenario 1	Scenario 2-H	Scenario 3-A	Scenario 4
Almost Never (<1%)	3 (4.6%)	11 (17%)	17 (26%)	26 (40%)
Rarely (1-10%)	1 (1.5%)	10 (15%)	18 (28%)	18 (28%)
Sometimes (11-50%)	18 (28%)	24 (37%)	20 (31%)	17 (26%)
Often (51-90%)	25 (38%)	14 (22%)	7 (11%)	1 (1.5%)
Almost Always (91-100%)	18 (28%)	6 (9.2%)	3 (4.6%)	3 (4.6%)

Ambulatory Anesthesia

Ambulatory Anesthesia - 1 Institutional Complications of Arteriovenous Fistulas in Hemodialysis Patients: A Retrospective Review

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Introduction: Arteriovenous fistulas (AVF) are a type of permanent vascular access available for hemodialysis. Although AVFs are preferred due to decreased long term vascular events, hemodialysis patients still present with complications including mechanical, infectious, and vascular.[1] Anesthetic options for the creation of AVFs include regional anesthesia (RA), general anesthesia (GA) and monitored anesthesia care (MAC). However, studies analyzing the relationship between anesthesia modality and AVF complications are limited. Therefore, the purpose of the study is to quantify the number of complications present in our institution compared to nationwide rates and determine whether complication rates differ depending on anesthesia modality.

Methods: Charts of 107 hemodialysis patients at our institution were reviewed between 2017-2021. Patients were divided into complications and no complications groups. In addition to baseline demographics, outcome variables studied were complications (mechanical, infectious, and vascular) and anesthesia used during AVF creation (GA, RA, or MAC). Complication rates at our institution were compared to complication rates nationwide.[2] Statistical analysis was performed using two population proportion tests and χ^2 test when appropriate. A p-value < 0.05 was considered significant.

Results: Subjects included in the study were patients who had an AVF created between 2017-2021. Of the 107 patients studied, 100 patients (93.5%) met inclusion criteria whereas 7 patients (6.5%) did not. Exclusion criteria included patients who were <18 years old and patients who had an AVF created before 2017. 53 patients (53%) had at least one complication following AVF creation while 47 patients (47%) had no complications. Patient demographics were similar between patients with and without complications except for race [Blacks ($p < 0.001$), Hispanics ($p = 0.031$), Other ($p = 0.071$)] and BMI ($p = 0.034$). There was a significant difference in overall complication rate at our institution compared to national complication rates (47% vs. 10.7%, $p < 0.001$), respectively. Specifically, thrombosis rates were significantly higher in our institution compared to national rates (42.55% vs. 21.37%, $p < 0.001$). There was no significant difference in infection (6.38% vs. 5.1%, $p = 0.697$) and ischemic steal syndrome (0% vs. 3.15%, $p = 0.215$) rates compared to national rates. There was no significant difference in anesthesia given during AVF creation and complication rates.

Conclusion: Our results demonstrate a significant difference in complication rates among our patients compared to the national rate, specifically thrombosis rates. Complications with the greatest incidence included malfunctioning AVF, thrombosis and stenosis. Anesthesia modality during AVF creation did not differ between the two groups studied. Institutional measures should be placed in order to reduce complication rates in hemodialysis patients with AVFs.

References: 1. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. 2020;75(4). 2. Complications of the Arteriovenous Fistula: A Systematic Review. 2017;28(6).

Table 1. Baseline demographics of patients who had an AVF created between 2017 and 2021.

Characteristic	No Complications (n=53)	Complications (n=47)	*p*-value
Age (years)	59.38±14.34	57.83±13.98	0.59
Race			
Black/African American	34 (64.2)	45 (95.7)	< 0.001*
Caucasian	7 (13.2)	2 (4.3)	0.119
Hispanic	5 (9.4)	0 (0)	0.031*
Other	6 (11.3)	0 (0)	0.017*
Undisclosed	1 (1.9)	0 (0)	0.342
Gender			0.359
Females	20 (37.7)	22 (46.8)	
Males	33 (62.3)	25 (53.2)	
BMI (kg/m^2)	28.57± 0.76	25.98± 0.95	0.034*
Comorbidities†			
Coronary Artery Disease	15 (28.3)	9 (19.1)	0.285
Congestive Heart Failure	13 (24.5)	13 (27.7)	0.719
Diabetes Mellitus	37 (69.8)	25 (53.2)	0.087
Hypertension	53 (100)	46 (97.9)	0.285
Peripheral Vascular Disease	1 (1.9)	3 (6.4)	0.250
Hyperlipidemia	25 (47.2)	24 (51.1)	0.697
Obesity	18 (34.0)	12 (25.5)	0.358

Data are expressed as mean ± SD or n (%)
†Some patients had multiple comorbidities; therefore, total percentages may exceed 100.

Table 2. Institutional Complications

Type of Complication	Number of Events
Thrombosis	20 (21.3)
Malfunctioning AVF	34 (36.2)
Failure of Maturation	5 (5.3)
Infection	3 (3.2)
Aneurysm/Pseudo-aneurysm	7 (7.4)
Stenosis	16 (17.0)
Swelling	3 (3.2)
Bleeding	1 (1.1)
Hematoma	2 (2.1)
Vein Transposition	3 (3.2)
Total	94

Table 3. Comparison of National and Institutional Complication Rates

Complication Type (%)	**National**	**Institutional**	***p*-value**
Infection	5.10	6.38	0.697
Ischemic Steal Syndrome	3.15	0.00	0.215
Thrombosis	21.37	42.55	< 0.001
Overall Complication Rate (%)	10.70	47.00	< 0.001

Table 4. Anesthesia Modality Given During AVF Creation

Anesthesia Modality	**No Complications (n=53)**	**Complications (n=47)**	***p*-value**
General Anesthesia	8 (15.1)	12 (25.5)	0.098
Monitored Anesthesia Care (MAC)	25 (47.2)	26 (55.3)	
MAC + Regional Anesthesia	20 (37.7)	9 (19.1)	

Data is expressed as n (%)

Anesthetic Pharmacology

Anesthetic Pharmacology - 1 Local anesthetics induce an anti-tumoral immune response in vitro and in tumor established in mice

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Introduction: Retrospective studies observed a surprising expended overall survival and significant less relapse after local anesthetics (LAs) injection during oncological surgery.1,2,3,4 We hypothesized that LAs may exert cytotoxic effects on tumor cells and trigger molecular signaling, which promote anticancer immune response.

Methods: Bupivacaine, chloroprocaine, levobupivacaine, lidocaine, ropivacaine and prilocaine were studied in vitro in human osteosarcoma wild-type cells or in cells stably expressing fusion proteins to investigate cell stress and cell death (U2OSwt, U2OS GFP-LC3, U2OS GFP-ATF4, U2OS GFP-ATF6 and U2OS venus-XBP1-RFP-FYVE). Results were validated in vivo in immunocompetent C57Bl/6 mice transplanted with subcutaneous murine fibrosarcoma (MCA205wt or MCA205 K3 knock-out designed with CRISPR-Cas9 technology or MCA205 Atg5 knock-down obtained with sh-RNA technology) and colon adenocarcinoma (MC38wt). Tumor growth, survival and immune response were investigated after treatment with lidocaine and ropivacaine alone or combined with immunotherapy (anti-PD-1). Data normality was tested by the Kolmogorov-Smirnov test. In vitro, statistical analyses were performed with a Student t-test to compare parametric data to a control. In vivo, statistical analyses were performed with a Wilcoxon-Mann-Whitney test for tumor growth and with a log-rank test for survival analysis. Algorithm was engineered with a deep learning approach. Data analysis was performed using R software. For all test, significance was assessed for $p<0.05$. Ethical Committee approvement: CEEA IRCIV/IGR n°26, French Ministry of Research, ref: 16946/2018100309413893v2,ref: 27492/2020100809149728v2

Results: LAs triggered premortem stress such as autophagy (Fig 1) and endoplasmic reticulum stress (Fig 2), which were both dependent on EIF2A kinase 3 and its downstream pathway phospho-eIF2alpha. LAs also mimicked mitochondrial uncouplers triggering mitochondrial toxicity and then cell death. In vivo, lidocaine and ropivacaine significantly decreased tumor growth and improved overall survival in different models of solid cancer (MCA205wt, MC38wt) established in immunocompetent mice (C57Bl/6). Associated with immune checkpoint blockade, these anticancer effects were significantly potentiated. Interestingly, LAs failed to induce antitumor responses in immunodeficient mice (nu/nu) or in tumors unable to trigger endoplasmic reticulum stress (MCA205 K3 knock-out) or autophagy (MCA205 Atg5 knock-down). Moreover, after rechallenge, cured mice did not develop tumors, proof of immunological memory development. Taken together, this data suggest that LAs-induced cellular stress triggers immune response that participate to the anticancer effect. Based on these findings, we designed an algorithm that allows to confront the biological effects of LAs with their physicochemical properties and to predict potential anticancer response of all clinically-employed anesthetic agents. Thus, intravenous agents such as propofol and ketamine seem to possess anticancer properties whereas opioids and volatile agents promote major procarcinogenic effects.

Conclusion: LAs enhance direct cytotoxicity in vitro and in vivo, which is preceded by premortem stress and mitochondrial dysfunction. LAs used as stand-alone agents trigger anticancer immune responses in vivo that can be enhanced by additional combination with standard anticancer immunotherapy. These observations led us to design an algorithm predicting effects of the different anesthetic agents. We suggest that the use of such 'immune-LAs' during oncological surgery may help clinicians to improve cancer care and clinical outcome.

References: Melanoma Research. 2000 Apr;10(2):165-9. Anesthesiology. 2006 Oct;105(4):660-4. Anesthesiology. 2008 Aug;109(2):180-7. Oncotarget. 2016 Mar 22;7(12):15262-73.

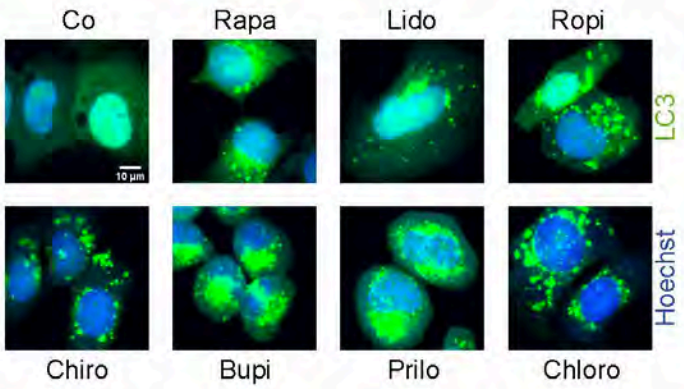

Figure 1. Local anesthetics induce autophagic flux
(Co: untreated, negative control ; Rapa: rapamycin, positive control; Lido: lidocaine;Ropi: ropivacaine;Chiro: chirocaine;Bupi: bupivacaine; Prilo: prilocaine; Chloro:chloroprocaine)

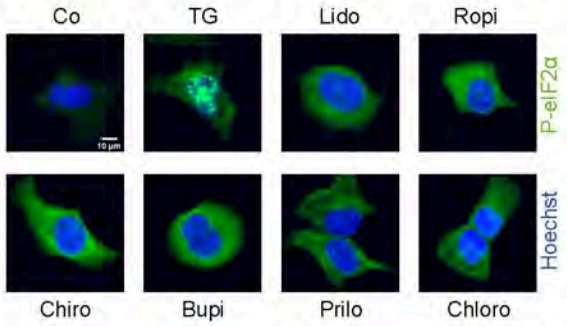

Figure 2. Local anesthetics induce endoplasmic reticulum stress
(Co: untreated, negative control ; TG: thapsigargin, positive control;Lido:lidocaine Ropi: ropivacaine;Chiro: chirocaine;Bupi: bupivacaine;Prilo:prilocaine;Chloro:chloroprocaine)

Anesthetic Pharmacology - 2

Understanding the effect of mitochondrial localization on anesthetic response

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Introduction: Worldwide, it is estimated that more than 230 million major surgical procedures are performed under general anesthesia each year. Despite our finesse with general anesthetic medications, we still do not fully understand how these small, structurally diverse compounds induce unconsciousness. A great deal of work has been done to identify the proteins targeted by anesthetics. One major class of proteins bound are those involved in the electron transport chain of the mitochondria. However, recent data demonstrated that propofol binds to kinesin motor protein, inhibiting its ability to transport cargo such as mitochondria1. Therefore, the effect of anesthetics on synapse energy homeostasis may be two-fold. First, as has been demonstrated in the past, from inhibiting the electron transport chain. Second, anesthetics bind to the motor proteins critical for movement of mitochondria to the neural synapse creating a relative decrease in energy available. To explore how kinesin movement and mitochondrial localization affects anesthetic response, we employed the larval zebrafish model and obtained loss of function mutants to two key proteins. Kinesin 5Aa (kif5Aa) has been shown to be important in mitochondrial movement down the synapse of neurons2. Kinesin binding protein (kbp) is a key regulator and removes kinesin proteins from microtubules3. We used these two mutations to explore how kinesin affects anesthetic response.

Methods: Using 5 days post fertilization (dpf) zebrafish larvae, we used a previously validated behavior, the startle response to a tap, to assess induction of anesthesia and response over time4. The larvae were placed in the previously defined EC50 for propofol and etomidate5 and tested by a tap stimulus was given every 30 seconds for 6 hours and responses were compared to wild type (wt). A single experiment contains 24 larvae per sample.

Results: We found that the kif5Aa mutants demonstrated a statistically significant decrease in response to propofol at 100 minutes (wt=0.32 ± 0.09 vs kif5Aa=0.50 ± 0.17, n=7). However, by 200 minutes the kif5Aa mutants returned to wild-type sensitivity. The kbp mutants also demonstrated a decrease in sensitivity to both propofol (wt=0.30 ± 0.07 vs kbp=0.55 ± 0.19, n=4-6) and etomidate (wt=0.40 ± 0.10 vs kbp=0.68 ± 0.16, n=3). The larvae remained resistant to both drugs throughout the course of the experiment.

Conclusion: Using the 5 dpf larval zebrafish, we found that both kif5Aa and kbp were resistant to propofol and kbp was resistant to etomidate. In the kif5Aa mutants, the resistance waned over time. Whereas, in the kbp mutants, the resistance was maintained. Using these mutations, we will be poised to understand how mitochondrial location within neurons affects anesthetic response. We will be able to dissect how mitochondrial localization affects synapse energy homeostasis and how a live animals respond to these drugs. Moreover, the transparent nature of the larvae will allow us to fully understand how these genes combined with different anesthetics affect neural signaling pathways.

References: Proc Natl Acad Sci U S A 2017; 114: E4281-E4287 J Neurosci 2014; 34: 14717-32 Curr Biol 2016; 26: 849-61 Elife 2019; 8 Sci Rep 2020; 10: 15789

Anesthetic Pharmacology - 3 Meta-analysis: a study of adverse effects and turnover rates of sugammadex versus neostigmine for neuromuscular blockade reversal

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Introduction: For many years, neostigmine, an acetylcholinesterase inhibitor, was the drug of choice for reversing neuromuscular blockades in the operating room. However, there are disadvantages to using neostigmine including autonomic dysfunction like bradycardia and post-operative nausea & vomiting (PONV), and the necessity to administer the drug at the correct time due to its lag time in effect. Recent studies have been performed on sugammadex, a new reversal agent, which does not have a 'lag time effect.' Although it is considered safer, some studies cite harmful effects. Given its rapid rise in usage, a more comprehensive characterization of the clinical and practical aspects of sugammadex compared to the standard of neostigmine is needed.

Methods: In accordance with the PRISMA guidelines, a systematic review of PubMed and Scopus databases was performed in search of publications that compared the efficacy and safety of sugammadex versus neostigmine. All publications that included either endpoints were included irrespective of date of publication, country of origin, language, age range of patients, type of surgical procedure, or ASA grade. Data were analyzed using Microsoft Excel.

Results: 57 articles totaling n = 66157 patients met inclusion criteria for this meta-analysis. Compared to neostigmine, sugammadex showed a significant reduction in extubation time (mean difference [MD] = -2.77 min, 95% CI (-3.95, -1.59)), Recovery to TOF >0.9 time (MD =-11.27 min, 95% CI (-12.7, -9.89)), OR discharge time (MD = -3.74 min, 95% CI (-4.77, -2.71)), and PACU discharge time (MD = -8.51 min, 95% CI (-14.9, -2.07)). Sugammadex shows a significant reduction in pneumonia (RR = 0.593, 95% CI (0.361, 0.671)) and bradycardia (RR = 0. 535, 95% CI (0.424, 0.675)), and a significant increase in PONV (RR = 1.21, 95% CI (1.05, 1.39)). No significant difference was found for atelectasis (RR = 0.964, 95% CI (0.853, 1.09)).

Conclusion: This study supports that administration of sugammadex as a reversal agent for neuromuscular blockade facilitates faster extubation time, OR turnover time, and PACU discharge time. Sugammadex is associated with lower risk of bradycardia and pneumonia, but higher risk of PONV. In an ongoing study, we are investigating the shorter times of sugammadex in the context of a cost-benefit analysis. These results serve as a strong basis for future work on neuromuscular blockage reversal agents, with large implications in improving the quality of patient care, bolstering the efficiency of the surgery and anesthesiology services, as well as improving healthcare costs of surgery and anesthesia.

Anesthetic Pharmacology - 4 An alternative way to reverse the sedative effect of dexmedetomidine rapidly by low dose atipamezole and caffeine in rats

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Introduction: Dexmedetomidine (Dex), an α2 adrenergic receptor agonist, may reduce the incidence of postoperative delirium and neurocognitive dysfunction in both very old and very young patient populations[1,2]. Emergence times from Dex sedation is slow, tying up resources[3]. Currently no drugs are used to reverse Dex clinically. Atipamezole (Ati) is an α2 competitive antagonist used in veterinary medicine, to reverse Dex. When tested in humans, high dosages of Ati were required to reverse Dex sedation (Ati:Dex ratio, 10:1 in rodents vs 40-100:1 in human); these high dosages were associated with unwanted effects[4]. Activation of α2 receptors leads to activation Gi protein, resulting in a decrease in [cAMP]i which inhibits neuronal activity. Our previous work showed that drugs that elevate cAMP levels, like caffeine, accelerated emergence from general anesthesia in both animals and humans[5,6]. We also observed that caffeine was able to directly reverse moderate sedation. The goal in this study was to devise a protocol to rapidly reverse Dex-induced deep sedation. We used low doses of Ati (Ati: Dex ratio, 0.5:1) to shift rats from deep sedation to moderate sedation, which then could be rapidly and completely reversed by caffeine. This strategy was extremely effective.

Methods: These studies were approved by the Univ of Chicago IACUC. Adult Sprague Dawley rats were divided into groups of 8 (female and male). They received Ati/caffeine or saline injections in a repeated measures design. All rats served as their own controls. Experiments were performed in the daytime at ~25 ◦C. A bolus of Dex was delivered via a tail vein IV. Ati/ caffeine or saline (control) was given 10 minutes after the Dex bolus. After drug injection, rats were placed in a cage on their backs and the time to recovery of righting reflex (RORR) was measured as a proxy for the time to emerge from sedation. A paired T-test or a repeated measures ANOVA with Tukey's multiple comparisons post-hoc test was employed. Data were expressed as mean ± standard deviation.

Results: A bolus of Dex (10 μg/kg) caused a group of female rats to lose their righting reflex for 30.0 ± 7.4 min after saline injection. Ati (5 μg/kg) or Ati (5 μg/kg) with caffeine (25 mg/kg) produced faster emergence time (13.6 ± 5.8 min or 3.0 ± 0.9 min, respectively), significantly different than saline ($p < 0.0001$). Ati/caffeine produced a much shorter emergence time than Ati alone ($p=0.0023$). In a different group of 8 rats with the same dosages, the emergence time was 34.2 ± 4.9 min, 25.7 ± 0.6 min or 4.3 ± 1.9 min, after saline, caffeine, or Ati/ caffeine, respectively. These differences were significant. Male rats showed similar behaviors.

Conclusion: The Ati doses employed in this study were 20-fold lower than that recommended by the manufacturer. The low dose Ati/caffeine combination reversed Dex sedation rapidly and completely. Future studies are needed to test the safety and efficiency of this combination in humans.

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Anesthetic Pharmacology - 5 EEG Profile for a Selective GABAA-Slow Agonist, Compared to Propofol, in Rats

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Introduction: Introduction: Anesthetic agents like propofol increase power in slow delta frequencies (0.1 to 3 Hz), with a general decrease in EEG frequencies above 30 Hz. Propofol is non-selective for GABAA response subtypes, it enhances all three GABAA-subtypes (slow, fast, and tonic). A new anesthetic, BB, selectively targets GABAA-slow synapses to depress brain responsiveness. We hypothesized that a selective GABAA-slow agonist, BB, would produce a different EEG signature compared to the broad spectrum GABAA agonist (propofol), and tested this using rat EEG recordings.

Methods: Methods: Male rats were used following IACUC approval from the US Army Medical Research Institute of Chemical Defense and the University of Michigan. Rats were anesthetized using isoflurane (3-5% induction, 1-3% maintenance; with oxygen @ 0.5-1.0 L/min. Stainless steel screws were used to capture cortical EEG activity.

Results: Results: Propofol administration generated increased power in slow delta frequencies (0.1 to 4 Hz) and a general decrease in EEG power above 30 Hz at loss of consciousness (LOC). By contrast, BB administration increased theta activity markedly (3-5 Hz and 8-10 Hz), and slightly increased delta power, but did not depress high frequency responses above 30 Hz. Neither agent produced burst suppression activity at LOC. Both anesthetics produced a characteristic flattening of time-delayed embeddings, similar to volatile and dissociative anesthetics at LOC. Propofol's EEG effects were in agreement with those seen in previous studies across individuals and species. At LOC a generalized slowing in EEG was seen with increased power in frequencies below 4 Hz. BB produced a markedly different EEG pattern, with a selective increase observed in the theta frequency range.

Conclusion: Conclusion: Increased theta frequencies are interesting because GABAA slow synapses have previously been suggested to underlie theta frequency oscillations, while fast synapses control high, gamma frequency oscillations (30-60 Hz). Tonic GABAA responses produce a generalized depression of neuronal activity across all frequencies. BB and propofol share the ability to flatten EEG time-delayed embeddings at LOC. Flattened embeddings are also observed in humans and thought to reflect a decrease in EEG information content at LOC. It appears that propofol's effects on fast and/or tonic responses contribute to its respiratory and cardiovascular unwanted side effects, since these were not produced by BB. Figure 1. Power spectral density plots comparing the effects produced by propofol (A & B) and BB (C & D). BB produced a selective increase in theta frequencies produced by prolonging GABA-slow synaptic inhibition following loss of consciousness (LOC-blue vs red-preLOC).

Anesthetic Pharmacology - 6 A propofol binding site on ryanodine receptor 1

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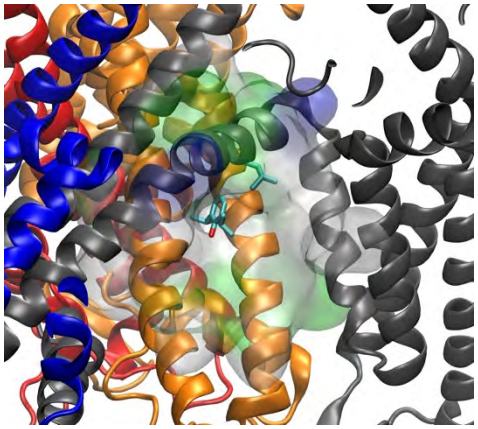
Introduction: Malignant hyperthermia (MH), as part of a spectrum of muscle pathologies, arises from the combination of triggering anesthetics and a mutant ryanodine receptor 1 (RyR1), a calcium channel embedded in skeletal muscle sarcoplasmic reticulum (1). The channel becomes biased open, resulting in a large calcium ion flux. Clearing the excess calcium from the cytoplasm generates a large metabolic load, which leads to the pathophysiologic sequelae of MH. Supportive care includes discontinuing triggering anesthetics in favor of non-triggering anesthetics such as propofol, which would then have an opportunity to bind to RyR1. Whether propofol binding occurs and its potential consequences are not yet understood. We have identified a propofol binding site on RyR1 using photoaffinity labeling and characterized it using molecular dynamics simulations.

Methods: Photoaffinity labeling was conducted using m-azipropofol (AziPm) (2), a photolabel analog of propofol. The RyR1 protein was incubated with AziPm and irradiated to form a reactive carbene version of AziPm which bonds covalently to RyR1 in the AziPm binding site. The adducted protein was then subjected to proteolysis and mass spectrometry. Identifying the peptides whose sizes grew by the size of the adduct allowed identification of adducted residues. In order to ascertain whether the identified site could be shared with propofol, a protection assay was conducted to determine whether co-incubation with propofol would competitively inhibit photoadduction by AziPm. Molecular dynamics (MD) simulations were conducted of the wild-type RyR1 transmembrane domain with a single propofol molecule placed in the photoaffinity-identified putative binding site on the tetrameric RyR1. This site is distinct from previous L4827 sites as it is among alpha helices with relatively little solvent exposure. Double-decoupling free energy perturbation (FEP) MD with a flat-well volume restraint (3) was used to calculate the standard binding free energy of each ligand.

Results: Photoaffinity labeling revealed an AziPm binding site at L4827 in RyR1. A protection assay was consistent with this also being a propofol binding site. This site is located in the transmembrane domain of RyR1. Since these experimental methods cannot quantify the affinity or configuration of these ligands in the site, we therefore conducted equilibrium MD simulations that suggested that propofol was stable in the site. FEP MD simulations with both closed and open state RyR1 predicted binding affinities of propofol that corresponded to dissociation constants KD = 0.5–3 μM. Examination of the bound propofol configuration shows that its hydroxyl group is oriented toward Y4851 with a distance roughly 9 Å.

Conclusion: Our data shows that propofol binds RyR1 at a clinically relevant concentration in the L4827 site on RyR1. Our previous work identified a propofol binding site near to this site with fewer interacting protein residues, also consistent with photoaffinity labeling of L4827, but with a lower affinity. As propofol is a nontriggering anesthetic, this is a novel example of the ability of a commonly-used non-triggering anesthetic to bind to RyR1. Future work would include reproducing these studies in RyR1 containing an MH-causative mutation.



Anesthetic Pharmacology - 7 Substituted Cysteine Modification-Protection Suggests Novel Anesthetic pTFD-di-iPr-BnOH Does Not Bind in α+/ γ− Pocket

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Introduction: Potent intravenous anesthetics act in part through pentameric γ-aminobutyric acid type A receptors (GABAARs), the major inhibitory ligand-gated ion channels in the central nervous system. Typical synaptic GABAARs contain two alpha, two beta, and one gamma subunit surrounding a central pore, arranged β-α-β-α-γ. This creates four distinct subunit interface types: α+/β−, α+/γ−, β−/ γ+, and two β+/α− (Fig 1). Etomidate binds in the two outer transmembrane β+/ α− interfaces, R–mTFD- MPAB binds to homologous α+/β− and γ+/β− sites, and propofol binds to all four of these interfaces. Until recently, no anesthetics were thought to bind in the outer transmembrane α+/γ− interface, leading to its designation as an "orphan site" (1, 2). However, exploratory hydrophobic mutagenesis and subunit-level photolabeling-protection studies suggest that pTFD-di-iPr-BnOH binds in outer transmembrane α+/β− and α+/γ− interfaces (3). The current study aimed to further map pTFD-di-iPr-BnOH binding using the Substituted Cysteine Modification-Protection (SCAMP) method, which correlates better than hydrophobic mutant function studies with anesthetic photolabeling results (2).

Methods: Xenopus laevis were used with IACUC. Harvested Xenopus oocytes were injected with messenger RNA mixtures encoding α1, β3, and γ2L subunits at 1α:1β:5γ ratios. SCAMP experiments were conducted in oocytes expressing four different cysteine mutants: α1S270Cβ3γ2L, α1β3L231Cγ2L, α1β3γ2LL246C, and α1β3γ2LI242C. Exposure to the sulfhydryl modifier, p-chloromercuribenzenesulfonic acid (pCMBS), was performed at room temperature in the presence of maximal-activating GABA (3 mM). pCMBS modification was detected using two-electrode voltage-clamp electrophysiology from changes in low:high GABA current response ratios (EC3 vs. 3 mM). Duplicate low:high ratios were measured before and after pCMBS + 3 mM GABA exposure, with intervening 5 min buffer washes. Modification ratios were calculated as average post-modification normalized to average pre-modification low:high ratios within oocytes. Control pCMBS exposures were chosen to produce 50% of the maximal modification ratio for each mutant receptor. In protection experiments, oocytes were pre-exposed to anesthetic for 30s before exposure to pCMBS + GABA + anesthetic. Modification ratio comparisons between control and protection used unpaired two-tailed Student's t-tests with n=3-5 oocytes per condition. Protection was inferred from significant concentration-dependent inhibition of modification.

Results: Modification conditions selected for the four mutants resulted in control modification ratios ranging from 3.7 to 9.2 (Fig 2). Notably, pTFD-di-iPr-BnOH weakly protected β3L231C and γ2LL246C but displayed no concentration-dependent protection at these sites (Fig 3). No protection was observed at γ2LI242C. Etomidate protected none of the four engineered cysteines (none are in the β+/α− interfaces), but enhanced modification in three (α1S270C, γ2LL246C and γ2LI242C). R-mTFD-MPAB protected α1S270C and β3L231C, consistent with previous results (2). MPAB protection at β3L231C was concentration-dependent and more profound than pTFD-di-iPr-BnOH at this site (Fig 3).

Conclusion: Our preliminary SCAMP results for etomidate and R-mTFD-MPAB are fully consistent with previous photolabeling, mutational analysis, SCAMP studies, and for etomidate, cryo-EM. Our results for pTFD-di-iPr-BnOH are not fully consistent with the hypothesis that this drug binds in the outer transmembrane α+/γ− "orphan" anesthetic site (3). No protection was observed at α1S270C. Weak protection at γ2LL246C was observed with 30 μM pTFD-di-iPr-BnOH, but not at 100 μM and no protection was observed one helical turn away at γ2LI242C. Additionally, 10 to 100 μM pTFD-di-iPr-BnOH similarly protected β3L231C. This lack of concentration-dependent protection and its weakness relative to R-mTFD-MPAB suggests an allosteric effect or possibly binding near only one of the two β3 subunits. Thus, our

results remain compatible with subunit photolabeling protection results suggesting that MPAB and pTFD-di-iPr-BnOH bind to one common site. However, current results only partially cover α+, γ−, and β− subunit faces. A more complete survey of potential anesthetic contact residues is underway. Funded by NIH R01GM089745 and R35GM141951

References: (1) Forman SA, Miller KW. Mapping General Anesthetic Sites in Heteromeric γ-Aminobutyric Acid Type A Receptors Reveals a Potential For Targeting Receptor Subtypes. Anesth Analg. 2016;123:1263–1273.

(2) Nourmahnad A, Stern AT, Hotta M, Stewart DS, Ziemba AM, Szabo A, Forman SA. Tryptophan and Cysteine Mutations in M1 Helices of α1β3γ2L γ-Aminobutyric Acid Type A Receptors Indicate Distinct Intersubunit Sites for Four Intravenous Anesthetics and One Orphan Site. Anesthesiology 2016;125:1144-58. (3) Shalabi AR, Yu Z, Zhou X, Jounaidi Y, Chen H, Dai J, Kent DE, Feng HJ, Forman SA, Cohen JB, Bruzik KS, Miller KW. A potent photoreactive general anesthetic with novel binding site selectivity for GABAA receptors. Eur J Med Chem. 2020 May 15;194:112261.

Figure 1. Schematic of GABAA receptor consisting of two alpha, two beta, and one gamma subunit with four distinct subunit interfaces: α+/ β−, α+/ γ−, β−/ γ+, and two β+/ α− sites. β_3L231C, α_1S270C, γ_{2L}L246C, and γ_{2L}I242C mutations are labeled on appropriate M1, M2, and M3 domains.

pCMBS Protection

Mutant	pTFD-di-iPr-BnOH	Etomidate	MPAB
$\alpha_1\beta_3\gamma_{2L}$S270C	No	No	Yes
$\alpha_1\beta_3$L231Cγ_{2L}	Yes	No	Yes
$\alpha_1\beta_3\gamma_{2L}$L246C	No*	No	No
$\alpha_1\beta_3\gamma_{2L}$I242C	No	No	No

Figure 3. Summary of anesthetic protection at four cysteine residues. *Note: $\alpha_1\beta_3\gamma_{2L}$L246C showed weak anesthetic protection with pTFD-di-iPr-BnOH at 30μm but this effect was not dose-dependent and no protection was shown at 100μm.

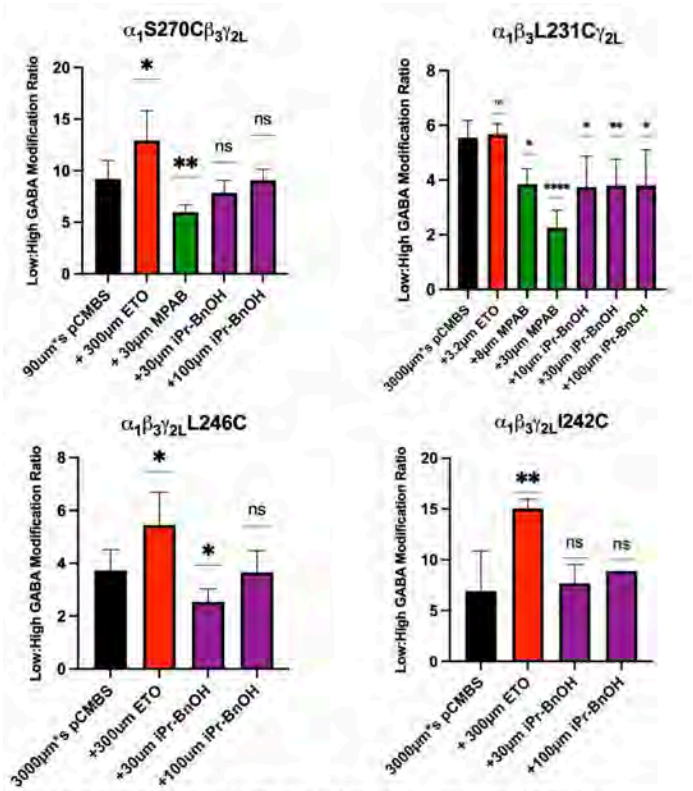

Figure 2. Substituted cysteine modification and anesthetic protection in α_1S270C$\beta_3\gamma_{2L}$, $\alpha_1\beta_3$L231Cγ_{2L}, $\alpha_1\beta_3\gamma_{2L}$L246C, and $\alpha_1\beta_3\gamma_{2L}$I242C mutants. The bar graph summarizes the pCMBS modification ratio in the presence of GABA alone and in the presence of ETO (red), R-mTFD-MPAB (green), or pTFD-di-iPr-BnOH (purple). P-values were calculated using student's t-test, with $p < 0.05$ as a significance threshold (****=p<0.0001, ***=p<0.001, **=p<0.01, *=p<0.05).

Anesthetic Pharmacology - 8 Direct inhibition of TLR7 by propofol sedation

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Introduction: Toll like receptors (TLRs) are major pattern recognition receptors that recognize a wide range of microbial components for host immunity. We have previously reported that a subset of anesthetics that we use in surgical arena and intensive care unit settings on daily basis directly bind and inhibit a group of TLRs. For example, volatile anesthetics directly inhibit the function of TLR2 and TLR4, both of which are critical TLRs to recognize gram positive and negative bacteria. In the middle of COVID-19 pandemic, a large number of patients has been required to have intensive care, including mechanical ventilation under sedation. As TLR7 variants including loss of function variants are associated with a significantly higher susceptibility to severe COVID-19 due to an impairment in type I and II interferon responses, the attenuation of TLR7 functions by drugs is likely less favorable. We tested the role of sedatives in TLR7 functions in this study.

Methods: TLR7 reporter assay Human TLR7 reporter cell line HEK-TLR9 cells containing NFŒ∫B-inducible secreted embryonic alkaline phosphate reporter were used to assess the effect of sedatives on TLR7 activation. They were stimulated with TLR7 agonist R837 (10 ¬µg/mL) for 24 hours. Sedatives (propofol, dexmedetomidine, ketamine, midazolam, fentanyl) were added to corresponding wells for 24 hours at a concentration of 1-100 ¬µM. The degree of NFkB activation was assessed by quantitating SEAP in the medium per the company protocol. Samples were subjected to a spectrophotometer analysis at 655 nm. Photolabeling and rigid docking m-azipropofol (AziPm) is a photoactivatable analogue of propofol. AziPm (final concentration 10 ¬µM) was equilibrated with TLR7 protein (1 mg/mL) in a reaction volume of 300 ¬µL for 10 min and then exposed to 350-nm light. The protein was separated on an SDS-polyacrylamide gel and stained with Commassie G-250. The protein gel band was excised for LC-MS/MS. After trypsin digestion, samples were injected into a nano-LC column with online electrospray into a LTQ linear ion trap. Raw data was acquired with Xcalibur, and Sequest was used to search b and y ions against the sequence of TLR7 for an AziPm mass modification on any amino acid of every peptide. To confirm the specificity of aziPm, competition was done by photolabeling TLR7 in the presence of propofol (200 ¬µM). Rigid docking was performed using adducted residues in a grid center by AutoDock. Glutaraldehyde crosslinking assay TLR7 protein concentration was adjusted to 25 ¬µM using buffer containing 10 mM HEPES-NaOH, pH 7.0, 150 mM NaCl. Propofol was added to the final concentration of 50 ¬µM followed by 10 ¬µM R837. The reactions were started by adding glutaraldehyde to a final concentration of 5 mM, incubated at room temperature for 25 min and quenched by adding Tris-HCl pH 7.5 to a final concentration of 100 mM. Crosslinked samples were analyzed by non-reducing SDS-PAGE. Lung slice culture After a mouse was euthanized, lung slice was obtained using slice cutter sterilely and cultured with R837 +/- propofol for 24 hours. Then, lung slice was subjected to RNA purification, cDNA creation and RT-PCR. Interferon genes were measured.

Results: Propofol attenuated TLR7 activation probed by reporter assays. Dexmedetomidine, fentanyl, midazolam and ketamine did not affect TLR7 functions. Photolabeling technique showed five different radducted residues. Rigid docking analysis showed that propofol bound to different pockets from R837. TLR7 is usually in a monomer, and R837 activation leads to a dimer formation. We found that propofol did not lessen dimer. Given TLR7 activation can be surrogated by TLR7-MyD88 interaction, we probed the interaction between TLR7 and MyD88 by immunoprecipitation. We found that MyD88 was less associated with TLR7 under propofol, indicating that propofol directly affected TLR7 and lessened TLR7 mediated signals. Of note, TLR7 antagonists can still keep a dimer per the previous report. Lastly we found that propofol attenuated the activation of interferon production in cultured lung slice.

Conclusion: We showed for the first time that propofol directly bound to TLR7 and inhibited the function of TLR7. Propofol is a popular choice of drugs as a sedative in intensive care settings. Although we do not know the clinical significance of propofol-mediated attenuation of TLR7 functions in the outcome of COVID-19 patients receiving propofol sedation, clinical studies are needed to evaluate this in vitro experimental findings.

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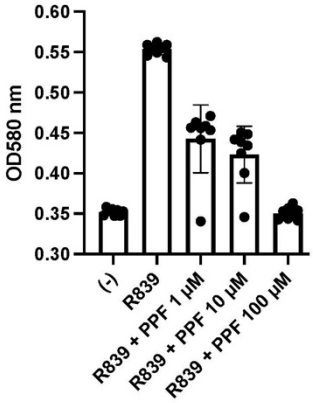


Fig. 1. Reporter assays of TLR7 activation
PPF; propofol

Fig. 2. Azi-propofol adducted residues (red)

Sequence coverage 88.2%
RSPWARWFPKTLPCDVTLDVSKNHVIVDCTDKHLTEIPGGIPTNTTNLTLTINHIPDISP
ASFHRLVHLVEIDFRCNCVPIRLGSKSNMCPRRLQIKPRSFSGLTYLKSLYLDGNQLLEI
PQGLPPSLQLLSLEANNIFSIRKEQLTELANIEILYLGQNCYYRNPCYVSYSIEKDAFLN
LTKLKVLSLKDNNVTTVPTVLPSTLTELYLYNNMIAEIQEDDFNNLNQLQILDLSGNCPR
CYNAPFPCTPCKNNSPLQIPVNAFDALTELKVLRLHSNSLQHVPPRWFKNINNLQELDLS
QNFLAKEIGDAKFLHFLPNLIQLDLSFNFELQVYRASMNLSQAFSSLKSLKILRIRGYVF
KELKSFQLSPLHNLQNLEVLDLGTNFIKIANLSMFKQFKRLKVIDLSVNKISPSGDSLVP
RGSSNARTSVESYEPQVLEQLYYFRYDKYARSCRFKNKEASFTSVQESCYKYGQTLDLSK
NSIFFIKSSDFQHLSFLKCLNLSGNLISQTLNGSEFQPLAELRYLDFSNNRLDLLHSTAF
EELRKLEVLDISSNSHYFQSEGITHMLNFTKNLKVLQKLMMNDNDISSSTSRTMESESLR
TLEFRGNHLDVLWRDGDNRYLQLFKNLLKLEELDISKNSLSFLPSGVFDGMPPNLKNLSL
AKNGLKSFIWEKLRYLKNLETLDLSHNQLTTVPERLSNCSRSLKNLILKNNQIRSLTKYF
LQDAFQLRYLDLSSNKIQMIQKTSFPENVLNNLKMLLLHHNRFLCTCDAVWFVWWVQHTE
VTIPYLATDVTCVGPGAHKGQSVISLDLYTCELDLTNEFLVPR

Fig. 3 Propofol and R837 binding sites

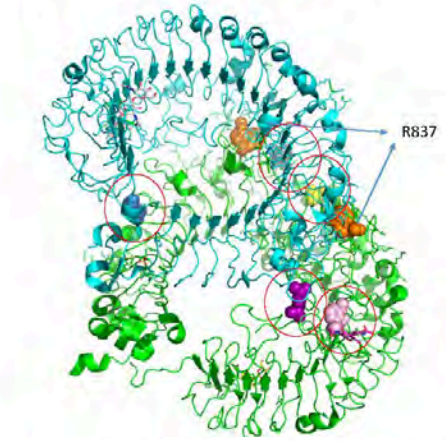


Fig. 4. Role of propofol in TLR7 dimerization (A) and the interaction between TLR7 and MyD88 (B)

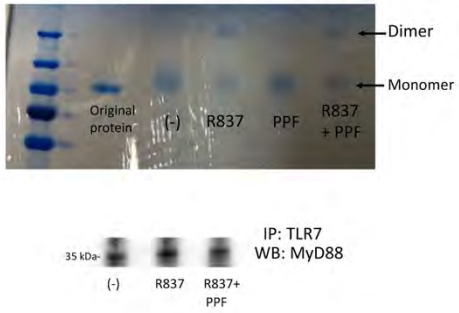
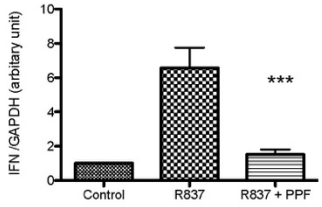


Fig. 5. The role of propofol on interferon production in lung



Blood Management

Blood Management - 1 Clinical Audit for introduction of Pre-filled Suxamethonium and Ephedrine syringes in Tallaght University Hospital.

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Introduction: Routine daily safety procedures in all theatre locations requires anaesthetists to have emergency intravenous medications immediately available for instances of severe reductions in blood pressure. However, the medications required for these emergencies are currently only available in glass ampoules which require a sterile drawing up procedure into disposable syringes for each case before they can be administered to the patient. The process of preparation area disinfection, opening syringes, drawing up needles, opening sterile ampoules, drawing up medications and labelling of syringes can last several minutes to perform. This constitutes an issue in anaesthetic emergencies that require immediate actions as well as in microbial contamination (1), drug administration errors (2) (3) and workplace efficiency (4). Pre-filled syringes (PFS) are now available and medications such as suxamethonium and ephedrine are supplied in individually wrapped pre-labelled and pre-filled syringes designed for immediate patient administration without the need for the prolonged drawing up process (4). We aimed to audit the cost-effectiveness of using PFS instead of glass ampoules and evaluate the benefit of these when considering waste disposal, environmental impact, infection risk and physician error.

Methods: An audit on all of the theatre events from January 2019 to January 2020 in Tallaght University Hospital was performed. We analysed data the amounts of suxamethonium and ephedrine drawn up, administered or disposed of without administration (waste) for all patients operated on for one calendar year. Accurate information was obtainable as all medication dispensed by pharmacy to theatre was provided by pharmacy and all administration of these drugs was recorded electronically in the anaesthesia information system GE Centricity.

Results: During the study period suxamethonium and ephedrine were made available for use in 8,519 patient theatre episodes. Taking current prices paid by the hospital for suxamethonium and ephedrine and comparing this to the indicative costs of pre-filled syringes, inclusion of PFS reflect an overall cost saving for the hospital of €7,831.00 per year. These calculations do not take into account peripheral costs such as needle stick injuries, waste, preparation of drugs, risk of microbial contamination, preparation errors and other financial burdens which are likely to be significantly reduced by the use of pre-filled syringes. Savings rise to €31,048.48 when considering these benefits of reduced medication error costs, reduced waste, reduced risk of microbial infection and patient safety.

Conclusion: There are great potential advantages to the use of PFS in theatre management of blood pressure as they have the potential to improve system safety and work efficiency from an economic, environmental, infection control, patient and staff safety viewpoint. Understanding this change at a hospital level from an organisational perspective, however, is key to implementing this and building safer systems in the future.

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Blood Management - 2 Survey Of Patient Blood Management Knowledge Among Anesthesiologists

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Introduction: Patient Blood Management (PBM) is an evidence-based, multidisciplinary approach to minimize blood loss and ensure hemostasis that improves outcomes and decreases cost. [1] Anesthesiologists order about half of hospital blood, [2] so they should have strong PBM knowledge. This study aims to assess PBM knowledge among US anesthesiology trainees and attendings.

Methods: Senior investigators designed a survey with 20 PBM content questions, and demographic questions. Content questions were checked by a PBM expert for clarity, accuracy, and one best answer. The assessment was distributed by e-mail to 15 U.S. anesthesiology residency programs and administered online. Using snowball recruitment, the Program Director recruited trainees at all levels, and attending anesthesiologists, via email. Completion of the survey was voluntary, and responses anonymous. The survey was also emailed to anesthesiology experts in PBM. The primary goals of the survey were to assess: 1) PBM knowledge of CA-3 residents (the survey was administered within 8 weeks of graduation); and 2) analyze differences in knowledge between training levels. A tertiary goal was to evaluate PBM knowledge among attending anesthesiologists. Experts were identified by leaders of PBM organizations. These experts were recruited to assess construct validity. Descriptive statistics and frequencies are reported. Analyses included tests for normality and parametric and non-parametric means comparison, with $p < 0.05$ considered significant.

Results: Five outliers (scores ≤ 20) were removed from the sample. Further work will consider if these comprise a specific subset of testees. The final dataset included 415 respondents. The distribution of cumulative scores both satisfied and violated assumptions of normality. Kolmogorov-Smirnov and Shapiro Wilk tests for normality indicated significance, $p < .001$. Visual inspection of data showed a typical histogram with no outliers, box plot with limited skewness, and linear Q-Q plot. Therefore, researchers pursued parametric and nonparametric tests to determine potential differences in means; similar results were derived from ANOVA with Tukey post-hoc comparisons and Kruskal-Wallis H-tests. Results for nonparametric (Kruskal-Wallis) are reported in this abstract. SPSS 28.0 was used for basic descriptives and non-parametric tests. The PBM exam will be further analyzed for construct validity to determine a potential cut score. For this abstract, training levels were compared to Experts. Mean (SD) scores increased with level of training, while Attendings' scores were lower than CA-4s and CA-3s (Fig. 1 and Table 1). Mean (SD) scores of CA-3s, 68 (11.76), and Attendings, 66.67 (14.28), were significantly lower than Experts, 79.07 (12.09), $p = 0.006$ and $p < 0.001$ respectively (Table 1). Mean (SD) of CA-4s, 72.50 (7.07) were not significantly different than Experts, $p = 0.383$ (Tables 1 and 2). Mean (SD) of CA-2s, 65.48 (12.34), were not significantly different than CA-3s, 68 (11.76), $p = 0.418$, but were significantly different than experts, $p < 0.001$ (Table 1 and 2). Differences in CA-3 mean scores between programs approximated significance, but the subsample of CA-3 residents constituted a limited n. Since CA-2 and CA-3 mean scores were not significantly different, we combined CA-2 and CA-3 residents within programs, and compared this subsample between programs and to Experts. The CA-2 and CA-3 group reached significance (Tables 3 and 4). Specifically, 10/15 programs' CA2-CA3s did not differ from Experts, while 5/15 (33.3%) programs' CA2-CA3s reached statistically-significant levels.

Conclusion: If construct validity and test reliability evidence can be confirmed, the data suggest 33.3% of programs stand to improve PBM education. Future validity and reliability considerations will include controlling for potential bias for specific sample demographics (ethnicity, gender, cognitive profile, languages spoken, country of birth), underlying latent constructs related to PBM, possible influences on test administration, and interpretations of final score.

References: 1. Robblee JA, Crosby E. Transfusion Medicine Reviews 1995;9(1):60-78 2. Leahy MF, Hofmann A, Towler S, et al. Transfusion 2017;57; 1347-1358

Figure 1. Box Plots of Mean Cumulative Score by Training Year

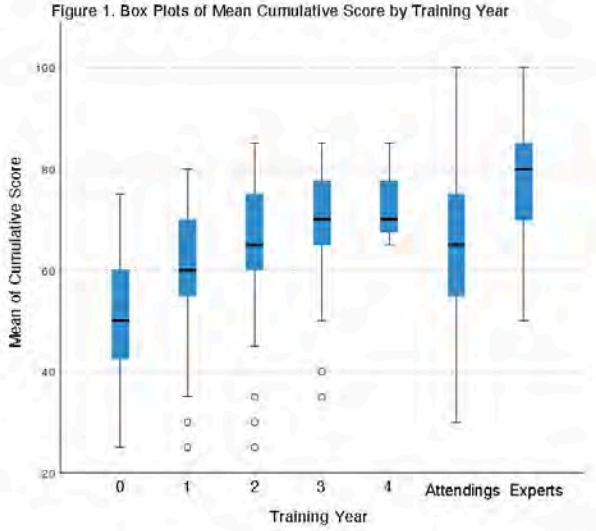

Table 1. Means of Cumulative Scores by Anesthesiology Training Year/Status

Training Year/Status	*n*	Mean	Standard Deviation	Range
CA-0	68	51.52	12.99	25-75
CA-1	45	60.11	14.00	25-80
CA-2	52	65.48	12.34	25-85
CA-3	40	68.00	11.76	35-85
CA-4	8	72.50	7.07	65-85
Attendings	171	66.67	14.28	25-100
Experts	27	79.07	12.09	50-100

n is lower within sub-populations (compared to total sample of 415) because four testees were removed because they did not indicate year of training.

Table 2. Kruskal-Wallis Pair-Wise Comparison of Means of Cumulative Score by Anesthesiology Training Year/Status

Sample 1	Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.
CA-0	CA-1	-68.051	22.696	-2.998	0.003
CA-0	CA-2	-114.281	21.757	-5.253	<.001
CA-0	CA-3	-134.405	23.534	-5.711	<.001
CA-0	CA-4	-174.305	44.145	-3.948	<.001
CA-0	Attendings	-115.512	16.932	-6.822	<.001
CA-0	Experts	-215.766	26.866	-8.031	<.001
CA-1	CA-2	-46.230	24.046	-1.923	0.055
CA-1	CA-3	-66.354	25.665	-2.585	0.010
CA-1	CA-4	-106.254	45.317	-2.345	0.019
CA-1	Attendings	-47.461	19.788	-2.399	0.016
CA-1	Experts	-147.715	28.751	-5.138	<.001
CA-2	Attendings	-1.231	18.704	-0.066	0.948
CA-2	CA-3	-20.124	24.839	-0.810	0.418
CA-2	CA-4	-60.024	44.854	-1.338	0.181
CA-2	Experts	-101.485	28.016	-3.622	<.001
Attendings	CA-3	18.893	20.744	0.911	0.362
Attendings	CA-4	58.793	42.723	1.376	0.169
Attendings	Experts	-100.253	24.458	-4.099	<.001
CA-3	CA-4	-39.900	45.742	-0.872	0.383
CA-3	Experts	-81.361	29.417	-2.766	0.006
CA-4	Experts	-41.461	47.542	-0.872	0.383

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same. Asymptotic significances (2-sided tests) are displayed. *Significant at $p < .05$

Table 3. Means of Cumulative Scores of CA-2 and CA-3 Residents by Program compared to Experts

Program	*n*	Mean	Standard Deviation	Range
Program 1	0	-	-	-
Program 2	1	-	-	-
Program 3	11	59.09	19.73	25-80
Program 4	5	69.00	13.87	55-85
Program 5	3	75.00	10.00	65-85
Program 6	15	65.33	11.72	35-85
Program 7	1	-	-	-
Program 8	1	-	-	-
Program 9	10	71.00	7.75	60-85
Program 10	8	65.00	7.56	55-75
Program 11	6	72.50	7.58	65-85
Program 12	18	66.39	9.04	45-80
Program 13	8	71.88	7.04	60-80
Program 14	1	-	-	-
Program 15	3	58.33	24.66	30-75
Experts	27	79.07	12.09	50-100

Means not reported for samples of $n = 1$.

Table 4. Kruskal-Wallis Pair-Wise Comparison of Means of Cumulative Score of CA-2 and CA-3 Samples by Program and Expert Status

Sample 1	Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.
Program 2 CA-2/CA-3	Experts	-70.741	34.799	-2.033	0.042
Program 10 CA-2/CA-3	Experts	-42.241	13.756	-3.071	0.002
Program 3 CA-2/CA-3	Experts	-41.377	12.223	-3.385	0.001
Program 6 CA-2/CA-3	Experts	-37.807	11.005	-3.436	0.001
Program 12 CA-2/CA-3	Experts	-36.352	10.398	-3.496	0.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. *Significant at $p < .05$

Cardiovascular Anesthesiology

Cardiovascular Anesthesiology - 1

Sulfide Quinone Oxidoreductase: A Novel Regulator of the Mitochondrial Permeability Transition Pore

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Introduction: The mitochondrial permeability transition pore (mPTP) is a voltage-gated, non-selective channel present on the inner mitochondrial membrane (1, 2). The mPTP plays a fundamental role in the pathophysiology of a variety of dis ease processes, from diabetes to ischemia-reperfusion injury (2,3). Regulation of mPTP opening is also essential for normal cellular development and homeostasis (4).While the precise proteinaceous identity of the mPTP remains unknown, certain key characteristics of the pore have been detailed. For instance, it is well accepted that the mPTP is voltage-dependent, such that depolarization of the inner mitochondrial membrane (IMM) leads to pore opening. There is a major gap in our knowledge, however, because it is unknown how mPTP voltage-gating is regulated. Prior work demonstrated that the redox status of vicinal thiol groups tunes the putative voltage sensor of the mPTP such that oxidation opens the pore at relatively higher ŒîΨ®s and thiol group reduction results in closed mPTP probability. In previous work, we identified a pathologically open mPTP within the forebrain of Fragile X syndrome (FXS) mice due to coenzyme Q (CoQ) deficiency and a relatively closed mPTP within the cardiomyocytes of FXS mice due to CoQ excess. In addition, CoQ replete FXS cardiomyocyte mitochondria appear to have altered voltage gating of their mPTP. Thus, it is clear that CoQ regulates the mPTP and may also contribute to its voltage gating. Interestingly, sulfide quinone oxidoreductase (SQOR), a mitochondrial enzyme that catalyzes the first step of catabolism of hydrogen sulfide (H2S), is a ubiquitously expressed IMM-associated protein, harbors redox-sensitive vicinal thiol groups, and binds CoQ as a requisite electron acceptor. These characteristics render SQOR an attractive candidate to be the voltage gate of the mPTP. We show that inhibition of SQOR in cardiomyocyte mitochondria with antimycin A altered the voltage sensing of the mPTP such that the probability of pore opening was significantly increased at relatively high ŒîΨ®s (when it should be closed).

Methods: The care of mice was in accordance with NIH and CUMC IACUC guidelines. We evaluated cardiac mitochondria harvested from male Fmr1 KO mice (FXS) along with FVB controls on P10 and 8wks. Oxygen consumption and mitochondrial membrane potential were measured simultaneously using polarography and a Tetraphenylphosphonium ion selective electrode. Complex II-dependent proton leak respiration was assessed using succinate, rotenone and oligomycin. In separate experiments, CsA was added at three membrane potential levels (low, intermediate and high) as the proton motive force declined in order to determine open or closed mPTP probability. Significance was assessed via chi-squared test with set $p < 0.05$. We determined the expression of the SQOR in cardiac mitochondria using Western blot. Finally, we evaluated the effect of the SQOR inhibitor, antimycin A, on voltage gating as described above except complex IV-dependent proton leak respiration was measured using N,N,N,N-tetramethyl-p-phenylenediamine /ascorbate, rotenone, malonate and oligomycin. Calcium loading capacity was determined using a calcium selective electrode.

Results: Mitochondria from both Fmr1 KOs and FVB controls demonstrated CsA sensitivity at low membrane potentials, suggesting open mPTP probability at or near 100%. Conversely, both groups showed CsA insensitivity at high membrane potential mitochondria, indicating closed mPTP probability. At median membrane potentials, we found open mPTP probability to be 89% in FVB controls samples compared to 45% in Fmr1 KOs, $p < 0.05$. Fmr1 KO cardiac mitochondria had a 20% increase in SQOR expression. Inhibition of SQOR with antimycin A led to opening of the mPTP at higher membrane potential where it would normally be closed.

Conclusion: We identified differences in voltage gating of the mPTP between Fmr1 KO and FVB controls and demonstrate differences in expression of the SQOR protein. We show that inhibition of SQOR disrupts normal voltage gating of the mPTP. This work identifies SQOR as novel regulator of mPTP voltage gating of the mPTP

References: 1. J. Bioenerg. Biomembr. 24:111-7, 1992 2. Apoptosis 12:815-33, 2007 3. Cell Cycle 9:3442-8, 2010 4. Dev. Biol. 426:1-7, 2017 5. FEBS J. 273:2077-99, 2006

Cardiovascular Anesthesiology - 2

Intravenous Waveform Analysis Correlates with Volume Status in Prone Positioning and Sternotomy in a Rat Model

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Introduction: Dynamic markers such as pulse pressure variation (PPV) are pivotal tools in volume management in the perioperative period. However, PPV validity does not extend to a large portion of operative cases including those with prone positioning and open chest.1, 2 Intravenous waveform analysis (IVA) is a novel marker of volume status that is thought to assess the relationship of pressure and volume in the right heart and venous system. It does this by isolating the amplitude of the frequency corresponding to heart rate, termed F1, within the venous waveform. As IVA does not assess changes in preload based on intrathoracic pressure variation it may not be subject to the same physiologic limitations. We hypothesized that IVA-derived F1 would fall in hemorrhage and rise in resuscitation corresponding to circulating volume status in subjects with either sternotomy or in prone positioning.

Methods: 12 male Sprague Dawley rats were anesthetized with isoflurane, intubated and mechanically ventilated. Estimated blood volume (EBV) was calculated by weight. Subjects were cannulated in the left femoral vein for blood withdrawal, left femoral artery for transduction of mean arterial pressure (MAP) and calculation of PPV, and the right femoral vein for venous waveform recording. Fast Fourier transform was performed on the venous waveform in MATLAB and amplitude of F1 measured. Heart rate (HR) was determined by electrocardiogram. 6 subjects were randomly assigned to each group, sternotomy, or prone positioning. Sternotomy was performed with mayo scissors, and ribs separated with an Alm retractor. Prone positioning was performed onto soft packing foam. Heparinization was then performed. Experimental protocol entailed withdraw of 5% of the EBV over 1 min repeated 4 minutes later, totaling 10% blood loss, and then return of 5% of the EBV over 1 min, repeated 4 minutes later to achieve euvolemia. Subjects were then over-resuscitated with crystalloid in 2 boluses with volumes equivalent to 5% of EBV. Repeated measures ANOVA with pairwise comparison was performed, and Sidak-adjusted p value significance was set at <0.05.

Results: In prone subjects F1 fell significantly in hemorrhage from baseline to 95% EBV, p=0.01, and did rise significantly in resuscitation from 95% EBV to 110% EBV, p=0.02 and from 100% EBV to 110% EBV p=0.04. MAP fell significantly in hemorrhage to 90% EBV, p=0.001 and rose in resuscitation to euvolemia, p=0.01. In subjects with sternotomy, F1 did not fall in hemorrhage, but once again rose during resuscitation from 95% EBV to 110% EBV, p=0.03. MAP fell in hemorrhage to 90% EBV, p=0.001, and rose in resuscitation to euvolemia, p=0.01. PPV did not change significantly at any timepoint in either group.

Conclusion: IVA outperformed PPV in both experimental settings. This proof-of-concept study demonstrates IVA sensitivity to hemorrhage and resuscitation under physiologic conditions where dynamic markers fail. Further evaluation into the widespread utility of IVA is warranted.

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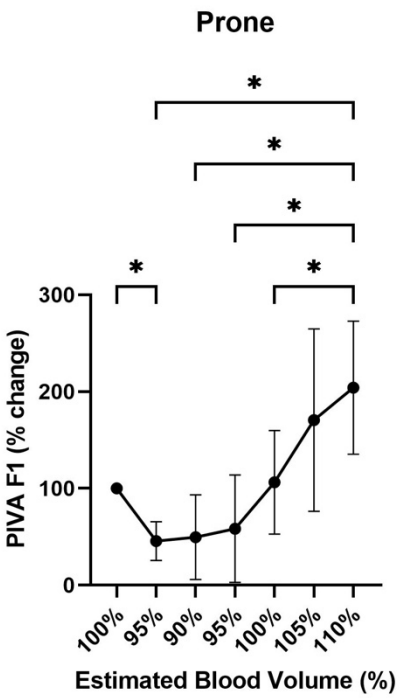
Prone
PIVA F1 (% change)
300
200
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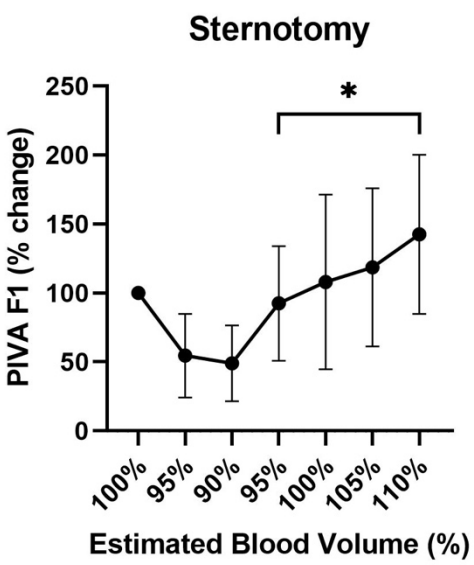
0
100%
95%
90%
95%
100%
105%
110%
Estimated Blood Volume (%)


Sternotomy
PIVA F1 (% change)
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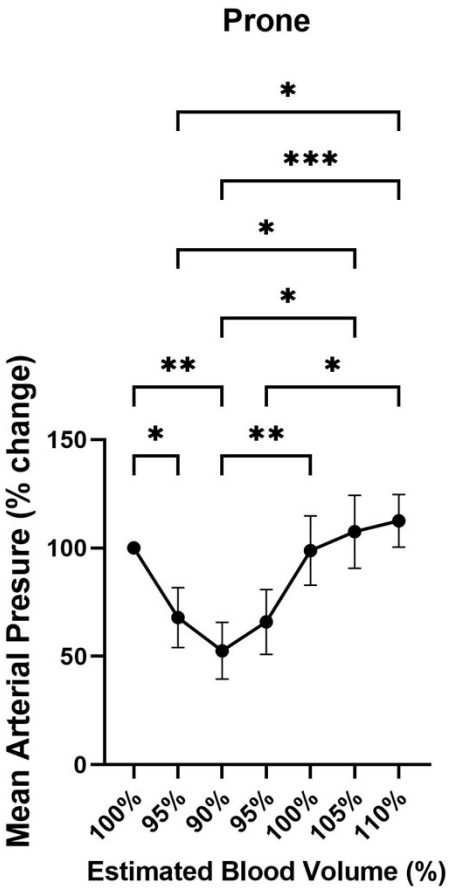
95%
100%
105%
110%
Estimated Blood Volume (%)


Prone
Mean Arterial Presure (% change)
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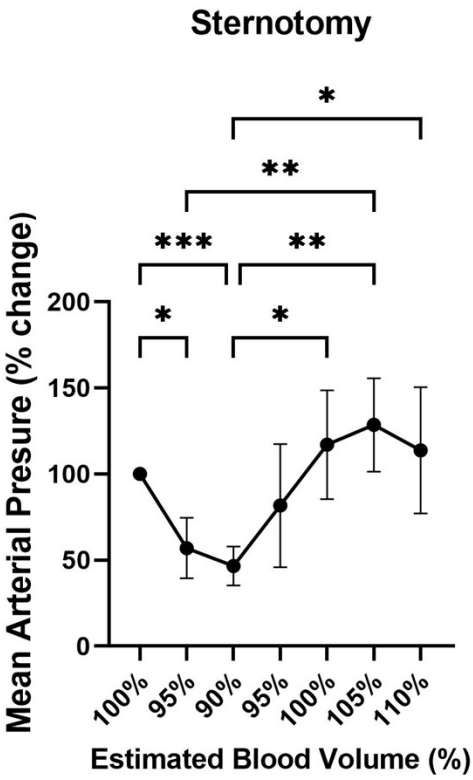
Sternotomy
Mean Arterial Presure (% change)
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95%
100%
105%
110%
Estimated Blood Volume (%)

Cardiovascular Anesthesiology - 3

Neural biomarkers do not predict postoperative delirium in cardiac surgery patients with cardiopulmonary bypass

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Introduction: Over 300,000 patients undergo cardiac surgery with cardiopulmonary bypass (CPB) annually in the United States.1 Delirium is commonly observed following CPB[2-4] and is associated with longer hospital stays, higher healthcare costs,[5,6] long-term cognitive impairment,[7,8] and increased mortality.[9,10] Phenotypical delirium following CPB may be due to oxidative reperfusion injury[11] and neuroinflammation.[12] Prior studies have demonstrated elevated neuronal biomarker levels, possibly reflecting these injury patterns, following CPB.[13] If these biomarkers are elevated in patients who develop postoperative delirium, then we would better understand the mechanism. Based on these findings, we hypothesized that elevated levels of neuronal biomarkers following CPB will be associated with delirium. To explore this association, we measured four biomarkers of neuronal injury at two distinct time points and conducted postoperative delirium assessments in adults undergoing cardiac surgery with CPB.

Methods: We conducted a nested case-control study of 46 participants originally enrolled in a single-center randomized controlled trial investigating the effects of hyperoxia versus normoxia on delirium and neurocognitive outcomes among cardiac surgery patients.[14] Blood samples were collected pre- and post-CPB; the serum concentrations of four biomarkers were measured using a custom R&D Human Premixed Multi-Analyte Panel. Two biomarkers (S100B and gamma enolase, ENO2, also known as neuron-specific enolase, NSE) were selected based on their validity in predicting neurocognitive outcomes supported by previous studies.[15,16] Two novel biomarkers that have not yet been studied in the context of post-operative delirium (ubiquitin carboxyl-terminal hydrolase isozyme L1, UCHL1 and chitinase-3-like protein 1, CH3L1) were also selected. Delirium was assessed using the Confusion Assessment Method (CAM-S). Pre-operative and post-operative biomarker levels were compared using paired student t-test. A series of stratified analyses was used to compare pre-operative and post-operative biomarker levels according to delirium/non-delirium status, hyperoxia/normoxia treatment, sex, CPB duration, and BMI. Finally, multiple regression analysis was used to model the relationship between delirium/non-delirium status and biomarker levels, hyperoxia/normoxia treatment, duration of CPB, or the interaction between these predictors.

Results: Twelve patients (26%) were delirium cases. Of the four biomarkers, UCHL1 was undetectable in the blood samples, and ENO2 and CHI3L1 were not elevated relative to baseline (Figure 1). Postoperative S100B levels were increased from baseline (8.04 to 10.14 pg/mL, $P<0.001$). Stratified analyses show that this effect was present regardless of delirium/non-delirium status ($P<0.001$), intraoperative oxygen treatment ($P<0.001$), BMI ($P<0.001$), or sex ($P=0.001$). Multiple regression analysis showed that neither postoperative change in S100B levels, duration of CPB, hyperoxia treatment, nor the interactions between these variables contributed significantly to the occurrence of delirium in this cohort.

Conclusion: In our study of four biomarkers of neuronal injury, only S100B was elevated from baseline following CPB. Elevated levels of S100B following cardiopulmonary bypass were not associated with post-operative delirium. Given the large burden of neurological injury following cardiac surgery, future studies are needed to examine the mechanism responsible for neurologic injury post anesthesia and cardiac surgery.

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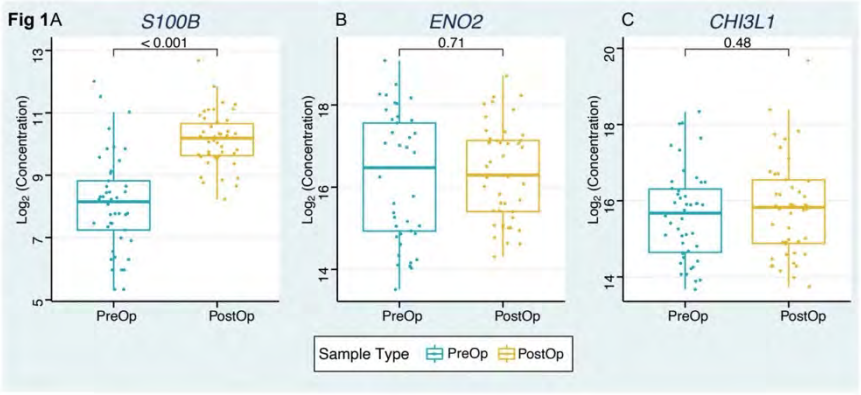

Cardiovascular Anesthesiology - 4

Interdependent Regulation of Vascular Endothelial Adenosinergic Signaling by Estrogen and Hypoxia: Implications for Microvascular Injury and Diastolic Heart Failure

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Introduction: Estrogen has multiple beneficial roles in the vasculature and protects premenopausal women from cardiovascular disease[1]. These salutary effects on the vasculature appear especially pronounced under experimental hypoxic conditions, which may be linked to increased generation of extracellular adenosine by CD39 and CD73[2]. The impacts of estrogen on the expression of these ectonucleotidases and modulation of adenosinergic pathways are largely unknown. We have therefore dissected out elements of the estrogen-hypoxia-adenosinergic pathways in vitro to define those mechanisms necessary for vascular protection in vivo.

Methods: Human umbilical venous endothelial cells (HUVECs) were exposed to hypoxia (1% oxygen for 24 hours) or Cobalt Chloride (100uM for 24 hours). HUVECs were then treated with estradiol (E2) and/or YC-1 compound (HIF-1α inhibitor). Expression levels of CD39, CD73, adenosine transporters (ENT1), HIF-1α and VEGFA and interactions were measured using western blotting, qRT-PCR, immunofluorescence studies and immunoprecipitation.

Results: Immunofluorescent expression of CD39 and HIF-1α was markedly increased under hypoxia following on E2 exposure. VEGFA expression increased likewise under hypoxia and/or E2 exposure, as measured by qRT-PCR. Increases in CD39, HIF-1α and VEGFA expression levels under hypoxic conditions and/or E2 exposure were attenuated by inhibition of HIF-1α. In contrast, ENT1 expression was down-regulated by E2 exposure and impacted by inhibition of HIF-1α. No differences were noted in expression of adenosine receptors (ADORA 2A or 2B). However, phosphorylation of ERK, a downstream adenosine signaling target, increased with E2 exposure, and was boosted by inhibition of HIF-1α. Estrogen receptor alpha (ERα) increased in hypoxic HUVECs, but no significant changes were observed with estrogen receptor beta (ERβ). ERα protein expression decreased with stimulation of aryl-hydrocarbon receptor (AhR), a transcription factor known to boost CD39 transcription, while AhR expression decreased following E2 exposure. No protein-protein interaction was observed between HIF-1α and ERα or between CD39 and either ERα or AhR. ERα interacted with AhR under hypoxic conditions, which increased in the presence of the proteosome inhibitor, MG-132.

Conclusion: We show that E2 treatment and/or hypoxia increase CD39 expression and decrease the expression of ENT1. These hormonal changes induced by E2 and/or hypoxia substantially increase extracellular adenosine availability and provide vascular protection. Altered regulation of ERα by AhR in hypoxia, likely through ubiquitination, infers additional regulatory mechanisms for E2 in mediating adenosinergic signaling. Further characterization of these regulatory pathways may provide effective, well tolerated therapeutic options to ameliorate post-menopausal cardiovascular disease, as noted in the Yentl syndrome.

References: 1. Circulation Research vol. 109 687-696 (2011). 2. Purinergic Signalling vol 2. 409 (2006).

Cardiovascular Anesthesiology - 5

Hypothermic circulatory arrest (HCA) does not impact cerebral autoregulation

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[1]University of Alabama at Birmingham, Birmingham, AL

Introduction: Hypothermic circulatory arrest (HCA) is associated with post-cardiac surgical neurologic impairment including, cognitive decline. Impaired cerebral pressure-flow autoregulation may contribute to neurologic injury through cerebral hypo-or hyper-perfusion. This study compares the cerebral autoregulation curves between patients who underwent aortic surgery with (HCA) and anterograde cerebral perfusion (ACP) and those who did not. The methodology for this single-center, retrospective observational study is novel in its use of a high-resolution data collection and device integration platform. We hypothesized that HCA alters cerebral autoregulation (CA) after separation from cardiopulmonary bypass. Specifically, we hypothesized that the lower limit of autoregulation (LLA), optimal arterial blood pressure (ABPopt), differs after HCA compared to pre-procedural baseline CA and with patients who underwent off-pump cardiac surgery.

Methods: Under IRB approval (IRB# 300005436), we analyzed high-resolution real-time waveform data that included systemic ABP and cerebral near-infrared spectroscopy (NIRS) via the Sickbay™ platform and a custom software package. Patients who underwent off-pump coronary artery bypass graft (OPCABG) surgery and those who underwent thoracic aortic arch repairs with HCA were included. LLA, ABPopt, and percent time below LLA were compared before and after HCA with ACP within the aortic repair group using a Welch's t-test. The same parameters were compared between the aortic group after separation from CPB and the OPCABG groups using the same statistical test.

Results: ABP and NIRS data were available for 38 patients undergoing arch repair with circulatory arrest and 28 undergoing OPCABG. Mean LLA before circulatory arrest for those undergoing arch repair was 65 ± 11 mmHg (standard deviation). After circulatory arrest, the mean LLA was 63 ± 6 mmHg. Likewise, the mean ABPopt before circulatory arrest was 77 ± 13 mmHg and 79 ± 8 mmHg after. None of these differences were statistically significant ($p>0.05$). There were no significant differences in those values post-arrest compared to patients who did not undergo arrest.

Conclusion: Cerebral autoregulation, as determined with noninvasive technology, was not impaired by hypothermic circulatory arrest. This result may consequently inform and refute underlying assumptions of the brain's vascular response to and recovery from HCA. Indeed, ACP might preserve autoregulation. Additionally, and importantly, we note that the average optimal mean arterial blood pressures obtained in this study are higher than the widely accepted population-based minimally recommended pressure of 65 mmHg.

Cardiovascular Anesthesiology - 6 Spinal Cord Neuromodulation alters Synaptic Connectivity and Neuroinflammation during Myocardial Ischemia in a Porcine Model

Kimberly Howard-Quijano[1], Sean Farris[1], Yuki Kuwabara[1], Tomoki Yamaguchi[1], Siamak Salavatian[1], Aman Mahajan[1]

[1]University of Pittsburgh, Pittsburgh, PA

Introduction: Sympathetic hyperactivity leads to cardiac arrhythmias during myocardial ischemia. Spinal cord stimulation (SCS) modulates efferent sympathetic output at the spinal level to attenuate ischemia triggered ventricular arrhythmias. The molecular mechanisms behind the therapeutic effect of SCS during cardiac ischemia have not been fully defined. Using single nuclei RNA sequencing, we aimed to identify molecular alterations in individual neuronal and glial cell populations associated with SCS in a porcine model of cardiac ischemia-reperfusion (IR).

Methods: RNA sequencing was performed on nuclei isolated from 2nd thoracic level (T2) spinal cord tissue in Yorkshire pigs (n=14) randomized to control (CON n=5), ischemia-reperfusion (n=4), or IR+SCS (n=5). Single nuclei suspensions were processed through 10x Genomic Chromium System and then sequenced on an Illumina NovaSeq with average of 50,000 reads per cell (Fig 1). Data were filtered, normalized, and cell clustering was performed using Partek flow software. Cell type identification was performed using top 20 genes for cluster identification, and genes with a threshold of absolute fold change >2 and a false discovery rate (FDR) <0.05 were considered as differentially expressed. Gene ontology and pathway enrichment analysis were further performed using ToppGene and Ingenuity Pathway Analysis.

Results: 5 cell types were identified: Neurons, Microglia, Astrocytes, Oligodendrocytes, and Meninges/Schwann. No difference in cell type number by experimental group or sex was found. In neurons, differential gene expression was found between all experimental conditions (Fig 2). With cardiac IR, neurotransmitter transport and trans-synaptic signaling biological processes were enriched. With IR+SCS, there was upregulation in genes and pathways for neurogenesis, neurotransmitter signaling and a down regulation in oxidoreductase and electron chain transport biological processes (Fig 3). Comparison analysis between differentially expressed neuronal genes in IR+SCS vs. IR and IR vs. CON demonstrated upregulation in synaptogenesis and transcriptional regulator restrictive element-1 silencing factor (REST) during SCS. Transcriptomic profiling in microglia showed enrichment in interleukin 15 (IL-15) production, and cell adhesion, with NYAP2 (Neuronal Tyrosine-Phosphorylated Phosphoinositide-3-Kinase Adaptor 2) being the most highly upregulated gene, and inhibition of Nitric Oxide and NFkB complex as upstream regulators (Fig 4). In astrocytes, cell adhesion and plasma membrane translocation were enriched and the anti-inflammatory cytokine gene CD19 was the most highly up regulated gene (Fig 5).

Conclusion: The data from this study for the first time, provides insights into molecular changes in the spinal cord through which SCS may reduce the arrhythmic effects of cardiac ischemia - by modulating neuronal cell identity and synaptic connectivity, neuronal-glial interactions, and glial regulated reductions in neuroinflammation.

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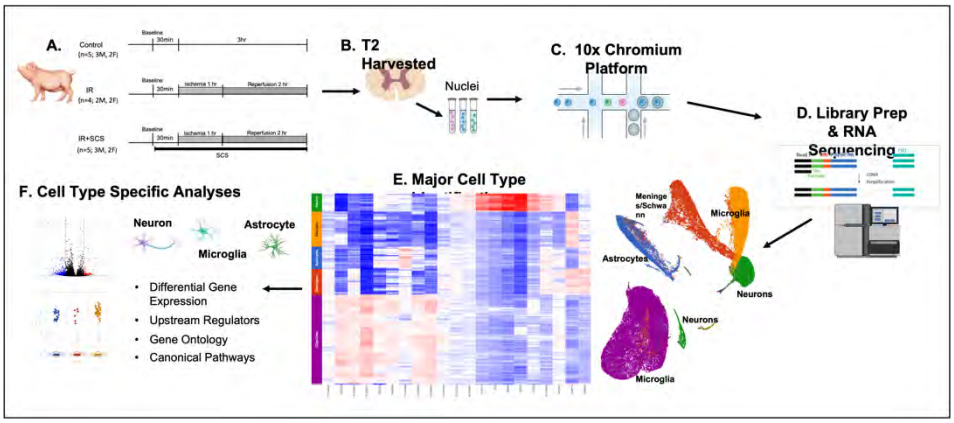

Figure 1. Study Design - RNA sequencing was performed on nuclei isolated from 2nd thoracic level (T2) spinal cord tissue in Yorkshire pigs randomized to Control (CON), Ischemia-reperfusion (IR) and IR with Spinal Cord Stimulation (IR+SCS). Single nuclei suspensions were processed through 10x Genomic Chromium System, sequenced on an Illumina NovaSeq and cell clustering was completed. Gene ontology and pathway enrichment analysis were further performed for each cell type.

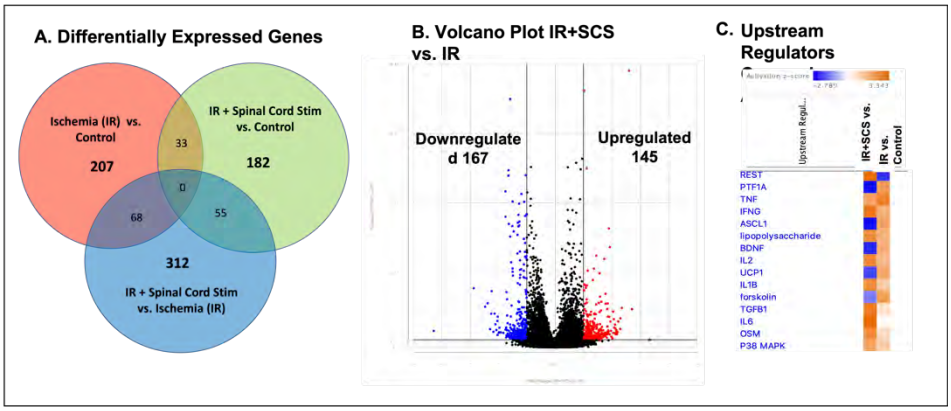

Figure 2. Neuronal cell results - **A.** Differentially expressed genes in neuronal cells as compared between experimental groups. **B.** Volcano plot demonstrating fold change and p-value specifically for differentially expressed genes between IR+SCS and IR alone. **C.** Comparison analysis of upstream regulators in IR+SCS vs. IR and IR vs. Control gene sets. Heat map demonstrates z-score change with blue representing decreased activity and orange representing increased predicted activity

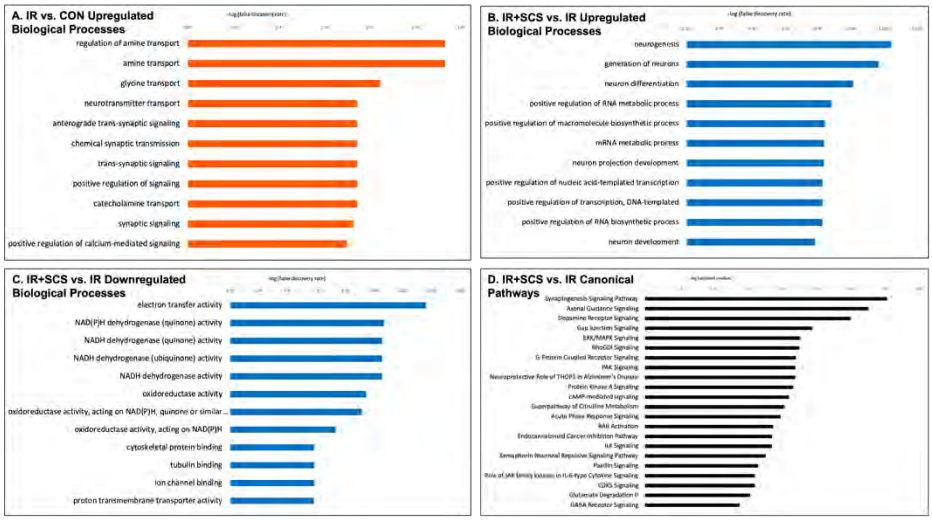

Figure 3. Neuronal Cell Gene ontology (GO) enrichment for differentially expressed genes in IR and IR+SCS – GO analysis on genes meeting differential expression criteria of FDR > 0.05 using Anova analysis. **A.** Biological Processes from upregulated genes in ischemia-reperfusion (IR) vs Control. **B.** Biological processes from upregulated genes in IR+ spinal cord stim (SCS) vs. IR. **C.** Biological Processes from downregulated genes in IR+SCS vs. IR. **D.** Enriched canonical pathways from differentially expressed genes in IR+SCS vs. IR.

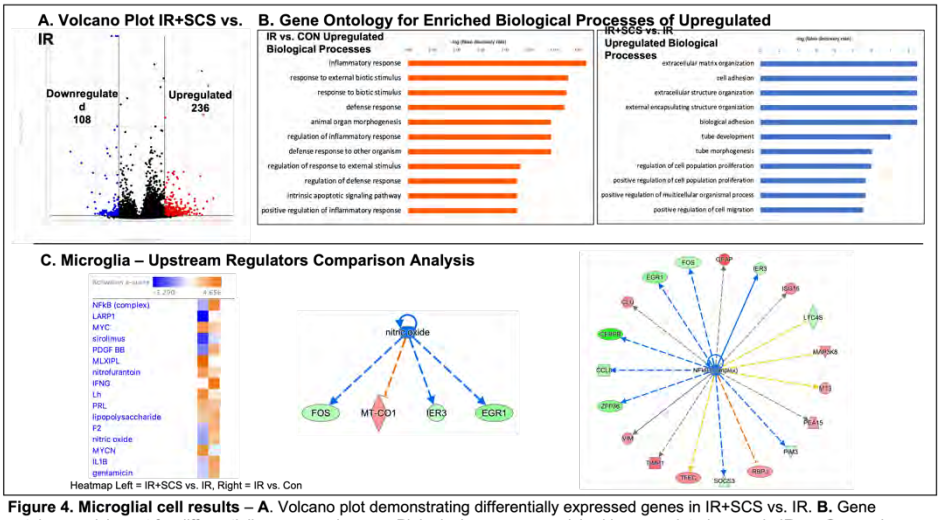

Figure 4. Microglial cell results – **A**. Volcano plot demonstrating differentially expressed genes in IR+SCS vs. IR. **B.** Gene ontology enrichment for differentially expressed genes. Biological processes enriched in upregulated genes in IR vs. Con and IR+SCS vs. IR. **C.** Comparison analysis of upstream regulators for differentially expressed genes IR+SCS vs. IR and IR vs Con. Heatmap demonstrates z-score with blue representing decreased predicted activity and orange representing increased activity.

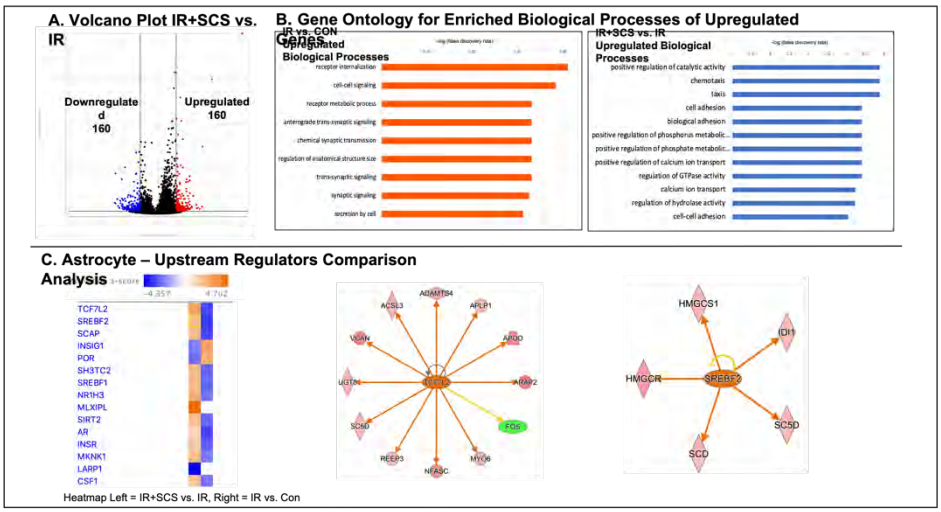

Figure 5. Astrocyte cell results – **A**. Volcano plot demonstrating differentially expressed genes in IR+SCS vs. IR. **B.** Gene ontology enrichment for differentially expressed genes. Biological processes enriched in upregulated genes in IR vs. Con and IR+SCS vs. IR. **C.** Comparison analysis of upstream regulators for differentially expressed genes IR+SCS vs. IR and IR vs Con. Heatmap demonstrates z-score with blue representing decreased predicted activity and orange representing increased activity.

Cardiovascular Anesthesiology - 7

Quantitative effect of positive end expiratory pressure on central venous pressure in closed and open thorax

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Introduction: Central venous pressure (CVP) is most commonly used monitoring tool to assess the volume status of patients during the perioperative period and intensive care units. The role of positive end expiratory pressure (PEEP) in keeping the lung recruited is not only employed for lung pathologies and left heart failure but also for ventilating normal lungs during intraoperative period as a part of protective ventilation strategy in aiming to prevent collapsing of alveoli. Mechanical ventilation and PEEP are known to influence the measurement of CVP through complex heart-lung interactions. Therefore, the exact volume status of the patient based on central venous pressure may be difficult to determine in patient with positive end expiratory pressure.This magnitude of change in CVP is expected to differ in patients with cardiac disease. Therefore, this study aimed to understand the physiological basis of rise in CVP after PEEP. To unravel the physiological mechanism, we compared the magnitude of change in CVP after PEEP application in closed and open thorax in patients with cardiac disease undergoing cardiac surgeries. Open thorax being referred to post median sternotomy incision over chest and opening of thorax during intraoperative period.

Methods: This prospective, quasi-experimental study was conducted in tertiary care centre in patients undergoing cardiac surgery. The study began after central trial registration, and ethical approval by the Institute Ethics Committee and the study followed Helsinki guidelines. After induction of anaesthesia and endotracheal intubation, hemodynamic parameters were obtained at baseline (PEEP at 0 cm of H20) and after application of two level of PEEP (5 cm and 10 cm). Three consecutive reading of hemodynamic parameters were obtained at 1, 2 and 3 minutes after application of PEEP in closed chest. Similar levels of PEEP were applied in open thorax after application of sternotomy retractor. The change in CVP after PEEP application was analysed in the closed and open thorax. Additionally, patients were stratified a priori and change in CVP was analysed in lower CVP group (<10 mm Hg) and higher CVP group (≥10 mm Hg), no TR group and TR group and low PCWP group (<15 mm Hg) and high PCWP group (≥15 mm Hg) in closed and open thorax. Sample size was estimated a priori based as per a previous study by N Kim et al. Power calculation for a 2 cm of H2O difference in CVP level, with an alpha level of 0.05 and power of 90%, yielded a sample size of 48 patients. Considering a drop out-rate of 25%, total sample size was calculated to be 62. Normality of distribution of variables was assessed using Shapiro-Wilk test. Paired t test, Independent t test, Repeated measure ANOVA were used. P-value <0.05 was considered statistically significant.

Results: Inclusion Criteria: Adult patients between age of 18-60 years, ASA grade I-III, Scheduled for elective cardiac surgery Exclusion criteria: Patient's refusal, Arrhythmia and hemodynamic instability. 62 patients were enrolled for PEEP intervention and all patients were eligible for final analysis. The mean age of participants was 46.2 ± 12.7yrs and mean body mass index (BMI) was 22.7 ± 3.2 kg/m2. Valvular heart disease and coronary artery disease were the most common cardiac disease. The mean difference (MD) in CVP at 5 cm H2O and 10 cm H2O of PEEP was 0.98±0.6 (95% confidence interval (CI), 0.83-1.13; p=0.001) and 2.33±1.13 (95% CI, 2.04-2.62, P=0.001) in closed thorax while the mean difference in open thorax at 5 cm H2O and 10 cm H2O 0.42±0.7 (95% CI, 0.6-0.89, P=0.001) and 1.02±0.77 (95%CI, 0.82-1.22, P=0.001), respectively. The increase in CVP was higher among patients who had a lower CVP group (2.64 ± 0.9 mm Hg vs 1.45± 1.17 mm Hg; p=0.001), without TR (2.64 ± 0.97 mm Hg vs 2.14 ± 1.2 mm Hg, p=0.09) and lower PCWP group (2.4 ± 0.9 mm Hg vs 2.3 ± 1.4 mm Hg, p=0.67) at 10 cm H2O PEEP in closed thorax. In the open thorax, magnitude of change in CVP was lower in all three groups.

Conclusion: Among cardiac patients, the loss in intrathoracic pressure does not abolish the effect of PEEP on rise in CVP completely. A 5 and 10 cm H20 of PEEP produced 0.98 and 2.33mm Hg rise in CVP respectively. There is overestimation of CVP values with application of PEEP in mechanically ventilated patients. Higher PEEP up to 10 cm H2O can be applied in cardiac patient if required as part of protective ventilation strategy without any compromise on hemodynamic during intraoperative period.

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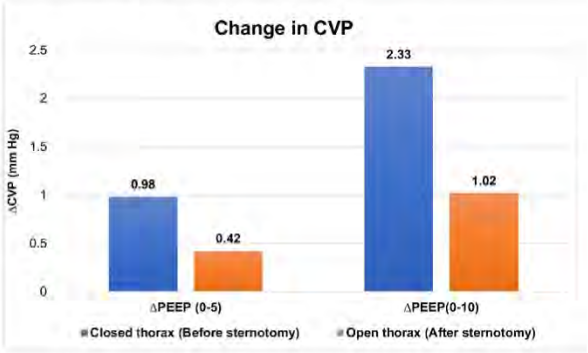
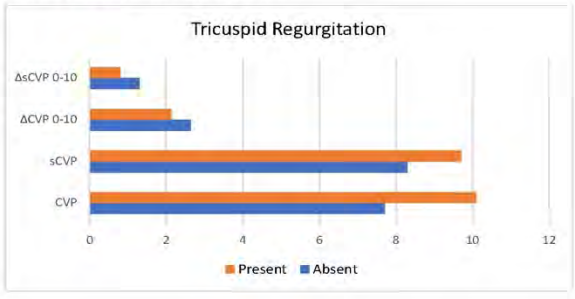
2. Doppler Tissue Imaging: A Noninvasive Technique for Evaluation of Left Ventricular Relaxation and Estimation of Filling Pressures. J Am Coll Cardiol 1997; 30(6):1527-1533. 3. Comparison of positive end-expiratory pressure-induced increase in central venous pressure and passive leg raising to predict fluid responsiveness in patients with atrial fibrillation. Br J Anaesth 2016; 116(3):350-356. 4. Effect of Positive End-Expiratory Pressure on Central Venous Pressure in Patients under Mechanical Ventilation. Emergency 2017; 5(1): e1 5. The influence of positive end-expiratory pressure on central venous pressure in patients with severe craniocerebral injury]. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue Chin Crit Care Med Zhongguo Weizhongbing Jijiuyixue 2012; 24(5):283-285.

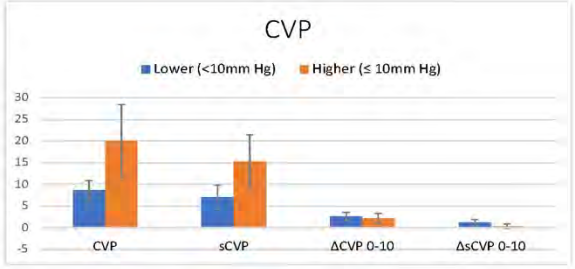
Figure 1 : Relation of Change in central venous pressure (CVP) with application of positive end expiratory pressure (PEEP) from baseline 0 cm H_2O (ZEEP) in closed and open thorax

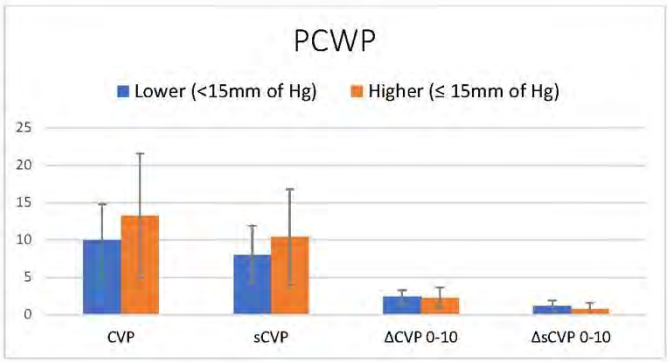


(ΔCVP is the change in central venous pressure measured in mm of Hg and ΔPEEP (0-5) and ΔPEEP (0-10) is the application of PEEP from baseline 0 cm H_2O to 5cm H_2O and 10 cm H_2O)

Effect of PEEP on various subset groups







Temporal sequence of changes in mean arterial pressure, heart rate with application of PEEP at different time points

Variables/Time points		Baseline (ZEEP)	1 min	MD	P-value	2 min	MD	P-value	3 min	MD	P-value
Closed Thorax (5 cm H_20 PEEP)	HR	76.3±21.02	75±21.33	1.3	0.06	75.5±21.63	0.75	0.9	75.08±21.6	1.2	0.06
	MAP	75.40±10.97	73.92±12.53	1.48	0.54	74.47± 12.33	0.93	1	74.53±12.28	0.87	1
Closed Thorax (10 cm H_20 PEEP)	HR	74.76±21.27	75.87±21.04	-1.1	1	76.1±20.97	-1.33	0.91	75.63±21.07	-0.87	1
	MAP	73.24±12.58	75.19±14.11	-1.95	0.43	73.9±13.78	-0.66	1	72.56±13.05	-0.67	1
Open Thorax (5 cm H_20 PEEP)	HR	80.39±20.86	80.45±20.45	-0.065	1	80.79±20.79	-0.403	1	80.44±20.93	-0.048	1
	MAP	81.52±11.69	80.48±12.33	1.03	0.88	80.11±12.34	1.40	0.36	79.19±12.58	2.32	0.055
Open Thorax (10 cm H_20 PEEP)	HR	81.44±21.04	80.45±20.28	0.98	1	80.08±20.34	1.35	0.53	80.26±20.65	1.17	0.81
	MAP	79.11±11.97	76.92±11.63	2.19	0.22	75.29±11.94	3.82	0.01	74.4±12.62	4.71	0.01

Cardiovascular Anesthesiology - 8

[TIMP-2]*[IGFBP7] as a marker of renal injury after multibranched thoracoabdominal endovascular aortic repair

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Introduction: Postoperative acute kidney injury (AKI) is a common and morbid complication after vascular surgery that may cause significant long-term decline in renal function. Up to 28% of patients sustain AKI after branched thoracoabdominal or paravisceral endovascular aortic repair (TEVAR). TIMP-2 and IGFBP7 are G1 cell cycle arrest proteins that have been utilized as urinary biomarkers for detection of renal stress as early as 6-12 h after surgery, prior to elevation in serum creatinine. Although urinary TIMP-2 and IGFBP7 have demonstrated modest success in early prediction of AKI after cardiac surgery, their utility after aortic surgery is less clear. We are analyzing urinary [TIMP-2]*[IGFBP7] in an existing cohort of patients who underwent branched-graft TEVAR. We hypothesize that urinary [TIMP-2]*[IGFBP7] will improve prediction of early postoperative AKI when combined with clinical predictors.

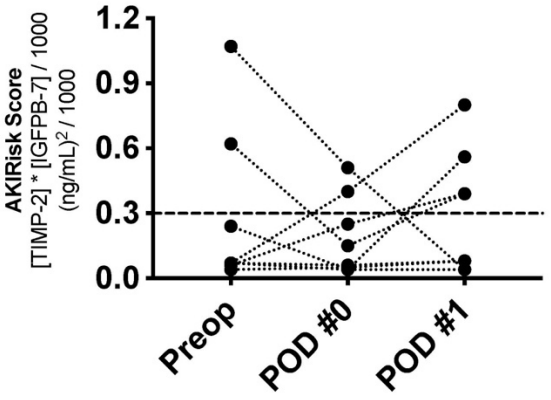
Methods: The study was approved by the local institutional review board and registered with ClinicalTrials.gov (NCT00483249). After informed consent, urine was collected from patients undergoing multibranched TEVAR at three time points: start of surgery, end of surgery, and postoperative day (POD) 1. Clinical data were recorded as part of an ongoing registry. For the pilot biomarker study, 8 patients (5 without AKI and 3 with AKI stage 1 or greater by Kidney Disease Improving Global Outcomes criteria) were selected for blinded measurement of [TIMP-2]*[IGFBP7] using a cartridge-based, commercially available immunoassay. Additionally, clinical variables associated with postoperative AKI stage 1 or greater were identified by univariate analysis. Upon receipt and processing of all three urine samples from all patients, we will conduct logistic regression and receiver operating characteristic analysis to determine if [TIMP-2]*[IGFBP7] improves prediction of postoperative AKI.

Results: Patients who underwent completion of multibranched TEVAR with baseline, POD 0, and POD 1 urine samples available for analysis were included in this retrospective cohort study. Individuals with preoperative end-stage renal disease (estimated glomerular filtration rate (eGFR) <15 mL/min and/or dialysis-dependent) or preoperative AKI requiring renal replacement therapy were excluded. Among 139 patients with complete data, 31.7% (44/139) of patients developed AKI stage 1 or greater within the first 3 days following surgery. Prevalence of major comorbidities in the cohort were as follows: chronic kidney disease (38.1%, 53/139), hypertension (95.7%, 133/139), hyperlipidemia (77.7%, 108/139), diabetes mellitus (16.5%, 23/139), prior cerebrovascular accident (18.0%, 25/159). Mean preoperative creatinine was 1.35 mg/dL (eGFR of 62.5 mL/min). Among the 8 patients in the pilot study, mean urinary [TIMP-2]*[IGFBP7] levels at baseline, POD 0, and POD 1 were 0.28, 0.19, and 0.30 $(ng/mL)^2/1000$, respectively. No statistically significant differences in [TIMP-2]*[IGFBP7] between time points were detected ($p=0.206$, Friedman test). Using the published cutoff of [TIMP-2]*[IGFBP7] > 0.3 $(ng/mL)^2/1000$ in any measured time point, 5 subjects were identified as being at risk for AKI, yielding a sensitivity of 0.67 and specificity of 0.40.

Conclusion: Urinary [TIMP-2]*[IGFBP7] levels have been measured in a pilot sample of individuals within a cohort of patients who underwent multibranched TEVAR. Blinded [TIMP-2]*[IGFBP7] measurements of the remaining cohort are ongoing.

References: 1. J Vasc Surg. 2018;68(3):916-928. 2. Eur Radiol. 2016;26(6):1613-1619. 3. J Trauma Acute Care Surg. 2016;80(2):243-249. 4. Crit Care Lond Engl. 2013;17(1):R25. 5. Crit Care Med. 2019;47(10):e820-e826. 6. PloS One. 2014;9(3):e93460. 7. J Intensive Care Med. 2020;35(10):1013-1025. 8. VASA Z Gefasskrankheiten. 2021;50(2):101-109.

9. PloS One. 2021;16(1):e0244658. 10. Kidney Int Suppl. 2012;2(1):19-36. 11. Nephrol Dial Transplant. 2014;29(11):2054-2061.



Cardiovascular Anesthesiology - 9

Effects Of Levosimendan On Right Ventricular Hydraulic Afterload During Acute Global Hypoxia In Anesthetized Rabbits

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Introduction: In situations of global hypoxia (Hx) (i.e., high altitude ascent), hypoxic pulmonary vasoconstriction (HPV) is generalized and results in elevated pulmonary arterial pressure (PAP), which, if exaggerated, may cause acute right-heart failure (1). Pulmonary vasoreactivity to Hx occurs predominantly in distal resistance pulmonary arteries (RPA). It varies significantly between species and is relevant to ventilation-perfusion (V/Q) matching. Levosimendan (LSM) produced different relaxation effects depending on proximal (conduit) to RPA, with higher relaxation potency in isolated RPA rings, reduced during Hx (2). We analyzed the stationary and pulsatile components of pulmonary hemodynamics response to normobaric acute global Hx and the effects of LSM by the PA pressure waveform analysis (PWA, time-domain) in anesthetized rabbits.

Methods: 14 females New Zealand rabbits (2.9 ± 0.1 Kg) were anesthetized and mechanically ventilated. A left thoracotomy was performed. Central venous (CVP) left atrial (LAP), and femoral arterial pressures (AoP) (fluid column catheter), and pulmonary arterial pressure (PAP) (Millar), and flow (PF) (Transonic) were monitored (Figure 1, LabChart, 1KHz). We assessed pulmonary vascular resistance (PVR); pulmonary arterial capacitance (PAC); input (Zo) and characteristic impedance (Zc, Li method); time (Ti); and magnitude (Ew) of the reflected wave; and augmentation index (AI) (Figure 2) (1,3). The animals were randomized to a control Hx group (n=6) (FiO2 0.1, for 5 min), and LSM Hx group (n=7) (Hx after 60 min LSM 0.2 µg/kg/min i.v., Hx-LSM).

Results: HPV stimulus (PsO2, Marshall equation) obtained during Hx was 24 ± 7 mmHg (4). HPV determined a significant increase in the dynamic afterload of the RV, both in stationary and pulsatile components, without a significant change of the AoP (Table 1). The high absolute values of Zc and Zo obtained could be associated with the reduced diameter of major vessels and fewer parallel vessels at any level of the vascular tree due to the small size of the rabbit. LSM infusion led to a decrease in mPAP, Zo, and the inflection pressure (Pi) (P <0.05) with an increase of PF and stroke volume (SV). However, Hx-LSM showed a similar hemodynamic response (relative change) without preventing the increase in PAP and RV hydraulic load secondary to the Hx (Table 2).

Conclusion: Pressure waveform analysis allowed the time-domain quantification of the dynamic RV afterload. HPV was associated with an increase in all the dynamic afterload parameters. Low-dose infusion of LSM did not prevent the increase in RV hydraulic load secondary to HPV.

References: 1. Physiol Rep 2021; 9:e15024 2. International Cardiovascular Forum Journal. 2017; 11:16-22 3. World J Cardiol 2011;3(10):322-28 4. Int Care Med 1994; 20:291-97

Figure 1: Representative tracings during Hypoxia

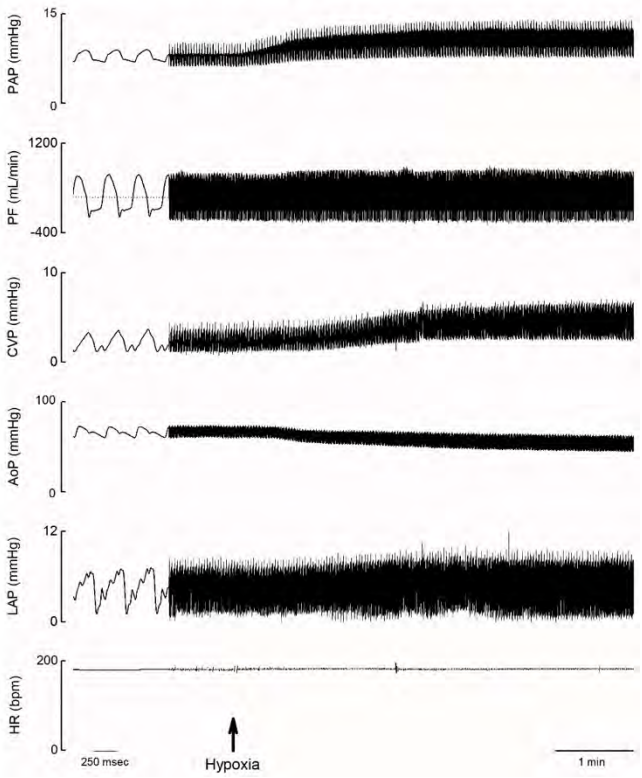

Figure 2: Representative tracings of the pulmonary arterial pressure (PAP), its second derivative ($dPAP^2/dt^2$) and pulmonary flow (PF) showing the pulse wave analysis and assessment of characteristic impedance (Zc).

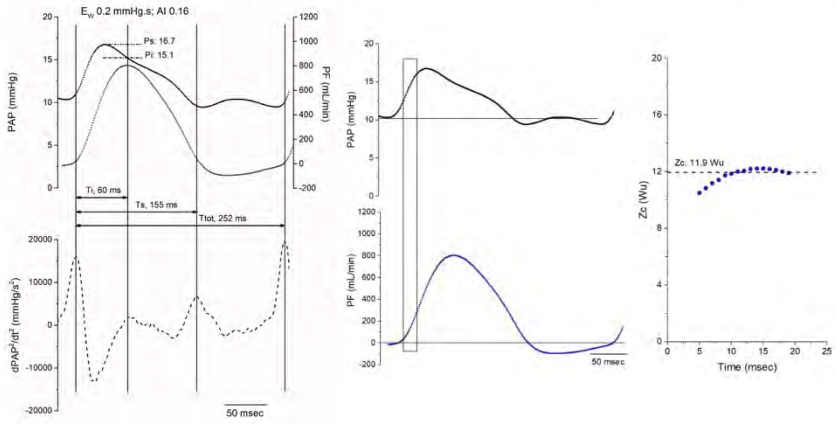

Table 1: Absolute grouped values of the two experimental situations

	Hypoxia group (n=7)		LSM-Hx group (n=7)		
	Basal	Hx	Basal	LSM	LSM-Hx
mAoP, mmHg	56±19	53±12	52±10	59±18	41±14*°
mPAP, mmHg	6.3±1.5	7.8±1.8*	7.8±2.9	6.8±3*	9.2±2.8°
pPAP, mmHg	8.3±1.5	10±1.7*	7.6±1.5	7.7±1.3	10.8±2.2*°
LAP, mmHg	2.0±1.1	2.1±1.5	2.3±2	1.4±0.4	1.2±0.9
RAP, mmHg	3.1±1.6	4.2±1.9*	2.2±1	2.6±1.2	4.4±1.3*°
PF, mL/min	220±62	191±76	190±40	240±90	170±80°
HR, bpm	194±20	181±27	180±28	175±16	173±27
SV, mL	1.1±0.3	1.0±0.3	1.1±0.3	1.4±0.4	0.95±0.3°
PVR, Wu	20±8	33±15*	29±14	25±13	56±35*°
Zo, Wu	30±6.5	47±15*	40±9	31±16*	64±35*°
PAC, mL/mmHg	0.14±0.05	0.1±0.04*	0.15±0.06	0.17±0.03	0.09±0.03*°
Pi, mmHg	11±1.9	13±1.8*	11.5±2.9	10.3±2.8*	13.3±3°
Ti, ms	60±11	50±11	70±20	60±10	50±10*°
Ti/Ttot	0.20±0.04	0.17±0.05*	0.21±0.04	0.17±0.05*	0.14±0.02*°
Zc, Wu	11±4	15±6*	6.7±2.1	7.6±2.6	9.4±3.4*
Ew, mmHg.s	0.10±0.07	0.19±0.1*	0.26±0.13	0.34±0.26	0.6±0.3*°
AI	0.07±0.05	0.10±0.08	0.19±0.09	0.21±0.12	0.28±0.12°

Mean ± SD. *P* <0.05 *vs. Basal; °vs. LSM

Table 2: Relative grouped values (%) of the two experimental situations

	ΔHx	ΔLSM-Hx
mPAP	23±9	25±15
pPAP	23±9	47±14
PF	-14±7	-6±2
HR	-6±5	-3±3
PVR	72±21	100±40
Zo	52±18	50±23
PAC	-22±8	-30±14
Ti/Ttot	-14±4	-32±8
Zc	33±7	44±21
Ew	158±63	171±90
AI	76±41	63±40

Mean ± SE. Δ: [(Hx-Basal)/Basal]*100

Cardiovascular Anesthesiology - 10

Continuous Propofol Infusion in patients with Brugada Syndrome. Preliminary results of a feasibility study.

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Introduction: Previous studies failed to provide any evidence that could confirm the alleged arrhythmogenicity of propofol in patients with Brugada syndrome. A single-bolus of propofol during induction of anaesthesia did not provoke malignant arrhythmias or clinically significant ST- QRS- or other electrocardiographic alterations. The hypothesis that increased propofol plasma concentrations are more likely to induce arrhythmias or similar electrocardiographic changes as during the provocation challenge with ajmaline, would be tested by providing total intravenous anaesthesia through target-controlled infusion.

Methods: The study was designed as a prospective, monocentric, non-randomised observational study. All patients underwent a routine, extensive preoperative evaluation before the scheduled surgery, as standard of care prescribes. Eligible patients were identified conform to inclusion and exclusion criteria and were approached for study participation and informed consent. For the current study, total intravenous anaesthesia was provided by an open-target-controlled infusion system incorporated in TCI-pumps, embedded with the pharmacokinetic-pharmacodynamic modelling of the effect-site concentration of Schnider (for propofol) and Minto (for remifentanil). Those models comprise algorithms depending on anthropomorphic characteristics (age, weight, gender, lean body mass and height) and ensure adequate anaesthetic depth. Co-administration of remifentanil-TCI was chosen in this design -as currently often performed-, to ensure a more vigilant approach by reducing propofol requirements up to 50%. The anaesthetic depth was continuously adjusted and fine-tuned during the procedure, based on the continuous intraoperative electroencephalographic (EEG) monitoring achieved by NeuroSENSE, the hemodynamic parameters and the (anticipated) surgical phases. The EEG monitoring was maintained until the emergence of the patient, and transport to the PACU. The NeuroSENSE device, rendered online raw and processed electroencephalographic activity (WAVCNS). A WAVCNS-value of 60-40 was targeted to help the attending anaesthesiologist adjust anaesthetic depth concordantly. Electrocardiographic data analysis occurred post-operatively by a cardiologist, who was not present during the anaesthetic procedure or data acquisition. Clearly this study is hampered by a clear rare disease, with low-prevalence, inclusion bottleneck. Therefore, only seven patients have been included up to date. PROCEDURE: Standard of care monitoring was implemented. Additionally, a modified 12-lead electrocardiogram (12-lead ECG with additional focus on the higher third intercostal space (IC3)) and a NeuroSENSE electroencephalographic (EEG) device were applied. The application of the EasyPrepTM Sensor Kit (EK-901) occurred while the patient was still awake. Adhesive defibrillator pads were connected to an external defibrillator device as a precautionary measure. The first ECG was registered, while the patient was awake, prior to administration of any medication. This was defined as the Baseline-ECG at T0. Consecutive ECG's were registered at intervals of at least ten minutes throughout the first hour of the surgical procedure. The second hour, the interval was increased to thirty minutes. ECG analysis occurred for all registrations. We present the preliminary measurements of the ST- and J-points. Due to low number of patients, no statistics were applied. We present te results in a summarizing table.

Results: Seven consecutive patients were included, scheduled for elective surgery. All of them received target controlled infusion of propofol, based on the effect-site concentration protocol of Schnider, during 60 to 120 minutes. In all seven patients, no changes could be noted at the ST-segment and the J-point, throughout the anaesthetic procedure. No clinical adverse events were noted during or after surgery. An additional ECG prior to discharge for the post-anaesthetic care unit confirmed the absence of ST-changes.

Conclusion: Based on prior findings and the preliminary results of unchanged ST-segments, and clinically uneventful anaesthetic procedures in patients with Brugada Syndrome, the authors believe that further collection and exploration of electrocardiographic findings is reasonable. A larger group of patients is required to enhance our knowledge on ECG changes during propofol infusion in patients with Brugada Syndrome.

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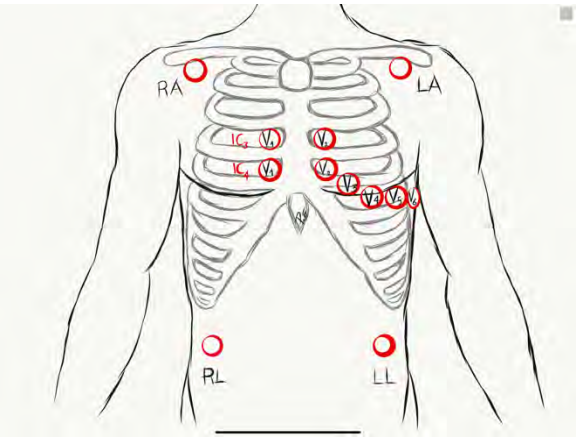

Cardiovascular Anesthesiology - 11

Gender Representation of Abstract Presenters at the Annual Meetings of the Society of Cardiovascular Anesthesiologists and American Society of Anesthesiology: 2016-2020

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Introduction: For the early-stage anesthesiologist, abstract presentation is an important mechanism of recognition and research collaboration for professional advancement. The purpose of this study was to compare gender trends in abstract poster presentation at the American Society of Anesthesiology (ASA) vs Society of Cardiovascular Anesthesiologists (SCA) Annual Meetings from 2016 through 2020.

Methods: This was a cross-sectional study using data from the ASA and SCA websites. Abstract data on presenting and senior authors were collected for the years 2016 through 2020 for both annual meetings, and gender was determined either through manual online search or Gender API software. Observed gender representation of abstract authors was compared to expected gender representation based on gender distribution of cardiac anesthesiologists for the SCA or of all anesthesiologists for the ASA.

Results: From 2016 to 2020, the percentage of woman physician abstract presenting authors at the ASA was consistently between 30-34% and was overrepresented compared to the expected proportion for each year (2016-2020: $p < 0.001$). The proportion of woman senior authors on abstracts was between 19-26% from 2016 to 2020, and was significantly underrepresented (2016-2019, $p < 0.05$). At the SCA meetings, the proportion of woman abstract presenting authors ranged from 25%-36%, and the proportion of women senior authors ranged from 18%- 27%. There was no significant difference in the observed vs expected proportion of woman presenting and senior authors.

Conclusion: While there was no significant underrepresentation of women physicians in both presenting and senior abstract author spots at the SCA meetings, there was significant overrepresentation of women as presenting authors and underrepresentation of women as senior authors at the ASA meetings. Our results suggest that in abstract presentation, women are appropriately represented at the ASA and SCA anesthesiology meetings, and that is not an area where barriers to academic advancement exist.

Table 1. Percentage of women presenting and senior authors at the American Society of Anesthesiologists Annual Conference, 2016-2020.

	Expected*	Observed Presenting Author			Observed Senior Author		
Year	*% Women*	*Total*	*Women N(%)*	*p-value*	*Total (N)*	*Women N(%)*	*p-value*
2016	25.1	914	275 (30.1)	p <0.001	984	203 (20.6)	0.001
2017	25.5	788	254 (32.2)	p <0.001	930	167 (18.0)	p <0.001
2018	25.7	921	312 (33.9)	p <0.001	1008	228 (22.6)	0.025
2019	25.9	709	240 (33.9)	p <0.001	810	170 (21.0)	0.001
2020	26.4	451	p <0.001	p <0.001	541	138 (25.5)	0.660

*Derived or extrapolated from AAMC Physician Specialty Data Report: Active Physicians by Sex and Specialty, 2017 & 2019

Table 2. Percentage of women presenting and senior abstract authors at the Society of Cardiovascular Anesthesiology Annual Conference, 2016-2020.

	Expected*	Observed Presenting Author			Observed Senior Author		
Year	*% Women*	*Total (N)*	*Women N(%)*	*p-value*	*Total (N)*	*Women N (%)*	*p-value*
2016	27.9	171	43 (25.1)	0.444	182	33 (18.1)	0.002
2017	30.1	220	61 (27.7)	0.508	207	52 (25.1)	0.129
2018	29.0	218	73 (33.5)	0.156	205	50 (24.4)	0.165
2019	25.6	172	51 (29.7)	0.296	153	35 (22.6)	0.407
2020	32.7	95	34 (35.8)	0.585	92	25 (26.3)	0.267

*Derived from ACGME Data Resource Book, Table C.21 Number of Active Residents by Specialty and Subspecialty and Sex

Table 3. Women-to-women mentorship at the ASA and SCA conferences, 2016-2020

Year	ASA	Cochran-Armitage p-value	SCA	Cochran-Armitage p-value
2016	25.1% (69/275)	>0.05	14.0% (6/43)	0.04
2017	17.7% (45/254)		29.5% (18/61)	
2018	26.9% (84/312)		32.9% (24/73)	
2019	23.8% (57/240)		27.5% (14/51)	
2020	27.0% (41/152)		29.4% (10/34)	

Critical Care

Critical Care - 1 The Complexity of Oxidative Stress After In Vitro Ischemia-Reperfusion Injury and Hypothermia: Not All Readouts Are The Same

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Introduction: Therapeutic Hypothermia (TH) is the gold standard treatment for neuroprotection in post-cardiac arrest patients. However, the TTM2 trial has raised controversy on its clinical application.[1] Additionally, TH's mechanisms are poorly understood and are still under investigation.[2] Oxygen & Glucose Deprivation followed by Reperfusion (OGD-R) is a well-established model for in vitro mechanistic studies on Ischemia and Reperfusion Injury (IRI).[3] Despite its limitations in translation to in vivo models of IRI, in vitro OGD-R represents a unique opportunity to characterize the individual biological response that different cell types experience after OGD-R and TH. Herein, we studied the effects on cell viability (CV), global reactive oxygen species (ROS) production, and lipid peroxidation using single cultures of neurons (NE) and astrocytes (AS) after OGD-R and TH protocols.

Methods: Neurons (HT-22) and Astrocytes (C8-D1A) were subjected to 6h OGD followed by 20h of Reperfusion (OGD-R). OGD is based on the combination of chemical ischemia (standard culture media depleted of glucose and other energy sources) and severe hypoxia (~ O2 1.5%) for 6h, while 20h of reperfusion consists of the addition of standard culture media and conditions (21% O2, 5% CO2, 37°C). TH group was set at 31.5°C during 20h reperfusion. CV was determined by ATP measurement with the CellTiter-Glo 2.0® assay (ProMega). Global ROS were assessed by the CellROX® assay (Thermo Fisher), while Lipid Peroxidation (LPO) was characterized by the Image-iT® Lipid Peroxidation Kit (Thermo Fisher).

Results: OGD-R decreased CV in NE (Fig. 1A, P value = 0.0001) and AS (Fig. 1B, P value = 0.0001). TH during reperfusion resulted in greater CV when compared with normothermia (NT) group, in both NE (Fig. 1A, P value = 0.0001) and AS (Fig. 1B, P value = 0.0001). In NE, OGD-R resulted in increased ROS production when compared with control, while TH after OGD-R downregulated ROS to control levels (Fig. 2A, P value = 0.0001). In AS, OGD-R resulted in increased ROS production when compared with control, while TH after OGD-R downregulated ROS to below control (Fig. 2B, P value = 0.01 and P value = 0.0001, respectively). In NE, OGD-R decreased LPO, while TH after OGD-R increased LPO when compared with NT group (Fig. 3A, P value = 0.05, P value = 0.08). In AS, OGD-R had no significant effect on LPO production, while, TH after OGD-R increased LPO versus NT (Fig. 3B, P value < 0.05).

Conclusion: The increased ATP production correlates with greater cell viability in NE and AS after TH, when compared with NT (Fig. 1A and Fig. 1B, respectively). TH was very effective in downregulating global ROS in NE and AS (Fig. 2A and Fig. 2B, respectively). Unexpectedly, in NE, OGD-R showed lower LPO levels versus control, while TH was associated with a higher LPO trend (Fig. 3A, P value = 0.08). In AS, TH was associated with higher LPO production versus OGD-R, NT group (Fig 3B, P value = 0.05). LPO is the product of ROS reacting with unsaturated fatty acids, which affects normal biological processes dependent on lipid function. These results suggest that oxidative stress characterization is complex and individual readouts like LPO may not be the best marker for simple ROS detection during OGD-R and TH settings. Further studies are required to properly characterize specific ROS behavior after OGD-R and TH.

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Fig.1A

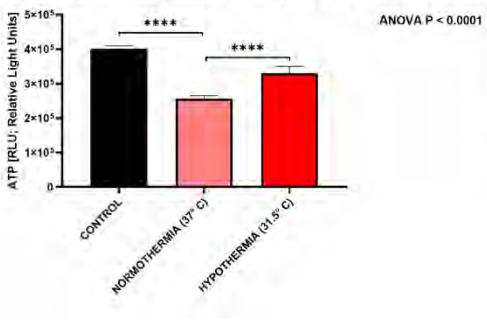


Fig.1B

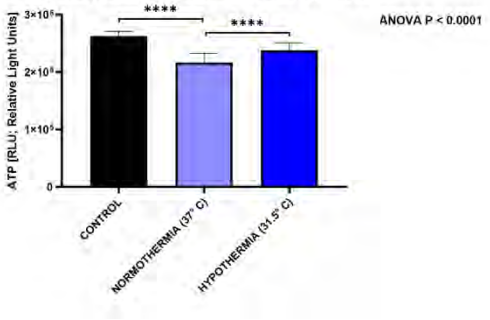


Fig. 2A

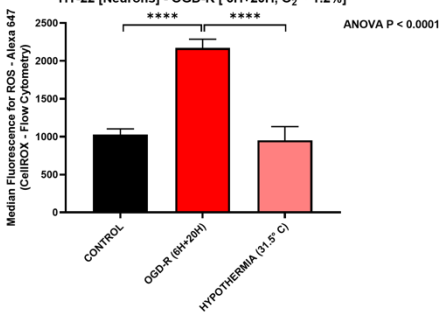


Fig. 2B

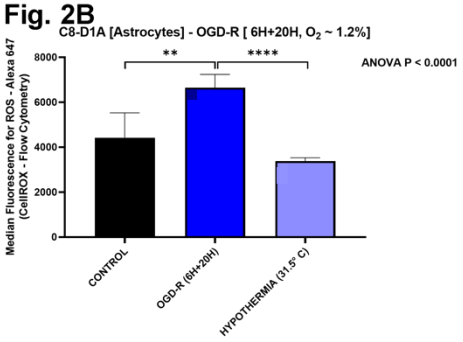


Fig. 3A

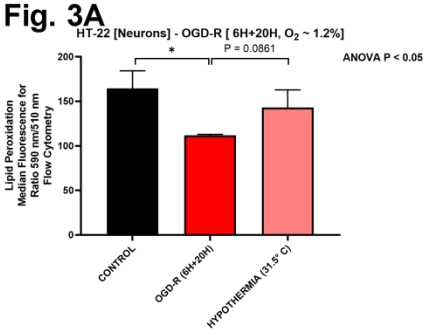
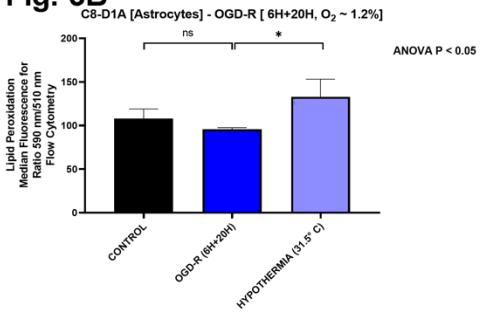


Fig. 3B



Critical Care - 2 Surgical futility: exploring early neonatal postoperative mortality

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Introduction: Determining whether surgery is unlikely to produce the desired outcome of rescuing a patient from mortality is a complicated, ethically challenging endeavor. Among adult medical patients, the concept of medical futility, defined as a situation when medical care is ineffective at producing the desired physiologic effect on or benefit for the patient, is well described in the bioethics literature.(1) Surgical futility is a relatively less examined and intensely debated subject.(2) Although pediatric postoperative mortality is highest among neonates,(4) to date the subject of neonatal surgical futility has not been examined. The purpose of this study was to examine factors associated with early (within 48 hr) postoperative mortality among neonates classified as American Society of Anesthesiologists (ASA) physical status ≥4 who underwent a surgical procedure.

Methods: Following IRB approval, we assembled a retrospective cohort of neonates who underwent an inpatient surgical procedure from the National Surgical Quality Improvement Program (2012 - 2019). Extreme risk was defined as ASA physical status ,â•4 and surgical futility was defined as death within 48 hr of the index surgery in these high-risk patients. We estimated the incidence and examined factors associated with surgical futility.

Results: Among a cohort of 42,016 neonates, 10,813 (25.7%) were classifiable as extreme pre-surgical risk. Of these 10,813 extreme pre-surgical risk neonates, 12.4% (n=1048) died within 30 days of surgery. Almost half of the mortality cases occurred within 48 hours of index surgery (47.7%, n=500). In the multivariable model, factors associated with surgical futility include emergency surgery, preoperative sepsis, prematurity, preoperative inotropic requirement. Of note, each kg increment in weight at the time of surgery was associated with a 13% reduction in the risk of surgical futility. Other predictor variables are detailed in Table 1. We derived and validated a scoring system that demonstrated an excellent discriminant ability to predict neonatal surgical futility (cross-validated AUC=0.911; 95%CI: 0.895, 0.922- Fig.1).

Conclusion: Although discussing surgical futility can be a difficult and emotive endeavor, we found, using a set of simple clinical and operative variables, that it is possible to predict with excellent discrimination neonates who died within 48hr of surgery. Our data may be used for preoperative risk profiling and counseling of parents and caregivers.

References: 1. Schneiderman LJ, Jecker NS, Jonsen AR. Medical futility: Its meaning and ethical implications. Ann Intern Med. 1990; 112:949 e954. 2. Grant SB, Modi PK, Singer EA. Futility and the care of surgical patients: Ethical dilemmas. World J Surg. 2014;38:1631e1637 3. Chiu AS, Jean RA, Resio B, Pei KY. Early postoperative death in extreme-risk patients: A perspective on surgical futility. Surgery. 2019 Sep;166(3):380-385. 4. Nasr VG, Davis JM. Anesthetic use in newborn infants: the urgent need for rigorous evaluation. Pediatr Res. 2015 Jul;78(1):2-6.

Characteristics	β coefficient	Odds ratio (95% confidence interval)	P-value	Score
Weight at the time of surgery, per kg increment	-0.14	0.87 (0.77—0.98)	0.02	-1
ASA class 5 vs. 4	1.30	3.66 (2.82—4.73)	<0.01	13
Ventilation support	0.97	2.63 (1.80—3.84)	<0.01	10
Inotropic support	1.17	3.22 (2.54—4.09)	<0.01	12
Transfusion prior to surgery	0.37	1.45 (1.14—1.84)	<0.01	4
Emergency case status	1.22	3.39 (2.57—4.46)	<0.01	12
Gastro-intestinal disorder	0.49	1.64 (1.24—2.16)	<0.01	5
Preoperative sepsis	0.72	2.05 (1.62—2.59)	<0.01	7
Prematurity	0.47	1.61 (1.15—2.24)	0.01	5

Figure 1. Multivariable logistic regression for the prediction of surgical futility and derivation of a prognostic index by incorporating demographic characteristics and pre-operative co-morbidities, NSQIP-P 2012-2019.
The cross-validated C-statistic was 0.911 (**Bias corrected 95% CI: 0.895-0.922**).
The derived prognostic index ranged from 0 to 66.
Abbreviations: ASA, American Society of Anesthesiology; NSQIP-P, National Surgical Quality Improvement Program-Pediatric; CI, confidence

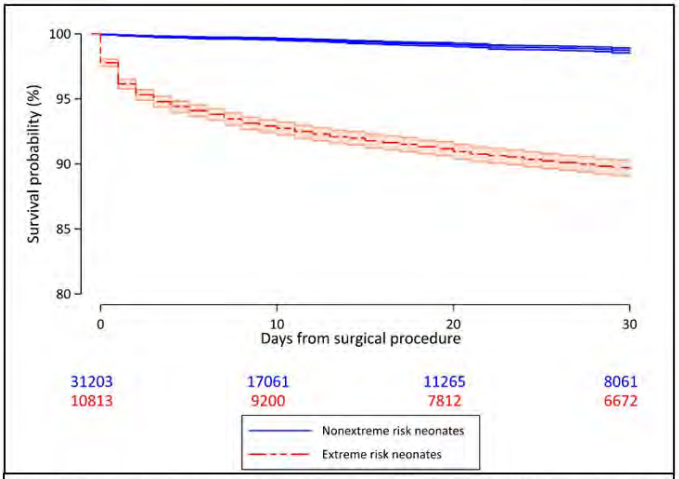

Figure 2. Time to mortality among extreme risk neonates (ASA classification≥ 4), who underwent inpatient surgery in hospitals participating in the National Surgical Quality Improvement Program (2012-2019).

Critical Care - 3 Specialized Pro-Resolving Mediators After LVAD, Cardiac, and Spine surgery

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Introduction: Inappropriate resolution of acute inflammation has been recognized as a maladaptive response that may lead to chronic disease.[1-3] Specialized pro-resolving mediators (SPMs) were recently identified as active mediators of inflammation resolution.[2,4-6] During the acute inflammatory phase, fatty acid metabolites prostaglandin (PG) and leukotrienes (LT) are produced to mediate the inflammatory response. At the height of neutrophil infiltration, lipid metabolism shifts to form SPMs rather than PGs and LTs to halt neutrophil recruitment and activate macrophages.[7] SPMs have been studied extensively in pre-clinical models. However, little data exist regarding SPMs in clinical models of acute inflammation. Cardiac surgeries, particularly the insertion of ventricular assist devices, incite a profound inflammatory reaction with outcomes depending on the relationship between rapid resolution of inflammation and the severity of surgery.

Methods: After IRB approval and written, informed consent, adult (≥18 years old) patients undergoing left ventricular assistance device (LVAD) implantation, cardiac, or spinal (as controls) surgery were recruited between May 2018 and August 2019. Plasma samples were collected in patients undergoing LVAD implantation preoperatively, daily for the initial 10 postoperative days, as well as at 30 and 90 days. In the cardiac and spinal patients, plasma samples were collected preoperatively and daily during their postoperative ICU course. The Lipidomics Core of Wayne State University analyzed for SPMs, prostaglandin metabolites, and metabolites of arachidonic acid pathways via liquid chromatography-mass spectrometry. Quantified cytokine assays (GM-CSF, IFNα2, IFNγ, IL-2, IL-6, IL-8, IL-10) were obtained by Eve Technologies. T-tests were used to determine significance in levels of cytokines and SPMs between LVAD and non-LVAD patients. Spearman's rank correlation coefficients were used to correlate peak cytokine and SPM levels among LVAD, cardiac, and spinal patients within the first 10 days postoperatively.

Results: 10 LVAD, 10 cardiac, and 4 spine surgery patients were enrolled. The SPMs, their associated mediators, and cytokines were analyzed with varying levels of success. A select group of SPMs and cytokines were further analyzed based on availability of data. Levels of RvD1 were the only SPMs reaching significance between LVAD and non-LVAD patients during each matched day of the post-operative period (Figure 1). Significant correlations were found between IL-6 and 11-HETE, 12-HEPE, 12-HETE, 13-HDoHE, 14-HDoHE, 15-HETE, 4-HDoHE, 5-HEPE, 5-HETE. Significant correlations were also found between IL-8 and 11-HETE, 13-HDoHE, 15-HETE, 18-HEPE, 4-HDoHE, 5-HEPE, 5-HETE. However, correlations overall were poor (Figure 2).

Conclusion: SPMs were detectable before and after LVAD implantation, cardiac, and spine surgeries. Strong correlations were not found between severity of surgery and levels of SPMs in the initial postoperative period. While significant differences were detected in RvD1 (which is thought to downregulate neutrophil activation in the acute inflammatory phase) between LVAD and non-LVAD patients, the overall lack of identifiable trends points towards the possibility that the conversion from acute to chronic SPMs occurs at a later stage following surgery.[8] Assessment of SPMs for longer periods postoperatively may potentially capture this conversion.

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omega-3 polyunsaturated fatty acids. Vol. 32, p.203-227, 2012. 5. Maresins: novel macrophage mediators with potent anti-inflammatory and pro-resolving actions. Vol. 206, p.15-23, 2009. 6. Discovery of specialized pro-resolving mediators marks the dawn of resolution physiology and pharmacology. Vol. 58, p.10-11, 2017. 7. Lipid mediator class switching during acute inflammation: signals in resolution. Vol. 2, p.612-619, 2001. 8. Resolvin D1 Alleviates the Lung Ischemia Reperfusion Injury via Complement, Immunoglobulin, TLR4, and Inflammatory Factors in Rats. Vol. 39, p.1319, 2016.

Figure 1. Select SPMs and cytokines before and after VAD, cardiac and spine surgeries.

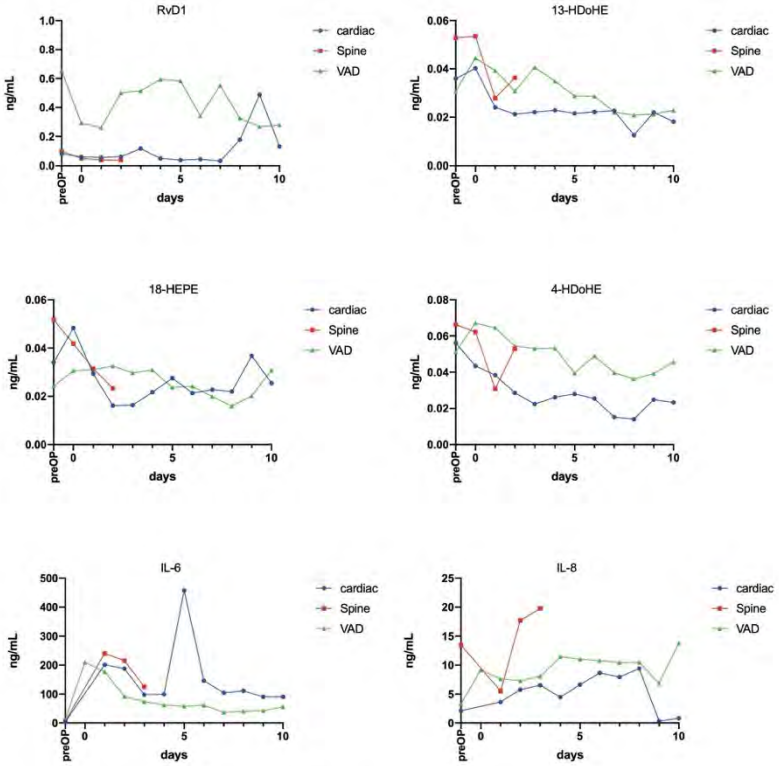

Figure 2. Spearman's rank correlation coefficients between select cytokines and SPMs.

Spearman	Peak IL-2	Peak IL-6	Peak IL-8
11-HETE	-0.043	0.43	0.522
12-HEPE	0.044	0.417	0.371
12-HETE	0.005	0.393	0.314
13-HDoHE	-0.059	0.434	0.648
14-HDoHE	0.035	0.417	0.354
15-HETE	-0.061	0.401	0.434
18-HEPE	0.006	0.381	0.568
4-HDoHE	-0.053	0.415	0.666
5-HEPE	-0.016	0.411	0.529
5-HETE	0.011	0.431	0.529
RvD1	-0.036	0.256	0.357

Critical Care - 4 Motion Analysis Tracks Improvements in Navy SEAL Combat Medics Performing Point-of-Care Ultrasound

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Introduction: Point of care ultrasound (POCUS) is commonly employed for imaging of the heart, lungs and abdomen in the clinical setting. Transthoracic echocardiography (TTE) is a critical component of POCUS that has been recently employed in austere environments by Navy SEAL combat medics for triage and diagnosis [1]. Despite its utility in both the clinical and combat settings, training for TTE remains largely unstandardized with regard to feedback to learners and indicators of proficiency [2,3]. Our group sought to employ motion analysis as a tool to measure progression in the performance of TTE by two groups of combat medics. We hypothesized that participants would exhibit significant improvements in a comprehensive series of motion metrics. We also hypothesized that motion metrics would exhibit an inverse relationship with expert ratings recorded by attending anesthesiologists.

Methods: Two groups of combat medics (5 and 10 individuals, respectively) underwent 5-day training courses in which they were taught TTE by a team of attending anesthesiologists. Participants used the same ultrasound probe, which was equipped with an electromagnetic sensor to record their motions. They each performed 2 rapid ultrasound for shock and hypotension (RUSH) exams for the latter 4 days of the course, totaling 8 trials per person. Three attending anesthesiologists graded the exams using a global rating scale (GRS). A generalized estimating equation (GEE) was used to analyze the trend of motion metrics exhibited by the ultrasound probe across all trials. These metrics included total distance travelled (path length), movements performed (translational motions), rotation performed (rotational sum) and time. Pearson correlation coefficients were assessed to determine the degree of correlation amongst motion metrics and expert ratings.

Results: Both groups exhibited negative trends in path length, translational motions, rotational sum, and time ($p < 0.001$) (Table 1). Expert ratings also significantly improved in all aspects ($p < 0.001$). Pearson correlation coefficients revealed weak to strong, inverse correlations amongst motion metrics and expert ratings (Table 2).

Conclusion: Motion metrics and expert ratings revealed significant improvements in Navy SEAL combat medics performing TTE. Motion metrics decreased as expert ratings improved, and exhibited weak-to-strong, inverse correlations. Objective analysis of performance may benefit trainees without access to formal training and feedback from experienced sonographers.

References: [1] Point-of-Care Ultrasound: A Trend in Health Care. 89 (2):127-138. 2017 [2] Special operator level clinical ultrasound: an experience in application and training. 10(2):16-21. 2010 [3] SOLCUS: Update On Point-of-Care Ultrasound In Special Operations Medicine. 16(1):58-61. 2016

Table 1: Trends of Motion Metrics Across Trials for Overall RUSH Exam

Metric	GEE Coefficient (95% CI)	p-value
Path Length (cm)	-269.49 (-327.06 to -211.92)	p < 0.001
Translational Motions	-326.30 (-437.59 to -215.00)	p < 0.001
Rotational Sum (degrees)	-3177.89 (-3859.85 to -2495.93)	p < 0.001
Time (s)	-34.53 (-40.97 to -28.09)	p < 0.001

RUSH: Rapid Ultrasound in Shock and Hypotension; GEE: Generalized estimating equations; CI: Confidence interval

Table 2: Correlation Coefficients between Motion Metrics and GRS Items

Cohort	Metric	Image finding	Image fine-tuning	Speed	Final Image Accuracy	Global Assessment
All	Path Length (cm)	-0.47 (p < 0.001)	-0.36 (p = 0.001)	-0.52 (p < 0.001)	-0.42 (p < 0.001)	-0.46 (p < 0.001)
	Translational Motions	-0.56 (p < 0.001)	-0.60 (p < 0.001)	-0.52 (p < 0.001)	-0.53 (p < 0.001)	-0.56 (p < 0.001)
	Rotational Sum (degrees)	-0.51 (p < 0.001)	-0.45 (p < 0.001)	-0.53 (p < 0.001)	-0.45 (p < 0.001)	-0.49 (p < 0.001)
	Time (s)	-0.64 (p < 0.001)	-0.60 (p < 0.001)	-0.67 (p < 0.001)	-0.58 (p < 0.001)	-0.65 (p < 0.001)

GRS: Global Rating Scale

Critical Care - 5 Safety and Efficacy of Awake Fiberoptic Intubation in Critically Ill Patients: A Retrospective Case Series

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Introduction: Intubation in critically ill patients is a high-risk procedure, with recent studies demonstrating that over 40% lead to hemodynamic instability, almost 10% lead to severe hypoxemia, and that propofol is significantly associated with cardiovascular instability (1). Video laryngoscopy does not shorten time to intubation nor improve first-pass success rates compared to direct laryngoscopy in critically ill patients, irrespective of operator experience (2). Awake fiberoptic intubation (AFOI) is a well-established tool for airway management in patients with known or suspected difficult airways and can reduce hemodynamic changes during induction (3-5). We sought to demonstrate the safety and efficacy of AFOI in critically ill patients irrespective of the presence of a difficult airway.

Methods: We performed a retrospective case series of patients who underwent AFOI attempts in the ICU of a large academic tertiary care hospital between April 2018 and September 2021. We obtained demographic and clinical variables at time of induction and recorded hemodynamic data throughout the peri-intubation period. Primary outcome was development of hemodynamic instability (either systolic pressure <65 at least once or <90 for 30 minutes during the peri-intubation period, new or increased need of vasopressors, or fluid bolus >15 mL/kg). Secondary variables were cardiac arrest during intubation, severe hypoxemia (oxygen saturation <80%), arrhythmia, aspiration, post-intubation ABG, in-hospital mortality, and 30-day mortality. A total of 21 ICU patients underwent AFOI. Indications for intubation and peri-intubation characteristics are shown in Table 1.

Results: All patients were successfully intubated using AFOI. 2 patients had hemodynamic instability during intubation and 1 patient had cardiac arrest. 2 patients had transient oxygen desaturations and 1 patient had severe hypoxemia in the setting of cardiac arrest. 0 patients aspirated. 2 patients had arrhythmias that were present prior to intubation. 15 patients died during hospitalization and 13 patients died within 30 days of intubation. Average post-intubation arterial pH was 7.35, average PaO2 was 135 (average FiO2 0.78), and average PCO2 was 48. Average change in heart rate from beginning to end of intubation was +4.5 bpm, change in blood pressure was -0.5mmHg, and change in oxygen saturation was +0.7 percent (Table 2, Figure 1, Figure 2).

Conclusion: In this retrospective series of 21 critically ill patients requiring intubation, we demonstrated that AFOI is a safe method of intubation that preserves hemodynamic stability and oxygenation. Notably, the period of hemodynamic instability, hypoxia, and cardiac arrest in one patient all occurred over 30 minutes after the intubation, suggesting other factors led to the outcome such as positive pressure ventilation and cardiogenic shock. Future studies will prospectively examine safety of AFOI in the ICU.

References: 1. JAMA. 2021;325(12):1164-1172 2. Crit Care. 2019;23(1):221 3. Anesthesia and Analgesia, v. 128, p. 971-980 4. Anesthesiology, v. 125, p. 105-114 5. Anaesthesia, v. 72, p. 694-703

Table 1: Peri-intubation Characteristics

Characteristic	
Indications	*Difficult airway (3)*
	Aspiration risk (2)
	Hypoxemic hypercapnic respiratory failure (6)
	Neck/mediastinal mass (2)
	Unstable cervical spine (2)
	Massive hemoptysis (1)
	Pulmonary hypertension (2)
	Cardiogenic shock/valvular disease (3)
Average age	57
Average Charlson Comorbidity Index (CCI)	6
Males (%)	10 (48%)
Females (%)	11 (52%)
Vasoactive infusions prior to intubation (%)	6 (29%)
Respiratory support	*HFNC (9)*
	BiPAP (8)
	HFNC and BiPAP (1)
	NC (3)
Patients on 100% FiO2 (%)	13 (62%)
Difficult mask ventilation (%)	5 (24%)
Sedation methods	*fentanyl (5)*
	dexmedetomidine (6)
	ketamine (1)
	hydromorphone (1)
	combination (3)
	none (5)

Table 2: Intubation Outcomes

Outcome	
Hemodynamic instability (%)	2 (9.5%)
Cardiac arrest (%)	1 (4.7%)
Severe hypoxemia (%)	3 (14.3%)
Aspiration (%)	0 (0%)
Arrhythmia (%)	2 (9.5%)
In-hospital mortality	15 (71.4%)
30-day mortality	13 (61.9%)
Performer of intubation	*Attending (8)*
	Fellow (10)
	Resident (3)
Average arterial pH	7.35
Average PaO2 (mmHg)	135
Average FiO2	0.78
Average PCO2 (mmHg)	48
Average PaO2:FiO2	173
Average change in MAP (mmHg)	-0.5
Average change in HR (bpm)	+4.5
Average change in SaO2 (%)	0.7

Figure 1: Heart Rate During AFOI

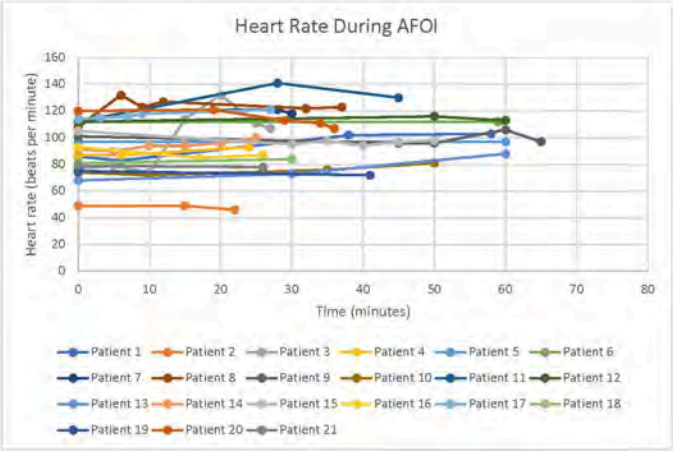


Figure 2: Mean Arterial Pressure (MAP) During AFOI

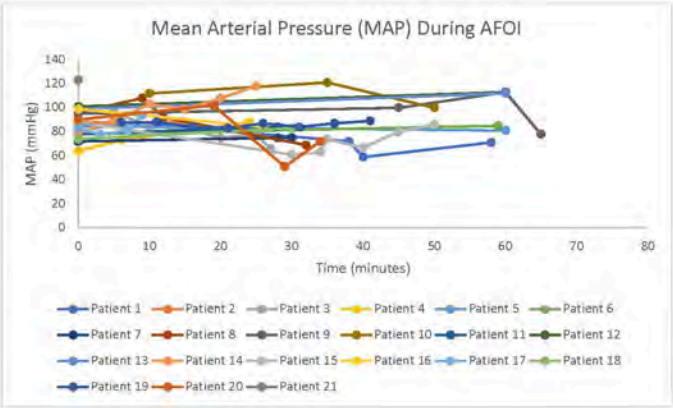
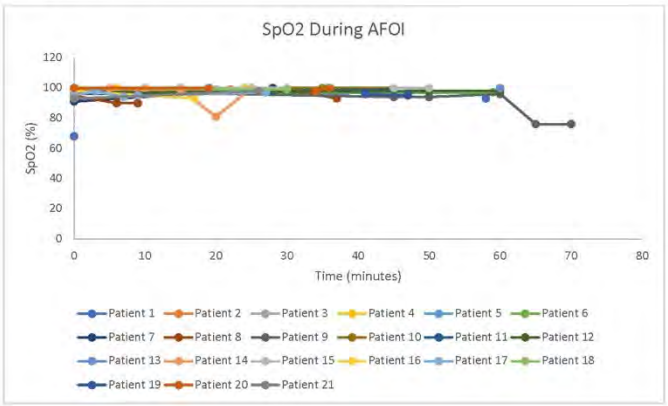


Figure 3: Oxygen Saturation (SpO2) During AFOI



Critical Care - 6 Neuromuscular morbidity on a long-term follow-up of COVID-19 ICU survivors

Dusan Hanidziar[1], Kathryn Baldyga[1], Jeanine P Wiener-Kronish[1], Zhongcong Xie[2]

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Introduction: Survivors of acute respiratory distress syndrome (ARDS) commonly experience persistent functional disability after discharge from the hospital. There is currently limited data on neuromuscular sequelae of COVID-19 critical illness. The goal of this study was to analyze the prevalence and types of neuromuscular morbidity on a long-term follow-up of COVID-19 ICU survivors.

Methods: We retrospectively analyzed a cohort of 35 adult patients (age ≥ 18 years) who were admitted to an ICU at Massachusetts General Hospital in Boston, MA between April 2, 2020, and May 4, 2020. These were consecutive admissions with PCR-confirmed COVID-19 pneumonia during the defined enrollment period of 33 days. All patients received invasive mechanical ventilation. The final date of study follow-up for all patients was October 15th, 2021. Electronic medical records from the index hospital admission, rehabilitation facilities, relevant outpatient visits (e.g., MGH Coronavirus Recovery Clinic, pulmonary medicine, neurology, psychiatry, physical therapy, home health services), and tests (CT, MRI, electromyography) were reviewed by two investigators (D.H and K.B), and queried for specific terms, including 'stroke', 'tracheostomy', 'decannulation', 'neuropathy', 'polyneuropathy', 'myopathy', 'weakness', 'deconditioning', 'disability', 'paresis', 'paresthesia', 'numbness', 'wheelchair', 'walker', 'cane', 'brace', 'gait', 'balance', 'physical therapy'. Active medication prescriptions on the day of follow-up were reviewed and the use of analgesics recorded. This detailed review allowed us to determine the rates and types of persistent neuromuscular morbidity following hospital discharge. Summary statistics were prepared using Microsoft Excel (Microsoft Corporation, Redmond, WA). This study was approved by the Partners Healthcare System Institutional Review Board as Protocol# 2020P001048. The Institutional Review Board waived the need for informed consent.

Results: Twenty-seven patients (77%) with median age of 56 years (IQR 52-67) were alive at the time of study follow-up. The date of follow-up was between 449 and 533 days (median 522, IQR 516-527) since hospital discharge. The hospital stay of this cohort was characterized by prolonged mechanical ventilation (median of 22.1 days, IQR 17-27.9) and high rates of tracheostomy (66.7%). The initial discharge destination for majority of patients (81.5%) was another healthcare facility. However, at the time of follow-up, most patients (92.6%) resided at home and all were decannulated (Table 1). We found high rates of neuromuscular morbidity in this cohort. Motor deficit in bilateral or unilateral extremities was documented in 12 (44.4%) patients, sensory neuropathy was documented in 6 (22.2%) patients, and post-COVID deconditioning (generalized weakness) in 18 (66.7%) patients between hospital discharge and follow-up. Five (18.5%) patients underwent formal electrodiagnostic testing (EMG) for the work-up of severe motor deficit. Over 365 days prior to follow-up, 10 (37%) patients required an assistive device (wheelchair, walker, or cane) or orthotics (brace) to facilitate mobility because of significant problems with the gait due to foot drop, leg weakness, or balance. In 8 (29.6%) patients, the need for assistive device started with critical illness, while 2 patients already used an assistive device before the critical illness. We found that the rates of neuromuscular morbidity gradually declined over time, suggesting propensity to improvement or recovery. Utilization of formal physical therapy services also declined over time. During the last 90 days preceding the follow-up, the ongoing motor deficit was documented in 3 (11.1%) patients, sensory neuropathy in 1 (3.7%) patient, and generalized weakness in 1 (3.7%) patient. At the time of follow-up, the most prescribed analgesics were gabapentinoids (29.6%), followed by NSAIDS (11.1%) and opioids (7.4%). (Table 2).

Conclusion: We found high rates of neuromuscular morbidity in survivors of COVID-19 critical illness. Neuromuscular morbidity was severe in at least one third of the patients who required various assistive devices to facilitate mobility after hospital discharge. Future studies are required to investigate potential

links between the observed neuromuscular sequelae and factors such as prolonged immobilization, deep sedation, use of neuromuscular blockade, and immune-inflammatory parameters, in order to improve the management and outcomes of patients with ARDS.

Patient characteristics	Value
Baseline characteristics	
Patients enrolled (April 2 - May 4, 2020), n	35
In-hospital mortality, n (%)	8 (22.9%)
Patients alive at the follow-up (October 15, 2021), n	27
Gender	
Men, n (%)	18 (66.7%)
Women, n (%)	9 (33.3%)
Age at the time of follow-up, years, median (IQR)	56 (52-67)
Hospital course (survivors)	
Duration of hospital stay, days, median (IQR)	35 (29-47)
Duration of mechanical ventilation, days, median (IQR)	22.1 (17-27.9)
Stroke, n (%)	2 (7.4%)
Received tracheostomy, n (%)	18 (66.7%)
Tracheostomy duration, days, median (IQR)	18 (13.8-33.8)
Days since decannulation, median (IQR)	522 (503.3-526.8)
Discharge characteristics	
Days since hospital discharge, median (IQR)	522 (516-527)
Initial discharge destination	
Home, n (%)	5 (18.5%)
Facility, n (%)	22 (81.5%)
Current residence	
Home, n (%)	25 (92.6%)
Facility, n (%)	2 (7.4%)

Neuromuscular morbidity	Value
Electrodiagnostic testing for weakness workup, n (%)	5 (18.5%)
Physical therapy	
Receiving PT during 90 days prior to follow-up, n (%)	2 (7.4%)
Receiving PT during 365 days prior to follow-up, n (%)	12 (44.4%)
Receiving PT at any point since hospital discharge	22 (81.5%)
Documentation of ongoing motor deficit	
90 days prior to follow-up, n (%)	3 (11.1%)
Upper extremity, n	0
Lower extremity, n	3
Bilateral	1
Unilateral	2
365 days prior to follow-up, n (%)	9 (33.3%)
Upper extremity, n	3
Lower extremity, n	8
Bilateral	4
Unilateral	5
Since hospital discharge, n (%)	12 (44.4%)
Upper extremity, n	4
Lower extremity, n	9
Bilateral	6
Unilateral	6
Documentation of ongoing sensory neuropathy	
90 days prior to follow-up, n (%)	1 (3.7%)
Upper extremity, n	0
Lower extremity, n	1
365 days prior to follow-up, n (%)	4 (14.8%)
Upper extremity, n	0
Lower extremity, n	4
Since hospital discharge, n (%)	6 (22.2%)
Upper extremity, n	2
Lower extremity, n	5
Documentation of ongoing post-COVID deconditioning	
During last 90 days, n (%)	1 (3.7%)
During last 365 days, n (%)	9 (33.3%)
Since hospital discharge, n (%)	18 (66.7%)
Utilization of assistive devices and orthotics during last 365 days, n (%)	
Brace, n (%)	1 (3.7%)
Cane, n (%)	2 (7.4%)
Walker, n (%)	4 (14.8%)
Wheelchair, n (%)	3 (11.1%)
Prescription of analgesic drugs at follow-up	
Gabapentinoids, n (%)	8 (29.6%)
NSAIDS, n (%)	3 (11.1%)
Opioids, n (%)	2 (7.4%)

Critical Care - 7 A Meta-analysis Comparing Colloid versus Crystalloid for Goal Directed Fluid Therapy in Major Abdominal Surgery

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Introduction: The main goal of fluid therapy during surgeries is to restore and maintain tissue fluid and electrolyte balance and central euvolemia, while avoiding excessive salt and water. This will facilitate tissue oxygen delivery without causing harm. Goal-directed fluid therapy (GDFT) is considered the gold standard of fluid therapy during surgeries. However, conflicting results were seen among the different studies on which fluid (colloid versus crystalloid) is better to be used in goal-directed fluid therapy (GDFT). This study is a Meta-analysis of previous literature, this will give updated summaries regarding this topic. In a clinical setting, identifying the advantages and disadvantages between the two will help clinicians weigh the benefits over the risks between the two choices. Furthermore, comparing the available literature will help in identifying special situations where colloids will be better used versus crystalloids, and vice versa. Presence of optimal IV fluid therapy improves perioperative outcomes. More so, in terms of developing evidence-based practice, the results of this study can be used as a reference for future researchers, as this Meta-analysis includes the most up-to-date literature associated with fluid of choice in GDFT.

Methods: A Meta-analysis was conducted which included randomized controlled studies that compared colloid versus crystalloid during intraoperative major abdominal surgery for goal directed fluid therapy. A search was performed in The Cochrane Library, MEDLINE, Pubmed, Clinicaltrial.gov, SCOPUS, Herdin, and Google scholar without language and publication date restrictions. The search strategy consisted of a combination of the following terms: 'colloids versus crystalloids'; 'abdominal surgery', and 'goal directed therapy'. Meta-analysis using pooled risk ratio to compare incidence of adverse events between colloid and crystalloid groups was done.

Results: Six randomized controlled trials with good methodologic quality were included in this Meta-analysis. Only two of the studies reported better patient outcomes associated with use of colloids as perioperative fluid of choice for goal directed fluid therapy. The rest of the studies reported no significant differences between colloid and crystalloid fluid therapies in terms of post-operative complications or adverse events. Pooled risk ratio also showed no significant difference in all adverse events assessed between the two groups (all p-values > 0.05).

Conclusion: Colloids in goal-directed fluid therapy protocol have no significant difference with crystalloid-based protocol in patients undergoing major abdominal surgeries with regards to the incidence of postoperative cardiac, respiratory, renal, gastrointestinal, infection, and coagulation complications.

References: Perioperative Fluid Therapy for Major Surgery [published correction appears in Anesthesiology. 132(2):405]. Anesthesiology. 2019;130(5):825-832. 2020 Perioperative Goal-Directed Fluid Therapy Is an Essential Element of an Enhanced Recovery Protocol? Anesth Analg. 122(5):1261-3. 2016

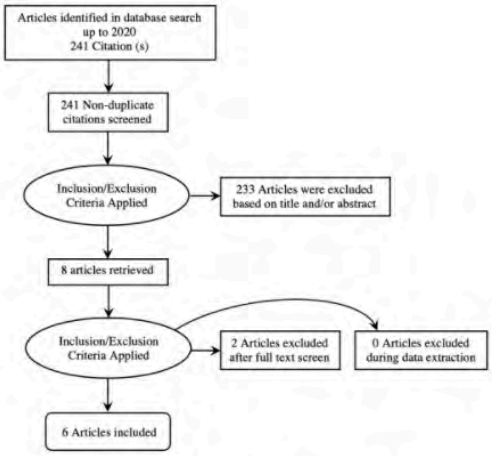

Figure 1. Flowchart of study selection

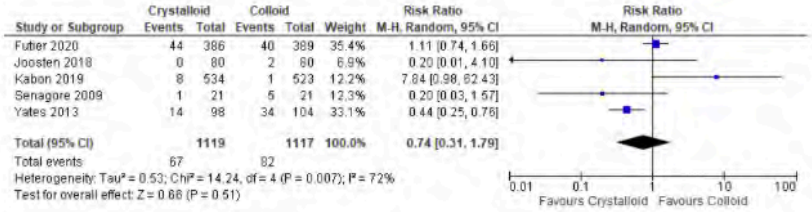

Figure 2. Cardiac related adverse outcomes

No significant difference in risk for respiratory related adverse outcomes was found between the two groups (RR=1.06, 95% CI=0.84-1.33, p-value=0.63).

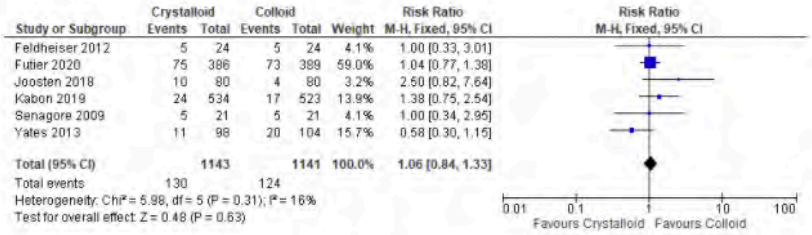

Figure 3. Respiratory related adverse outcomes

No significant difference in risk for renal related adverse outcomes was found between the two groups (RR=0.81, 95% CI=0.63-1.03, p-value=0.09).

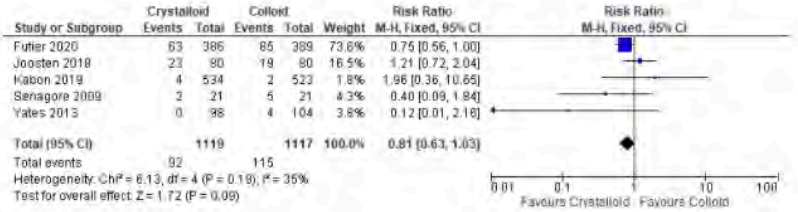

Figure 4. Renal related adverse outcomes

No significant difference in risk for gastrointestinal related adverse outcomes was found between the two groups (RR=0.97, 95% CI=0.52-1.81, p-value=0.92).

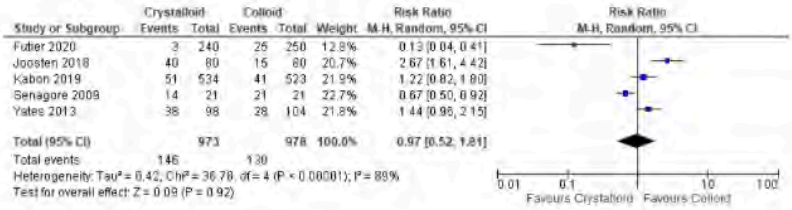

Figure 5. Gastrointestinal adverse outcomes

No significant difference in risk for infection related adverse outcomes was found between the two groups (RR=1.00, 95% CI=0.80-1.25, p-value=0.99).

Figure 6. Infection related adverse outcomes

No significant difference in risk for coagulation related adverse outcomes was found between the two groups (RR=0.81, 95% CI=0.47-1.39, p-value=0.45).

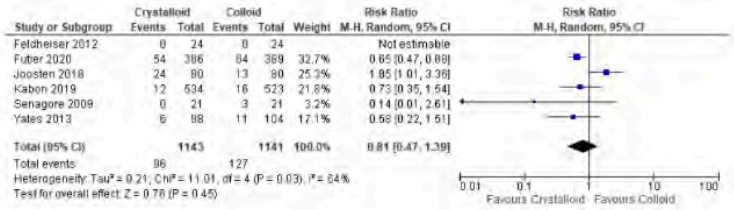

Figure 7. Coagulation related adverse outcomes

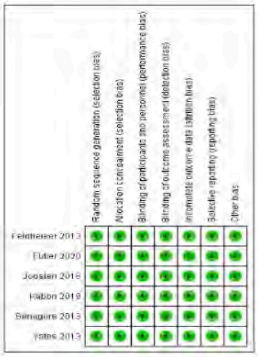

Figure 8. Risk of bias summary of included studies (Cochrane Risk of Bias Assessment Tool).

Table 1. Risk of bias table of included studies (Jadad Quality Assessment Scale).

Author, Year	Randomization	Concealment	Blinding	Withdrawal	Overall
Senagore, 2009	Appropriate	Appropriate	Appropriate	Described (minimal)	Good
Feldheiser, 2012	Appropriate	Appropriate	Appropriate	Described (minimal)	Good
Yates, 2013	Appropriate	Appropriate	Appropriate	Described (minimal)	Good
Joosten, 2018	Appropriate	Appropriate	Appropriate	Described (minimal)	Good
Kabon, 2019	Appropriate	Appropriate	Appropriate	Described (minimal)	Good
Futier, 2020	Appropriate	Appropriate	Appropriate	Described (minimal)	Good

Critical Care - 8 Pre-menopausal age in females is associated with protection from development of post-operative acute kidney injury, but not mortality following AKI

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[1]Department of Anesthesiology, Duke University Medical Center, Durham, NC, [2]Duke University Hospital, Durham, United States of America, [3]Duke University School of Medicine, Durham, NC, [4]Duke University, Durham, NC, [5]Duke Medical Center, Durham, NC, [6]Duke University Hospital, Durham, NC, [7]University of Michigan Medicine, Ann Arbor, MI, [8]University of Virginia, Charlottesville, VA

Introduction: Acute kidney injury (AKI) is one of the most common forms of perioperative organ injury. Preclinical and clinical studies examining the influence of sex on AKI have yielded conflicting results. The objective of our study was to determine the association of sex and age on the development of postoperative AKI; and mortality following AKI. We hypothesized that pre-menopausal-aged females would display lower incidence of postoperative AKI, and mortality following AKI, than males of similar age; and the protection would be lost in post-menopausal-aged females.

Methods: This was a retrospective observational study of the Multi-center Perioperative Outcomes Group database (MPOG). We reviewed surgical patients at 46 institutions between 2013-2019. Our primary exposure was between age younger or older than 50 years and sex. Our primary outcome was development of AKI by KDIGO criteria. A mixed effects multivariable logistic regression was used to determine the association of sex hormone status with postoperative AKI and mortality. Secondary analyses consisted of investigating the association of ascending age deciles over 40 years and postoperative AKI.

Results: After excluding patients with CKD5 and cardiac, transplant, urologic and obstetric procedures, among 390,382 patients undergoing index surgeries, 25809 (6.6%) developed postoperative AKI. In the adjusted model, the lowest risk of AKI was in women under 50 (OR 1.0), with higher risk in men under 50 (OR 1.90 [1.79, 2.01]; p<.0001), women over 50 (OR 1.51 [1.43, 1.59]; p<.0001), and men over 50 (OR 2.06 [1.96, 2.17]; p<.0001). In the secondary analysis, risk of AKI gradually increased in women as they aged, whereas men had very little change in risk based on age (Fig. 1). Of the 24,716 patients who developed postoperative AKI with known hospital mortality data, there was no clear pattern in mortality data, and mortality was broadly similar between men and women at each age group (Fig. 2).

Conclusion: Younger age in females is associated with a significantly lower risk of postoperative AKI; and the protective effect is gradually lost with ageing. A similar effect was not found for mortality after AKI. These results suggest that female sex hormones might protect against postoperative AKI.

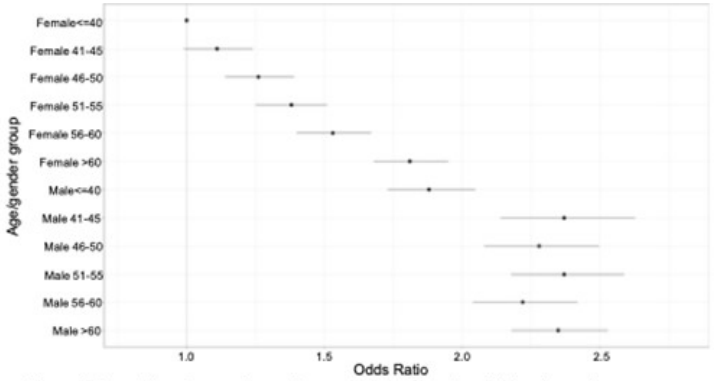

Figure 1: Association of sex and ascending age with post-operative AKI development.

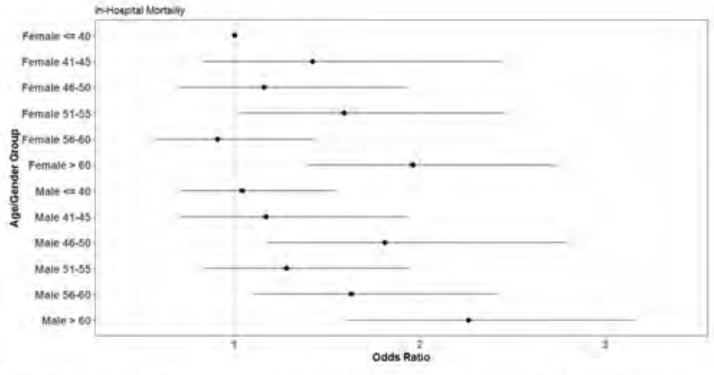

Figure 2: Odds ratio of in hospital mortality data among men and women of differing age groups

Critical Care - 9 Racial and Ethnic Differences in the Prevalence of Advanced Directives Among Geriatric Patients with Traumatic Brain Injury

Alex Girden[1], Krista L Haines[2], Megan Fah[3], Tetsu Ohnuma[3], Vijay Krishnamoorthy[3]

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Introduction: With improvements in health care, the older adult population continues to constitute a large portion of the population now accounting for approximately 30% of the US population1,2. As the aging population continues to grow so does the number of older adult traumas with trauma now ranking as the seventh leading cause of geriatric mortality.1 For patients aged 65-74, rate of hospitalization for traumatic brain injury (TBI) was 87.9 per 100,000 and for those >75 years of age, 104.6 per 100,000.2 Over the past decade, there has been an emphasis on the role of advanced directives (AD) to preserve patient wishes and avoid undesired care by health professionals.3 Despite this focus on advanced directives, the prevalence of ADs in the older adult population with TBI only ranges from 6-18%.4 In addition, the Institue of Medicine (IOM) Unequal Treatment report concluded that racial disparities are rampant in health care and are associated with worse outcomes in minorities.5 While recent studies have investigated the prevalence of ADs in this population, no studies have examined the association between race/ethnicity with the utilization of ADs. We hypothesize that the prevalence of advanced directives in older adult severe TBI will be low, and patients of minority race/ethnicity will have a lower prevalence of ADs, compared to White patients.

Methods: We conducted a retrospective cohort study using the National Trauma Databank (NTDB), which houses the largest collection of trauma data in the United States. We examined data from participating hospitals in the NTDB 2007-2016. We included geriatric patients (age > 65 years) with severe TBI, defined as admission Glasgow Coma Scale score (GCS) < 8. We excluded patients who were not admitted to the hospital or died within 24 hours of hospital admission. Our exposure of interest was race/ethnicity and outcome was the presence of an advanced directive on admission, defined as a documented Do Not Resuscitate (DNR) order. Multivariable logistic regression models, adjusting for demographic and clinical covariates, were used to examine the association between race/ethnicity and the presence of an advanced directive.

Results: Table 1 describes the demographic and clinical characteristics of the cohort. As we focused on severe TBI, no patient had a Glasgow coma scale >8 with a median GCS of 3 and mean of 3.4. Our patient population included 81% White patients, 6.3% Black patients, 8.5% Hispanic patients, 3.3 % Asian patients, and 3.0% other races. XX% of patients had an advanced directive at hospital admission. The most common mechanism of injury was via fall, with 59% of patients without advanced directives and 67.3% patients with an advance directive presenting after fall. The mean(SD) injury severity score was 22.7(10.6) in the no advanced directive group and 22.4(9.5) in the advanced directive group. Compared to White patients, Black patients (OR 0.48, 95% CI 0.35-0.64), Hispanic patients (OR 0.54, 95% CI 0.40-0.70), and Asian patients (OR 0.63, 95% CI 0.44-0.90) had a decreased odds of having an advanced directive at hospital admission (Table 2).

Conclusion: This analysis shows that disparities do exist with regard to ADs in older adults with TBI. Non-White older adult TBI patients have a lower prevalence of ADs compared to white patients of the same category. Prior research has illustrated that in general, minorities have higher rates of mortality due to chronic disease compared to non-minorities. In addition, minorities have been shown to have lower quality end of life and more intensive treatment than non-minorities. A multitude of factors contributes to the observed racial disparities including differences in quality of health care, ability to access health centers, difference in economic status, and implicit bias of care providers. 6,7 Further studies should examine whether these differences in advanced directives have effects on patient outcomes such as healthcare utilization, mortality, and quality of death.

References: 1. J Trauma Acute Care Surg. 2015;78(6):1197-1209. 2. Crit Care Med. 2008;36(1):282-290. 3. Int J Crit Illn Inj Sci. 2011;1(2):132-137. 4. Journal of Trauma and Acute Care Surgery: September 14, 2021. 5. Health Serv Res, 47: 1232-1254. 6. World J Emerg Surg 13, 40 (2018). 7. Journal of general internal medicine, 21(6), 667-669.

Table 1: Patient population

Category	No Advanced Directive	With Advanced Directive
Total Number	28,782	1,878
Gender	F: 11,153 (38.8%) M: 17,621 (61.2%)	F: 860 (46%) M: 1019 (54%)
Age (years)	Mean: 75.6, SD 7.16	Mean: 79.2, SD: 6.82
Glasgow Coma Scale	Mean: 4.24, SD 1.79	Mean: 4.64, SD: 1.90
Injury Severity Score	Mean: 22.72, SD: 10.59	Mean: 22.41, SD 9.46
Injury Mechanism (%)*	1: 20.79, 2. 59.05, 3: 1.66, 4:3.17, 5: 1.98, 6: 13.36	1: 20.11, 2: 59.55, 3: 1.64, 4: 3.05, 5: 1.90, 6: 13.75

*Key: 1=Motor vehicle trauma, 2=Fall, 3=Firearm, 4=cyclist,pedestrian accident, 5: struck by, against, 6=other

Table 2: Likelihood of having an advanced directive vs white patient's

Race	Odds Ratio	P > |z|	95% CI
White	Ref		
Black	0.48	<0.001	0.35-0.64
Hispanic	0.54	<0.001	0.40-0.74
Asian	0.63	0.01	0.44-0.90
Other	0.49	<0.001	0.33-0.74

Critical Care - 10 Role of megalin and sex in AKI-CKD transition due to cardiorenal syndrome type1

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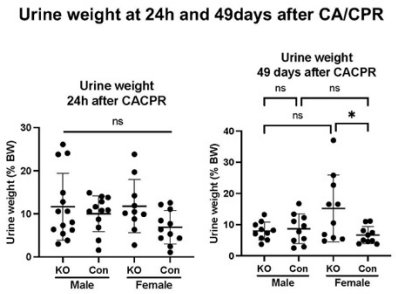
Introduction: Cardiorenal syndrome type 1 (CRS-1) is acute kidney injury (AKI) due to rapid worsening of cardiac function, and is a common perioperative complication. The megalin-mediated endocytic system is an important component of renal function which may influence AKI and which likely influences development of chronic kidney disease (CKD). Since CKD may be a long-term perioperative outcome, we tested whether megalin deletion affects the severity of CRS-1 and consequential CKD.

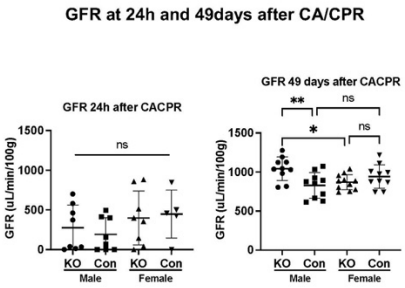
Methods: Male and female proximal tubule-specific inducible megalin deletion mice (iMegKO, LRP2 fl/fl NDRG1-CreERT2) and cre-negative littermate controls received tamoxifen (150 mg/kg) for 5 days, 16 days before cardiac arrest and cardiopulmonary resuscitation (CA/CPR). Urine was collected for 24h after CA/CPR and again 49 days after CA/CPR. Renal function was assessed as glomerular filtration rate (GFR; uL/min/100g body weight) at 24h and 49 days after CA/CPR. Briefly, fluorescein isothiocyanate (FITC)-sinistrin was injected retro-orbitally, then elimination of FITC-sinistrin fluorescence was subcutaneously monitored by using a fluorescence detector (MediBeacon). GFR was calculated from the half-time (t1/2). Significance was assessed by one-way ANOVA with Tukey test, or log-rank test.

Results: All animals had abnormally reduced GFR and oliguria 24h after CA/CPR. Resuscitation time and epinephrine dose were not different between groups. 49-day survival was not different among groups (p=0.66, n=12-14/group). Change in body weight was not different at 24h and 49 days after CA/CPR between groups. Body weight-corrected urine weight (urine weight (g)/body weight (g)x100 (%)) at 24 hours after CA/CPR was not different between iMegKO and cre-littermate control (p=0.17, n=10-14/group; KO male:11.7%, Cont male:10.0%, KO female:11.8%, Con female:6.9%). At 49 days after CA/CPR, urine weight was higher in iMegKO mice than in littermate control in female, but there was no difference in male (p=0.02, n=10/group; KO male: 8.0%, Cont male: 8.7%, KO female: 15.2%, Con female: 6.6%). 24h after CA/CPR, GFR was similar in iMegKO mice and controls (p=0.36, n=5-8/group; KO male: 275.1 uL/min/100gBW, Cont male: 192.0 uL/min/100gBW, KO female: 398.1 uL/min/100gBW, Con female: 446.9 uL/min/100gBW). 49 days after CA/CPR, however, GFR in iMegKO males was preserved compared with control male or iMegKO female (p=0.0001, n=10-11/group; KO male: 1043 uL/min/100gBW, Cont male :827.7 uL/min/100gBW, KO female: 869.1 uL/min/100gBW, Con female: 943.2 uL/min/100gBW).

Conclusion: Megalin deletion does not alter susceptibility to or resuscitation from cardiac arrest, survival, or CA/CPR-induced AKI (CRS-1) as indicated by GFR. Megalin deletion ameliorates long-term loss of GFR due to CRS-1 in males, but not in females. This tantalizing sex difference suggests sexually dimorphic mechanisms of AKI-CKD transition, and for the first time implicates this important transporter system in the development of CKD.

References: JASN. 2021;32(10):2579-2594, Nephron. 2020;144(12):629-633, JCI insight. 2019;4(4):e122130, Nat Rev Mol Cell Biol. 2002;3:258-267, Current Hypertension Report. 2020;22(30), J. Vis. Exp. 2018; (140), e58520


Urine weight at 24h and 49days after CA/CPR
Urine weight
24h after CACPR
Urine weight (% BW)
ns
KO Con KO Con
Male Female
Urine weight
49 days after CACPR
ns ns
ns *


GFR at 24h and 49days after CA/CPR
GFR 24h after CACPR
GFR (uL/min/100g)
ns
KO Con KO Con
Male Female
GFR 49 days after CACPR
** ns
* ns

Critical Care - 11 The Association of Discharge Medication Burden on Long-Term Outcomes Among Intensive Care Unit Survivors

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Introduction: Intensive care unit (ICU) survivors are at increased risk for inappropriate continuation of centrally acting medications. The Drug Burden Index (DBI) is a validated measure of exposure to these medications, with higher DBI associated with worsened cognitive impairment and mortality in non-hospitalized older adults. These associations have not yet been investigated among ICU survivors who also frequently exhibit cognitive impairment and subsequent mortality. We sought to investigate the independent association of centrally active medication burden at hospital discharge, measured by the DBI, on long-term cognitive function and 90-day mortality among ICU survivors.

Methods: We performed a cohort study of medical and surgical ICU survivors admitted with respiratory failure and/or septic shock previously enrolled in prospective investigations. Pre-admission and discharge medication lists were extracted retrospectively from electronic health records. DBI was calculated as the sum of each sedative and anticholinergic drug burden values. A score of 0 represents no exposure, <1 represents low exposure, and >1 represents high exposure. Cognitive impairment was assessed 3 to 6 months following hospital discharge using validated batteries and defined as ≥2 standard deviations (SDs) in 1 cognitive test or ≥1.5 SDs in any 2 cognitive tests. Only patients with at least one follow-up cognitive test completed were included in cognitive impairment analysis. 90-day mortality was obtained by chart review and/or surrogate contact. Multivariable proportional odds logistic regression was used to investigate the independent association of discharge DBI on cognitive impairment, adjusting for pre-specified covariates. Cox proportional hazards regression was used to investigate 90-day mortality, adjusting for the same pre-specified covariates.

Results: A total of 676 patients, including 478 with follow-up cognitive assessment, were included in our cohort with a median age 57.6 (47.8-66.6) years, median ICU stay of 4.9 (2.6-10.1) days, and median discharge DBI of 3.1 (2.0-4.3) (Table 1). Overall prevalence of long-term cognitive impairment was 56.1%, and 90-day mortality was 13.6%. We did not find a statistically significant overall association between hospital discharge DBI and long-term cognitive impairment (p=0.19). We found, however, an approximate 20% increased probability of cognitive impairment when hospital discharge DBI increased from 0 to 4 as shown in Figure 1a. We found no statistically significant association between discharge DBI and 90-day mortality (p=0.56), as shown in Figure 1b.

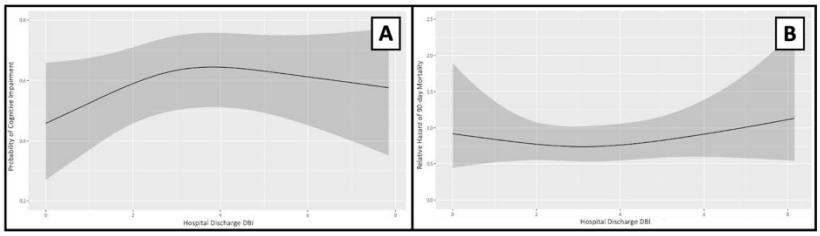
Conclusion: We found a high burden of centrally active medications prescribed at discharge in ICU survivors. This burden, as measured by DBI, was not significantly associated with long-term cognitive impairment or 90-day mortality among ICU survivors. There was a potential relationship between discharge DBI and cognitive impairment up to DBI score of 4. Investigation into the differential impact of drug burden on cognitive impairment may identify patients with modifiable medication regimens who could benefit from medication optimization.

Table 1: Baseline Patient Characteristics

Baseline Characteristic	Study Cohort (n=676)
Age (years)	57.6 [47.8-66.6]
Sex (males)	362 (53.6%)
Race (white)	598 (88.5%)
Education (high school or less)	396 (58.6%)
Body Mass Index (BMI)	29.7 [24.8-36.8]
Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)	3.0 [3.0-3.2]
Charlson Comorbidity Index	2 [1-4]
Sepsis (yes)	183 (27.1%)
Acute Brain Dysfunction Duration (days)	3 [1-7]
Total Mechanical Ventilation (days)	2.2 [0.9-6.1]
Total ICU stay (days)	4.9 [2.6-10.1]
Hospital Discharge DBI	3.1 [2.0-4.3]

Variables are presented as median [interquartile range] or count (%), as appropriate.

Figure 1: Analysis of Hospital Discharge DBI on Probability of Cognitive Impairment and Hazard of 90-Day Mortality



Critical Care - 12 Assessment of Bedside Physiologic Parameters as a Predictive Tool for Unplanned Surgical Intensive Care Unit Admission

Dhruv Choudhry[1], Annandita Kumar[1], Shaun Yockelson[1], John-Paul Sara[1], Adrian Alexis-Ruiz[1], Brian Strollo[1], Jeffanne Millien[1], Conor Coogan[1], Jonathan Babin[1], Bobby D Nossaman[1]

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Introduction: The Modified Early Warning Score (MEWS) had been proposed to warn healthcare providers of adverse events, but subsequent studies were unable to show the benefits of this scoring system (5). The possibility exists that the components for MEWS were not properly vetted for inclusion into this early warning system (6). We evaluated all measured bedside vital signs including those used in MEWS during bedside evaluation for unplanned escalation of care as predictors for hospital mortality.

Methods: Following IRB approval, 495 consecutive unplanned admissions into a surgical intensive care unit over one year were entered into this study. Patient characteristics and vital signs measured during bedside evaluation for unplanned escalation of care were extracted from electronic medical records. A logistic regression model was developed to analyze the interactions of these bedside measurements with future hospital mortality. Diagnostic accuracies of the logistic models were analyzed with misclassification rates calculated with 95% confidence intervals (CI) (6). Lack-of Fit-test (Goodness-of Fit-test) was utilized to determine whether the multivariate analysis model contained enough information (degrees of freedom) for prediction of future hospital mortality or whether more factors and/or complex terms were needed (6). P values for associated frequentist tests were set at <0.005 for statistical significance to minimize false discovery rates (6).

Results: In this series of 495 consecutive patients, the incidence of hospital mortality following unplanned escalation of care was 32.9% CI 28.9-37.2%. The associations of individual vital sign measurements to the incidence of hospital mortality are shown in Figure 1. When vital sign measurements are grouped by prognosis (Fig. 2), no discernable difference is observed. A logistic regression model was developed to assess the interactions of these vital sign measurements to hospital mortality obtained with the results of that model shown in Table 1. The association of vital signs under these conditions to hospital mortality was not statistically significant (Table 1A; P=0.0306). In contrast, the Lack-of-Fit Chi-Squared statistic (Table 1B) was significant suggesting the model needs more factors and/or complex terms. A misclassification rate of 29.5% CI 25.8%-34.4% (Table 1A) was observed with this association.

Conclusion: Vital signs obtained at the time of bedside assessment for unplanned escalation of care provided no statistical predictive risk for future hospital mortality. The high misclassification rates indicate these measurements under these conditions do not provide the discriminatory support needed to identify patients at risk for hospital mortality. The results in the Lack-of Fit-test suggest more factors and/or complex terms are needed in this predictive model.

References: 1. A prospective controlled trial of the effect of a multi-faceted intervention on early recognition and intervention in deteriorating hospital patients. Resuscitation. Jun 2010;81(6):658-66. 2. The effect of implementing a modified early warning scoring (MEWS) system on the adequacy of vital sign documentation. Aust Crit Care. Feb 2013;26(1):18-22. 3. Identification of deteriorating patients on general wards; measurement of vital parameters and potential effectiveness of the Modified Early Warning Score. J Crit Care. Aug 2012;27(4) 4. An early warning scoring system for detecting developing critical illness. Clin Intensive Care. 1997;8(2):S100. 5. The Modified Early Warning Score as a Predictive Tool During Unplanned Surgical Intensive Care Unit Admission. Ochsner J. Summer 2020;20(2):176-181. 6. Why the C-statistic is not informative to evaluate early warning scores and what metrics to use. Crit Care. Aug 13 2015;19:285.

Figure 1

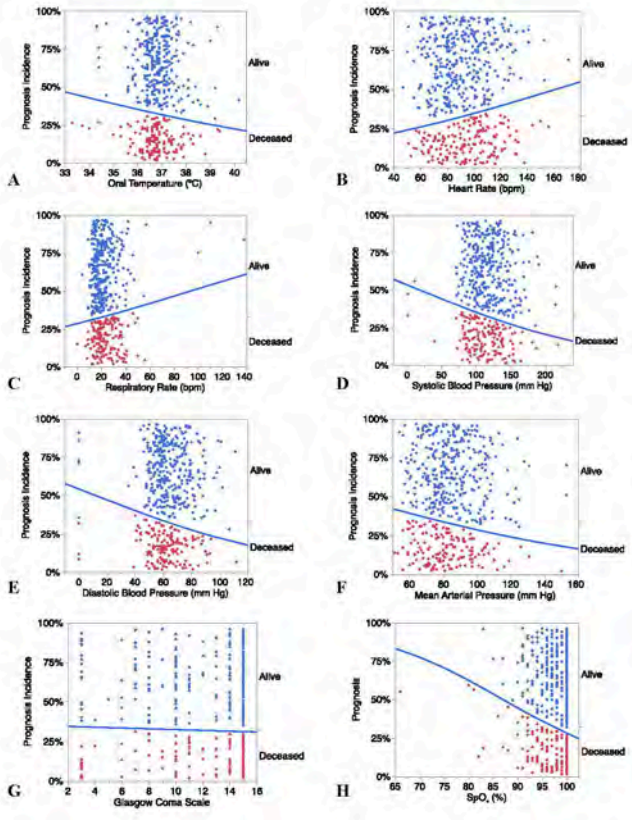

Figure 2

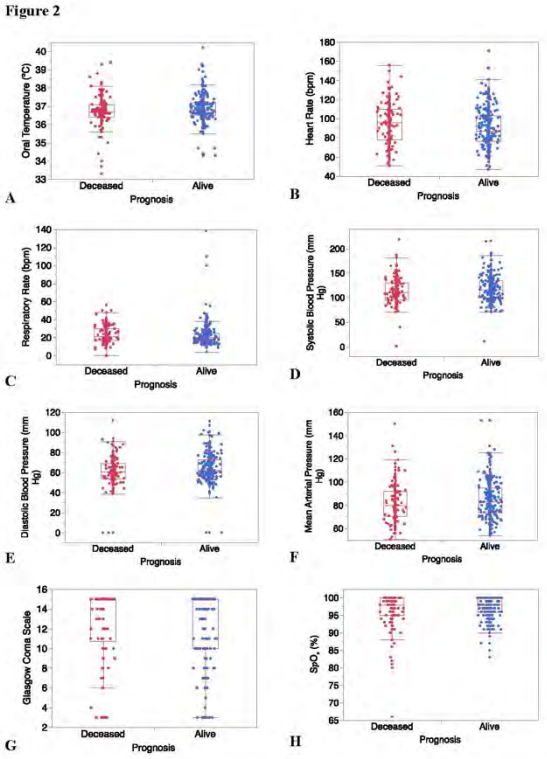

Figure Legends

Figure 1 Logistic fit graphs of hospital mortality to vital sign measurements obtained in 495 surgical patients undergoing bedside evaluation for unplanned escalation of care. The blue lines indicate the incidence of mortality. Red dots identify decreased patients. Blue dots identify alive patients. **A**: Oral Temperature, ChiSquare=1.5, P=0.2212, Misclassification Rate=0.32; **B**: Heart Rate, ChiSquare=4.9, P=0.0268, Misclassification Rate=0.33; **C**: Respiratory Rate, ChiSquare=1.4, P=0.2365, Misclassification Rate=0.34; **D**: Systolic Blood Pressure, ChiSquare=4.1, P=0.0425, Misclassification Rate=0.32; **E**: Diastolic Blood Pressure, ChiSquare=4.7, P=0.0304, Misclassification Rate 0.33; **F**: Mean Arterial Pressure, ChiSquare=3.7, P=0.0557, Misclassification Rate=0.33; **G**: Glasgow Coma Score; ChiSquare=0.18, P=0.6696, Misclassification Rate=0.32; **H**: SpO_2, ChiSquare=7.6, P=0.0057, Misclassification Rate=0.32. P values <.005 are statistically significant.[13]

Figure 2 Boxplots of vital signs grouped by prognosis in 495 surgical patients undergoing bedside evaluation for unplanned escalation of care. **A**: Oral Temperature, ChiSquare=1.9, P=0.1662; **B**: Heart Rate, ChiSquare=5.8, P=0.0165; **C**: Respiratory Rate, ChiSquare=5.4, P=0.0201; **D**: Systolic Blood Pressure, ChiSquare=3.6, P=0.0566; **E**: Diastolic Blood Pressure, ChiSquare=4.3, P=0.0381; **F**: Mean Arterial Pressure, ChiSquare=4.1, P=0.0427; **G**: Glasgow Coma Score; ChiSquare=0.22, P=0.6421; **H**: SpO_2, ChiSquare=4.0, P=0.0467. P values <.005 are statistically significant.[13]

Table 1: Nominal Logistic Regression Model for Hospital Mortality by Vital Signs Measurements during Unplanned Escalation of Care in 495 Surgical Patients

A

Terms	Estimate	95%CI	Std Error	ChiSquare	Prob>ChiSq
Intercept	-11.5	-22.6 to -0.86	5.5	4.7	0.0369
Oral Temperature	-0.16	-0.12 to 0.44	0.14	1.2	0.2703
Heart Rate	0.007	-0.08 to 0.003	0.005	1.9	0.1645
Respiratory Rate	0.005	-0.22 to 0.14	0.009	0.3	0.5914
Systolic Blood Pressure	-0.003	-0.011 to 0.018	0.008	0.2	0.6511
Diastolic Blood Pressure	-0.02	-0.009 to 0.056	0.016	1.7	0.1880
Mean Arterial Pressure	0.005	-0.044 to 0.030	0.019	0.1	0.7694
Glasgow Coma Scale	-0.0002	-0.058 to 0.057	0.029	0.0	0.9957
SpO_2	-0.06	-0.007 to 0.11	0.028	4.9	0.0277

SpO_2: Pulse oximetry; 95%CI: 95% Confidence interval; ChiSquare: Chi-Square statistic; Prob>ChiSq: Probability that the Chi-Square statistic is due to chance; Whole model ChiSquare statistic of 17.0 with 8 degrees of freedom and an associated P-value of 0.0306; Misclassification rate: 29.5% CI 25.8%-34.4%. P values <.005 are statistically significant.[13]

B

Lack-of-Fit (Goodness-of-Fit) test

Source	DF	-LogLikelihood	ChiSquare
Lack Of Fit	435	275.5	551.1
Saturated	443	0.0	**Prob>ChiSq**
Fitted	8	275.5	0.0001

DF = degrees of freedom; -LogLikelihood; computed by taking twice the difference in negative log-likelihoods between the Fitted model and the Saturated model; ChiSquare: formed by twice the difference in the log-likelihoods due to the hypothesis. Probability > ChiSq: the probability that the P-value is greater than the ChiSquare statistic.

Critical Care - 13 Plasma extracellular microRNA profiling and their potential role in innate immunity and sepsis

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[1]University of Maryland School of Medicine, Baltimore, United States of America, [2]Massachusetts General Hospital, Charlestown, MA, [3]The University of Texas MD Anderson Cancer Center, Houston, United States of America, [4]University of Maryland at College Park, College Park, United States of America

Introduction: Sepsis is a critical condition induced by a dysregulated host immune response to infection. The pattern recognition receptors such as Toll-like receptors (TLRs) are an essential part of the innate immunity and recognize pathogen-associated molecular patterns (PAMPs), e.g., endotoxin and viral nucleic acids. While these PAMPs are well known for their roles in triggering host immune response, the contribution of endogenous danger-associated molecules, such as host RNAs and DNAs, in body's innate immune response and in sepsis pathogenesis remains poorly understood. In this study, using small RNA sequencing, we profiled plasma extracellular (ex) miRNAs in mice and humans. We identified miR-146a-5p as one of the most abundant plasma miRNAs in both septic mice and humans. We discovered the underlying molecular mechanism by which miR-146a-5p activates TLR7 and modulate cellular IRAK-1 expression, a kinase critical for innate immune signaling. Finally, we tested the contributory role of miR-146a-5p in the pathogenesis of murine sepsis and its association with clinical manifestations of septic patients.

Methods: All human and animal studies were approved by the IRB and IACUC, respectively. C57BL/6J mice were subjected to CLP (cecum ligation and puncture), or sham (laparotomy). Plasma RNAs were isolated using Trizol and profiled by small RNAseq. Cytokines were assayed by ELISA. Innate immune cells were analyzed by flow cytometry. Transthoracic echocardiography was performed in non-anesthetized mice to assess cardiac function.

Results: Using small RNA sequencing, we identify that miRNAs are the most abundant RNA species in the plasma and differentially expressed in murine and human sepsis, such as miR-146a-5p. Exogenous miR-146a-5p, but not its double-stranded duplex precursor, induces a strong immunostimulatory response through a newly identified UU-containing nucleotide motif and TLR7 activation, and an immunotolerance by rapid IRAK-1 protein degradation via TLR7,ÜíMyD88 signaling and proteasome activation, whereas its duplex precursor acts by targeting 3' UTR of Irak-1 gene via Ago2 binding. miR-146a knockout in mice offers protection against sepsis with attenuated IL-6 storm and organ injury, improved cardiac function, and better survival. In septic patients, the plasma miR-146a-5p concentrations are closely associated with the two sepsis outcome predictors, blood lactate and coagulopathy.

Conclusion: This study demonstrates that 1) miRNAs are the predominant RNA biotype in the plasma and markedly altered in sepsis, 2) ex miR-146a-5p stimulates innate immune response via a UU-motif and TLR7 activation, 3) ex miR-146a-5p downregulates IRAK-1 protein through TLR7 and proteasome activation, and 4) Plasma miR-146a-5p is associated with sepsis predictors and plays a role in sepsis. Thus, our study establishes the important role of extracellular miR-146a-5p in innate immune regulation and sepsis pathogenesis.

Critical Care - 14 Long term renal outcome of patients requiring de novo renal replacement therapy after cardiac surgery

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Introduction: Outcomes after cardiac surgery are generally good but occasionally patients may acquire organ failure and specifically acute kidney injury (AKI) due to hemodynamic instability, hypoperfusion and high vasopressor requirements. While the incidence of AKI is up to 30% after cardiac surgery, only a few patients will require (continuous) renal replacement therapy (CRRT) if they had no end-stage renal disease (ESRD) requiring dialysis prior to surgery. Twenty-four % of medically critical ill patients with AKI who require CRRT and survive critical illness will chronically need dialysis[1]. We do not know however if this statistic holds true for patients who require de novo CRRT after cardiac surgery.

Methods: We retrospectively studied all patients who underwent cardiac surgery at an academic medical center in 2011. We identified patients who required CRRT postoperatively and assessed if they had pre-existing ESRD or if this was their first episode of RRT. Chronic dialysis dependence was defined as patients who continued to require RRT 90 days and one year after surgery. Dialysis-free survival was plotted using Kaplan-Meier curve.

Results: All 1551 patients who underwent cardiac surgery at an academic medical center in 2011 were included in this study. As previously reported [2] 449 patients developed AKI defined by Kidney Disease: Improving Global Outcomes (KDIGO) criteria. 20 patients (1.28%) required CRRT perioperatively. 15 of these (75%) had pre-existing chronic kidney disease. Two of the 20 patients required CRRT before surgery, four immediately after surgery and 12 within 1 to 15 days after surgery. Six patients required CRRT for less than a week, four less than two weeks and three less than 90 days. Of the remaining seven patients, four patients required RRT for less than a year (three of these died 18 +/- 1 days after surgery) and three required long-term RRT. The figure depicts the liberation from RRT during the first year.

Conclusion: Seven of 20 patients who required CRRT after cardiac surgery continued to require RRT after 90 days. One of them was liberated from RRT and the remaining either died or continued to require RRT after one year. This data will help us provide necessary information to families who frequently must make the difficult decision if starting CRRT will help provide good long-term outcomes despite severe multi-organ failure and critical illness.

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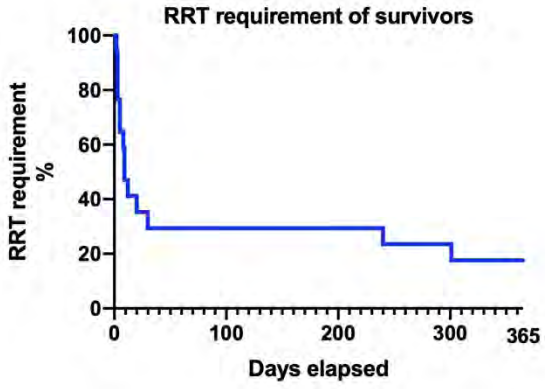


Critical Care - 15 Cardiovascular Phenotypes of 196 Perioperative Hypotensive Patients using the Echocardiographic Assessment using Subxiphoid onlY (EASY) Exam

Benjamin Hoenig[1], Michelle Burmistrova[1], David King[1], Rhagav Narravula[1], Ariana Adamski[2], Cheshta Prasad[1], Ashar Ata[2], Khrystyna Korostil[1], Tejas Kollu[1], Priya Uppal[1], Aliaksei Pustavoitau[3], Nibras Bughrara[2]

[1]Albany Medical Center, Albany, NY, [2]Albany Medical College, Albany, NY, [3]Johns Hopkins University, Baltimore, MD

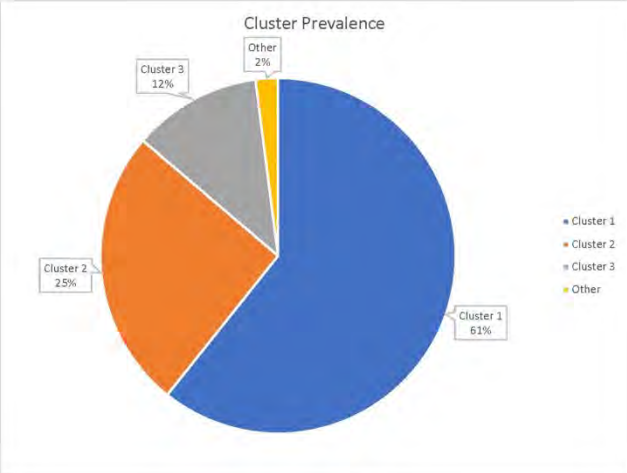
Introduction: Focused Critical Care Echocardiography (FCCE) can aid in diagnosing undifferentiated shock.1-4 Organization of cardiovascular presentation on ultrasound into clusters allows for rapid selection of hemodynamic support.1-2 We implemented a standardized curriculum to use the Echocardiographic Assessment using Subxiphoid OnlY (EASY) exam to initially evaluate patients in shock in lieu of a more comprehensive FCCE exam. The EASY exam is based on pattern recognition of 7 proposed phenotypes grouped into 3 clusters based on similar management using a single subcostal four chamber view of the heart and IVC.1 Cluster 1 is normal to hyperdynamic ventricular function, cluster 2 is LV systolic dysfunction, and cluster 3 is isolated RV dysfunction. The goal of this study is to determine the prevalence of these phenotypes in patients with hypotension and to determine their outcome.

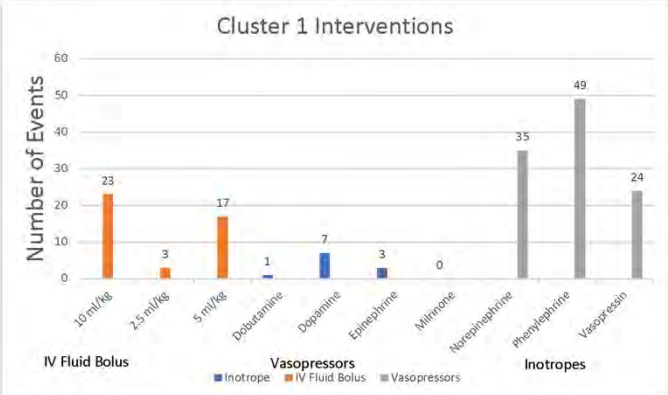
Methods: We reviewed EASY exams performed by trained anesthesia residents on perioperative patients in the POCU, PACU, ICU, and OR from August 2017 to June 2021. 196 patients who received a consult due to diagnosis of arterial hypotension (MAP < 65) are included here for analysis.

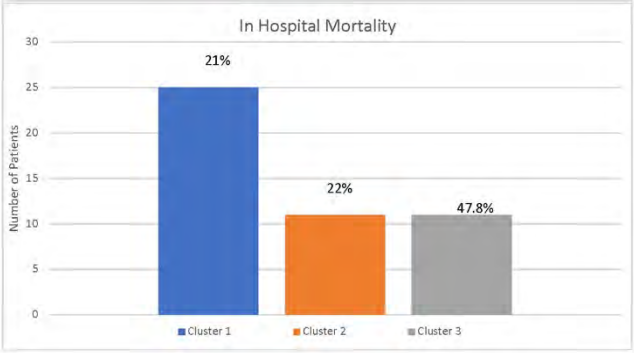
Results: In our cohort, 55% were male and mean age was 64. Prevalence for clusters 1-3 respectively, was 61%, 26%, and 12%. 2 patients had pericardial tamponade. For clusters 1-3, respectively: mean ICU LOS was 13.2 days, 13.8 days, and 9.5 days. ICU mortality was 19.3%, 20%, and 47.8%. The most common 2 interventions in each cluster 1-3 respectively, were: IV fluid boluses given 43 times to 119 patients and phenylephrine (49 (41.2%) patients); norepinephrine (26 (52%) patients) and phenylephrine (15 (30%) patients); norepinephrine (17 (74%) patients) and vasopressin (11 (47.8%) patients); Across all clusters, 69 patients had a diagnosis of sepsis. Across all clusters, the EASY exam duration was 4.7 minutes and interpretable images were obtained in 166 (84.6%) patients. Imaging changed patient management in 113 (57.6%) cases.

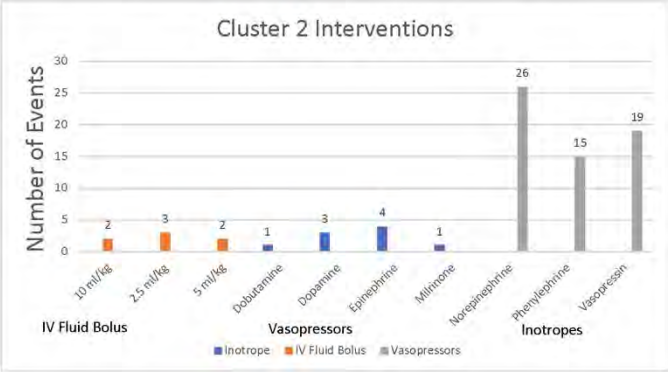
Conclusion: The EASY exam is a novel approach to evaluating hemodynamic status using a subcostal only view of the heart. Trained physicians obtained interpretable images and assigned a phenotype which guided patient management in most of our cohort. The EASY exam and 7 proposed phenotypes show potential for streamlining care for patients with complex pathology and warrants further investigation and multidisciplinary validation.

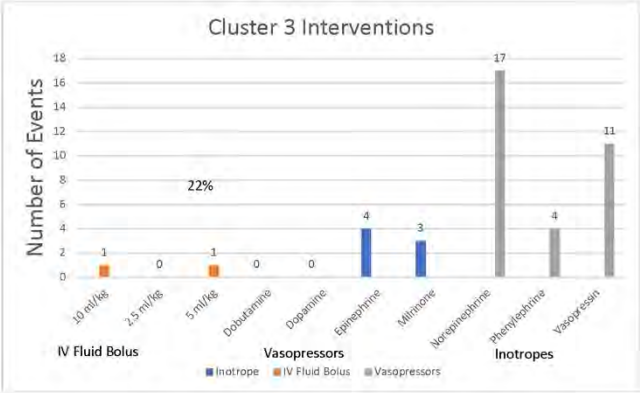
References: 1. Bughrara, N., et al. (2020). 'Perioperative Management of Patients with Sepsis and Septic Shock, Part II: Ultrasound Support for Resuscitation.' Anesthesiol Clin 38(1): 123-134 2. Nikravan, S., et al. (2020). 'Focused ultrasonography for septic shock resuscitation.' Curr Opin Crit Care 26(3): 296-302. 3. Heiberg, J., et al. (2016). 'Focused echocardiography: a systematic review of diagnostic and clinical decision-making in anaesthesia and critical care.' Anaesthesia 71(9): 1091-1100. 4. Oren-Grinberg, A., et al. (2013). 'Focused critical care echocardiography.' Crit Care Med 41(11): 2618-2626


Cluster Prevalence
Other 2%
Cluster 3 12%
Cluster 2 25%
Cluster 1 61%
Cluster 1
Cluster 2
Cluster 3
Other


Cluster 1 Interventions
Number of Events
10 ml/kg
2.5 ml/kg
5 ml/kg
Dobutamine
Dopamine
Epinephrine
Milrinone
Norepinephrine
Phenylephrine
Vasopressin
IV Fluid Bolus
Vasopressors
Inotropes
Inotrope
IV Fluid Bolus
Vasopressors


In Hospital Mortality
Number of Patients
21%
22%
47.8%
Cluster 1
Cluster 2
Cluster 3


Cluster 2 Interventions
Number of Events
10 ml/kg
2.5 ml/kg
5 ml/kg
Dobutamine
Dopamine
Epinephrine
Milrinone
Norepinephrine
Phenylephrine
Vasopressin
IV Fluid Bolus
Vasopressors
Inotropes
Inotrope
IV Fluid Bolus
Vasopressors


Cluster 3 Interventions
Number of Events
22%
10 ml/kg
2.5 ml/kg
5 ml/kg
Dobutamine
Dopamine
Epinephrine
Milrinone
Norepinephrine
Phenylephrine
Vasopressin
IV Fluid Bolus
Vasopressors
Inotropes
Inotrope
IV Fluid Bolus
Vasopressors

Critical Care - 16 Proteomic analysis of murine heart mitochondria during sepsis

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Introduction: Sepsis-induced cardiomyopathy (SIC) is a major contributing factor for morbidity and mortality in sepsis. Accumulative evidence has suggested that cardiac mitochondrial oxidative phosphorylation is attenuated in sepsis, but the underlying molecular mechanisms remain incompletely understood.

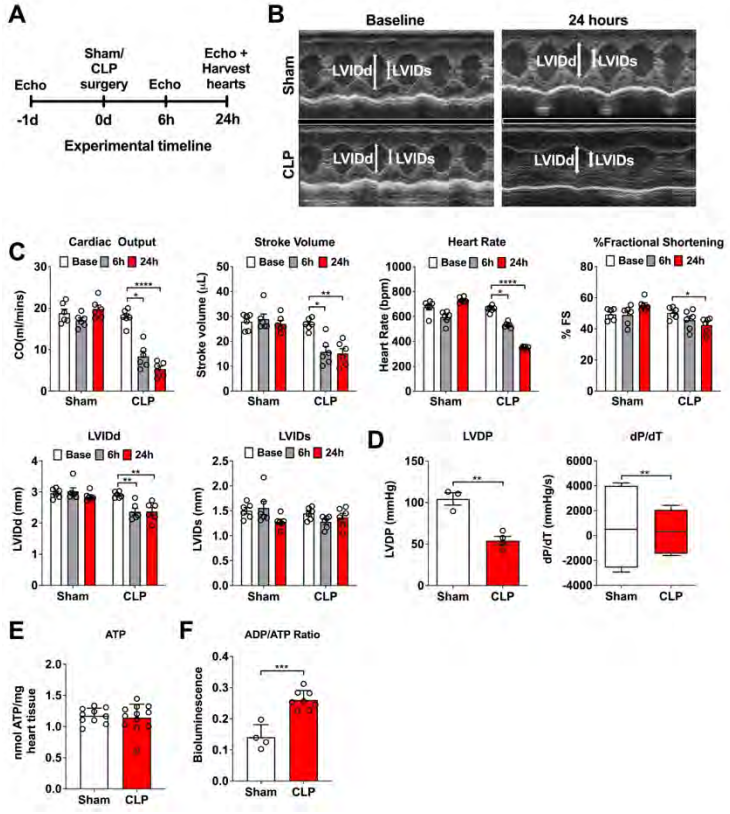
Methods: Adult male mice of 9 to 12 weeks old were subjected to sham or cecal ligation and puncture procedure. Echocardiography in vivo and Langendorff perfused hearts were used to assess cardiac function 24 h after the procedures (Figure 1). Unbiased proteomics analysis was performed to profile mitochondrial proteins in the hearts of both sham and SIC mice.

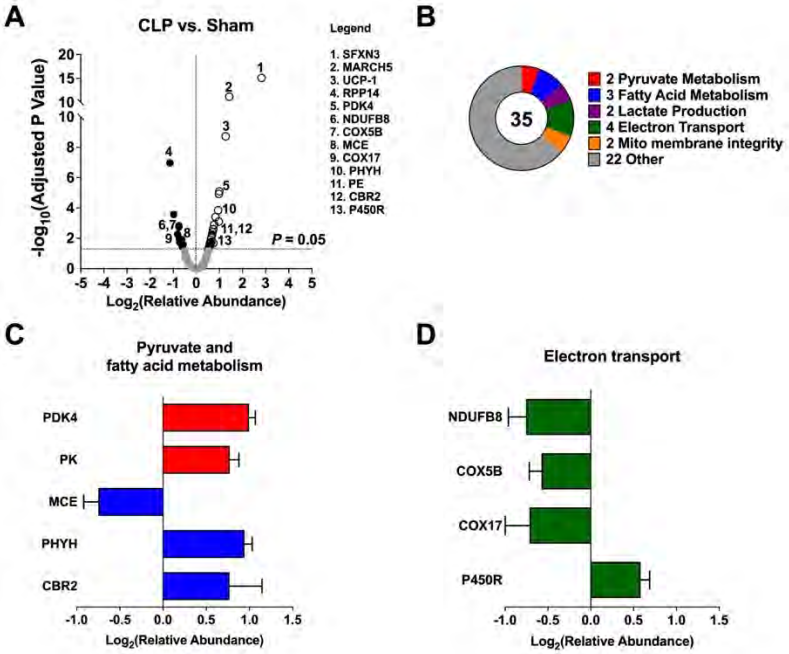
Results: Of the 665 mitochondrial proteins identified in the proteomics assay, 35 were altered in septic mice (Table 1). The mitochondrial remodeling involved various energy metabolism pathways including subunits of the electron transport chain, fatty acid catabolism, and carbohydrate oxidative metabolism (Figure 2). Some of the notable proteins involved in the electron transport chain include NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 8 (NDUFB8), a subunit of complex I, cytochrome C oxidase subunit 5B (COX5B) and cytochrome C oxidase copper chaperone 17 (COX17), two subunits of complex IV, and NADPH-cytochrome P450 reductase (P450R), an enzyme that is required for electron transfer from NADPH to cytochrome P450. Interesting fatty acid catabolism proteins included methylmalonyl-CoA epimerase (MCE) involved in odd chain-length fatty acid catabolism, phytanol-CoA 2-hydroxylase (PHYH), important for alpha-oxidation of 3-methyl branched fatty acids, and carbonyl reductase [NADPH] 2 (CBR2), involved in carbonyl metabolism from aldehydes and ketones derived from lipid peroxidation. There were also two proteins involved in pyruvate metabolism, pyruvate kinase (PK), and pyruvate dehydrogenase kinase 4 (PDK4), a kinase that plays a key role in the regulation of pyruvate and fatty acid metabolism through reversible inactivation of pyruvate dehydrogenase (PDH) via phosphorylation of the subunits PDHA1 and PDHA2, and is the major isoform in the heart. Consistent with the notable increase in PDK4 expression via proteomics, we also identified a significant increase of pyruvate dehydrogenase (PDH) kinase 4 (PDK4) and inhibition of PDH activity in septic hearts (Figure 3).

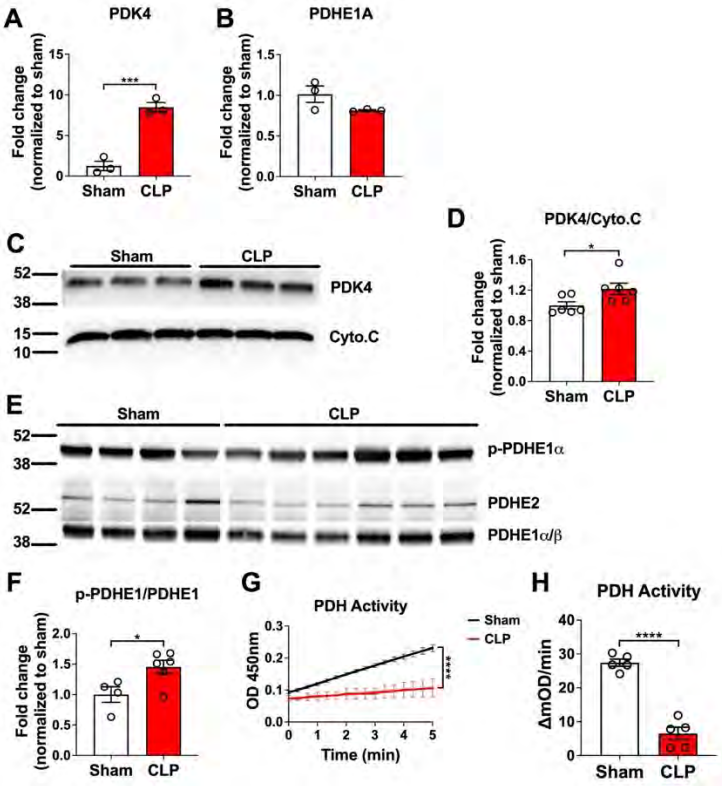
Conclusion: These data demonstrate a broad mitochondrial protein remodeling, PDH inactivation, and provide a molecular framework for further exploration.

Table 1. Proteomics analysis of cardiac mitochondrial proteins: 35 differentially expressed proteins between sham and CLP mice.

#		*Accession*	*Gene Name*	*Abundance Ratio (CLP/sham)*
	Pyruvate Metabolism			
1	Pyruvate kinase	P52480	PKM	1.706
2	Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 4	O70571	PDK4	1.993
	Fatty Acid Metabolism			
3	Methylmalonyl-CoA epimerase	Q9D1I5	MCEE	0.595
4	Carbonyl reductase [NADPH] 2	P08074	CBR2	1.704
5	Phytanoyl-CoA dioxygenase, peroxisomal	O35386	PHYH	1.921
	Lactate Production			
6	L-lactate dehydrogenase B chain	P16125	LDHB	1.481
7	L-lactate dehydrogenase	A0A1B0GSX0	LDHA	1.668
	Electron Transport			
8	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 8, mitochondrial	Q9D6J5	NDUFB8	0.592
9	Cytochrome c oxidase subunit 5B	Q9D881	GM11273	0.671
10	Cytochrome c oxidase copper chaperone	P56394	COX17	0.609
11	NADPH--cytochrome P450 reductase	P37040	P450R	1.497
	Mito Membrane Integrity			
12	MICOS complex subunit MIC10	Q7TNS2	MINOS1	0.508
13	E3 ubiquitin-protein ligase MARCH5	Q3KNM2	MARCH5	2.685
	Other			
14	Glyceraldehyde-3-phosphate dehydrogenase	A0A0A0MQF6	GAPDH	1.660
15	Cathepsin D	P18242	CTSD	1.607
16	Mitochondrial brown fat uncoupling protein 1	P12242	UCP-1	2.410
17	Phosphate carrier protein	Q8VEM8	SLC25A3	1.575
18	Cathepsin B	P10605	CTSB	1.777
19	Sideroflexin-3	Q91V61	SFXN3	7.061
20	Keratin, type II cytoskeletal 5	Q922U2	KRT5	2.413
21	B-cell receptor-associated protein 31	Q61335	BCAP31	1.631
22	39S ribosomal protein L15	Q9CPR5	MRPL15	1.571
23	Transforming protein RhoA	Q9QUI0	RHOA	1.964
24	Transport and Golgi organization 2 homolog	P54797	TANGO2	1.514
25	Fructose-bisphosphate aldolase	A6ZI44	ALDOA	1.549
26	Tripeptidyl-peptidase 1	O89023	TPP1	1.457
27	Mitochondrial thiamine pyrophosphate carrier	Q9DAM5	SLC25A19	0.645
28	Solute carrier family 35 member F6	Q8VE96	SLC35F6	1.577
29	Ribonuclease P 14 subunit (Human)	J3QMX0	RPP14	0.453
30	Coiled-coil domain-containing protein 58	Q8R3Q6	CCDC58	1.907
31	Haloacid dehalogenase-like hydrolase domain-containing protein 3	Q9CYW4	HDHD3	0.602
32	tRNA methyltransferase 10 homolog C	Q3UFY8	TRMT10C	1.503
33	Deaminated glutathione amidase	Q8VDK1	NIT1	0.571
34	LETM1 domain-containing protein 1	Q924L1	LETMD1	0.656
35	Aurora kinase A-interacting protein	Q9DCJ7	AURKAIP1	1.610




A
CLP vs. Sham
Legend
1. SFXN3
2. MARCH5
3. UCP-1
4. RPP14
5. PDK4
6. NDUFB8
7. COX5B
8. MCE
9. COX17
10. PHYH
11. PE
12. CBR2
13. P450R
-log10(Adjusted P Value)
Log2(Relative Abundance)
P = 0.05
B
35
2 Pyruvate Metabolism
3 Fatty Acid Metabolism
2 Lactate Production
4 Electron Transport
2 Mito membrane integrity
22 Other
C
Pyruvate and fatty acid metabolism
PDK4
PK
MCE
PHYH
CBR2
Log2(Relative Abundance)
D
Electron transport
NDUFB8
COX5B
COX17
P450R
Log2(Relative Abundance)


A
PDK4
Fold change (normalized to sham)
Sham
CLP
B
PDHE1A
Fold change (normalized to sham)
Sham
CLP
C
Sham
CLP
PDK4
Cyto.C
D
PDK4/Cyto.C
Fold change (normalized to sham)
Sham
CLP
E
Sham
CLP
p-PDHE1α
PDHE2
PDHE1α/β
F
p-PDHE1/PDHE1
Fold change (normalized to sham)
Sham
CLP
G
PDH Activity
OD 450nm
Time (min)
Sham
CLP
H
PDH Activity
ΔmOD/min
Sham
CLP

Critical Care - 17 Prolonged unconsciousness is common in severe COVID-19 and is associated with hypoxemia

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[1]Weill Cornell Medical College, New York, NY, [2]Columbia University, New York, NY, [3]Massachusetts General Hospital, Boston, MA, [4]Columbia University Medical Center, New York, NY, [5]Harvard Medical School, Cambridge, MA

Introduction: For survivors of severe coronavirus disease 2019 (COVID-19), the re-emergence of consciousness is often prolonged[1], leading to clinical and ethical uncertainty surrounding neurologic prognosis and goals of care[2]. Early in the pandemic, we and others observed a high incidence of prolonged disorders of consciousness in patients with ARDS from severe COVID-19[3-5], often in those with prior hypoxemia[2,5-7]. However, the natural history of prolonged unconsciousness in severe COVID-19 remains unknown. Here, in a retrospective study of 795 intubated patients with severe COVID-19 at three medical centers during the initial surge (March–July 2020), and 427 patients during the second surge (October 2020–April 2021), we determined the time to recovery of command following and its association with hypoxemia.

Methods: Patients were included if admitted to one of three academic hospitals with a clinical presentation of severe COVID-19[3], endotracheal intubation for at least seven days, and impairment of consciousness, defined by a Glasgow Coma Scale (GCS) motor score less than six[8]. We estimated the time from intubation to recovery of command following (defined as a GCS motor score of six) using Kaplan-Meier cumulative incidence curves. Our primary outcome was recovery of consciousness, specifically the last recovery of command following during hospitalization. Our primary exposure was hypoxemia, defined as a partial pressure of oxygen (PaO_2) value below two set thresholds (55 mmHg and 70 mm Hg) based on ARDSNet protocols[9]. For the initial surge (n = 795), we estimated the hazard of hypoxemia on time to recovery of command following using univariate Cox proportional-hazards regression models, with multivariate adjustment for demographics (age, sex, race/ethnicity), level of sedation (cumulative sedative dose, days of sedation), and severity of illness (lowest P:F ratio on day of intubation, days of continuous neuromuscular blockade, use of continuous renal replacement therapy). We further computed Kaplan-Meier cumulative incidence curves for 1) the subset of patients in the first surge with no evidence of structural neurologic injury on head imaging (n = 199) and 2) intubated patients in the second surge (n = 427).

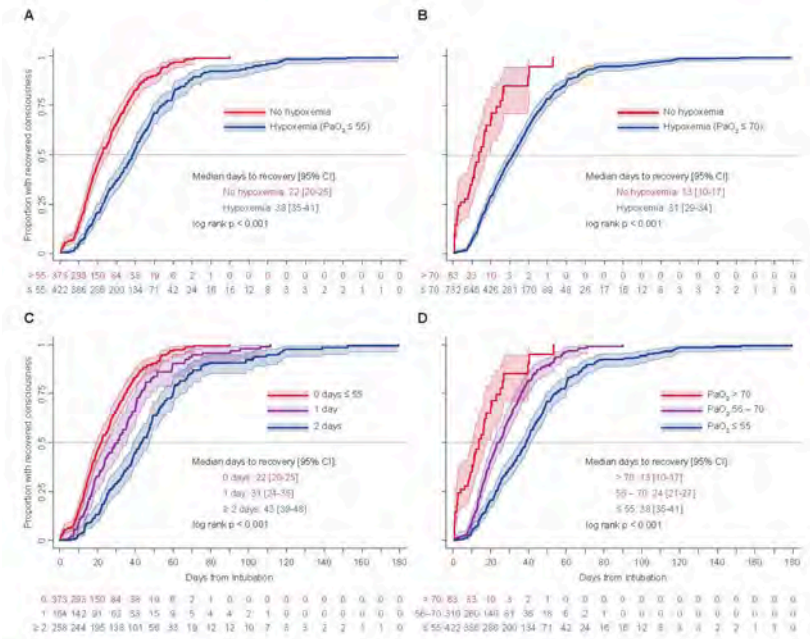
Results: In the initial surge, 571 of the 795 included patients recovered command following. The median time to recovery of command following was 30 days (95%-confidence interval [CI]: 27-32). Median time to recovery of command following increased by 16 days for patients with at least one episode of an arterial partial pressure of oxygen (PaO_2) value ≤ 55 mmHg ($p<0.001$), and 25% recovered ≥ 10 days after cessation of mechanical ventilation (Figure 1). The time to recovery of consciousness was associated with hypoxemia (PaO_2 ≤ 55 mmHg hazard ratio (HR): 0. 56, 95%-CI: 0.46 – 0.68; PaO_2 ≤ 70 HR: 0.88, 95%-CI: 0.85 – 0.91), and each additional day of hypoxemia decreased the likelihood of recovery, after accounting for cofactors including level of sedation and severity of illness (Figure 2). Our findings were confirmed in the subset of patients without any imaging evidence of neurologic injury (n = 199; Figure 3), and in a non-overlapping second surge cohort (n = 427; Figure 4).

Conclusion: The results of this multi-center, retrospective cohort study demonstrate that in severe COVID-19 recovery of command following 30 days after intubation is common if supportive care is provided. Prolonged unconsciousness is associated with hypoxemic events in a dose-dependent manner. Hypoxemia remains associated with time to recovery of command following in severe COVID-19 after adjustment for demographics, sedation exposures,

and disease severity. This prolonged time to recovery, particularly exhibited in patients with hypoxemia, was observed in three large medical centers, and confirmed in patients without evidence of neurologic injury as well as an out-of-sample cohort from the second surge. Prolonged time to recovery of command following, as observed in our study, should be considered in goals of care discussions between clinicians and surrogate decision makers. Further, our results underscore the need to investigate the underlying mechanisms of prolonged recovery of consciousness following severe COVID-19 and motivate studies to identify laboratory, imaging, and electrophysiological predictors of recovery.

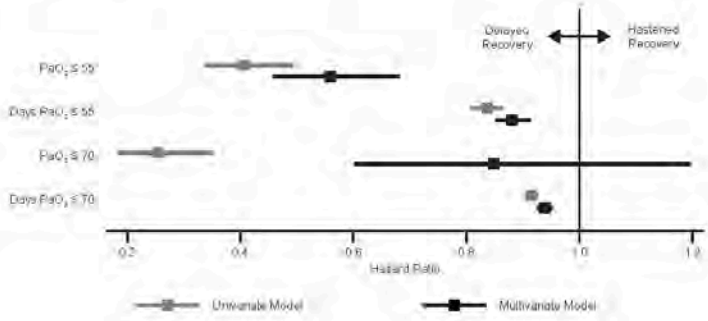
References: 1. Edlow BL et al. Neurocrit Care. 2020;33(3):627-629 2. Waldman GJ et al. Ann Neurol. 2020;88(4):653-655 3. Berlin DA et al. N Engl J Med. 2020;383(25):2451-2460 4. Abdo WF et al. Neurology. 2021;96(10):e1437-e1442 5. Fischer D et al. Ann Neurol. 2020;88(4):851-85. 6. Mao L et al. JAMA Neurol. 2020;77(6):683-690 7. Paterson RW et al. Brain. 2020;143(10):3104-3120 8. Teasdale G, Jennett B. Lancet. 1974;2(7872):81-84 9. Acute Respiratory Distress Syndrome Network, et al. N Engl J Med. 2000;342(18):1301-1308

Figure 1. Kaplan-Meier cumulative incidence curves for recovery of consciousness in patients with and without hypoxemia for initial surge (n = 795; March – July 2020).



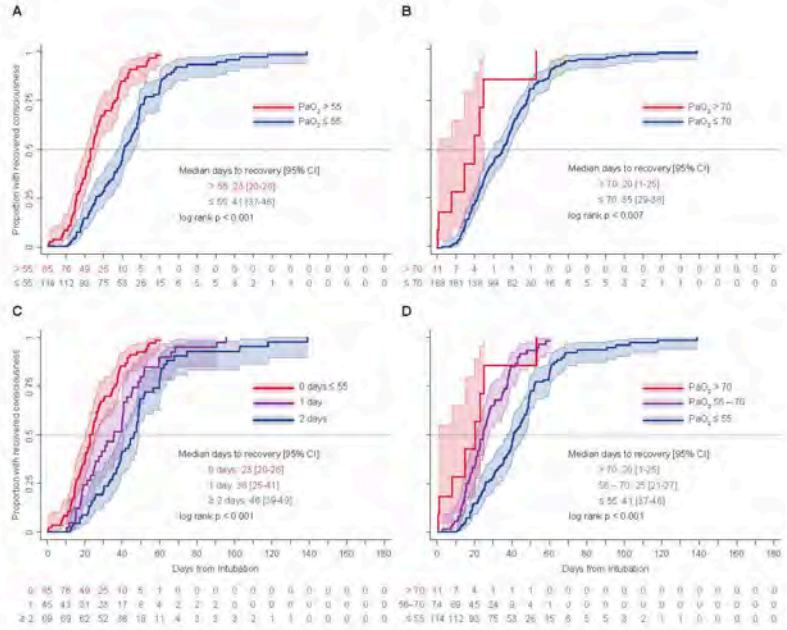
Kaplan-Meier (K-M) curves for recovery of command following in patients grouped by: A) minimum $PaO_2 \leq 55$ mmHg versus > 55 mmHg; B) minimum $PaO_2 \leq 70$ mmHg versus > 70 mmHg; C) number of days of $PaO_2 \leq 55$ mmHg; D) minimum PaO_2 per patient.

Figure 2. Pooled univariate and multivariable hazard ratios of primary hypoxemia exposure from Cox proportional hazard regressions clustered by site, initial surge (March – July 2020).



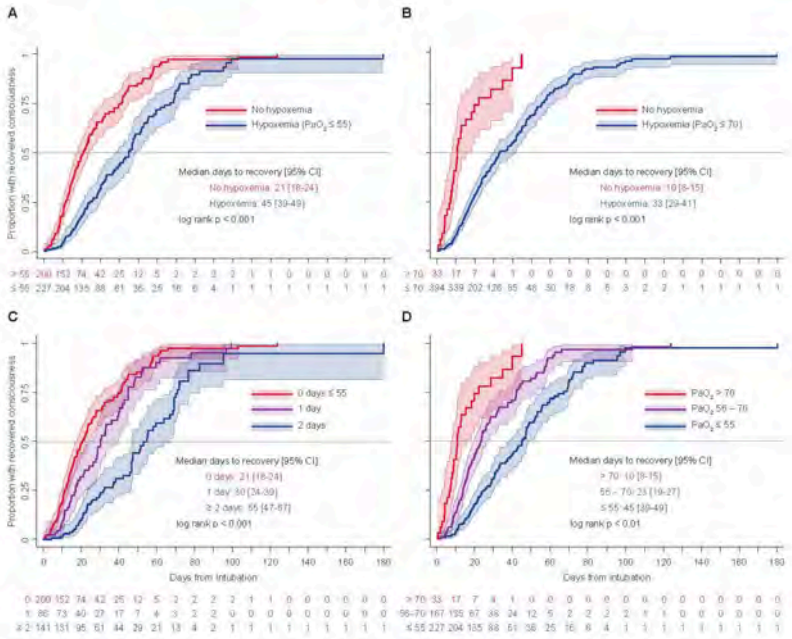
Each point estimate represents an independent regression model; 95% confidence intervals are associated with corresponding bars. Multivariable regressions included the exposure listed as well as covariates for demographics (age, sex, race/ethnicity), level of sedation (cumulative analgesic and sedative dose, duration of continuous analgesic and sedative), and severity of illness (ARDS severity, neuromuscular blockade, CRRT).

Figure 3. Kaplan-Meier cumulative incidence curves for recovery of consciousness in patients in initial surge (March – July 2020) with head imaging and without evidence of neurologic injury (n = 199).



Kaplan-Meier (K-M) curves for recovery of command following in patients grouped by: A) minimum $PaO_2 \leq 55$ mmHg versus > 55 mmHg; B) minimum $PaO_2 \leq 70$ mmHg versus > 70 mmHg; C) number of days of $PaO_2 \leq 55$ mmHg; D) minimum PaO_2 per patient.

Figure 4. Kaplan-Meier cumulative incidence curves for recovery of consciousness in patients with and without hypoxemia for second surge (n = 427; October 2020 – April 2021).



Kaplan-Meier (K-M) curves for recovery of command following in patients grouped by: A) minimum $PaO_2 \leq 55$ mmHg versus > 55 mmHg; B) minimum $PaO_2 \leq 70$ mmHg versus > 70 mmHg; C) number of days of $PaO_2 \leq 55$ mmHg; D) minimum PaO_2 per patient.

Critical Care - 18 Toll-like receptor 7 drives lung inflammation by sensing miR-146a and causes acute respiratory distress syndrome in murine sepsis

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Introduction: Sepsis is the leading cause of acute respiratory syndrome (ARDS). Septic patients with ARDS have high morbidity and mortality. Our recent findings suggest that circulating miR-146a-5p, released during sepsis, functions as a danger molecule and induces a robust innate immune response via Toll-like receptor 7 (TLR7), a single stranded RNA sensor. Furthermore, mice lack of TLR7 have attenuated systemic inflammation, organ injury, and lower mortality in sepsis. However, whether miR-146a-5p,ÜíTLR7 signaling has any impact to lung injury in sepsis remains unclear. In this study, we tested the hypothesis that TLR7 in immune cells activated by miR-146a-5p causes endothelial barrier disruption and lung inflammation (Fig. 1).

Methods: Polymicrobial sepsis was created by cecal ligation and puncture (CLP). Albumin in the bronchoalveolar lavage (BAL) was tested by ELISA. Cytokines were detected by ELISA and qRT-PCR. Conditioned media were collected from macrophages (MœÜ) treated with lipofectamine (lipo) or miR-146a-5p (50 nM) for 24h. Endothelial barrier function was assessed by transendothelial electric resistance and XPerT assay. All animal experiments were approved by IACUC. The null hypothesis was rejected for $p < 0.05$ with two tails.

Results: Sepsis significantly augmented miR-146a-5p level in the BAL at 24 h (Fig. 2A). Intratracheal administration of miR-146a-5p (20 µg) in miR-146a KO mice induced pulmonary inflammation as evidenced by a marked increase in BAL IL-6 (Fig. 2B) and robust neutrophil infiltration in the lung. Absence of TLR7 almost completely blocked the injurious effect of exogenous miR-146a-5p, indicating that miR-146a-5p induced lung injury is exclusively TLR7-dependent. Most importantly, in a CLP sepsis model, TLR7KO mice had preserved alveolar-capillary barrier function (Fig. 2C) and attenuated proinflammatory cytokines when compared with WT mice (Fig. 2D). To decipher the molecular mechanism responsible for miR-146a-5p→TLR7-mediated barrier disruption and activation, we treated endothelial cells (ECs) with miR-146a mimics. Because ECs do not express TLR7, direct treatment of miR-146a-5p, a TLR7 activator, exhibited no impact on permeability. In contrast, the EC permeability increased dramatically when ECs were incubated with conditioned media from miR-146a-treated WT Mφ or WT septic sera. Absence of TLR7 either in Mφ or septic mice preserved the barrier function (Fig. 2 E, F). To identify the downstream effectors, cytokine array was performed and revealed over 70 increased cytokines between WT and TLR7KO septic sera. Pathway enrichment analysis implies TNFα singling pathway to be the most promising effector for endothelial barrier dysfunction (Fig. 2G). Indeed, sera from WT-CLP mice lost the ability to induce barrier leaky in the ECs when incubated with anti-TNFα Ab (Fig. 2H).

Conclusion: We demonstrate a pivotal role of miR-146a-5p and TLR7 sensing in mediating lung injury induced by polymicrobial sepsis.

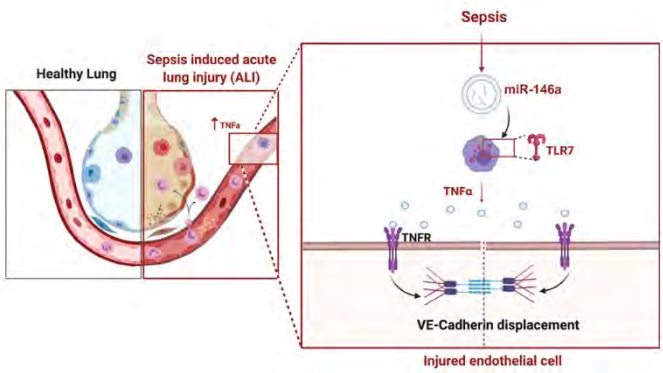

Figure 1. Schematic hypothesis that TLR7 in immune cells activated by miR-146a-5p causes endothelial barrier disruption and lung inflammation in part via TNFα. . Increased lung injury secondary to sepsis was characterized by pulmonary inflammation and alveolar-capillary barrier dysfunction. Increased miRNA in circulation by sepsis activates the immune cells by recognizing TLR7 signaling to release multiple proinflammatory cytokines, including TNFα, which leads to pulmonary barrier damage through disrupting VE-cadherin junctions on endothelial cells.

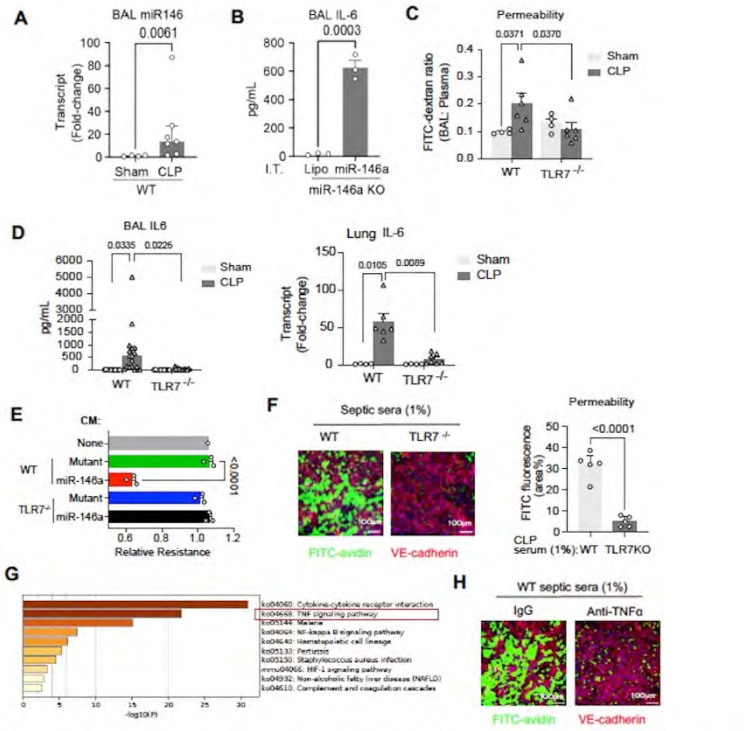

Figure 2. Absence of TLR7 attenuated lung injury elicited by exogenous miR-146a and polymicrolial sepsis. ***A.*** BAL miR-146a tested at 24h after sham and CLP procedure. n=4-7. ***B.*** BAL IL-6 in miR-146a KO mice at 24 h following the intratracheal injection of miR-146a-5p (20μg). n=3. ***C-D.*** WT and TLR7$^{-/-}$ mice are subjected to sham or CLP, permeability (***C***) and IL-6 (***D***) were evaluated at 24 h. n=4-17. ***E.*** miR-146a increases endothelial permeability via macrophage TLR7. ECs were incubated with conditioned media (CM) collected from miR-146a- or mutant- treated WT and TLR7KO macrophage. Resistance was measured at 8 h. ***F.*** Endothelial permeability visualized and quantified by area percentage of FITC-avidin at 24h following treatment of 1% septic sera from WT and TLR7$^{-/-}$ mice. n=5. ***G.*** Pathway enrichment analysis. ***H.*** WT septic sera were preincubated with IgG or anti-TNFα (10ng/mL) prior to the treatment with EC. Permeability was visualized with FITC-avidin.

Critical Care - 19 Validity of SOFA Score in Patients with Severe Respiratory Distress Secondary to COVID 19 Pneumonia.

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Introduction: SOFA scoring has been validated to predict mortality in patients admitted to ICU [1]. Since COVID-19 pandemic, there is conflicting evidence regarding the accuracy of SOFA score to predict mortality in patients with severe respiratory distress secondary to COVID-19 pneumonia and the concern of that population not being represented in the original SOFA studies [2,3]. The purpose of our study is to evaluate correlation between SOFA score and mortality prediction in patients suffering from COVID-19 pneumonia complicated by severe respiratory distress who needed or not mechanical ventilation. It also aimed at further analysis to determine the best cutoff for discrimination for mortality risk and to compare with previous studies in general ICU population.

Methods: We performed a retrospective chart review of the patients admitted to Henry Ford Hospital from March to December 2020 whose principal diagnosis were COVID 19 pneumonia complicated by severe respiratory distress. We defined respiratory distress as oxygen saturation below 93% and/or respiratory rate above 30 breaths per minutes for 2 hours. We compared their initial SOFA scores (at time of diagnosis of severe respiratory distress) to mortality outcomes using a grouped analysis. Patients were split into 7 levels of SOFA score (0-1, 2-3, 4-5, 6-7, 8-9, 10-11 and >11) and comparison of mortality in between groups was performed using Chi-square test followed by a Linear trend Analysis. We used ROC curve for analysis of the performance of SOFA score as mortality predictor and to find the optimal discrimination score. All statistical tests were 2-tailed and a P value >0.05 was considered significant.

Results: There was a total of 320 patients, out of these 111 underwent intubation and mechanical ventilation. Overall mortality was 22%, and mortality for patients who needed mechanical ventilation was 50% (Table 1). Grouped SOFA score analysis showed steep correlation with mortality rate, with ranges from 0% mortality for SOFA 0-1 to 100% mortality rate for SOFA scores above 11 (Figure 1). ROC curve for analysis of performance of SOFA as mortality predictor showed an area under the curve = 0.883, which is comparable to the range of performance previously seen in non-COVID-19 population. The optimal point for discrimination (best balance between false positive fraction and true positive fraction) was for SOFA =5. In the population studied, mortality for SOFA score equal or less than 5 was 8.3% (18/217) versus 51.4% (52/101) for SOFA score above 5 (Figure 2).

Conclusion: SOFA score in COVID-19 patients complicated by severe respiratory distress showed strong correlation with mortality rate and could be used as mortality predictor for this population as well. However, the best point of discrimination found was lower (SOFA = 5) than previously seen for non-COVID-19 population, when that point was in the range of 7-8. It is valid to use SOFA scores to predict mortality in COVID-19 patients, but patients seemed to have an increased mortality rate with a lower SOFA score than the general ICU population.

References: 1. Ferreira FL, Bota DP, Bross A, M√©lot C, Vincent J-L. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. JAMA [Internet]. 2001 Oct 10;286(14):1754-8. Available from: https://doi.org/10.1001/jama.286.14.1754
2. Fayed M, Patel N, Yeldo N, Nowak K, Penning DH, Vasconcelos Torres F, et al. Effect of Intubation Timing on the Outcome of Patients With Severe Respiratory Distress Secondary to COVID-19 Pneumonia. Muacevic A, Adler JR, editors. Cureus [Internet]. 2021 Nov 16;13(11):e19620. Available from: https://www.ncbi.nlm.nih.gov/pm 3. Yang Z, Hu Q, Huang F, Xiong S, Sun Y. The prognostic value of the SOFA score in patients with COVID-19: A retrospective, observational study.2-Niraj Gowda, Gifty Dominah, Hayley Rogers, Amira Elshikh, Suraj Gowda, Ivy Benjenk, david yamane, EVALUATING APACHE AND SOFA SCORING SYSTEMS IN PATIENTS WITH COVID-19, Chest, Volume 160,

Issue 4, Supplement, 2021, Page A1077, ISSN 0012-3692, https://doi.org/10.1016/j.chest.

SOFA Score	Intubated COVID-19 N	Intubated patients mortality N (%)	Total COVID-19 patients N	Total COVID Mortality N (%)	Expected mortality by SOFA in non-COVID-19 patients %
Number total	111	56 (50%)	320	70 (22%)	
0-1	1	0 (0%)	79	0 (0%)	0
2-3	7	1 (14.3%)	71	4 (5.6%)	6.4%
4-5	26	9 (35%)	67	14 (20.9%)	20.2%
6-7	33	12 (36%)	51	18 (35.3%)	21.5%
8-9	22	13 (59%)	26	13 (50%)	33.3%
10-11	14	11 (79%)	17	14 (82.3%)	50%
12-14	6	6 (100%)	6	6 (100)	95.2%
>14	1	1 (100)	1	1 (100%)	95.2%

Table 1. SOFA score and associated mortality in COVID-19 patients with severe respiratory distress.

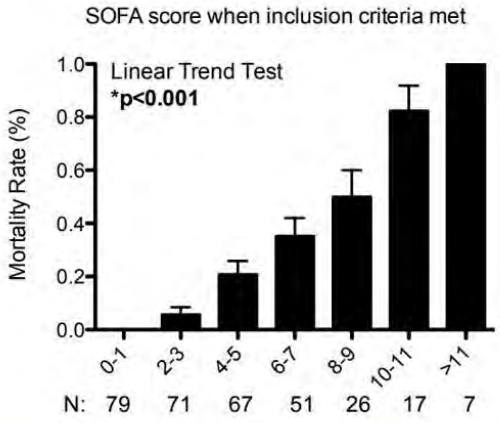

Figure 1. Grouped mortality rate for 7 different levels of SOFA score. Groups differ in between them (Chi-square test, *p<001) and there is linear association between SOFA score level and mortality (Linear Trend Test, *p<0.001).

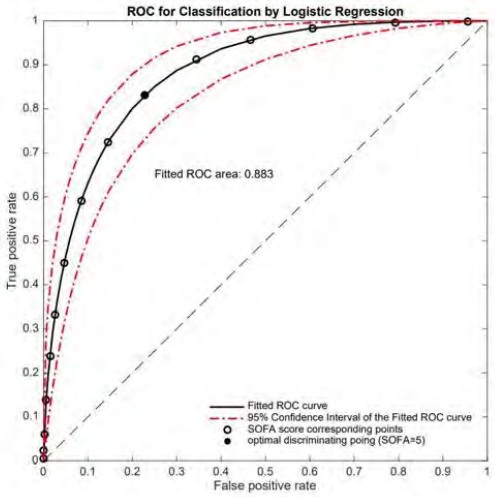

Figure 2. ROC curve for classification by Logistic Regression. Each classifier level corresponded to a discrete SOFA score level (from 0 to equal or greater than 14). Optimal discrimanation point was calculated as the corresponding classifier point closer to the left upper corner of the graph (coordinates (0,1)).

Critical Care - 20 Nucleic acid sensing mediates brain inflammation in murine sepsis

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Introduction: Sepsis is a critical condition with life-threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis-associated encephalopathy (SAE) occurs in sepsis survivors and is reportedly caused by the blood-brain barrier (BBB) breakdown, brain inflammation, and neurological dysfunction. Extracellular (ex) miR-146a-5p is increased significantly in the plasma of septic mice and humans, and is capable of inducing potent pro-inflammatory cytokines and complement activation via TLR7 signaling, a single-stranded RNA sensor. In the current study, we delineated the impact of ex-miRNAs and TLR7 in SAE.

Methods: All animal experiments were approved by the IACUC. WT (C57BL/6J) and TLR7-/- mice were employed. Polymicrobial sepsis was created by cecal ligation and puncture. A battery of behavioral tests was conducted. Blood-brain barrier (BBB) breakdown was measured by leakage of the blood sodium fluorescein (376 Da) to the brain. Microglial cells were isolated from neonatal mice and cytokines were tested using ELISA and qRT-PCR. Brain immune cell infiltration was evaluated by flow cytometry. Statistical analysis was performed using GraphPad Prism 9 software. The null hypothesis was rejected for $p < 0.05$ with two tails

Results: Sepsis significantly increased plasma RNA concentrations and miR-146a-5p for up to 7 days (Fig. A). To test whether miR-146a-5p causes neuroinflammation, we treated microglia cultures or intact brain via intracerebroventricular (ICV) injection with miR-146a-5p mimics. miR-146a-5p, but not its U→A mutant, led to a marked increase in cytokine production in WT microglia cultures (Fig.B). Deficiency of TLR7 (TLR7-/-), but not TLR3 (TLR3-/-, a double-stranded RNA sensor), abolished miR-146a-5p's effect (Fig. B). Additionally, ICV injection of miR-146a-5p mimics upregulated cortical cytokine IL-6, TNFα and chemokine CXCL2 gene expression at 24 h. Flow cytometry analysis within the same time frame revealed a robust increase in the numbers of myeloid cells including monocytes and neutrophils. Importantly, sepsis induced brain inflammation for up to 14 days and neurological dysfunction. Lack of TLR7 attenuated miR-146a-5p-triggered innate immune response manifested as reduced cytokine production (Fig. C) and limited immune cell infiltration (Fig. D). Ablation of TLR7 in TLR7-/- mice preserved BBB integrity at 24 h (Fig. E), reduced microglial expansion and leukocyte infiltration up to 14 days (Fig. F), and attenuated GSK3β signaling in the brain, but did not improve neurobehavioral recovery following sepsis (data not shown).

Conclusion: We established a clinically relevant mouse model of SAE and identified the importance of ex-miRNAs-TLR7 signaling in brain inflammation in murine sepsis.

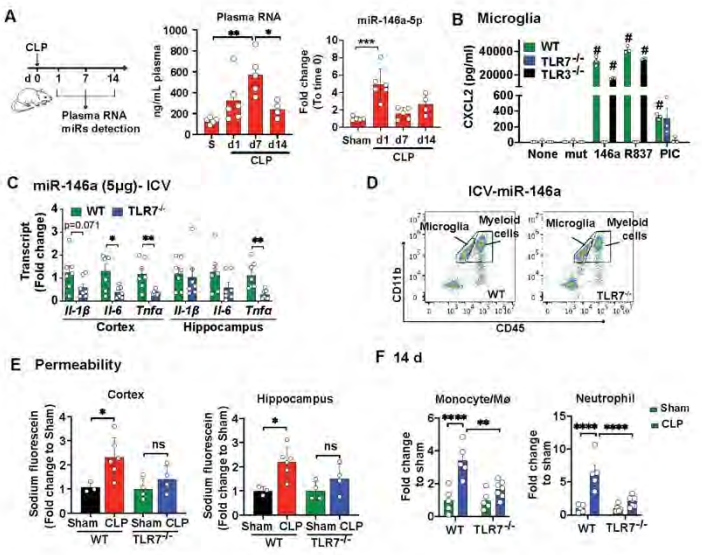

Figure. Absence of TLR7 attenuated neuroinflammation triggered by miR-146a and attenuated sepsis-associated encephalopathy. *A.* Circulating RNA and miR-146a-5p level in the plasma collected at d1, d7, and d14 following CLP. S = sham. n = 4-6/group. *p<0.05, **, p<0.01, *** p<0.001. ***B.*** miR-146a-5p and R837-induced CXCL2 production was abolished in TLR7-deficient microglia. WT, TLR7$^{-/-}$, and TLR3$^{-/-}$ microglia were treated with lipofectamine-complexed miR-146a-5p mutant control (mut, 50 nM), miR-146a-5p (146a, 50 nM), the TLR7 ligand R837 (1 μg/ml), and the TLR3 ligand poly I:C (PIC, 10 μg/ml). n = 7/group. #$p < 0.001$ *vs.* None. ***C.-D.*** Deficient in TLR7 suppressed cytokine transcripts in the cortex and hippocampus (C), and myeloid cell infiltration (D) caused by intracerebroventricular (ICV) injection of miR-146a-5p (5μg). n = 7/group, *$p < 0.05$, **$p < 0.01$. ***E.*** BBB permeability as assessed by leakage of sodium fluorescein from blood to brain tissue at 24 h after CLP. n = 3-6/group. *$p < 0.05$. F. Flow cytometry analysis of brain monocyte and neutrophils at 14 days after sham/CLP in WT and TLR7$^{-/-}$ mice. n= 5-7/group. **$p < 0.01$, ****$p < 0.0001$.

Critical Care - 21 Opportunities in Tele-Critical Care: Analysis of Transfer Center Outcomes of a Large Academic Center

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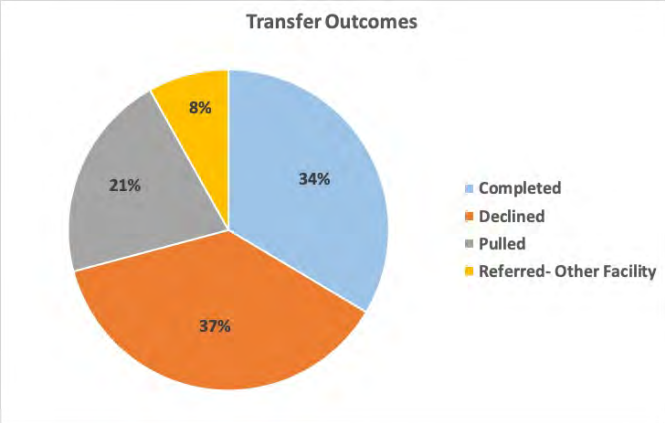
Introduction: Involvement of critical care specialists has been shown to improve patient outcomes [1], yet many community-based hospitals lack access to intensivists [2]. Tele-Critical Care (TCC) has evolved to provide specialized critical care services to remote sites [2,3] with evidence supporting that it may improve ICU patient safety, cost-effectiveness, and health care quality [4,5,6]. The purpose of this study is to quantify transfer requests at a large academic hospital and proportion of transfers accepted. We hope to better understand which critically ill patients can and cannot be cared for in the community and how TCC could help larger hospitals better partner with regional hospitals to improve diverse outcomes.

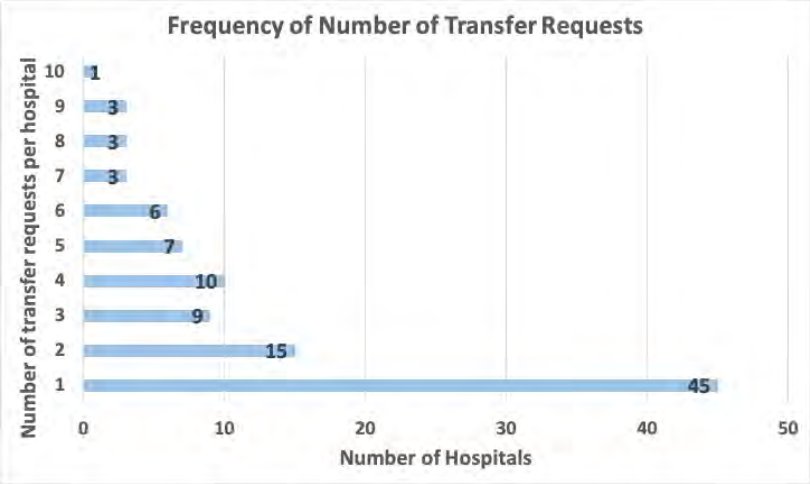
Methods: In partnership with hospital leadership and an academic tertiary care hospital transfer center, de-identified data from 4/13/2021 to 5/13/2021 regarding consecutive requests to transfer a critically ill patient from community hospitals to the tertiary care center were obtained. Transfer request rationale and ultimate transfer success were analyzed.

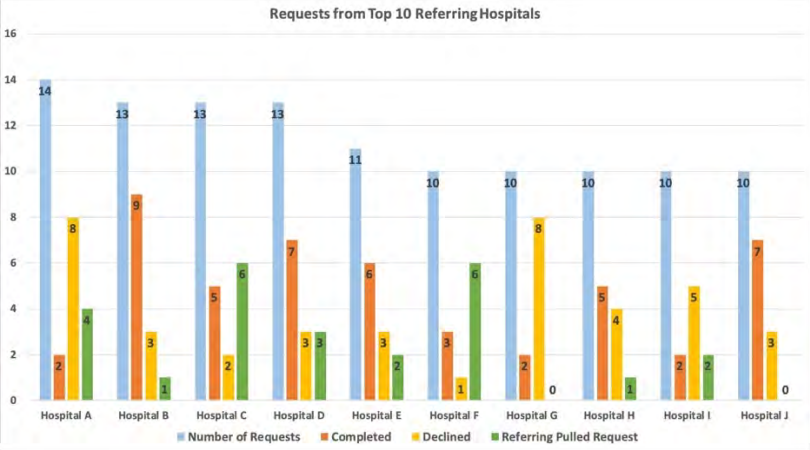
Results: In the one- month period, 907 requests were submitted. As TCC services would not impact requests due to a clinical service line not available at the community hospital (i.e., neurosurgical services, interventional cardiology, etc), data were analyzed concerning requests for 'higher level of care' and 'patient/family request'. This yielded 295 transfer requests from 102 different hospitals. 99 (34%) of requests ultimately resulted in actual patient transfer from the community hospital to the academic tertiary care hospital. 110 requests (37%) were declined by the tertiary care hospital, 62 (21%) requests were withdrawn by the community hospital, and 24 (8%) of requests resulted in the patient being transferred away from the community hospital but not to the tertiary care hospital (Figure 1). 45 hospitals had 1 request during the study period, 15 hospitals had 2 requests, 9 hospitals had 3 requests, 10 hospitals had 4 requests, 7 hospitals had 5 requests, 6 hospitals had 6 requests, 3 hospitals had 7 requests, 3 hospitals had 9 requests, 3 hospitals had 9 requests, and 1 hospital had 10 requests (Figure 2). The results of the requests from Top 10 referring hospitals are shown in Figure 3. Reasons for transfer decline varied (Figure 4), with the primary reason for decline being 'no bed availability' (24% of all transfer requests).

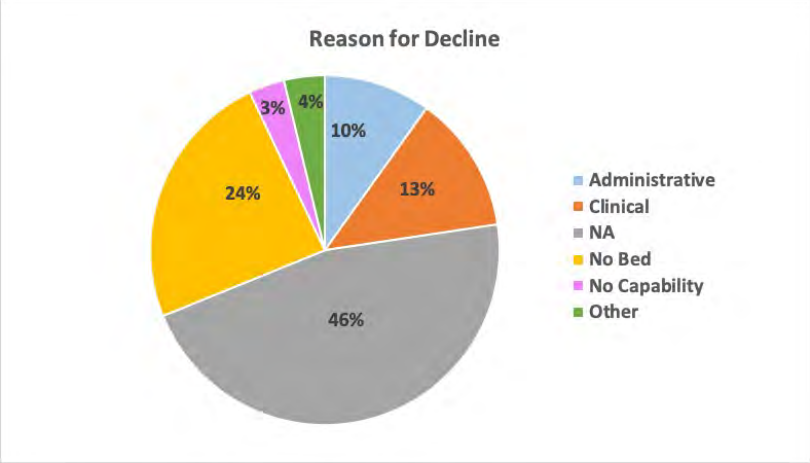
Conclusion: Our data suggest that a large academic center may receive numerous requests to transfer a critically ill patient but that less than half actually result in a successful transfer. There also may be a small subset of hospitals that frequently request a transfer and thus, may be more likely to utilize and benefit from TCC services. Further investigation into rationales for transfer request and whether or not community hospitals would utilize a TCC service are needed.

References: [1] JAMA 2002; 288:2151-2162. [2] Crit Care Med 2017; 45:298-304. [3] Crit Care Med 2020; 48:553-561. [4] Health Services Research 2017; 53(4):2099-2117. [5] Chest 2020; epub ahead of print. [6] Crit Care Med 2019; 47(5):659-667.




Frequency of Number of Transfer Requests
Number of transfer requests per hospital
10
9
8
7
6
5
4
3
2
1
1
3
3
3
6
7
10
9
15
45
0
10
20
30
40
50
Number of Hospitals


Requests from Top 10 Referring Hospitals
16
14
12
10
8
6
4
2
0
Hospital A
Hospital B
Hospital C
Hospital D
Hospital E
Hospital F
Hospital G
Hospital H
Hospital I
Hospital J
Number of Requests
Completed
Declined
Referring Pulled Request


Reason for Decline
10%
13%
46%
24%
3%
4%
Administrative
Clinical
NA
No Bed
No Capability
Other

Critical Care - 22 Studying Unconscious bias in End-of-Life care

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Introduction: Introduction Nearly one in five adults will die in the intensive care unit with substantial scholarship dedicated to maximizing dignity for both patients and their families and evaluating disparities in care. Prior investigators have identified greater intensity of care at the end-of-life in the ICU among patients who are non-white, although whether this stems from differences in physician communication, differences in hospital use, or cultural differences in end of life preferences has yet to be fully elucidated. In the context of the severe COVID-19 pandemic, we conducted a single-center study of care at the end of life in our ICUs (including both medical ICUs and surgical ICUs) by race and ethnicity.

Methods: A retrospective data review was conducted on EHR data collected from all ICU admissions between June 2019 until and December 2020 in a tertiary care center in Boston, MA. The primary outcome was death and secondary outcomes included 'code status,' broken down into the designations: Do Not resuscitate (DNR), DNR/Do not Intubate (DNI) and Comfort measures only (CMO) before death occurred in the ICU. Race and ethnicity categories were determined by patient self-identification of these categories and are described in Table 1. We categorized different 'code statuses' at death by race and ethnicity, and the percentage of patients who died with markers of aggressive care (e.g., ongoing feeding, vasopressors, dialysis, restraints) or markers of conflict (ethics consult).

Results: A total of 13,212 ICU patients were included in the analysis. 1302 patients died (9.9%) and the rest were discharged alive (Fig 1). 4581 (34.7%) were discharged home, and 435 (3.3%) discharged to hospice (home plus medical facility). 9.6% were DNAR +/- DNI, and 8.6% were CMO. 53.5% were males, 6.8% were Hispanic/ Latino, 13.8% were Black and 3.6% were Asian. 10,273 had an HCP available (77.7%). The mean age was 63.3 (± 17.2) (Table 1). 716 patients (5.4%) were COVID positive in the ICU. Of those who died 74.5% were non-Hispanic/ Latino, 13.2% were Black and 57.1% were White. Of Black patients, 9.4% died whilst 8.5% of White patients died. These differences were statistically significant ($p<0.0001$) (Table 2a). The average age of Black patients who died was 69 years (sd 15.2) versus 71.4 years (sd 14.5) among White patients (Table 2 b). At the time of death, White patients were most likely to be DNAR/DNI or CMO (84.1%) as compared with Black patients (77.9%) or Hispanic/Latino patients (67.7%). Black patients were more likely to be DNAR/OK to Intubate (15.1%) as compared with White patients (9%) (Table 3). At the time of demise 53% were intubated, 53.7% were being infused vasopressors, 22.8% had feeding orders, 17% were on dialysis, 31.4% had restraint orders, 87% had a Palliative care consult, 4.8% had an Ethics consult, the mean time between DNR decision and demise in hours was 151 (± 229.8). The median LOS in the ICU was 2.2 (IQR 1,5) and hospital LOS was 6 (IQR 3,12) (Table 4). the mean time between DNR decision and demise in hours was 131.2 (± 137.4). The mean time between DNR decision and demise in hours was 139.9 (± 162.3) hours amongst Black patients and 126.9 (±125.9) hours amongst White patients (Table 5). When comparing this difference prior to and during the COVID pandemic surge (March 2020) younger patients were admitted to the ICU post pandemic (62.9 years (sd 17.1) vs 64 years (sd 17.4) ($p=0.0003$). Table 6 shows a better ICU outcome in this larger cohort. However, compared to pre-pandemic, more Black and Hispanic patients were admitted to the ICU after March 2020. This was opposite to the effect seen with White patients where there was a decrease in ICU admissions ($p=0.023$).

Conclusion: Our data has identified several statistically significant disparities within dying patients by race and ethnicity. These include a difference in overall mortality rate, likelihood of being transitioned to 'Comfort Measures Only' status and time between DNR decision and demise. The pandemic also had a disproportionately worse effect on Black and Hispanic patients. This data opens opportunities to move from disparities to equity.

Table 1. Descriptive

Variable	Encounters (n=13212)
DNAR/DNI, No. (%)	917 (6.9)
DNAR/OkInt, No. (%)	352 (2.7)
CMO, No. (%)	1136 (8.6)
Full Code, No. (%)	10807 (81.8)
Gender, No. (%)	
Male	7071 (53.5%)
Ethnicity, No. (%)	
Non Hispanic/Latino	10958 (82.9)
Unobtainable	1357 (10.3)
Hispanic/Latino	897 (6.8)
Race, No. (%)	
American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander	76 (0.6)
Asian	472 (3.6)
Black	1826 (13.8)
Other	648 (4.9)
Unknown	1487 (11.3)
White	8703 (65.9)
Age, Mean (SD)	63.3 (17.2)
Discharged Home, No. (%)	4581 (34.7)
Discharged to Hospice, No. (%)	
Hospice-Home	153 (1.2)
Hospice-Medical Facility	282 (2.1)
Patients died, No. (%)	1302 (9.9)
Covid Status, No. (%)	
COVID +	716 (5.4)
Prior COVID +	38 (0.3)
Not COVID +	12458 (94.3)
LOS	
Median (IQR)	6 (3, 12)
Mean (SD)	10.1 (14.2)
[min, max]	[1, 384]
ICU LOS	
Median (IQR)	2.2 (1, 5)
Mean (SD)	4.6 (7.5)
[min, max]	[0, 170.3]

Table 2a. Mortality by Race and Ethnicity

	Patients who died (n=1302)	Patients discharged alive (n=11910)	P-value
Ethnicity, No. (%)			<0.0001
Non Hispanic/Latino	970 (74.5) – (8.9)	9988 (83.9) – (91.2)	
Unobtainable	267 (20.5) – (19.7)	1090 (9.2) – (80.3)	
Hispanic/Latino	65 (5.0) – (7.3)	832 (7.0) – (92.8)	
Race, No. (%)			<0.0001
American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander	10 (0.8) – (13.2)	66 (0.6) – (86.8)	
Asian	42 (3.2) – (8.9)	430 (3.6) – (91.1)	
Black	172 (13.2) – (9.4)	1654 (13.9) – (90.6)	
Other	45 (3.5) – (6.9)	603 (5.1) – (93.1)	
Unknown	290 (22.3) – (19.5)	1197 (10.1) – (80.5)	
White	743 (57.1) – (8.5)	7960 (66.8) – (91.5)	

Table 2 b. Average age by race among patients who died

Age in years	American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander (n=10)	Asian (n=42)	Black (n=172)	White (n=743)	Other (n=45)	Unknown (290)
Mean (SD)	75.7 (13.5)	70.6 (17)	69 (15.2)	71.4 (14.5)	68.8 (15.3)	64.3 (17.8)

Table 3. Code status by race/ethnicity among patients who died (n=1302).

	DNAR/DNI (n=134)	DNAR/OkInt (n=143)	Full Code (n=112)	CMO (n=913)
Ethnicity, No. (%)				
Non Hispanic/Latino	105 (78.4) – (10.8)	99 (69.2) – (10.2)	71 (63.4) – (7.3)	695 (76.1) – (71.7)
Unobtainable	26 (19.4) – (9.7)	32 (22.4) – (12)	32 (28.6) – (12)	177 (19.4) – (66.3)
Hispanic/Latino	3 (2.2) – (4.6)	12 (8.4) – (18.5)	9 (8) – (13.9)	41 (4.5) – (63.1)
Race, No. (%)				
American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander	2 (1.5) – (20)	0 (0.0)	2 (1.8) – (20)	6 (0.7) – (60)
Asian	7 (5.2) – (16.7)	4 (2.8) – (9.5)	5 (4.5) – (11.9)	26 (2.9) – (61.9)
Black	20 (14.9) –(11.6)	26 (18.2) – (15.1)	12 (10.7) – (7)	114 (12.5) –(66.3)
Other	3 (2.2) – (6.7)	7 (4.9) – (15.6)	8 (7.1) – (17.8)	27 (3) – (60)
Unknown	26 (19.4) – (9)	39 (27.3) – (13.5)	34 (30.4) – (11.7)	191 (20.9) – (65.9)
White	76 (56.7) –(10.2)	67 (46.9) – (9)	51 (45.5) – (6.9)	549 (60.1) – (73.9)

Table 4. Markers of Aggressive care or conflict at death

Variable	N=Died (1302)
Intubation at demise	693 (53)
Vasopressors at demise	700 (53.7)
Feeding orders at demise	297 (22.8)
Dialysis at demise	221 (17)
Restraint orders at demise	409 (31.4)
Palliative care consult	1134 (8.7)
Ethics consult	63 (4.8)

Table 5. Time between DNR decision and demise by race (only among patients who died and who were not full code (n=1214)

Time between dnr decision and demise (in hours)	American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander (n=6)	Asian (n=44)	Black (n=149)	White (n=869)	Other (n=33)	Unknown (113)	Total Group (n=1214) (p=0.237)
Mean (SD)	314.7 (333.9)	178.8 (179.4)	139.9 (162.3)	126.9 (125.9)	98 (84.2)	134.8 (155.5)	131.2 (137.4)
Median (IQR)	198.9 (23.5, 724.8)	116.1 (60, 262.4)	93.7 (43.6, 162.2)	91.8 (45.5, 167.8)	66.4 (32.7, 146.2)	73.5 (43.1, 168.7)	91.7 (45.3, 168.3)
[min, max]	[17.5, 724.8]	[18.3, 836.6]	[0.9, 1053.8]	[0.7, 1080.8]	[6, 354.3]	[2.4, 873.2]	[0.7, 1080.8]

Table 6. Pre and post pandemic surge (row%) – (col%)

Variable	Pre-COVID (n=4840)	Post-COVID (after March surge 2020) (n=8372)	p-value
Code status, No. (%)			<0.0001
DNAR/DNI	395 (43.1) – (8.2)	522 (56.9) – (6.2)	
DNAR/Okflnt	129 (36.7) – (2.7)	223 (63.4) – (2.7)	
CMO	487 (42.9) – (10.1)	649 (57.1) – (7.8)	
Full Code	3829 (35.4) – (79.1)	6978 (64.6) – (83.4)	
Gender, No. (%)	2596 (36.7) – (53.6)	4475 (63.3) – (53.5)	0.838
Male			
Ethnicity, No. (%)			0.131
Non-Hispanic/Latino	4017 (36.7) – (83)	6941 (63.3) – (82.9)	
Unobtainable	518 (38.2) – (10.7)	839 (61.8) – (10)	
Hispanic/Latino	305 (34) – (6.3)	592 (66) – (7.1)	
Race, No. (%)			0.023
	35 (46.1) – (0.7)	41 (54) – (0.5)	
American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander			
Asian	178 (37.7) – (3.7)	294 (62.3) – (3.5)	
Black	616 (33.7) – (12.7)	1210 (66.3) – (14.5)	
Other	224 (34.6) – (4.6)	424 (65.4) – (5.1)	
Unknown	569 (38.3) – (11.8)	918 (61.7) – (11)	
White	3218 (37) – (66.5)	5485 (63) – (65.5)	
Age, Mean (SD)	64 (17.4)	62.9 (17.1)	0.0003
Discharged Home, No. (%)	1506 (32.9) – (31.1)	3075 (67.1) – (36.7)	<0.0001
Discharged to Hospice, No. (%)	191 (43.9) – (4)	244 (56.1) – (2.9)	0.0014
Patients died, No. (%)	537 (41.2) – (11.1)	765 (58.8) – (9.1)	0.0003
LOS			<0.0001
Median (IQR)	7 (3, 13)	5 (2, 11)	
ICU LOS			<0.0001
Median (IQR)	2 (1, 4.2)	2.4 (1, 5.7)	

Critical Care - 23 Identifying pro-inflammatory miRNA motifs using an exhaustive computer search algorithm in murine sepsis and trauma

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Introduction: Organ dysfunction occurs following traumatic injury or septic shock and is due, in part, to body's inappropriate immune responses[1]. The DAMPs such as cellular nucleic acids have been implicated in the immune response in sepsis and trauma[2]. We have reported that many plasma miRNAs are upregulated upon sepsis and ischemia, and some are pro-inflammatory via TLR7[3-4], a RNA sensor. However, while uridine and guanosine are essential for the miRNA-mediated innate immune response[5], neither the specific nucleotide sequence preference nor motifs essential for their activity is known[6].

Methods: All animal experiments were approved by the IACUC. Anesthetized C57BL/6J mice were subjected to Trauma (bowel ischemia, tibia fracture, and muscle crush), CLP (Cecum ligation and puncture), or Sham (Laparotomy). Blood was collected at 6h and 24h after surgery and plasma RNA isolated using Trizol and profiled by small RNAseq. Cytokines were assayed by ELISA. Brute force search was performed for miRNA motifs of length 4-7 within the two miRNA lists (18 pro-inflammatory vs. 15 non-inflammatory miRNAs). Sequences with at least 10 matches within the pro-inflammatory miRNA list and 0 matches in the non-inflammatory list were selected as potential motifs of interest.

Results: RNAseq identified 1044 and 1206 mature miRNAs in trauma and septic mouse plasma, respectively, among which 65 and 99 miRNAs were upregulated. A list of the upregulated miRNAs (**Fig. 1A**, *training* set, n=33) were tested for their abilities to induce IL-6/CXCL-2 production *in vitro*. Among them, 18 miRNAs induced IL-6/CXCL-2, while 15 did not. Initial receiver operating characteristic analysis of the nucleotide sequence demonstrated that uridine content predicted inflammatory properties (**Fig. 1B**). Brute force search identified ten uridine-containing sequences that were associated the pro-inflammatory miRNAs (**Fig. 1C**). Two of sequences (UU...U and U..UU) occurred in 55.6% and 61.1% of cases, respectively; thereby correctly classifying 15 out of 18 inflammatory miRNAs (**Fig. 1D**) and an overall predictive accuracy of 90.9% (sensitivity: 83.3%, specificity: 100%) in discriminating pro- from non-inflammatory miRNAs. To experimentally test the necessity of UU…U motif, we made a series of single mutations in miR-146a-5p (**Fig. 2A**) and discovered that the mutations outside of the motif, i.e. $U_1$1→A or U_8→A, had no impact on IL-6 production (**Fig. 2B**). However, mutations within the motif: U_{12}→A or U_{13}→A completely, and U_{17}→A partially, abrogated IL-6 production. Finally, to validate the predictive value of the two motifs, an independent *testing* set of 20 miRNAs (**Fig. 3A**) were tested (**Fig. 3B**). These data demonstrate that the two motifs achieved an overall prediction accuracy of 75% (sensitivity: 69%, specificity: 86%).

Conclusion: This study demonstrates that many plasma miRNAs following traumatic injury and sepsis possess strong pro-inflammatory properties. Two nucleotide motifs are identified that are highly associated pro-inflammatory miRNAs.

References: (1) J Trauma. 1996;40(4):501-510. (2) Injury. 2007;38(12):1336-1345. (3) J Immunol. 2016;196(6):2788-2798. (4) J Immunol. 2017;199:2106-2117. (5) Nat Neurosci. 2012;15(6):827-35. (6) Immunity. 2016;45(4):737-748.

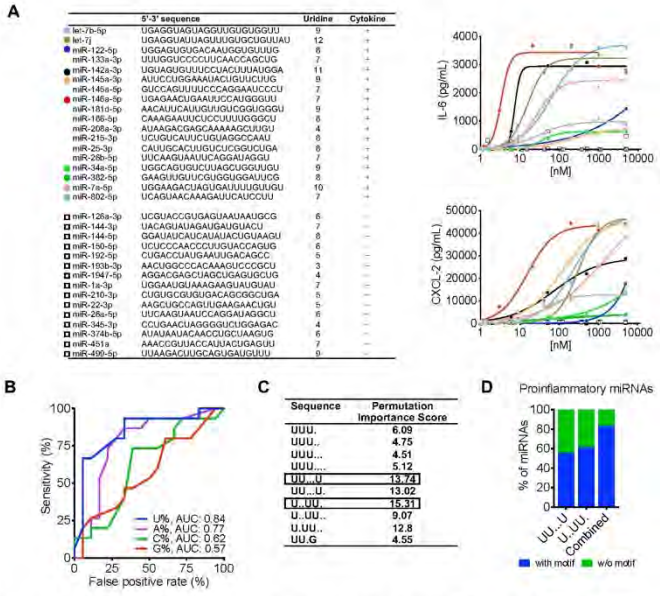

Figure 1. Identification and characterization of pro-inflammatory miRNA motif. A. Two groups of miRNAs that are pro- or non-inflammatory (cytokine production) and used as the *training* set; **B.** AUC analysis of the nucleotide sequences of miRNAs; **C.** Ten uridine-rich nucleotide motif in miRNAs identified by a computer search algorithm; **D.** Presence of the two motifs in the 18 pro-inflammatory miRNAs.

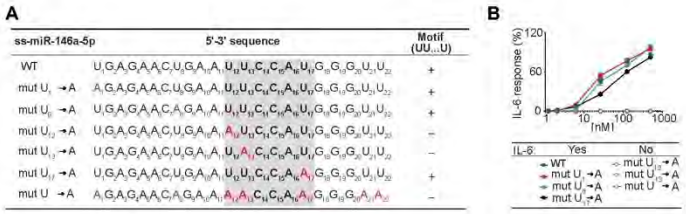

Figure 2. Importance of UU…U motif in miR-146a-5p-induced IL-6 production in macrophages. A. Nucleotide sequences of single-stranded miR-146a-5p and its various U→A mutants. The $U_{12}U_{13}…U_{17}$ motif sequence is highlighted in shade. U→A mutants are in red. **B.** Dose-response of IL-6 production in bone marrow-derived macrophages treated with miR-146a-5p or its various U→A mutants (50 nM), n=3.

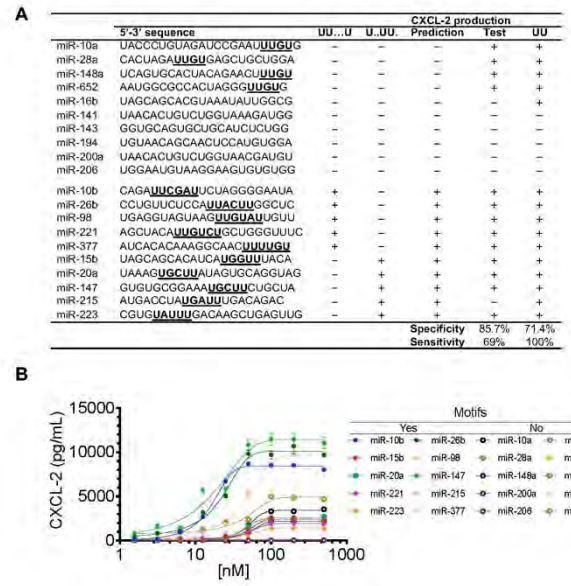

Figure 3. Validation of UU…U and U..UU motif in their association with pro-inflammatory properties of various miRNAs. A. A list of miRNAs with or without the two motifs and their predictive accuracy of CXCL-2 production. **B.** Dose-dependency of cytokine production in cells treated with various doses of miRNA mimics.

Critical Care - 24 Utilizing the Echocardiographic Assessment using Subcostal view only (EASy) exam in hypotensive peri-operative patients: A single-site retrospective review

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Introduction: POCUS has been useful in diagnosing and treating cases of hemodynamic instability (1-2). Its use in peri-operative settings has been documented in a limited number of studies (3-6). Of note, the subcostal approach to echocardiograms as a single view has the potential to become the superior view due to its ease of access, efficiency, and ability to visualize the IVC consistently (7). This study seeks to demonstrate how the echocardiographic assessment using subcostal view only (EASy) approach was effective in directing clinical decision making for hypotensive patients using standardized criteria to categorize patient's echocardiograms within etiologic clusters and common cardiac phenotypes.

Methods: 2075 POCUS exams were collected at Albany Medical Center, an urban level 1 trauma center, between August 2017 and June 2021 and were reviewed for the study. Training of residents to perform the EASy exam consisted of a 4-day ultrasound course with opportunity to gain proficiency in the PACU. We included all patients with hypotension as reason for anesthesia consult who had a completed EASy exam with saved images that were available for review. Patients were then divided into three cohorts: those with an EASy exam completed pre-operatively, intra-operatively, or post-operatively in the post-anesthesia care unit (PACU).

Results: 78 patients were included across the 3 study cohorts. 70 (86.5%) EASy exams were of good/adequate quality upon review, and 91% of exams were completed in less than 5 minutes with an average duration of 2.54 minutes per EASy exam. The other 8 patients' exams were of poor quality or unable to obtain view, thus were corroborated with a FATE exam between apical and parasternal views. At least 50% or more of the exams were completed successfully by anesthesia residents, the rest being completed by attendings. Mortality rates were highest in the pre-op and intra-op patient cohorts and lowest in the PACU cohort (20%, 18.75%, and 1.92%, respectively). All patients who received EASy exams with good/adequate quality (N = 70) or a FATE exam (N = 8) when EASy was poor quality or unable to be obtained benefited from having an exam done as it provided diagnostic information at minimum. The majority of patients also benefited from having an EASy exam +/- FATE due to its ability to aid in clinical interventions: 80%, 81.2%, and 69.2% in the pre-op, intra-op, and PACU cohorts, respectively. Most common interventions included IV volume boluses, administration of pressors and inotropes, and other interventions (procedures, surgery, diuresis).

Conclusion: The EASy exam is a novel approach to evaluating hemodynamic status in patients, especially so in a variety of peri-operative settings: pre-operatively, intra-operatively, and immediately post-operatively in the PACU. Training of residents to perform the EASy exam has been demonstrated as both feasible and desirable given the high success rate, alluding to the need for further implementation of this method of POCUS. Mortality rates trending higher in the pre- and intra-operative cohorts could indicate that these patients were sicker and in greater need of acute care (i.e. transfer directly from OR to ICU) than their peers in the PACU. In future studies, we hope to further demonstrate the EASy exam's efficacy in other settings and patient populations.

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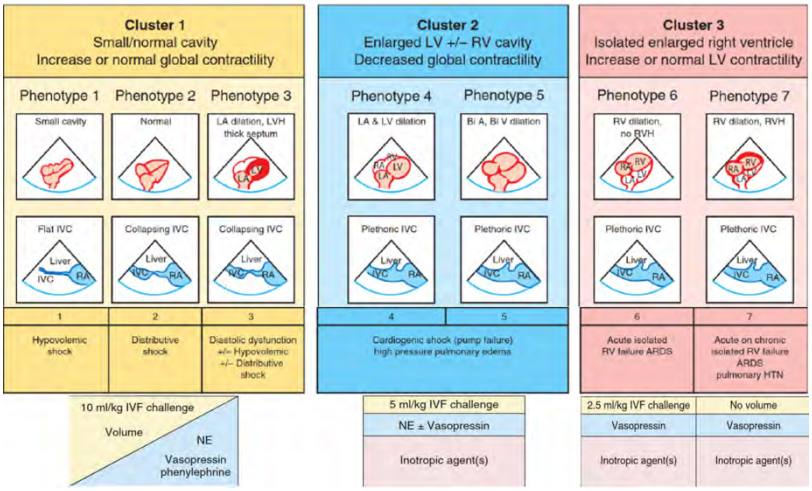
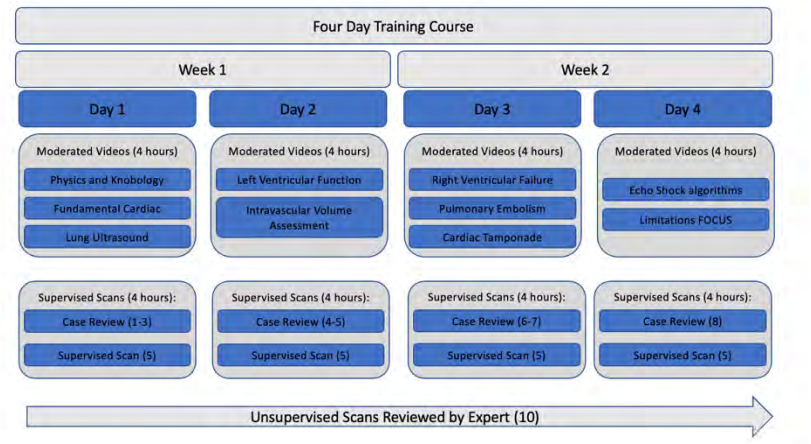
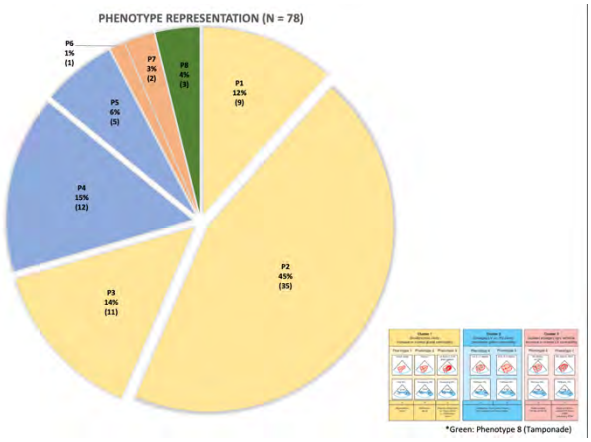


Cohort (N)	% Male (N)	Avg BMI	Average Days in Hospital	Average Days in ICU (N)	Average Days Ventilated (N)	Mortality % (N)	Average Time of EASY Exam (min)	% Exams w/ good or adequate quality (N)	% Exams completed by resident (N)
Pre-op (10)	50.0 (5)	27.71	16.8	8.6 (8)	2.3 (5)	20.0 (2)	2.6	100 (10)	50.0 (5)
OR (16)	62.5 (10)	28.46	20.13	10.81 (13)	4.13 (9)	18.75 (3)	2.14	93.75 (15)	50.0 (8)
PACU (52)	44.23 (23)	27.95	9.83	2.76 (25)	0.45 (6)	1.92 (1)	2.88	86.5 (45)	86.5 (45)



Intervention Type	Pre-op			Intra-op			PACU		
Total pts (N = 78)	*Cluster 1 (N = 3)*	*Cluster 2 (N = 4)*	*Cluster 4 (N = 3)*	*Cluster 1 (N = 11)*	*Cluster 2 (N = 4)*	*Cluster 3 (N = 1)*	*Cluster 1 (N = 41)*	*Cluster 2 (N = 9)*	*Cluster 3 (N = 2)*
No additional interventions	1	1	0	0	1	0	6	5	1
IV Bolus	1	1	0	1	0	0	24	19	1
Stop IV Fluids	0	0	0	1	0	0	0	0	0
Blood Transfusion	0	2	1	3	0	0	5	5	0
Pressors (Norepinephrine, phenylephrine, vasopressin)	2	1	0	10	4	1	23	19	0
Inotropes (Dopamine, Epinephrine, milrinone)	0	0	0	0	0	0	2	2	0
Stop/reduce Pressors	0	1	1	1	0	0	6	5	0
Stop/reduce inotropes	0	1	0	0	0	0	2	2	0
Other Interventions (procedure, diuresis, surgery, albumin)	1	3	3	5	0	0	13	11	0



Critical Care - 25 Initial Pulse Oximetry Readings in Patients Suspicious for SARS-CoV-2 (COVID-19): A Predictor for Hospital Death?

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Introduction: Early recognition of patient deterioration has been identified as the primary successful determinant of medical intervention.[1, 2] However, recognition of patient deterioration requires measurements with timely decisions based upon these values[3-6] as tissue hypoxia can lead to death under stress-load conditions.[7] We examined the initial vital signs assessments in the Emergency Department (ED) in patients suspicious for COVID-19 and who were subsequently admitted to the ICUs at Ochsner Health.

Methods: Following IRB approval, initial vital signs in all patients 18 years and older with a diagnosis of COVID-19 were reviewed during ED admission leading to transfer to the COVID ICU. These values underwent multivariable and recursive partitioning analyses. Probability values for all frequentist tests were set at <.005 for statistical significance to minimize the risk for false discovery rates.[8]

Results: In this preliminary study of 121 patients, the overall hospital mortality rate was 22.3 95%CI 15.8-30.5%. The initial vital signs assessments in the ED were entered into a nominal logistic fit model for hospital mortality. The results of that model are shown in Table 1. Temperature, heart rate, respiratory rate, systolic and diastolic blood pressures were not statistically associated with hospital mortality (Table 1). In contrast, pulse oximetry (SpO2) was statistically associated with hospital mortality ($\chi 2=8.1$, P=0.0045). The misclassification rate was 24%. The relationship of hospital mortality to initial SpO2 readings are shown in Figure 1. A progressive increase in hospital mortality was observed with decreasing SpO2 values (Fig. 1). Cut-points for initial SpO2 values based upon hospital mortality were calculated using recursive partitioning and the results of that analysis are shown in Figure 2. A cut-point of 88% identified two groups at different risk for hospital mortality (Fig. 2).

Conclusion: These preliminary results in patients suspicious for COVID-19 suggest that SpO2 values during initial ED assessment require earlier attention by healthcare personnel.

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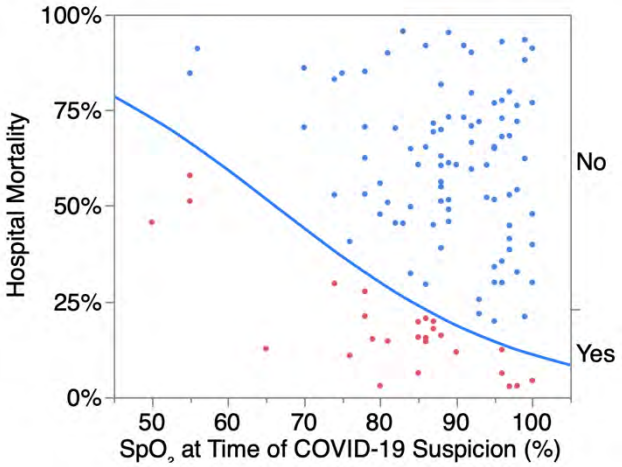
Table 1: Nominal Logistic Model of Initial Vital Signs in the ED for ICU admission for COVID-19

Parameter Estimates at Time of COVID-19 Suspicion

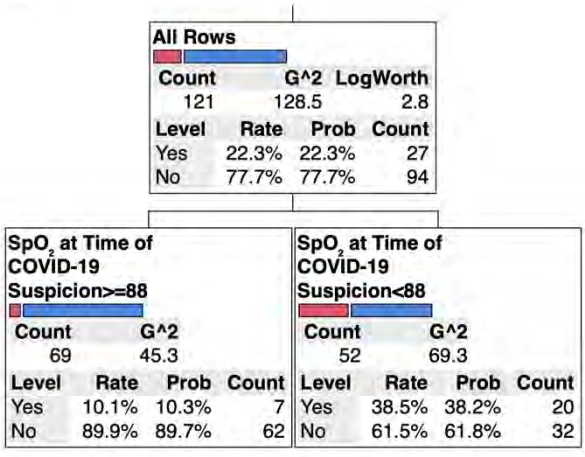
Terms	Estimate	Std Error	ChiSquare	Prob>ChiSq
Intercept	6.43	4.69	1.9	0.1701
Temperature	-0.03	0.10	0.1	0.7506
Heart Rate	0.02	0.01	1.5	0.2179
Respiratory Rate	-0.08	0.05	2.2	0.1382
Systolic Blood Pressure	-0.01	0.01	0.3	0.6042
Diastolic Blood Pressure	0.01	0.02	0.1	0.7762
SpO_2	-0.07	0.02	8.1	0.0045

ED: Emergency Department; Std Error: Standard error of the estimates; Prob>ChiSq: Probability that the ChiSquare statistic is due to chance. Values <.005 are statistically significant.[8]

Figure 1



Nominal logistic fit of hospital mortality by SpO_2 readings at time of COVID-19 suspicion. The blue line plots the probability of hospital mortality by SpO_2 readings. Red dots identify deceased patients. Blue dots identify alive patients. The blue line is the incidence of hospital mortality plotted across the SpO_2 readings in this patient population. n=121, ChiSquare=9.3, P=0.0022. P values <.005 are statistically significant.[8]



Recursive Partitioning of S_pO_2 readings during initial Emergency Department assessment in patients suspicious for COVID-19. Upper box: the overall incidence of hospital mortality was 22.3% in this patient population. When S_pO_2 was greater than 88%, the incidence of hospital mortality decreased to 10.1% (lower, left box). When S_pO_2 was <88%, the incidence of hospital mortality increased to 38.5% (lower, right box).

Economics, Education and Policy

Economics, Education and Policy - 1

Interprofessional Anesthesia Simulation: Education of Resident Physicians and Student Anesthetists

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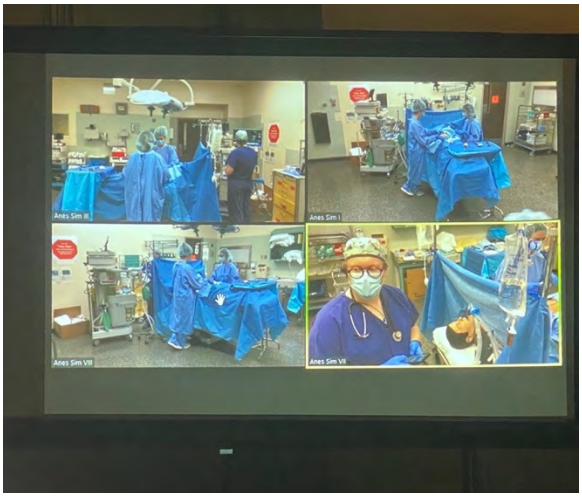
Introduction: Many anesthesia groups across the United States practice in an Anesthesia Care Team Model using medical direction or medical supervision. Few, if any, ACGME approved residency programs in anesthesiology include interprofessional training on how to work in an anesthesia team. We propose our innovative interprofessional simulation event as a way to close this educational gap in anesthesia resident physician training.

Methods: Fifty three Clinical Anesthesia Year 2 and 3 anesthesia resident physicians participated in interprofessional simulations with a team of approximately ten Student Anesthesiologist Assistants (SAAs) over two years. Each resident physician was in the 'hot seat' for one simulation where they provided medical direction to two simulated operating room cases with SAAs playing the role of anesthetist as an embedded participant. Scenarios included every day situations where anesthesiologists need to prioritize which room, patient, and anesthetist demanded their clinical attention and presence. The simulation day also included a discussion, question, and answer period on anesthesia billing: medical supervision vs. medical direction vs. QZ.

Results: Overall feedback from both resident physicians and SAAs was positive. In 2020, feedback from CA3s was to move the simulation to CA2 year when residents are looking for jobs, with the majority of residents noting they wish they had been told about anesthesia billing practices before they signed contracts for jobs. In 2021, only one third to one half of CA2s already had signed for jobs after residency graduation at the time of the simulation. This encouraged a robust and interactive conversation about anesthesia billing practices across our state of Indiana. Debriefing conversations were qualitatively themed across all groups. All debriefings included a discussion of how participants felt being needed in two places at the same time as well as the obstacles of the scenario. Topics discussed with every group also included how to communicate best, technology challenges with communication, how to plan for breaks, how to ask for help from colleagues, how to effectively use your circulating nurse, and how to maintain professionalism in stressful situations. Many participants noted how hard it was to both take care of a patient and send messages at the same time. We also discussed that relationships between anesthesiologists and anesthetists take time to develop and there is a balance in managing the art of an anesthetic versus asking someone to follow evidence based best practice. Topics such as errors in handoff communication, second victim, error disclosure, and best practices in use of a medical translator were covered as they arose in the simulated scenarios.

Conclusion: Interprofessional simulations with resident physician anesthesiologists and anesthetists in training are possible to run and can provide a psychological safe learning environment for the practice of the seven steps of medical direction. Education on anesthesia billing is well perceived by anesthesia residents and should take place at all training institutions.



Economics, Education and Policy - 2

Projecting Future Pediatric Post-Surgical Mortality in the United States: Current Trends and Racial/Ethnic Disparities

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Introduction: Despite advances in medical care, pediatric postoperative mortality varies across groups defined by race and ethnicity in the United States, with minority children bearing the highest burden. Forecasting changing trends is imperative to make essential adjustments to prevailing public health policies, priorities for health research, and fiscal investments. In this report, we evaluated trends in pediatric post-surgical mortality rates by race/ethnicity between 2000 and 2019 and projected these rates to 2029. We also estimated the impact of potential policy changes on mortality, quantifying the degree of mortality reduction needed to eliminate the disparities within the next decade.

Methods: We performed a population-based study using a large, nationally representative sample of pediatric inpatient surgery patients between 2000 and 2019. We included children <18 years of age who were admitted for intermediate to high-risk surgery, as previously defined (n=265,440).[1] The primary outcome was risk-adjusted mortality rates across racial and ethnic groups. We estimated the annual risk-adjusted mortality rates for 2020-2029 by race/ethnicity using Age-Period-Cohort models, as used in previous studies.

Results: Between 2000 and 2019, surgical mortality declined across racial categories, with Black children having the lowest rate of decline (Average annual percent changes [AAPCs]: -1.7% for White children, -0.9% for Black children, and -1.8% for Hispanics). Despite the overall decline, the risk-adjusted mortality rates trended consistently higher for Black and Hispanic children, compared to White children, with no evidence of narrowing of the disparity gap (Pairwise tests of parallelism of the AAPCs not statistically significant)-Figure 1. If Black and Hispanic children had post-surgical mortality rates comparable to their White peers, 3210 deaths would have been avoided in the last two decades. If the current trends continue, these disparities are projected to result in 1,493 excess deaths in children of minority race/ethnicity over the next 10 years. Mortality rates would need to decline by 6.4% per year for Black children and 1.9% per year for Hispanic children to eliminate the disparity gap by the end of 2029.

Conclusion: Despite a steady decline in pediatric post-surgical mortality across all groups, persistent racial/ethnic disparity existed over the past two decades. Pediatric post-surgical mortality rates need to decline 7-fold faster than the current rates if disparity gaps are to be eliminated within the next decade. Targeted, robust actions are imperative to ensure equitable pediatric surgical health.

References: 1. Kraemer K, Cohen ME, Liu Y, Barnhart DC, et al. Development and Evaluation of the American College of Surgeons NSQIP Pediatric Surgical Risk Calculator. J Am Coll Surg. 2016 Nov;223(5):685-693.

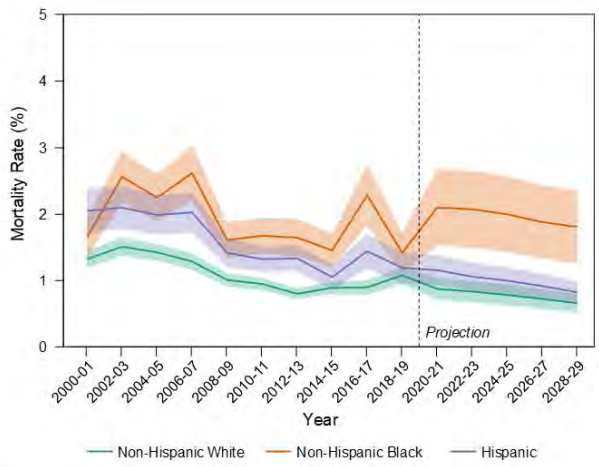

Figure 1. Observed and projected risk-adjusted postoperative mortality rates for children <18 years between 2000 to 2029(inclusive).

Economics, Education and Policy - 3

Burnout in Anesthesiologists Underrepresented in Medicine

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Introduction: Burnout is characterized by emotional exhaustion, depersonalization, and low sense of personal accomplishment, [1] and is associated with poorer quality of care and patient safety.[2, 3] Anesthesiologists are at high risk for burnout with an alarming 59.2% of US anesthesiologists reporting emotional exhaustion and/or depersonalization. [4, 5] In this study we evaluated the risk factors for burnout among anesthesiologists who identify as underrepresented based on race (UiM) and/or consider English as a second language (ESL).

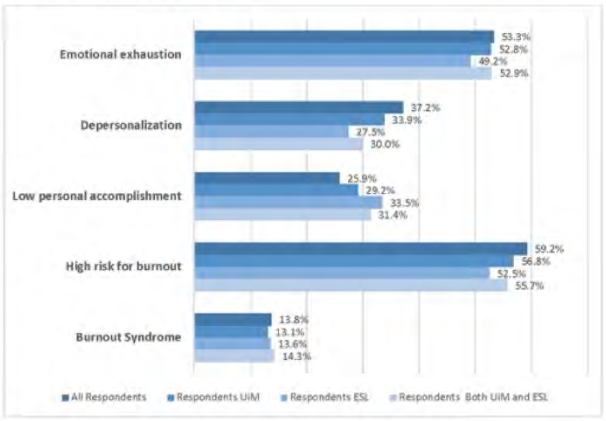
Methods: Data for this subgroup analysis was collected from a national survey of US attending anesthesiologists conducted between March 6, 2020, and March 30, 2020. Burnout was assessed using the Maslach Burnout Inventory Human Services Survey. [1] We considered high scores in emotional exhaustions and/or depersonalization to indicate high risk for burnout. Burnout syndrome was defined by the presence of the three dimensions of burnout. Additional questions were added to the survey, focusing on personal and occupational risk factors for burnout. For each subgroup univariate comparisons by high risk for burnout were performed. Multivariate logistic regression analysis was performed to investigate the association between identifying as UiM and/or ESL and burnout.

Results: When compared to all respondents (3,898), those who identify as UiM (398), ESL (236) and both UiM and ESL (70) had similar rates of burnout syndrome (13.8% vs 13.1% vs 13.6% vs 14.3%) and high risk for burnout (52.9% vs 56.8% vs 52.5% vs 55.7%). When compared to their non-UiM counterparts, UiM anesthesiologists at high risk for burnout reported significantly lower rates of having someone available to safely talk about concerns at work (26.0% vs 17.7%). Among those considered high risk for burnout, adjusted odds of lack of support in work-life were significantly higher in those who identify as UiM (OR, 19.7; 95% CI, 9.74-39.7), ESL (OR, 7.56; 95% CI, 3.26-17.5) and both UiM and ESL (OR, 10.4; 95% CI, 2.21-49.4) when compared to all respondents (OR, 6.7; 95% CI, 5.3-8.5).

Conclusion: Anesthesiologists who identify as racial/ethnic minorities report burnout at comparable rates to their non-minority counterparts. Lack of support in the workplace is the independent risk factor most strongly associated with high risk for burnout among UiM and ESL anesthesiologists. The association of lack of support in work-life and high risk for burnout is significantly greater among UiM anesthesiologist when compared to all respondents. Our study suggests that burnout rate alone, as it is currently measured and reported, does not tell the entire story of burnout among UiM physicians. Our study also suggests that the true identity of burnout among UiM physicians rests in the details of the workplace environment that UiM physicians face.

References: 1.Evaluating stress: A book of resources.1997,p. 191-218. 2. Annals of surgery, 2010. 251(6): p. 995-1000. 3.Journal of general internal medicine : JGIM, 2017. 32(4): p. 475-482. 4.Anesthesiology, 2021. 134(5): p. 683-696. 5.Archives of internal medicine (1960), 2012. 172(18): p. 1-9.

Figure 1: Dimensions associated with Burnout



UiM vs Non-UiM

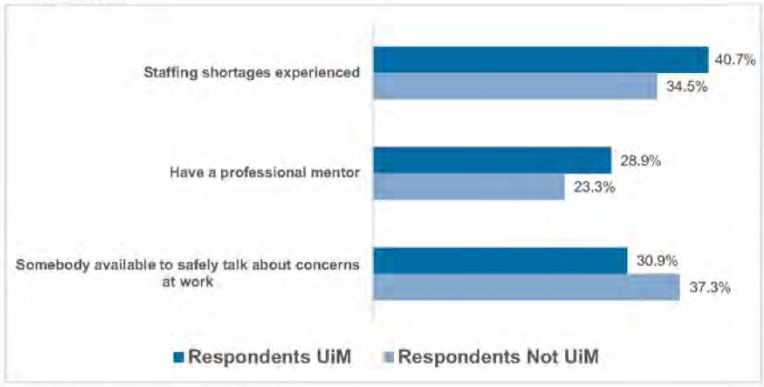
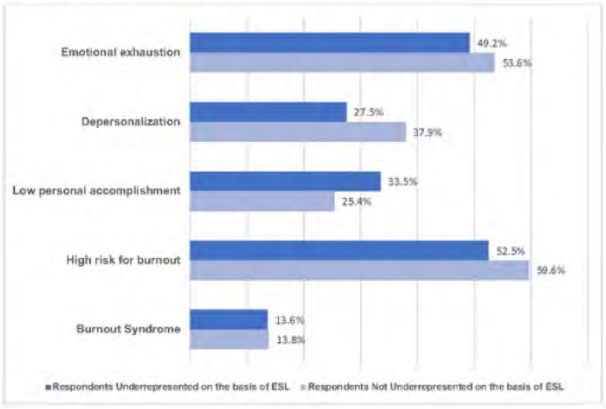
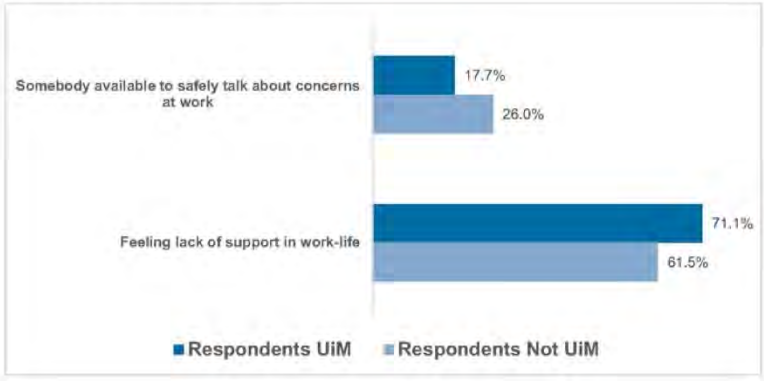


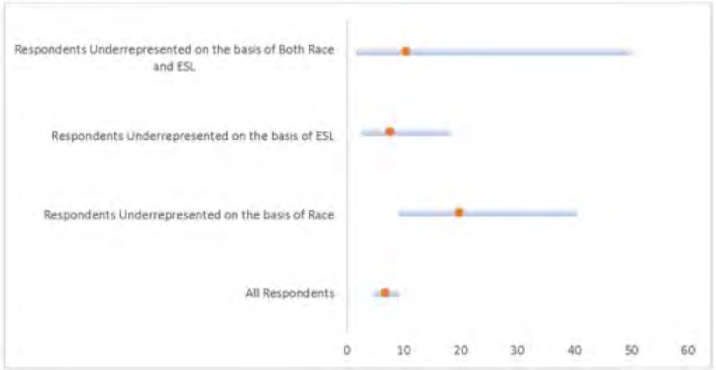
Figure 2: Dimensions associated with burnout in ESL compared to non-ESL



High Risk for Burnout: UiM vs Non-UiM



Adjusted Odds Ratio for Lack of Support in Work-Life Among High Risk for Burnout



Economics, Education and Policy - 4

Multimodal, coached telehealth prehabilitation has high compliance and improves exercise and cognitive capacity prior to surgery: a pilot study

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Introduction: Over 30 million surgeries are performed annually in the US, with up to 30% or patients experiencing recovery delays, prolonged pain, opioid consumption and functional impairment, contributing $8 billion annually to US health care costs. Novel interventions that improve pain resolution, minimize opioid exposure, and accelerate functional recovery are urgently needed. Multi-modal pre-operative optimization programs (prehab) integrating exercise with nutrition counseling and stress reduction have been shown to decrease postoperative complications, hasten recovery of functional capacity, decrease length of hospital stay, and decrease healthcare costs (1-5). Preoperative cognitive training can decrease the incidence of postoperative cognitive decline(6) and postoperative delirium(7). However, prehab programs are underutilized and compliance remains an issue, as lack of personalized guidance, motivation, and convenient transportation remain as barriers to consistent patient participation. Our approach tested a patient-centered, multimodal, coached prehabilitation program combining telehealth physical exercise training with nutritional counseling, cognitive training, and guided meditation designed to optimize each patient's ability to cope with the physical and mental stress of surgery and to recover faster, with fewer complications.

Methods: Adult patients (N = 12) scheduled for major elective surgery under general anesthesia were recruited(8). Baseline cognitive and exercise capacity was assessed using the quick mild cognitive impairment (qMCI) test, the six-minute walk test (6MWT), timed up and go (TUG), five times sit to stand test (5XSTST), and timed wall squat. All patients underwent coached prehabilitation (32.6±15.2 days, 10.67±3.38 sessions) via telehealth. Patients were also prescribed a home regimen of daily exercises, cognitive training with the Lumosity application, Mediterranean Diet nutrition instructions, and guided meditation recordings. Patients repeated the cognitive and fitness tests after the program, and compliance measures were recorded.

Results: High overall patient compliance with nutrition (88%) and physical exercises (72%) was observed, while compliance on the guided meditation (55%) and cognitive exercises (33%) was moderate. We observed significant improvement between baseline and post-prehab scores on the qMCI ($p = 0.001$, 1-tailed, paired t tests), 6MWT ($p = 0.01$), and TUG ($p = 0.03$), as well as a trend towards longer wall squat time ($p = 0.05$). In addition, program length correlated iwth qMCI improvement ($r = 0.69$, $p = .03$), exercise compliance and correlated with 5TSTS improvement ($r = 0.87$, $p = .03$), qMCI improvement, and TUG improvement ($r = 0.90$, $p = .02$).

Conclusion: A multimodal, coached telehealth prehab program had high patient compliance for nutrition and physical exercise programs, resulting inimproved exercise and cognitive capacity prior to surgery. Comparative studies between coached telehealth prehab and standard prehab programs will be important to determine whether a high-compliance prehab program can positively alter clinical and biological (including immunological) risk factors for adverse post-operative outcomes.

References: 1. Eur J Prev Cardiol. 25:404-417. 2018 2. Surgery. 160:1189-1201. 2016 3. Anesthesiology. 121:937-47. 2014 4. Front Surg. 19;8:628848. 2021 5. J Am Coll Surg. 230:306-313.e6. 2020 6. Med Sci Monit. 21:798-805. 2015 7. JAMA Surg. 156:148-156. 2021 8. World J Surg. 44:2211-2219. 2020

Economics, Education and Policy - 5

Assessing Anesthesiology Needs in Simulation Based Medical Education

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Introduction: New Accreditation Council for Graduate Medical Education (ACGME) milestones emphasize competency-based training with objective performance measures.[1,2] Simulation-based medical education (SBME) is linked to superior clinical performance and skill acquisition.[3] This study's primary aim was to determine how training programs currently use SBME.

Methods: An anonymous 10-question survey was created in REDcap to assess where and how SBME occurs, which SBME resources are available, frequency of and barriers to SBME's use, and perceived utility of a departmental education lab dedicated to SBME.[4] The survey can be seen in Supplemental File 1. Publicly available contact information was obtained for 148 out of 161 US anesthesiology residency program directors listed on the Fellowship and Residency Electronic Interactive Database (FREIDA).[5] General survey reminders were sent twice (once weekly) following initial distribution on December 7, 2020, followed by targeted emails to nine respondents over approximately 3 weeks (April 22,2021 to May 7, 2021). The targeted respondents were selected due to being considered likely to respond to direct survey requests, and / or had recently assumed positions from preceding directors.

Results: The survey response rate was 30.4% (n=45 out of 148) and included respondents from all US Census regions; full survey results are displayed in Table 1. SBME typically occurred at shared on-campus labs (64.4%), with residents typically participating in SBME one to four times per year (64.4%). Frequently practiced skills included airway management, trauma scenarios, non-technical skills, and ultrasound techniques (all ≥ 77.8%; details displayed in Chart 1). Mannequins, dedicated task trainers, and ultrasound / echocardiography simulators were generally available resources (100%, 84.4%, and 77.8% respectively; details in Chart 2). Frequently cited logistical barriers (details in Chart 3) included COVID-19 precautions (75.6%), scheduling (57.8%), and lack of trainers (48.9%). Most respondents believed a dedicated departmental education lab would be useful or very useful (77.8%).

Conclusion: Our findings aligned with other similar surveys: particularly of non-technical skills being frequently practiced via SBME[6] and scheduling difficulties being a prominent SBME barrier.[6,7] A 2018 national survey of ACGME accredited pediatric anesthesiology fellowship programs also notably reported 87% of respondents believed standardized simulation curricula should be developed for voluntary use. When considered alongside our survey's revelation that most anesthesia residency programs consider dedicated education labs as useful or very useful resources, it appears there is a national interest in increased opportunities for / implementation of SBME. As our specialty moves towards competency based-training, it is increasingly important to provide learners with opportunities to improve skills with greater frequency and flexibility.

References: 1. Educating Anesthesiologists During the Coronavirus Disease 2019 Pandemic and Beyond. Anesth Analg. 2021;132(3):585-593. 2. The Anesthesiology Milestones 2.0: An Improved Competency-Based Assessment for Residency Training. Anesth Analg. 2021; 133(2):353-361 3. Does simulation-based medical education with deliberate practice yield better results than traditional clinical education? A meta-analytic comparative review of the evidence. Acad Med. 2011;86(6):706-11. 4. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research

informatics support, J Biomed Inform. 2009;42(2):377-81 5. The AMA Residency & Fellowship Database. FREIDA. https://freida.ama-assn.org/. Accessed July 8, 2021. 6. Barriers to use of simulation-based education. Can J Anaesth. 2005;52(9):944-950. 7. Medical simulation utilization among pediatric anesthesiology fellowship programs. Paediatr Anaesth. 2020;30(7):823

Table 1. Survey Results

Question[a]	Responses
1) Geographic area	- Northeast US (ex: Massachusetts, New York, Pennsylvania, etc.) - 15 (33.3%) - South US (ex: Texas, North/South Carolina, Florida, etc.) - 13 (31.1%) - Mid-West US (ex: Michigan, Wisconsin, Illinois, etc.) - 9 (20.0%) - West US (ex: California, Oregon, Colorado, Hawaii, etc.) - 7 (15.6%)
2) Frequency of scheduled simulation education for residents	- 1 to 4 times per year (I.e. quarterly / annually) - 28 (62.2%) - Approximately once a month - 10 (22.2%) - 2 to 4 times per month (I.e., weekly / every other week) - 3 (6.7%) - Other[d] - 4 (8.9%)
3) Estimated participation rate of residents & scheduled simulations	- 80 – 100% - 36 (80%) - 60 – 79% - 8 (17.8%) - 40 – 59% - 0 (0%) - 20 – 39% - 1 (2.2%) - 0 – 19% - 0 (0%)
4) Locations of simulation-based training (Check all that apply)[c]	- On-campus central simulation lab shared with other departments - 38 (84.4%) - Off-campus simulation lab which is not directly affiliated with your organization - 9 (20.0%) - Dedicated space designed exclusively for anesthesia department - 16 (35.6%) - Anesthesia departments break rooms / lounges - 8 (17.8%) - Conference rooms / auditoriums (shared spaces) - 11 (24.4%) - Other[e] – 13 (28.9%)
5) Primary simulation-based training location (Choose one)	- On-campus central simulation lab shared with other departments – 29 (64.4%) - Off-campus simulation lab which is not directly affiliated with your organization–5 (11.1%) - Dedicated space designed exclusively for anesthesia department – 6 (13.3%) - Conference rooms / auditoriums (shared spaces) - 2 (4.4%) - Other[f] – 3 (6.7%)
6) Simulation skills & activities practiced at primary location (Check all that apply)[c]	- Airway management skills (ex: direct laryngoscopy, supraglotticairway placement, etc.) - 42 (93.3%) - Trauma / case scenarios - 39 (86.7%) - Non-technical skills training (ex: communication, leadership skills, etc.) - 37 (82.2%) - Ultrasound imaging - 36 (80.0%) - TEE - Transesophageal Echocardiography - 32 (71.1%) - Fiberoptic skills - 30 (66.7%) - Spinal / epidural placement - 28 (62.2%) - Arterial line placement - 23 (51.1%) - IV placement- 26 (57.8%) - ACLS Training - Advanced Cardiovascular Life Support - 26 (57.8%) - Regional anesthesia - 21 (46.7%) - Didactics - 16 (35.6%) - Research studies - 9 (20.0%) - Other[g] - 6 (16.7%)
7) Resources at primary simulation location (Check all that apply)[c]	- Mannequins - 45 (100%) - Dedicated task trainers (ex: ultrasound-compatible phantoms) - 38 (84.4%) - Ultrasound / echocardiography simulators - 35 (77.8%) - Dedicated staff to manage the space - 35 (77.8%) - Virtual Reality / Augmented Reality software programs - 11 (24.4%) - 3D printing models - 6 (13.3%) - Other[h] - 2 (4.4%)

8) Barriers to simulation (Check all that apply, or N/A)[c]	- COVID-19 precautions - 34 (75.6%) - Scheduling difficulties with participants - 26 (57.8%) - Lack of trainers / staff availability to facilitate training - 22 (48.9%) - Booking availabilities with the simulation lab - 19 (42.2%) - Financial costs for supplies - 13 (28.9%) - Inadequate equipment for desired training - 10 (22.2%) - Costs for renting simulation lab - 9 (20.0%) - Not enough space to accommodate teaching groups - 9 (20.0%) - Difficulty traveling to simulation site(s) - 5 (11.1%) - N/A - I am not aware of any such barriers - 1 (2.2%) - Other[g] - 3 (6.7%)
9) Utility of a departmental education lab as described	- "5 - Very Useful" - 28 (62.2%) - "4" - 7 (15.6%) - "3" - 6 (13.3%) - "2" - 2 (4.4%) - "1 – Not Very Useful" - 2 (4.4%)
10) Desired resources for a departmental education lab (Check all that apply, or N/A)[c]	- Fiberoptic scope (or equivalent simulator) - 37 (82.2%) - Ultrasound / echocardiography simulator - 36 (80.0%) - Ultrasound machine - 35 (77.8%) - Airway management mannequins / trainers - 34 (75.6%) - Regional anesthesia trainers - 31 (68.9%) - Virtual Reality / Augmented Reality simulators - 27 (60.0%) - Staff dedicated to managing the space - 27 (60.0%) - 3D printer - 12 (26.7%) - N/A - I do not believe such a center is necessary for our department at this time - 2 (4.4%) - Other[h] - "Neuraxial" - 1 (2.2%)

[a]Abbreviations for the question's core concept are listed in this table; the full text of each question can be seen in Supplemental File 1.

[b]Responses are reported in the following format: Answer selected, number of responses (percentage of respondents who selected answer).

[c]These questions allowed respondents to select multiple options simultaneously, as applicable; thus, percentages for those questions total to over 100%. Otherwise, respondents could only select one of the available options.

[d]Other responses to question #2 consisted of one of each of the following responses: "quarterly beginning in June of intern year," "6-8 times a year," "five labs in 12 months," and "6 1 ½ hour sessions during internship, 50 hours during [clinical anesthesia] orientation, intermittent manikin, [point-of-care ultrasound] and [transesophageal echocardiography] throughout residency."

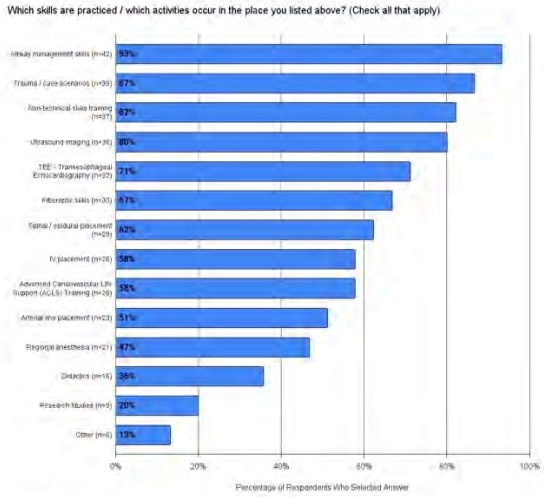
[e]Other responses to question 4 consisted of in-situ at actual clinical locations / operating rooms (n=8); central simulation lab for course staff and virtual participation for learners (n=1); an off-campus, affiliated center shared between departments (n=2); cadaver lab (n=1); and virtual simulation training (n=1). [f]Other responses to question 5 consisted of one of each of the following responses: an off campus, affiliated, shared lab, empty ORs; and a central shared lab which is on campus for the medical school, but off campus for the center's department.

[g]Other responses to question 6 consisted of one of each of the following responses: introduction to pediatrics rotation; clinical scenarios, OSCE (Objective Structured Clinical Examination) preparations, and cadaver lab; specific anesthesia complications; point-of-care ultrasound; and crisis resource management. One respondent did not provide details for their selection of "other" for this question.

[h]Other responses to question 7 consisted of one of each of the following responses: video, and standardized patients.

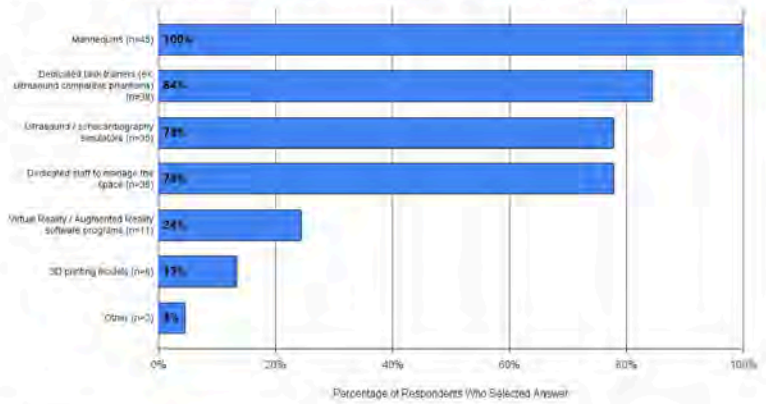
[i]Other responses to question 8 consisted of one of each of the following responses: "faculty time / availability," "time away from clinical duties," and "clinical schedule and clinical work demands." [j]Other response to question 10 consisted of one respondent who wrote "Neuraxial."

Chart 1. Skills and Activities at Primary Simulation Spaces.



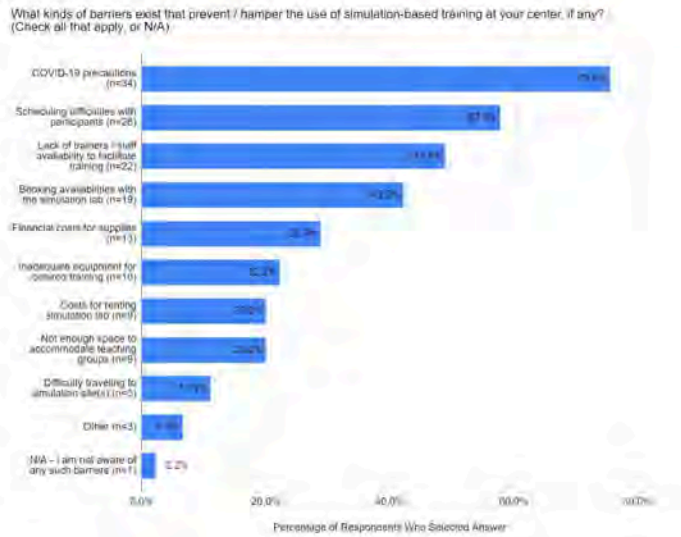
The above bar chart in Chart 1 depicts the distribution of respondents' answers for question 6 of our survey (n=45): "Which skills are practiced / which activities occur in the place you listed above [i.e., at the primary simulation space]," in descending order by percentage of respondents who selected each skill. This question allowed respondents to select multiple options simultaneously, as applicable; thus, percentages for the answers total to over 100%. Other responses to this question consisted of one of each of the following responses: introduction to pediatrics rotation; clinical scenarios, OSCE preparations, and cadaver lab; specific anesthesia complications; point-of-care ultrasound; and crisis resource management. One respondent did not provide details for their selection of "other" for this question.

Chart 2. Resources at Primary Simulation Spaces.

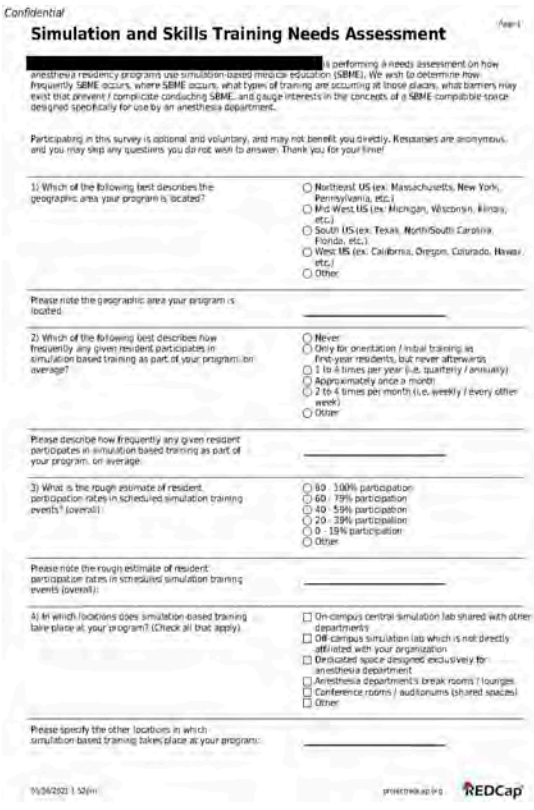


The above bar chart in Chart 2 depicts the distribution of respondents' answers for question 7 of our survey (n=45): "What resources are available at the primary center for simulation-based training," in descending order by percentage of respondents who selected each resource. This question allowed respondents to select multiple options simultaneously, as applicable; thus, percentages for the answers total to over 100%. Other responses to this question 7 consisted of one of each of the following responses: video, and standardized patients.

Chart 3. Barriers to Simulation.



The above bar chart in Chart 3 depicts the distribution of respondents' answers for question 8 of our survey (n=45): "What kinds of barriers exist that prevent / hamper the use of simulation-based training at your center, if any," in descending order by percentage of respondents who selected each resource. This question allowed respondents to select multiple options simultaneously, as applicable, or select "N/A I am not aware of any such barriers;" thus percentages for the answers total to over 100%. Other responses to this question consisted of one of each of the following responses: "faculty time / availability," "time away from clinical duties," and "clinical schedule and clinical work demands."



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Simulation and Skills Training Needs Assessment

[redacted] is performing a needs assessment on how anesthesia residency programs use simulation-based medical education (SBME). We wish to determine how frequently SBME occurs, where SBME occurs, what types of training are occurring at those places, what barriers may exist that prevent / complicate conducting SBME, and gauge interests in the concepts of a SBME-compatible space designed specifically for use by an anesthesia department.

Participating in this survey is optional and voluntary, and may not benefit you directly. Responses are anonymous, and you may skip any questions you do not wish to answer. Thank you for your time!

1) Which of the following best describes the geographic area your program is located?
- ○ Northeast US (ex: Massachusetts, New York, Pennsylvania, etc.)
- ○ Mid-West US (ex: Michigan, Wisconsin, Illinois, etc.)
- ○ South US (ex: Texas, North/South Carolina, Florida, etc.)
- ○ West US (ex: California, Oregon, Colorado, Hawaii, etc.)
- ○ Other

Please note the geographic area your program is located:

2) Which of the following best describes how frequently any given resident participates in simulation based training as part of your program, on average?
- ○ Never
- ○ Only for orientation / initial training as first-year residents, but never afterwards
- ○ 1 to 4 times per year (i.e. quarterly / annually)
- ○ Approximately once a month
- ○ 2 to 4 times per month (i.e. weekly / every other week)
- ○ Other

Please describe how frequently any given resident participates in simulation based training as part of your program, on average:

3) What is the rough estimate of resident participation rates in scheduled simulation training events? (overall):
- ○ 80 - 100% participation
- ○ 60 - 79% participation
- ○ 40 - 59% participation
- ○ 20 - 39% participation
- ○ 0 - 19% participation
- ○ Other

Please note the rough estimate of resident participation rates in scheduled simulation training events (overall):

4) In which locations does simulation-based training take place at your program? (Check all that apply)
- ☐ On-campus central simulation lab shared with other departments
- ☐ Off-campus simulation lab which is not directly affiliated with your organization
- ☐ Dedicated space designed exclusively for anesthesia department
- ☐ Anesthesia department's break rooms / lounges
- ☐ Conference rooms / auditoriums (shared spaces)
- ☐ Other

Please specify the other locations in which simulation-based training takes place at your programs:

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5) In which location does the majority of simulation-based training take place at your program? (Choose one)
- ○ On-campus central simulation lab shared with other departments
- ○ Off-campus simulation lab which is not directly affiliated with your organization
- ○ Dedicated space designed exclusively for anesthesia department
- ○ Anesthesia department's break rooms / lounges
- ○ Conference rooms / auditoriums (shared spaces)
- ○ Other

Please specify the location in which the majority of simulation-based training takes place at your programs:

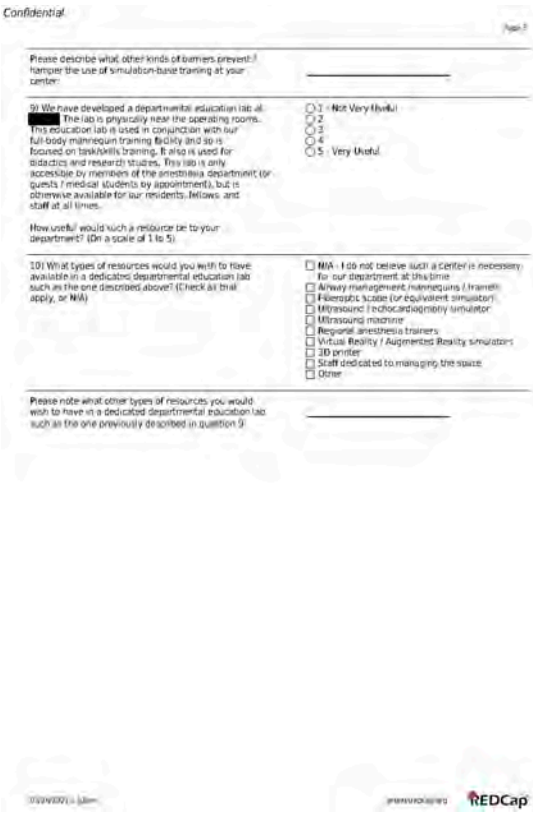
6) Where skills are practiced / which activities occur in the place you listed above? (Check all that apply)
- ☐ Airway management skills (ex: direct laryngoscopy, supraglottic airway placement, etc.)
- ☐ Fiberoptic skills
- ☐ Arterial line placement
- ☐ IV placement
- ☐ Ultrasound imaging
- ☐ TEE - Transesophageal Echocardiography
- ☐ Spinal / epidural placement
- ☐ Regional anesthesia
- ☐ Trauma / code scenarios
- ☐ Non-technical skills training (ex: communication, leadership skills, etc.)
- ☐ ACLS Training - Advanced Cardiovascular Life Support
- ☐ Didactics
- ☐ Research studies
- ☐ Other

Please specify what other skills / activities are practiced at the primary location for simulation-based training:

7) What resources are available at the primary center for simulation-based training? (Check all that apply)
- ☐ Mannequins
- ☐ Dedicated task trainers (ex: Ultrasound-compatible phantoms)
- ☐ Ultrasound / echocardiography simulators
- ☐ Virtual Reality / Augmented Reality software programs
- ☐ 3D printing models
- ☐ Dedicated staff to manage the space
- ☐ Other

Please note what other resources are available at the primary center for simulation-based training:

8) What kinds of barriers exist that prevent / hamper the use of simulation-based training at your center, if any? (Check all that apply, or N/A)
- ☐ Booking availabilities with the simulation lab
- ☐ Scheduling difficulties with participants
- ☐ Financial costs for supplies
- ☐ Costs for renting simulation lab
- ☐ Inadequate equipment for desired training
- ☐ Not enough space to accommodate teaching groups
- ☐ Lack of trainers / staff availability to facilitate training
- ☐ COVID-19 precautions
- ☐ Difficulty traveling to simulation site(s)
- ☐ N/A - I am not aware of any such barriers
- ☐ Other



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Please describe what other kinds of barriers prevent / hamper the use of simulation-base training at your center:

9) We have developed a departmental education lab at [redacted]. The lab is physically near the operating rooms. This education lab is used in conjunction with our full-body mannequin training facility and so is focused on task/skills training. It also is used for didactics and research studies. This lab is only accessible by members of the anesthesia department (or guests / medical students by appointment), but is otherwise available for our residents, fellows, and staff at all times.

How useful would such a resource be to your department? (On a scale of 1 to 5)
- ○ 1 - Not Very Useful
- ○ 2
- ○ 3
- ○ 4
- ○ 5 - Very Useful

10) What types of resources would you wish to have available in a dedicated departmental education lab such as the one described above? (Check all that apply, or N/A)
- ☐ N/A - I do not believe such a center is necessary for our department at this time
- ☐ Airway management mannequins / trainers
- ☐ Fiberoptic scope (or equivalent simulator)
- ☐ Ultrasound / echocardiography simulator
- ☐ Ultrasound machine
- ☐ Regional anesthesia trainers
- ☐ Virtual Reality / Augmented Reality simulators
- ☐ 3D printer
- ☐ Staff dedicated to managing the space
- ☐ Other

Please note what other types of resources you would wish to have in a dedicated departmental education lab such as the one previously described in question 9:

Economics, Education and Policy - 6

Pilot Implementation of Entrustable Professional Activities in Seven United States Anesthesiology Residency Training Programs

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Introduction: Entrustable Professional Activities (EPAs) represent a practical and informative framework to assess trainee competency and provide just-in-time feedback. EPAs can also be mapped to ACGME milestones to document trainee progress.[1-7] A set of EPAs for US anesthesiology programs was recently developed and published8 but has yet to be formally implemented or tested.

Methods: A three-month trial of EPA implementation via a mobile app (APP) was completed at seven anesthesiology residency training programs. Trainee and faculty satisfaction with EPA usage was assessed via a survey prior to and immediately following the trial. The number of individual EPA assessments during the trial was compared to the quantity of competency assessments in the three-month period immediately prior to the trail using the pre-existing assessment system at each program. EPA results were also tabulated and reported as average scores stratified by post-graduate year in training.

Results: Trainee survey results showed improvements in metrics of timeliness, quality, specificity and amount of feedback after EPA app implementation but not in the perceived frequency of receiving feedback, or the perception of faculty dominating the feedback conversation (Figure 1). Based on faculty survey results, supervising physicians found EPAs and the APP easy to use, preferred the use of EPAs over other assessments, used the EPA APP more frequently than pre-existing assessments, and found EPAs to be a useful tool to assess competency (Table 1). Use of the EPA APP resulted in a larger quantity of feedback submissions as compared to previous feedback formats (Figure 2), and scores in all EPAs had a positive correlation with level of training (Figure 3).

Conclusion: A multi-center trial of anesthesiology EPA implementation showed largely positive effects of EPAs on the quality and quantity of feedback from faculty and were found to be user friendly, intuitive and in some ways preferred over other existing forms of competency assessment. EPAs have the potential to improve the assessment of trainee competency in anesthesiology programs, improve feedback discussions, and document individual trainee progression along the ACGME milestone continuum. While this study was limited to seven programs, they were of varying geography and program size. Future directions include studying the validity of the EPAs and how they fit into a larger program of competency assessment to address all anesthesiology milestones.

References: 1. Med Teach. 2015;37:983-1002. 2. Acad Med. 2016;91:943-950. 3. J Gen Intern Med. 2014;29:1177-1182. 4. Med Teach. 2017;39:582-587. 5. Acad Med. 2015;90:479-484. 6. Med Educ. 2016;50:93-100. 7. Anesth Analg. 2021;132(6):1579-1591.

Figure 1. Trainee survey results comparing average response to each item before (n=126) and after (n=93) pilot.

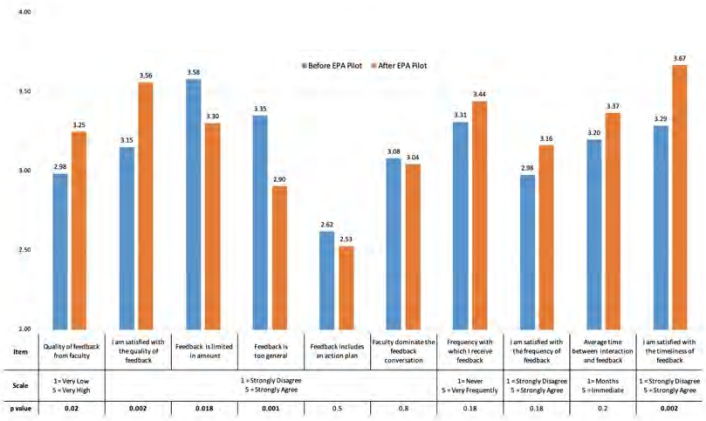


Table 1. Faculty survey results immediately following EPA pilot (n=131).

Item # and Stem	Scale	Average	SD
1. I would like to use this APP frequently	1 = Strongly Disagree 5 = Strongly Agree	3.39	1.19
2. I thought the APP was easy to use	1 = Strongly Disagree 5 = Strongly Agree	3.79	1.04
3. I found the APP to be too complex	1 = Strongly Disagree 5 = Strongly Agree	2.24	0.86
4. I think that I would need the support of a technical person to be able to use this APP	1 = Strongly Disagree 5 = Strongly Agree	1.79	0.94
5. I would imagine that most people would learn to use this APP very quickly	1 = Strongly Disagree 5 = Strongly Agree	4.02	0.73
6. I found the APP very awkward to use	1 = Strongly Disagree 5 = Strongly Agree	2.46	1.08
7. I felt very confident using the APP	1 = Strongly Disagree 5 = Strongly Agree	3.81	0.90
8. I needed to spend a lot of time with the APP before I could use it effectively	1 = Strongly Disagree 5 = Strongly Agree	2.10	0.96
9. Overall, I would rate the user friendliness of this APP as	1= Awful 5 = Excellent	3.69	0.93
10. I would use this APP frequently to submit resident assessments	1 = Strongly Disagree 5 = Strongly Agree	3.50	1.22
11. Assessment data collected from the APP would be useful to evaluate resident competency	1 = Strongly Disagree 5 = Strongly Agree	3.50	1.06
12. I prefer the style of evaluation in the APP compared to the other assessments I am supposed to complete	1 = Strongly Disagree 5 = Strongly Agree	3.38	1.19
13. I filled out the APP evaluations alongside the trainee	1 = Never 5 = All of the time	2.11	1.23
14. I shared my evaluation scores I entered in the APP with the trainee	1 = Never 5 = All of the time	2.50	1.40
15. I discussed with trainee why I assigned the evaluation score	1 = Never 5 = All of the time	2.45	1.39

Average=Average survey response; APP=mobile EPA app; SD=standard deviation

Figure 2. Number of assessment submissions by month comparing EPAs to pre-existing assessment system (average assessments submitted per trainee per month).

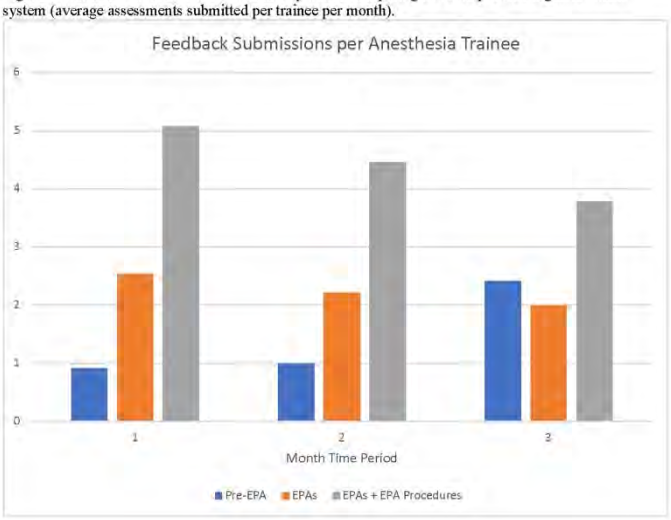
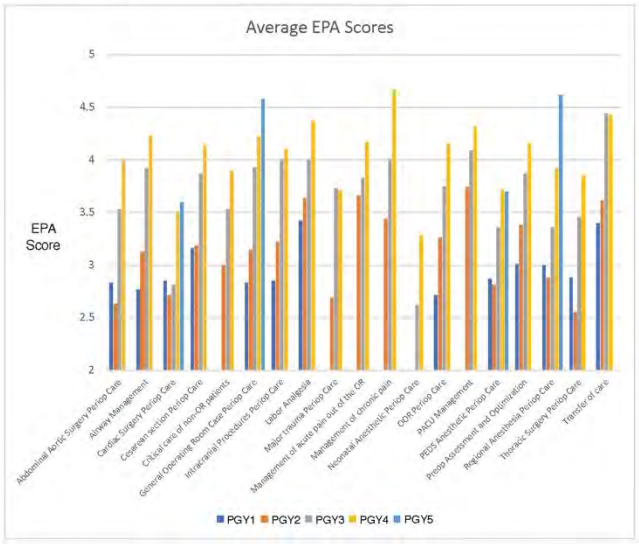


Figure 3. Average scores for each EPA by PGY-year.



Economics, Education and Policy - 7

Anesthesiology Resident Educational and Personal Wellbeing Experiences during the Covid 19 Pandemic-National Survey Results

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Introduction: The effect of the Coronavirus disease 2019 (COVID-19), has been devastating. We conducted a national survey in the United States through the ASA(American Society of Anesthesiology) to understand the impact of this pandemic on the clinical training, didactics and wellbeing of resident doctors in the Anesthesiology. Trainees were embracing new norms while plagued by uncertainty about their clinical training, educational endeavors, and most importantly their health and emotional well-being. Across the country different training programs have had different experiences. There have been no surveys or studies on effect of the pandemic on anesthesiology residents in particular. There have been some viewpoints, blogs and letters to the editor but no published surveys. Information collected by this national survey of Anesthesiology trainee experience during the Covid-19 pandemic addressed a priority issue for ASA members. The purpose of this survey was to confirm and possibly quantify the real anxiety and fear among anesthesiology trainees. Our hypothesis is that COVID-19 has had a significant impact on educational experience, mental health ,wellbeing of trainees in anesthesiology.

Methods: The study was approved by the appropriate Institutional Review Board (IRB), and the requirement for written informed consent was waived by the IRB. Email-based surveys were generated using Survey Monkey software and sent to anesthesiology residents across the country anonymously. The survey was sent to 5469 residents across the United States whose emails were registered with the ASA and included PGY1-PGY4 residents. 450 residents(approximately 10%) filled out the survey voluntarily from May 2020 to July 2020 The survey collected both quantitative and qualitative data. To obtain quantitative data, residents were given a grading score from 0 - 5 (0 = never, 5 = always) which then was translated into an impact score with 0 being low impact and 100 being the highest impact. Qualitative data was ascertained with free text responses.

Results: The survey looked at the effects COVID 19 had on three broad categories: 1.Resident wellness, 2.Academics 3.Clinical responsibilities. Resident wellness questions focused on personal well-being and the impact on residents' personal relationships. Table 2 illustrates the survey questions that evaluated the well-being of residents during the COVID pandemic with average impact scores amongst 450 participants. The highest concern rated by the residents was the possibility of unknowingly infecting their family members with COVID 19 with an average score of 60, answered by total of 450 residents. Many residents did indicate feeling anxious when it comes to balancing workload and family life during the pandemic. Furthermore, the impact score on exercise and sleep, reducers of stress, were 47 and 51 respectively. The impact score for financial hardship during the pandemic was low. Overall, 77% of residents indicated their programs did provide support and assistance during the pandemic. The average score for academic disruption was 61. Residents were asked to free-text what different education modalities were added to their curriculum during this time to assist with continuing education. Clinical Training During the initial COVID 19 surge, elective surgical cases were cancelled or postponed. Residents indicated their OR and NON-OR clinical training was adversely affected with an impact score of 56 and 46 respectively. The average score for the residents' ability to control their own case selection was 18, indicating low control. Residents did indicate low impact score on feeling unsafe while doing their clinical duties with a score of 27. Table 3 illustrates a list of potential sources that could contribute to feeling unsafe in the hospital and the percentage of residents who filled out the survey who indicated such concerns. The highest reason for feeling unsafe was the fear of getting infected while performing clinical duties (58.89%).

Conclusion: The resident experience during the Covid pandemic is real and should be acknowledged and addressed by program directors. This survey addresses the hardships that trainees experienced. Moving forward Program Directors need to keep that in mind in assessing resident well being and in planning educational curriculum in the post pandemic times

References: 1. J Educ Perioper Med. 2021 Jan-Mar; 23(1): E659. 2.Can Med Educ J. 2020 Sep; 11(5);e126-e128. 3.J Neurosurg Anesthesiol 2021 Jan;33(1):82-86.

Table 1

Categories	Impact score Average (0-100)	Female Average	Male Average
Resident Wellness Questionnaire			
I feel anxious balancing workload and family	45	52	41
This pandemic has negatively affected my relationship with family	33	34	31
I am worried that I may unwittingly infect my family	60	62	59
I experience feelings of anxiety/depression/helplessness during this pandemic	42	54	35
I am able to exercise or perform other activities that relax me	47	49	45
I am able to sleep well during this pandemic	51	48	52
I am undergoing financial hardship during this pandemic	20	19	20
Academics			
I feel that education was disrupted during this time	61	65	58
Clinical			
My clinical training in the OR locations has been adversely affected by the COVID 19 pandemic	56	59	54
My clinical training in the NON-OR locations has been adversely affected by the COVID 10 pandemic	46	48	45
I have control of my case selection when I am working in the clinical environment	18	16	18
I feel unsafe while doing clinical work in the hospital	29	33	26
I was offered a possibility to exempt myself from clinical work during the pandemic	27	27	27

Table 2

Sources of feeling unsafe performing clinical duties

Inadequate support or training	17.78%
Inadequate personal protective equipment	40.44%
Fear of getting infected	58.89%
Unavailability of adequate testing protocols	37.78%

Table 3 – Top 5 strategies to ease anxiety

1. Exercise (105)
2. Family/Friend Support (104)
3. Work Support (39)
4. Time away from clinical duties/Vacation/Reduced Case load (32)
5. Mindfulness/Yoga (27)

Economics, Education and Policy - 8

Anesthesiologists with Advanced Degrees in Education: A Qualitative Study of a Changing Paradigm

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Introduction: Anesthesiology education has undergone profound changes over the past century, from a clinical apprenticeship model to novel, comprehensive curricula based on andragogic learning theories. Combined with institutional and regulatory requirements, these new curricula have propagated the professionalization of the clinician-educator role. A significant number of clinician-educator anesthesiologists have pursued formal health professions education (HPE) training, yet there is no published guidance describing the benefits or costs.

Methods: Investigators performed a qualitative study of anesthesiologists with HPE degrees working at academic medical centers. Interviews were analyzed via an iterative process. They were coded for recurring themes using a grounded theory approach, and representative quotations were compiled.

Results: Seven anesthesiologists were interviewed, representing diverse geographic regions, subspecialties, and medical institutions. Analyses of interview transcripts resulted in six core themes: outcomes, extrinsic motivators, intrinsic motivators, investment, experience, and recommendations. Interviewees noted advantages of HPE training for those wishing to pursue leadership and scholarship in medical education but noted opportunity cost in relation to preexisting commitments and family time. Interviewees also highlighted considerations regarding optimal timing of HPE training.

Conclusion: There are numerous professional and personal benefits to pursuing HPE degrees for faculty interested in education leadership and scholarship. Making an informed decision to pursue HPE training can be challenging when considering the competing pressures of clinical work and personal obligations. The experiences of the interviewed anesthesiologists offer direction to future anesthesiologists and chairs in their decision-making process of whether, and when, to pursue HPE training.

Code	Definition	Representative statements
Outcomes	Intended and unintended impacts of the degree on one's career; including how they have utilized the degree and practical day to day application of skills/knowledge	• "It's definitely a factor to get you noticed by people like chairs when they have educational leadership roles to fill." • "I think it has been a good opportunity for me to... further push those key projects...[and] get a better understanding of where the problems are in care delivery within my department." • "I think it influenced much of what I did even beyond education. When I look back, what really happened in the years just after, it just gave me that desire to know my own self, to just go for it. And that was really great to develop more confidence in your own abilities outside of what you do." • "I mean, like the job offers I'm getting, it's insane."
Extrinsic Motivators	Reasons for an individual seeking a degree based on attaining a known, external reward	• "Pretty much... [the chair] told me I had to do it to become faculty." • "I would say that [for] the department and my division, definitely, it was an expectation that I would pursue the degree." • "... my career goals were to kind of move up [to] med ed administration and to publish in medical education." • "My mentor... was a very key proponent in me getting my masters because... to continue to move up that that would be a skill set and a degree that would look good from an experience standpoint."
Intrinsic Motivators	Reasons for an individual seeking a degree for its own sake without an external reward; including emotions, values, goals	• "I was just frustrated with myself. And I felt like I just needed a formalized process and I needed everything at once and I was tired of trying to find it on my own." • "I felt like I needed to know the language and I needed to know the theory behind why things are done the way they're done in medical education. And so that prompted me to get my masters." • "I really wanted advanced training and knowledge in education in general, which I thought would be helpful, just to understand more what's going on" • "I started to really become interested in studying educational processes, and team dynamics even, and the ways we think and how it influences the way we act and just everything like that."
Investment	Positive and negative aspects of obtaining an HPE degree; including personal or financial sacrifices, opportunity costs, time commitment	• "The biggest stressor was that I had to negotiate with my family because of time." • "I didn't jump into the program my first year as an attending even though I was advised to, because I felt like I really needed to lay my ground as a clinician. ... We work a lot of days in a row. And that makes doing an online curriculum while you're a full-time employee very difficult..." • "When I enrolled in the program, I had the added pressure to really get through it as fast as possible... because there was this tension with my family, basically." • "First of all, it's a time commitment. ...If you just stay in your clinical practice, right, and you try to do things within the division or department, it's already very busy."
Experience	Overall perspectives about the degree program, including opinions about the process of obtaining the degree (i.e. satisfaction with the content covered, mode/format of delivery, and suggestions for improvement)	• "I would have liked more statistics work. But otherwise, I was pretty happy with a lot of the courses." • "It reviews a lot of the scientific methodology that we all appreciate even in other aspects of research. There's an emphasis on leadership, which I really appreciated. I especially appreciated that understanding of ourselves. There was an emphasis on understanding your MBTI scores and what that meant, which really gets into where you understand your strengths, and what works well." • "But what I wish the program did was potentially focus less on individualized projects and potentially allow more collaboration and group projects for your Capstone... It would be really interesting to use the program more to develop interprofessional projects than having everybody do one individual project." • "I think what I really would have loved is if there was somebody in there who could help you either write a case report, you know, or help you with the research part as you're doing it, or help you write a grant."
Recommendations	Advice that the participant would offer to someone interested in pursuing an HPE degree regarding timing, factors to consider, aspects of a program to look for or avoid	• "If you think, look, I love to teach... you don't need a master's degree to be a teacher of residents, right, anybody in an academic center is going to teach residents. But if you think you want to be involved in residency leadership or medical school leadership, if you see yourself as being a program director one day or you know, dean for curriculum of a medical school, that kind of thing, then I think it is a good step because as I said before, I think it will get you noticed when those kinds of opportunities come up." • "I think right out of training, you don't necessarily know which person you are. What I usually advise is to do some workshops, figure out if you just want to become a really good teacher. I think you don't need a master's to do that." • "I think if you want to study teaching and you want to have a foundation in adult learning theory and you want to be able to become an administrator or become a researcher in med[ical] ed[ucation] that I would advise the [HPE degree]." • "If you're going to use this degree, you're pretty much marrying yourself to academics. But then I would also say that I think that there's a lot of opportunities for innovation, and a lot of interesting ways to use the master of education. And I would also say that I would sort of make sure that I had an academic or administrative niche that, you know, you can really start applying the coursework early on. So that you know, like, you can sort of build your academic portfolio while you're working on the degree."

Economics, Education and Policy - 9 The Impact of Social Media on Applicant Perceptions of Anesthesiology Residency Programs during the COVID-19 Pandemic

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Introduction: Visiting medical student rotations have traditionally been effective opportunities for medical students to gain a better understanding of the residency program, meet current residents and faculty and to showcase their abilities and interest in a program. Although anesthesiology residency programs have increased their social media presence in recent years to help attract applicants, many programs have been slow to adopt social media. The COVID-19 pandemic disrupted the residency application process in 2020-2021 as it greatly reduced elective surgical procedures, restricted visiting medical student rotations, as well as forced the transition to virtual interviews. There is limited data regarding the effectiveness and impact of social media on anesthesia residency applicants' evaluation of potential programs, particularly in the context of the COVID-19 pandemic. We hypothesized that given the COVID-19 restrictions, social media presence of anesthesiology residency programs would play a greater role in how applicants evaluated residency programs.

Methods: The study was approved by the Mayo Clinic IRB. Email addresses of all anesthesia residency applicants who applied to the authors' program were collected from ERAS and sent a link to the survey along with statements regarding the confidentiality, anonymity, and optional nature of the survey. There was no incentive to complete the survey. Applicants were sent an email reminder to complete the survey one month after the original email. The 20-item survey was hosted on Qualtrics and collected no identifying information. It included questions regarding sub-internship rotation completion, social media resource use, social media impact, and general demographics. Microsoft Excel was used to perform descriptive statistics.

Results: The survey was sent out to 1,091 individuals who applied to the Mayo Clinic - Arizona anesthesiology residency program and 640 unique responses were recorded for a response rate of 58.6%. Many respondents reported an inability to complete 2 or more planned sub-internships due to COVID-19 restrictions (55.9%), with 25% of applicants reporting inability to do any visiting medical student rotations (Figure 1). The majority of applicants reported using residency program-based social media. Official websites (91.5%), Doximity (47.6%), Instagram (38.5%), and Twitter (19.4%) were reported as the most used resource by applicants. A large proportion of applicants agreed that social media was an effective means to inform applicants (67.3%) and that it positively impacted their perception of the program (57.5%). Applicants reported that social media helped convey a program's culture and transparency, with posts of social events rated as most impactful. A third of applicants agreed that social media presence will continue to impact future application cycles (Table 2).

Conclusion: As a result of COVID-19 restrictions in 2020-2021, many anesthesiology applicants were unable to complete planned visiting medical student rotations. Social media played a significant role in applicants' perception of programs. It was an effective means to inform applicants and generally positively impacted applicants' perception of programs. Aside from the traditional official website, applicants utilized social media platforms, like Instagram, to gather insight into a program's culture and transparency, with social event posts being the most successful at engaging applicant's interest. Thus, anesthesia residency programs should consider investing time and resources towards building a social media presence as it is an important factor towards recruitment of potential anesthesia residency applicants.

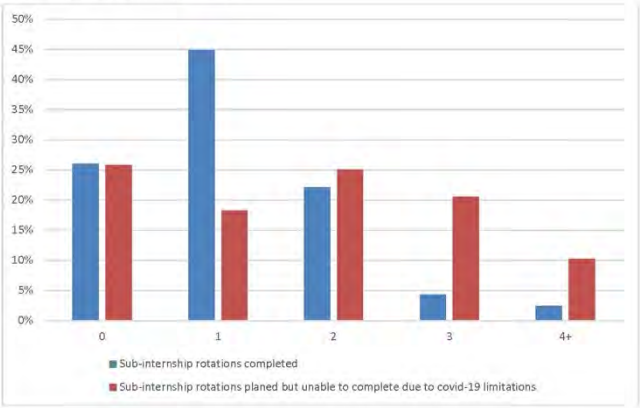
References: Renew JR, Ladlie B, Gorlin A, Long T. The Impact of Social Media on Anesthesia Resident Recruitment. J Educ Perioper Med. 2019;21(1):E632. Schweitzer J, Hannan A, Coren J. The role of social networking web sites in influencing residency decisions. J Am Osteopath Assoc. 2012;112(10):673-

679. Final Report and Recommendations for Medical Education Institutions of LCME Accredited, U.S. Osteopathic, and Non-U.S. Medical School Applicants. https://www.aamc.org/system/files/2020-05/covid19_Final_Recommendations_05112020.pdf.

Table 1: Demographics	n (%)
Gender	
Female	197 (34.3%)
Male	372 (64.8%)
Gender Variant	1 (0.2%)
Age	
Less than 25	24 (4.2%)
25 -30	439 (76.5%)
31-35	78 (13.6%)
36-40	23 (4.0%)
Greater than 40	8 (1.4%)
Race/Ethnicity	
Black	32 (5.6%)
Native American	2 (0.3%)
White	288 (50.3%)
Asian	136 (23.7%)
Native Hawaiian/Pacific Islander	4 (0.7%)
Hispanic	46 (8.0%)
Multiracial	31 (5.4%)
Unknown	3 (0.5)

Table 2: Impact of Social Media	Strongly Agree	Somewhat Agree	Neither Agree nor Disagree	Somewhat Disagree	Strongly Disagree
Pages Available and Accessible	108 (18.9%)	259 (45.3%)	135 (23.6%)	54 (9.4%)	16 (2.8%)
Effective Way to Inform Applicants	152 (26.5%)	233 (40.7%)	117 (20.5%)	53 (9.3%)	17 (3.0%)
Impact on Perception of Program	123 (21.7%)	197 (34.7%)	159 (28.0%)	44 (7.7%)	45 (7.9%)
Positive Impact on Opinion of Program	121 (21.2%)	207 (36.3%)	203 (35.6%)	20 (3.5%)	20 (3.5%)
Improved Programs Professional Image	119 (20.8%)	176 (30.8%)	224 (39.2%)	38 (6.7%)	14 (2.5%)
Improved Perception of Programs Prestige	63 (11%)	135 (23.6%)	274 (47.9)	62 (10.8%)	38 (6.6%)
Helps Exhibit Programs Culture and Camaraderie	228 (39.9%)	194 (34.0%)	123 (21.5%)	15 (2.6%)	11 (1.9%)
Improved Programs Transparency	149 (26.0%)	216 (37.8%)	158 (27.6%)	30 (5.2%)	19 (3.3%)
Due to COVID-19, social media will have significant impact on perception of programs.	170 (29.8%)	207 (36.3%)	125 (21.9%)	52 (9.1%)	17 (3.0%)
Social media will have less of an impact on applicant during future interview cycles not limited by COVID-19.	42 (7.3%)	149 (26.0%)	188 (32.9%)	164 (28.7%)	29 (5.1%)

Figure 1: 2020 – 2021 Sub-Internship Rotations



Economics, Education and Policy - 10

Association Between "Balance Billing" Legislation and Anesthesia Payments in California: A Retrospective Analysis

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Introduction: When a patient receives care from an out-of-network (OON) practitioner, they may receive a "balance bill" for the difference between the practitioner's charge and their insurer's usual contracted rate.[1-4] AB72 was implemented in California in 2017 to ban balance billing in specific situations, including provision of anesthesia care. This law requires insurance plans to pay the greater of the local average in-network (IN) contracted rate or 125% of the Medicare reimbursement rate for OON services.[5] By tying payments for OON care to Medicare rates, the law raised concerns that it would strengthen insurers' bargaining power, resulting in decreased payments for anesthesia services.[6] This study examined the association between AB72 and payments for IN and OON anesthesia care.

Methods: We used payment data from Truven MarketScan®, a database of healthcare claims for commercially insured individuals, to conduct a retrospective analysis of payments for anesthesia care in California before and after implementation of AB72. These data spanned 2013 to 2019 and included annual average amounts paid for procedure (Current Procedural Terminology®; CPT) codes at the county level, further stratified by IN or OON status. We isolated payments for 15 common anesthesia CPT codes as well as payments for physician office (Evaluation and Management; E&M) visits (CPT 99201-99205), which were not affected by the law. Our final sample consisted of 15,871 county-year-CPT code-network status (i.e., IN or OON) combinations. We first analyzed changes in IN and OON payments for anesthesia services after AB72 took effect on September 1, 2017, defining 2018 and 2019 as the "post-law" period and 2013-2017 as the "pre-law" period. To minimize confounding (i.e., changes in insurer bargaining power over the study period) we then performed a difference-in-differences analysis in which we compared the differential effect of AB72 on payments for anesthesia services versus payments for non-anesthesia services (E&M) not affected by the law.

Results: Following passage of AB72, the average IN payment for the 15 anesthesia CPT codes fell from $1,132 in 2017 to $1,095 in 2019 (difference $37; 95%CI -$66 to $6; p=0.021), while the OON payment fell from $1,543 to $1,309 (difference $234; 95%CI -$397 to -$70; p<0.001). However, these declines were broadly mirrored in the non-anesthesia CPTs (Figure 1). Difference-in-differences analysis found that AB72 was associated with significant decline in payments for OON anesthesia services (13.6% decline; 95%CI -17.9 to -9.2%; p<0.001), but no significant change for IN anesthesia services (0.4% increase, 95%CI 1.6% decline to 2.5% increase; p=0.68; Figure 2).

Conclusion: AB72 was associated with significant declines in OON payments but with no significant change in IN payments, suggesting that the law may have had limited impact on changing negotiating dynamics between insurers and healthcare practitioners.

References: 1. JAMA 2020; 323: 538-547 2. JAMA Health Forum 2021; 2: e211460 3. Health Aff (Millwood) 2020; 39: 783-790 4. Health Aff (Millwood) 2017; 36: 177-181 5. Health Care Coverage: Out-of-Network Coverage, AB-72. United States of America, California Legislative Information, 2016 6. Am J Manag Care 2019; 25: e243-e246

Figure 1: Average Payments for Anesthesiology and Evaluation & Management (E&M) Services Pre- and Post-AB72 (2017), by In- or Out-of-Network Status

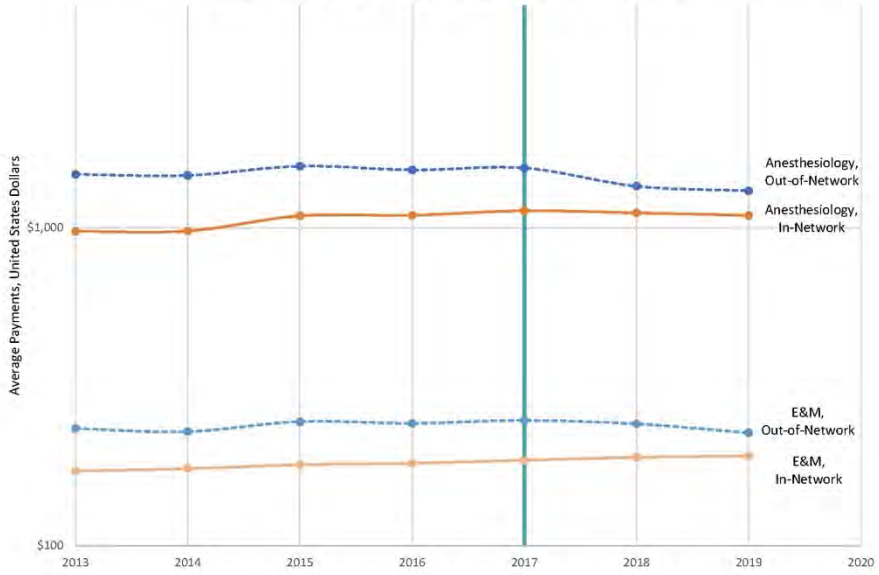

Figure 1 shows unadjusted average payments over time for in-network and out-of-network anesthesiology and evaluation and management (E&M) services, before and after implementation of AB72 in 2017. AB72 affected payments for anesthesiology services but did not affect E&M services. Payments increase in all groups until 2017, after which out-of-network payments for anesthesiology and E&M decrease.

Figure 2: Adjusted Percent Change in Payments for Anesthesiology Services Following AB72 Implementation

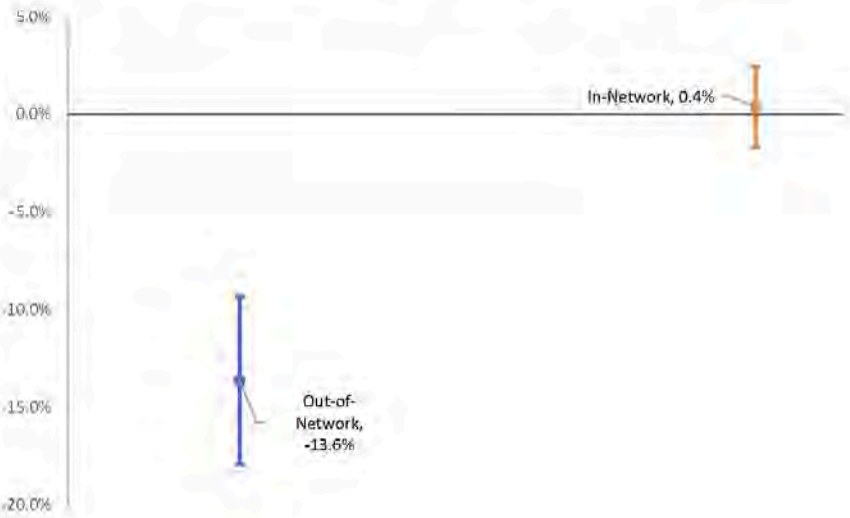

Figure 2 shows adjusted in-network and out-of-network percent change in payments from 2017 (pre-AB72) to 2019 (post-AB72) for anesthesiology services, calculated using difference-in-difference analysis.
Out-of-network payments were significantly lower (13.7% lower, 95% CI -17.9 to -9.2%; p<0.001) post-AB72 implementation; in-network payments were not.

Economics, Education and Policy - 11

Health Care Burden Associated with Pediatric Prolonged Opioid Use After Surgery

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Introduction: Prolonged opioid use after surgery (POUS), filling ≥ 1 opioid prescription 90-180 days after surgery, increases healthcare costs and utilization in adult populations; however, its economic burden in pediatric patients is unknown. We sought to determine whether POUS is associated with increased healthcare cost and utilization in adolescent surgical patients.

Methods: Design: Retrospective cohort study Setting: Insurance claims data from Optum's Clinformatics Data Mart Database from January 1, 2003 and June 30, 2019 Participants: Opioid-naive patients 12-21 years of age in the US who received outpatient prescription opioids Exposure: Prolonged opioid use after surgery Main Outcomes and Measures: Total healthcare costs (prescription drug and inpatient, emergency, and outpatient/other medical costs) and healthcare visits (inpatient, emergency, and outpatient/other) in the 730 day period following the surgical encounter. Multivariable regression analyses accounting for cohort asymmetry in the available surgical and demographic factors were used to determine adjusted healthcare cost and visit differences in dollars and days, respectively.

Results: A total of 126,338 unique patients undergoing 132,107 procedures were included in the analysis, with 4,867 patients meeting criteria for POUS for an incidence of 3.9%. Adjusted mean total healthcare costs in the 730 days after surgery were 52% higher in patients with POUS than in non-POUS patients ($13,443 versus $8,824), with adjusted costs higher for inpatient ($2,163 versus $1,222), emergency ($1,142 versus $602), and outpatient/other ($7,967 versus $5,265) medical visits. Adjusted mean prescription drug costs in the 730 days after surgery were also higher in patients with POUS ($2,083 versus $1,517). Patients with POUS had more adjusted mean days of inpatient (0.54 versus 0.32), emergency (2.04 versus 1.08), and outpatient/other (22.35 versus 16.43) healthcare visits in the 730 days after surgery ($p<0.0001$ for all comparisons).

Conclusion: In adolescents, POUS was associated with increased total healthcare costs and utilization in the 730 days following their surgical encounter. Given the increased healthcare burden associated with POUS in adolescents, further investigation of preventative measures for high-risk individuals and additional study of the relationship between opioid prescription and outcomes may be warranted.

Economics, Education and Policy - 12 A comprehensive analysis of direct hospital costs associated with the use of sugammadex versus neostigmine: A multicenter cohort study.

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Introduction: Residual neuromuscular blockade (NMB) after surgery increases the risk of postoperative respiratory complications and may lead to higher costs of care during a patient's hospital stay (1-2). Sugammadex can eliminate residual NMB and may mitigate associated complications and healthcare utilization, but the drug is more expensive than generic alternatives, and variably used (3-4). In this study, we hypothesized that the use of sugammadex compared to neostigmine for reversal of NMB is associated with decreased direct hospital costs.

Methods: Adult patients who underwent surgery under general anesthesia and received NMB agents and reversal with neostigmine or sugammadex at two tertiary academic healthcare networks in Massachusetts and New York between January 2016 and June 2021 were included in this retrospective cohort study. The primary exposure was the administration of either neostigmine or sugammadex and the primary outcome was direct hospital costs, defined as costs arising from patient-care related activities of specific departments (e.g., surgery, anesthesia, etc.), such as staffing, or supply costs attributed to the patient's hospital stay during which the index surgery was performed. To maintain confidentiality, we used proportionally modified direct hospital costs (multiplied by a fixed factor) for analysis; these were then log-transformed, and a multivariable generalized linear model adjusted for a priori defined patient demographics, comorbidities, intraoperative factors, year of surgery, and the healthcare network, was applied. Effect modification was assessed for the most prominent cost-driving factors based on clinical significance in the primary model. Model estimates with 95% confidence intervals (95% CI) are provided and a P-value of <0.05 was considered as statistically significant.

Results: Among 79,474 patients included in this study (Figure 1), 59,643 (75.0%) received neostigmine and 19,831 (25.0%) received sugammadex for reversal of NMB. Sugammadex use varied by the healthcare network. In addition, surgical cases involving sugammadex administration were generally more complex, and the patients were older and had more comorbidities (Table 1). The proportion of sugammadex use versus neostigmine increased during the first years of the study period until arriving at a steady-state status in 2019 (Figure 2). The median (IQR) proportionally modified direct hospital costs were 21,449 Units (13,133-37,744) in patients who received neostigmine and 22,085 Units (12,549-43,245) in patients who received sugammadex. The primary model indicated good model calibration (Figure 3). In the full study cohort and after adjustment for a priori defined confounding factors, the use of sugammadex versus neostigmine was associated with a small but statistically significant decrease in proportionally modified direct hospital costs by 1.3% (adjusted model estimate: 0.987; 95% CI 0.978-0.995; P=0.002; Table 2A). This effect was modified by the healthcare network, admission type, surgical duration, preoperative hospital length of stay, preoperative stay in the Intensive Care Unit (ICU), and by a high American Society of Anesthesiologists (ASA) physical status classification. The use of sugammadex versus neostigmine was associated with decreased direct hospital costs in one healthcare network, in patients undergoing ambulatory surgery or shorter procedures, and in patients who had a lower ASA physical status classification, spent preoperatively less time in the hospital and no time in the ICU. By contrast, sugammadex was associated with higher direct hospital costs in more complex, hospitalized patients with longer preoperative stays (Table 2B). Additional adjustment of the primary model for these interactions confirmed the primary findings of decreased costs with sugammadex (Table 2A).

Conclusion: The effect of reversal agent (neostigmine versus sugammadex) on direct costs of perioperative care is small compared to other predictors such as hospital practice, comorbidities, procedural severity, and admission status, which modified the primary association tested. Our study suggests lower direct hospital costs associated with sugammadex versus neostigmine use in an ambulatory setting and among procedures of shorter duration, whereas sugammadex was associated with higher costs among more complex hospitalized patients. The restriction of sugammadex, which may have had an impact on costs, could not be examined in this study.

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Table 1. Cohort characteristics.

ASA, American Society of Anesthesiologists; SPORC, Score for Prediction of Postoperative Respiratory Complications; NMBA ED95 dose, median effective dose of neuromuscular blocking agents required to achieve a 95% reduction in maximal twitch response from baseline.

Characteristic	Neostigmine (n = 59,643)	Sugammadex (n = 19,831)	Standardized difference
Primary exposure			
Neostigmine dose, mg	3.00 (3.00–4.00)	–	–
Sugammadex dose, mg	–	200.00 (200.00–300.00)	–
Demographics			
Age, years	52.66 ± 16.96	56.15 ± 16.91	-0.205
Sex, female	22,060 (37.0%)	8,360 (42.2%)	-0.106
Body mass index, kg/m^2	30.18 ± 7.60	30.15 ± 7.99	0.027
ASA physical classification III or IV	26,061 (43.7%)	10,904 (55.0%)	-0.227
Federal insurance	30,620 (51.3%)	10,353 (52.2%)	-0.017
Healthcare network			-0.320
Healthcare network 1	21,586 (36.2%)	10,282 (51.8%)	
Healthcare network 2	38,057 (63.8%)	9,549 (48.2%)	
Preoperative factors			
Opioid prescriptions within 90 days	13,015 (21.8%)	3,668 (18.5%)	0.083
Preoperative hospital length of stay			-0.001
0 days	48,324 (81.0%)	16,242 (81.9%)	
1 to 3 days	8,024 (13.5%)	2,404 (12.1%)	
4 to 7 days	2,266 (3.8%)	741 (3.7%)	
>7 days	1,029 (1.7%)	444 (2.2%)	
Emergency surgery	4,178 (7.0%)	14,31 (7.2%)	-0.008
Preoperative ICU stay	1,093 (1.8%)	488 (2.5%)	-0.043
Admission type			0.024
Ambulatory surgery	20,827 (34.9%)	7,222 (36.4%)	
Same-day admission	11,319 (19.0%)	3,589 (18.1%)	
Inpatient surgery	27,497 (46.1%)	9,020 (45.5%)	
Surgical service			-0.111
Cardiac surgery	2,448 (4.1%)	532 (2.7%)	
Colorectal surgery	1,034 (1.7%)	591 (3.0%)	
Ear, nose, and throat	3,326 (5.6%)	1,229 (6.2%)	
Gastroenterology	553 (0.9%)	411 (2.1%)	
General surgery	18,824 (31.6%)	4,922 (24.8%)	
Gynecology	8,496 (14.2%)	2,209 (11.1%)	
Neurosurgery	2,574 (4.3%)	1,532 (7.7%)	
Orthopedic surgery	5,998 (10.1%)	1,928 (9.7%)	
Other	740 (1.2%)	506 (2.6%)	
Plastic surgery	5,049 (8.5%)	1,397 (7.0%)	
Surgical oncology	561 (0.9%)	246 (1.2%)	
Thoracic surgery	1,460 (2.4%)	1,219 (6.1%)	
Transplant surgery	1,241 (2.1%)	637 (3.2%)	
Trauma surgery	1,233 (2.1%)	454 (2.3%)	
Urology	3,648 (6.1%)	1,281 (6.5%)	
Vascular surgery	2,458 (4.1%)	737 (3.7%)	
Comorbidities			
Charlson Comorbidity Index	0 (0–1)	1 (0–2)	-0.144
Cancer diagnosis during index stay	9,715 (16.3%)	3,752 (18.9%)	-0.069
Diabetes mellitus	9,588 (16.1%)	3,370 (17.0%)	-0.025
Severe diabetes mellitus	4,454 (7.5%)	1,810 (9.1%)	-0.060
Heart failure	3,624 (6.1%)	1,724 (8.7%)	-0.100
Coronary artery disease	6,334 (10.6%)	2,430 (12.3%)	-0.051
Atrial fibrillation	2,876 (4.8%)	1,427 (7.2%)	-0.100
Peripheral vascular disease	4,740 (7.9%)	1,811 (9.1%)	-0.042
Renal disease	5,123 (8.6%)	2,172 (11.0%)	-0.080

History of drug abuse	1,862 (3.1%)	681 (3.4%)	-0.018
History of smoking	7,721 (12.9%)	3,081 (15.5%)	-0.074
Chronic pulmonary disease	8,999 (15.1%)	3,304 (16.7%)	-0.043
SPORC Score ≥ 7	2,896 (4.9%)	1,426 (7.2%)	-0.098
Intraoperative factors			
Duration of surgery, min	156 (111–229)	142 (96–221)	0.076
Work relative value units	14.91 (10.05, 20.38)	14.04 (8.28, 20.38)	0.055
Neuraxial anesthesia	57 (0.1%)	6 (0.0%)	0.026
NMBA ED95 dose, mg	2.16 (1.55–3.10)	2.53 (1.83–3.67)	-0.291
NMBA type			0.046
Rocuronium only	59,437 (99.7%)	19,809 (99.9%)	
Vecuronium only	85 (0.1%)	8 (0.0%)	
Both	121 (0.2%)	14 (0.1%)	
Packed red blood cell units			-0.017
0	58,665 (98.4%)	19,452 (98.1%)	
1	473 (0.8%)	196 (1.0%)	
>1	505 (0.8%)	183 (0.9%)	

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range [25th-75th percentile], values separated by dash).

Table 2. Results.

2A. Effects of sugammadex versus neostigmine on direct hospital costs

Outcome	Neostigmine (n=59,643)	Sugammadex (n=19,831)	Adjusted Analysis [a] Model estimate (95% CI)	Adjusted Analysis [a] Change with sugammadex in % (95% CI)	P-value
Primary analysis					
Proportionally modified direct hospital costs (n=79,474)	21,449 Units (13,133–37,744)	22,085 Units (12,549–43,245)	0.987 (0.978–0.995)	–1.3% (–2.3 to –0.5%)	0.002
Primary analysis with additional adjustment for all interactions [b]					
Proportionally modified direct hospital costs (n=79,474)	—	—	0.950 (0.934–0.968)	–5.0% (–6.6 to –3.2%)	<0.001

Proportionally modified direct costs data are expressed as median (interquartile range [25th-75th percentile], values separated by dash). Statistical analyses were performed using a multivariable generalized linear model of the gaussian family with identity link. For analyses, the primary outcome was log-transformed and used as dependent variable in the regression model. Model estimates are reported for regression analyses as results of the exponential transformation of model coefficients. 95% confidence intervals (CI) are provided and a P-value <0.05 was considered as statistically significant.

[a] Analyses were adjusted for a priori defined confounders, including patient demographics (age, sex, body mass index, insurance status), comorbidities (American Society of Anesthesiologists physical status classification, smoking status, drug abuse, renal disease, SPORC [Score for prediction of postoperative respiratory complications], cancer diagnosis during index stay, Charlson Comorbidity Index, diabetes mellitus, arterial hypertension, heart failure, chronic pulmonary disease, liver disease, cancer, tumor with metastasis, coronary artery disease, peripheral vascular disease), preoperative factors (healthcare network, emergency status, admission type, preoperative hospital stay, opioid prescriptions prior to surgery, preoperative stay in the Intensive Care Unit), and intraoperative factors (surgical service, duration of surgery, work relative value units, use of neuraxial anesthesia, neuromuscular blocking agent dose, packed red blood cell units) as well as the year of surgery and the proportion of surgical volume.

[b] Additional adjustment of the primary regression model for all interaction terms as provided in Table 2B.

2B. Effect modification analyses

	Neostigmine (n=59,643)	Sugammadex (n=19,831)	Adjusted Analysis [a] Model estimate (95% CI)	Adjusted Analysis [a] Change with sugammadex in % (95% CI)	P-value	P-for-Interaction
Effect modification by healthcare network						
Healthcare network 1 (n=31,868)	17,189 Units (9,528–32,513)	17,949 Units (9,557–31,820)	0.913 (0.902–0.924)	–8.7% (–9.8 to –7.6%)	<0.001	<0.001
Healthcare network 2 (n=47,606)	23,619 Units (15,589–40,304)	28,488 Units (16,815–62,164)	1.059 (1.048–1.071)	5.9% (4.8 to 7.1%)	0.001	
Effect modification by ambulatory versus non-ambulatory surgery						
Ambulatory surgery (n=28,049)	11,948 Units (8,124–18,147)	11,370 Units (7,667–18,135)	0.935 (0.923–0.947)	–6.5% (–7.7 to –5.3%)	<0.001	<0.001
Non-ambulatory surgery (n=51,425)	28,903 Units (18,975–49,989)	32,044 Units (19,853–62,780)	1.018 (1.007–1.028)	1.8% (0.7 to 2.8%)	0.001	
Effect modification by surgical duration [b]						
Short surgical duration (n=48,666)	16,407 Units (10,505–24,208)	16,712 Units (9,930–27,818)	0.949 (0.939–0.959)	–5.1% (–6.1 to –4.1%)	<0.001	<0.001
Long surgical duration (n=30,808)	34,640 Units (22,904–56,213)	38,338 Units (23,800–71,034)	1.018 (1.004–1.032)	1.8% (0.4 to 3.2%)	0.012	
Effect modification by preoperative hospital length of stay [c]						
Short preoperative hospital stay (n=74,994)	20,415 Units (12,691–34,073)	20,857 Units (12,055–37,957)	0.982 (0.973–0.990)	–1.8% (–2.7 to –1.0%)	<0.001	<0.001
Long preoperative hospital stay (n=4,480)	68,873 (46,472–110,986)	90,361 (54,358–151,356)	1.090 (1.057–1.124)	9.0% (5.7 to 12.4%)	<0.001	
Effect modification by preoperative Intensive Care Unit (ICU) stay						
Preoperative ICU stay (n=1,581)	64,370 Units (45,994–107,492)	77,814 Units (46,273–153,527)	1.058 (1.007–1.111)	5.8% (0.7 to 11.1%)	0.025	0.005
No preoperative ICU stay (n=77,893)	21,134 Units (13,007–36,487)	21,614 Units (12,373–41,171)	0.985 (0.977–0.993)	–1.5% (–2.3 to –0.7%)	<0.001	

Figure 1. Study flow diagram.

MA, Massachusetts; NY, New York; ASA, American Society of Anesthesiologists; SPORC, Score for Prediction of Postoperative Respiratory Complications; NMBA ED95 dose, median effective dose of neuromuscular blocking agents required to achieve a 95% reduction in maximal twitch response from baseline.

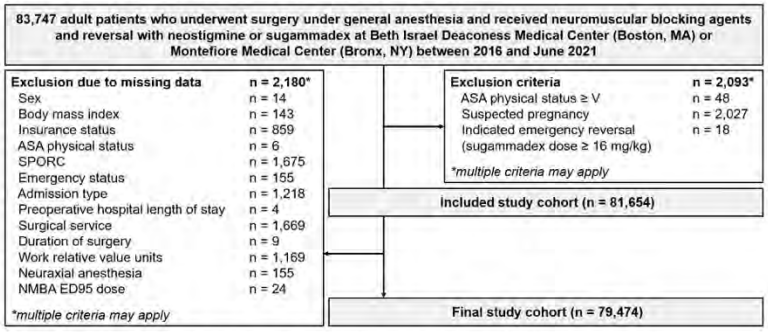


Figure 2. Change in reversal agent use in study cohort over years.

The use of sugammadex (light grey line) and neostigmine (dark grey line) is shown over the years included in this study cohort. The use of sugammadex versus neostigmine significantly increased after 2016 and has arrived at a steady-state status since 2019.

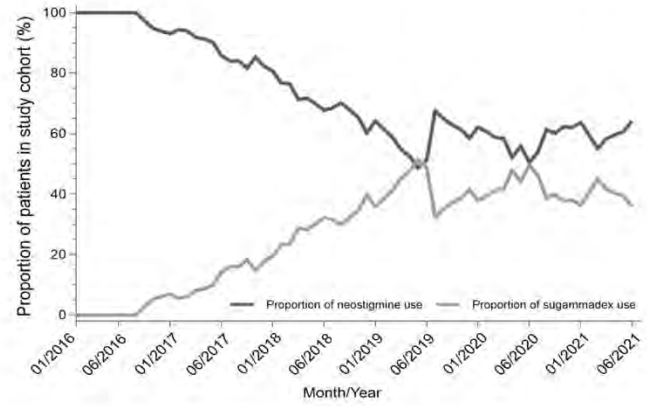
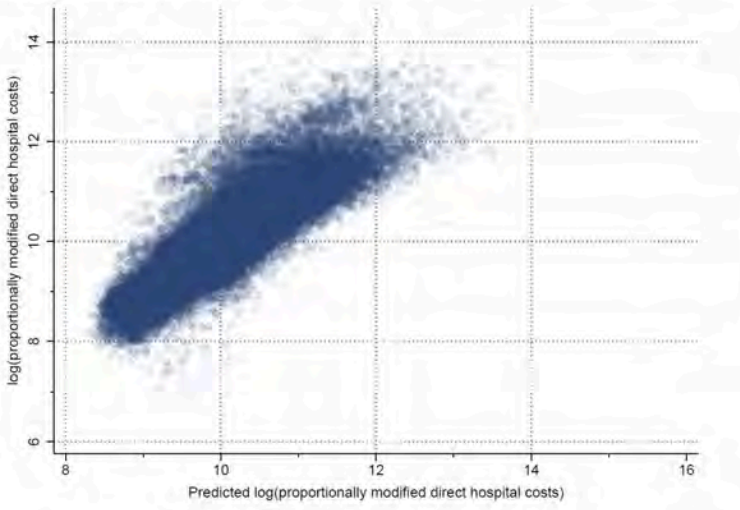


Figure 3. Calibration plot of the primary model.

Calibration plot of the primary generalized linear model showing the log-transformed primary outcome (log(proportionally modified direct hospital costs)) on the y-axis as a function of the predicted log-transformed proportionally modified direct hospital costs (predicted log((proportionally modified direct hospital costs)) on the x-axis. Each individual blue dot displays one observation in the study cohort. An optimal calibration is indicated by a linear increase at same values for x and y.



Economics, Education and Policy - 13

Comparing the costs of Sugammadex vs. conventional muscle blockade reversal for laparoscopic cholecystectomy procedures.

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Introduction: Laparoscopic cholecystectomy, the 3rd most commonly performed outpatient surgery, provides a model to examine outpatient Sugammadex utilization. Sugammadex can quickly and reliably reverse profound neuromuscular blockade. A study using the Multicenter Perioperative Outcomes Group database concluded that approximately 40% of cases receiving neuromuscular blockade utilized Sugammadex for reversal in 2018.1 Conversely, the relatively high cost of Sugammadex compared to that of other conventional reversal drugs such as neostigmine is reported as a significant limitation in its routine use.2 Therefore, our goal was to evaluate cost differences between Sugammadex and conventional reversal for laparoscopic cholecystectomies.

Methods: We used the Premier Healthcare database to analyze cost data for outpatient laparoscopic cholecystectomy procedures performed at a large sample of hospitals in the United States, from January of 2016 to June of 2018. The sample was limited to procedures where patients received a neuromuscular blockade along with either Sugammadex or a conventional reversal drug (neostigmine, edrophonium, pyridostigmine, glycopyrrolate, or atropine). We then compared the mean total cost for procedures using Sugammadex (along or with other blockade drugs) versus any other used conventional reversal, without and with confounding adjustment including patient and hospital characteristics as well as time trends. We also performed the same comparison among Medicare patients, for whom we know the reimbursement rate for the procedure. Finally, we compared the change in costs between 2016 and 2018 among hospitals (a) switching from exclusively using conventional reversal to primarily using Sugammadex to (b) those that continued to exclusively use conventional blockade reversal.

Results: We found an unadjusted difference in total costs per case of $5.89 (95% CI -$42.68 - $54.46), indicating no clinically meaningful difference in cost. However, the fully adjusted model identified that Sugammadex is associated with $42.25 (95% CI -$1.69 - $86.19) lower costs (Table 1). Among patients having Medicare, Sugammadex was associated with $87.67 (95% CI, -$7.84 - $183.18) in cost savings in the adjusted model (Table 2). Among the Medicare population, this increased 26.6% (95% CI -2.4% - 55.7%) on the average profit per procedure. We found no evidence that Sugammadex adoption is associated with increased costs at the hospital level (Table 3).

Conclusion: Numerous studies have demonstrated an increase in cost-effectiveness of outpatient surgery,3-5 making adoption of Sugammadex in the outpatient setting of particular interest, despite its higher costs when compared to neostigmine. Our results indicate that Sugammadex use is associated with cost reduction across different scenarios. Further investigation of complications and costs is recommended to assist institutions in developing policies regarding the optimal choice of neuromuscular blockade reversal. Supported in part by a research grant from Investigator-Initiated Studies Program of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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Table 1: Adjusted Cost Differences

	Model 1	Model 2	Model 3	Model 4
Sugammadex Use	5.89	-84.21***	-167.86***	-42.25
Standard Error	24.78	24.47	24.97	22.42
Controls				
Patient Characteristics	No	Yes	Yes	Yes
Year-Month Fixed Effects	No	No	Yes	Yes
Hospital Fixed Effects	No	No	No	Yes

Patient characteristics include sex, age, type of payer, race, the presence of each comorbidity used to calculate the van Walraven score, the use of IV acetaminophen, and the use of liposomal bupivacaine. Standard errors are heteroskedasticity-robust. * p<.05, ** p<.01 *** p<.001.

Table 2: Adjusted Cost Differences in Medicare Patients

	Model 1	Model 2	Model 3	Model 4
Sugammadex Use	-71.06	-172.78***	-262.21***	-87.67
Standard Error	52.10	51.71	53.08	48.73
Controls				
Patient Characteristics	No	Yes	Yes	Yes
Year-Month Fixed Effects	No	No	Yes	Yes
Hospital Fixed Effects	No	No	No	Yes

Sample is limited to patients with Traditional Medicare as their primary payer. Patient characteristics include sex, age, type of payer, race, the presence of each comorbidity used to calculate the van Walraven score, the use of IV acetaminophen, and the use of liposomal bupivacaine. Standard errors are heteroskedasticity-robust. * p<.05, ** p<.01 *** p<.001.

Table 3: Hospital-Level Cost Differences by Sugammadex Adoption Status

	Model 1	Model 2	Model 3	Model 4
Adopts Sugammadex	-178.10*	-105.86	-104.57	
	(88.09)	(57.68)	(86.96)	
After Potential Adoption	77.58***	70.45***		
	(12.68)	(12.45)		
Adoption x Post	-19.51	77.78	60.92	-292.10***
	(127.58)	(122.38)	(122.58)	(80.10)
Controls				
Patient Characteristics	No	Yes	Yes	Yes
Year-Month Fixed Effects	No	No	Yes	Yes
Hospital Fixed Effects	No	No	No	Yes

Sample is limited to patients treated from January to June in 2016 or 2018 at hospitals that adopted or did not adopt Sugammadex. Patient characteristics include sex, age, type of payer, race, the presence of each comorbidity used to calculate the van Walraven score, the use of IV acetaminophen, and the use of liposomal bupivacaine. Standard errors given in parentheses are heteroskedasticity-robust and clustered at the hospital level. * p<.05, ** p<.01 *** p<.001.

Economics, Education and Policy - 14

Gender-Based Discrimination experienced by surgeons and anesthesiologists: a survey study on its prevalence, forms, perpetrators, and impact in the perioperative setting

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Introduction: Gender-based discrimination (GBD) has been well described in a variety of professions [1-4]and also in academic medicine.[5-8] Recent studies have detailed the experiences of surgical trainees[9,10] and faculty members[11,12] with GBD in the workplace; however, few explore GBD among attending surgeons and anesthesiologists. The sources of GBD for attending physicians is little studied but could be useful to inform interventions to address GBD. There is evidence suggesting a small number of individuals are responsible for a large portion of workplace misconduct through repeated offenses.[13,14] In our study, we hypothesized that surgeons and anesthesiologists would report a high level of GBD, that women would report a higher level of GBD, including sexual harassment, than would their male colleagues, and that we would observe the presence of repeat offenders.

Methods: After exempt designation from our institution's review board, we invited all attending surgeons and anesthesiologists at a large academic medical center via departmental email listserv to complete a 15-minute survey on 'experience in OR environment'. REDCap was used to distribute the survey and collect and manage confidential data. The survey consisted of 30 initial items. Participants who indicated any experience with GBD at work received eleven additional items assessing the frequency, source, and impact of their experience, and whether they used available reporting mechanisms. De-identified responses from completed surveys were analyzed. Categorical responses were presented as frequencies and proportions and differences in responses between male and female participants were assessed with a chi-square or Fisher exact test, as appropriate. Ordinal responses were assessed with a Mantel-Haenszel chi-square test or exact test, as appropriate, to compare responses between men and women. Response rates in each category are visually presented with bar graphs. Continuous responses, such as values entered from a scroll bar are presented as median, inter-quartile range (IQR), after confirming with the Shapiro-Wilk test that the data did not follow a normal distribution. Differences in responses between women and men were assessed with a Wilcoxon Rank-Sum test. Statistical significance was defined as a twosided p-value < 0.05. Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results: 125 of the 213 faculty members invited to participate completed all items of the survey, representing a 58.7% completion rate. 33.6% (42) of participants were women and 66.4% (83) were men. Refer to Table 1 for participant demographics. Overall, 72.8% of faculty reported experiencing GBD during their practice as an attending physician. More women (97.6%) experienced GBD compared to men (60.2%, $p<0.001$). Women experienced more GBD more frequently than men in all except one form studied (all $p<0.001$, Figure 1). Forty percent of all faculty (71.4% of women and 24.1% of men) reported experiencing sexual harassment at some point in their career as an attending, and 31% of women and 9.6% of men reporting sexual harassment at least once per year or more. Women experienced GBD most commonly from surgeons (78.4%) and patients (73%), whereas men experienced GBD most commonly from patients (45.5%) and nurses (36.4%, Figure 2). Forty-two percent of respondents indicated that at least one of the offenders was responsible for two or more of their experienced incidents of GBD. Significantly more women (66%) reported experience with repeat offenders than did men (18%, $p<0.001$.) Women reported their experiences with GBD had more severe impacts on their job satisfaction, personal risk of burn-out, personal well-being, self-doubt, and personal safety (all $p<0.006$) than did men (Figure 3).

Conclusion: This study uniquely demonstrates high levels of GBD experienced by both women and men attending surgeons and anesthesiologists working in the peri-operative setting. The primary source of the GBD for women was surgeons whereas for men it was patients. The majority of women reported the GBD they experienced was from repeat offenders, and this was in contrast to the men's experience. Women were significantly more likely to experience GBD and to experience the negative psychosocial effects. Since GBD experiences impact physician job satisfaction, personal risk of burn-out, personal well-being, as well as quality of patient care, our study underscores the urgent need for intervention.

References: Am J Public Health, 1999. 89(3): p. 358-63 J Occup Health Psychol, 2001. 6(1): p. 64-80 Law Hum Behav, 2011. 35(1): p. 25-39 Journal of Management, 2013. 39(6): p. 1579-1605 West J Emerg Med, 2020. 21(2): p. 252-260 JAMA, 2016. 315(19): p. 2120-1 Acad Med, 2014. 89(5): p. 817-27 Ann Intern Med, 2000. 132(11): p. 889-96 Acad Med, 2019. 94(11): p. 1691-1698 Ann Surg, 2020. 271(4): p. 608-613 Am J Surg, 2013. 206(2): p. 263-8 Medical Education Online, 2015. 20(1) Can J Anaesth, 2017. 64(2): p. 128-140 JAMA, 2020. 323(15): p. 1503-1505

Table 1. Demographic characteristics on survey respondents

Characteristic	N = 125
Gender, No. (%)	
Female	42 (33.6)
Male	83 (66.4)
Ethnicity, No. (%)	
Hispanic or Latino	6 (4.8)
Not Hispanic or Latino	115 (92.0)
Prefer not to answer	4 (3.2)
Race, No. (%)	
White	77 (62.6)
Black or African American	1 (0.8)
Asian	30 (24.4)
Multi-Racial	3 (2.4)
Other	4 (3.3)
Prefer not to answer	8 (6.5)
Leadership role in your department, No. (%)	
Yes	65 (52.4)
No	59 (47.6)
Specialty, No. (%)	
Surgeon	69 (55.7)
Anesthesiologist	54 (43.5)
Other	1 (0.8)
Years in clinical practice, mean (SD)	14.2 (11.0)
Age, mean (SD)	47.8 (10.2)

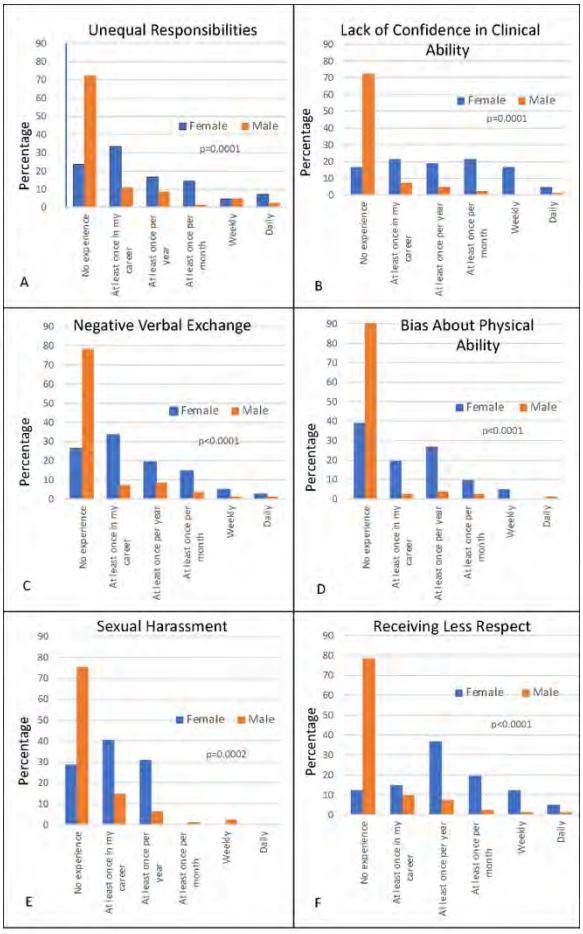

Figure 1. Forms of gender-based discrimination experienced by participants, as reported by men versus women. A. Received unequal (in quantity or significance) administrative or clinical responsibilities from your superiors. B. Perceived lack of confidence in ability to care for patients. C. Negative or inappropriate verbal exchange specific to gender. D. Gender bias about your physical ability to perform clinical work. E. Sexual harassment. F. Receiving less recognition or respect from other health care providers than colleagues of a different gender.

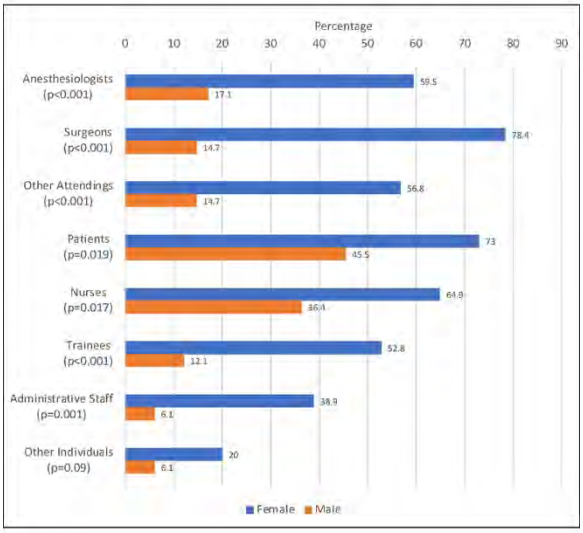

Figure 2. Sources of gender-based discrimination, as reported by men versus women. Participants were asked to report all sources of their experienced incidents of gender-based discrimination, therefore the sum of the percentages will be greater than 100.

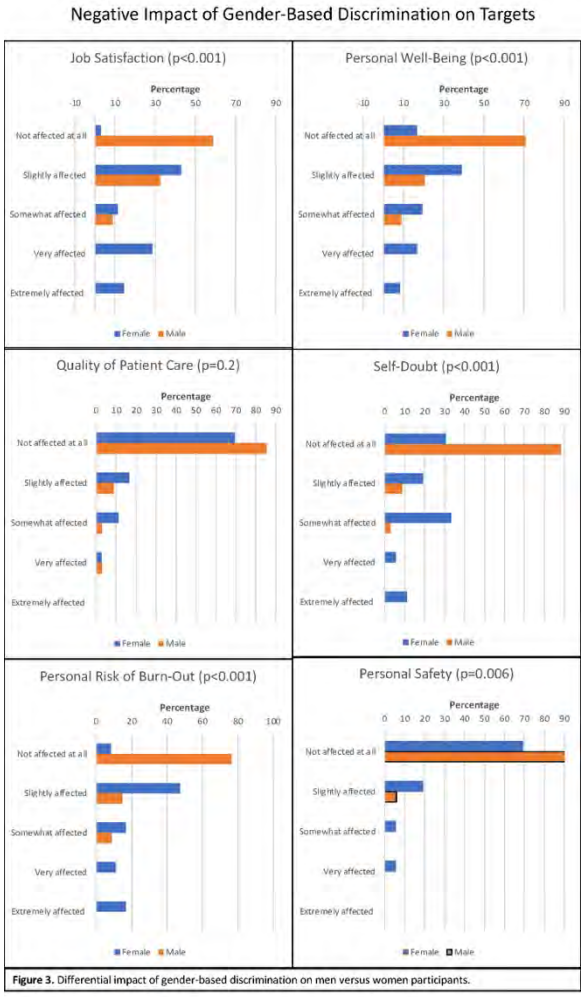

Figure 3. Differential impact of gender-based discrimination on men versus women participants.

Economics, Education and Policy - 15

Anesthesiologist Ethnicity and Sex Influence Patient Perceptions of Physician Competence

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Introduction: Explicit and implicit biases affect patient perceptions of their physician and influence the physician-patient relationship. We previously demonstrated that factors such as a physicians age, sex and body language influence patient perception of anesthesiologist.(1,2) However, the effect of ethnicity on patient perceptions has not been studied previously. In this follow-up study, we hypothesized that patients display preferences for physicians based on sex and ethnicity and that white male anesthesiologists would be preferred over black female anesthesiologists.

Methods: 300 consecutive adult, English-speaking patients were recruited in the Preanesthesia Evaluation and Testing Center. Patients were randomized (150 per group) to view a set of 4 pictures with paired audio recordings in random order. Each picture displayed for 90 seconds each featured either a white male, black male, white female, or black female anesthesiologist with a paired audio recording of an actor reciting the same script describing general anesthesia. Patients ranked each anesthesiologist on confidence, intelligence, and likelihood of choosing the anesthesiologist to care for their family member. Patients also chose the one anesthesiologist who seemed most like a leader.

Results: 300 patients viewed the picture with associated audio recording and completed the study questionnaire. Black anesthesiologists had greater odds of being ranked more intelligent (odds ratio, 1.81; 95% CI, 1.39 to 2.36; P < 0.0001), more confident (odds ratio, 1.44; 95% CI, 1.10 to 1.68; P = 0.008), were more likely to be chosen to care for a family member (odds ratio, 1.85; 95% CI, 1.14 to 2.43; P < 0.0001) and had greater odds of being considered a leader (odds ratio, 1.39; 95% CI, 1.08 to 1.20; P < 0.0001) when compared with white anesthesiologists. Female anesthesiologists had greater odds of being ranked more intelligent (odds ratio, 1.34; 95% CI, 1.07 to 1.68; P = 0.01) and more likely to be chosen to care for one's family member (odds ratio, 1.55; 95% CI, 1.25 to 1.92; P < 0.001) compared with male anesthesiologists. These findings were consistent even after adjusting for the respondents' age, sex and ethnicity.

Conclusion: Patients display preferences for certain anesthesiologists. Patients preferred black anesthesiologists on the measures of confidence, intelligence, likelihood of choosing the anesthesiologist to care for a family member and leadership. Patients also preferred female anesthesiologists on the measures of intelligence and choice for family care. Understanding how these preferences influence physician-patient relationships may lead to improved cultural competency and better patient outcomes.

References: 1. Anesthesiology. 2019;130(2):314-321. 2. Anesthesiology. 2021;134(1):103-110.

Economics, Education and Policy - 16

Effectiveness of Opioid Disposal Kits and Education Methods: A Systematic Review of Randomized Controlled Trials

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Introduction: More than 70,000 individuals died from opioid overdose in 2017, with over 17,000 deaths attributed to prescription opioid overdose.1 Notably, of the 9.7 million individuals who misused opioids in 2019, more than 50% received opioids from a friend or family member.2 Leftover prescription opioids create a reservoir of unused pills that are vulnerable to misuse and diversion. This study aims to determine the effectiveness of two interventions, patient education through verbal or written instruction and opioid-inactivating disposal kits, on opioid disposal rates among patients with leftover prescription medication.

Methods: A systematic review was performed using PubMed, Scopus, and Cochrane databases for studies describing prescription opioids and opioid disposal methods. Search terms included 'opioids' and 'disposal', 'take back', 'disposal kit', 'opioid diversion', or 'buyback'. Using the systematic review tool Covidence, 476 unique studies were identified. Inclusion criteria included randomized controlled trials (RCTs) involving human subjects in the United States from January 1999 to August 2021. Primary or secondary outcomes included measurement of opioid disposal rate as a result. Two independent reviewers screened study abstracts and titles, reviewed full text, extracted relevant data, and assessed the quality of the studies.

Results: Nine RCTs fulfilled inclusion criteria and collectively included 1,814 patients (Figure 1). In total, 591 patients comprised the control group, 851 received educational intervention, and 372 received an opioid disposal kit. There were no statistically significant age or gender differences for the three groups (Table 1). There was a high risk of bias in blinding of participants and personnel across all studies (Figure 2, 3). Eight trials followed patients up to 6 weeks postoperatively, while one trial followed medical or surgical patients who received short-term (≤7 days) opioid prescriptions (Table 1). One study was not included in the analysis of disposal rate due to reporting of intended disposal and actual disposal rate as a single outcome. The average opioid disposal rate was similar in the control group (30.50%) and the education group (30.85%). Provision of an opioid disposal kit was associated with the highest rate of disposal (51.88%), with a 21.38% increase in disposal participation compared to the control group (Table 2).

Conclusion: Our findings suggest that providing an opioid disposal kit increases patient participation in disposing of unused opioids prescribed for short-term use. Patient education minimally influenced patient behavior, suggesting that verbal or written patient instruction does not increase participation in opioid disposal. Rather, widespread distribution of opioid disposal kits could serve as an effective, actionable measure to improve the safe disposal of unused prescription opioids and therefore decrease opioid misuse and diversion in the community.

References: 1. '2019 Annual Surveillance Report of Drug-Related Risks and Outcomes - United States Surveillance Special Report', Page 9; 2019. 2. 'Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health', Page 24; 2020.

Table 1. Description of randomized controlled trials included in systematic review

First Author	Year	Intervention Arms	Surgical Specialty	Total # of Patients (Analyzed*)	% Sex	Age	Method of Obtaining Data	Follow up time
LeAnn Lam	2021	Education	Cesarean Sections	162	100 % Female	No statistically significant difference between groups	Email, text message or phone call	2 weeks
Cornelia Keyser	2020	Disposal Kit	Outpatient Foot and Ankle Surgery	47	No statistically significant difference between groups	Not provided	Survey	6 weeks
Cindy R. Nahhas	2020	Education: 1.Pamphlet 2.Pamphlet & Text Message	Total hip arthroplasty Total knee arthroplasty Unicompartmental knee arthroplasty	489	No statistically significant difference between groups	No statistically significant difference between groups	Survey	6 weeks
Mark C. Bicket	2021	1.Education 2. Education & Disposal Kit	Nonsurgical (Any patient with short term opioid prescription)	227	No statistically significant difference between groups	No statistically significant difference between groups	Phone survey	6 weeks
Kristen Buono	2021	Education (Counseling)	Pelvic Reconstruction Surgery	101	100 % Female	No statistically significant difference between groups	Survey	2 weeks
Terri Voepel-Lewis	2020	1.Education 2.Disposal Kit 3.Education and Disposal Kit	Various	368	No statistically significant difference between groups	No statistically significant difference between groups	Survey	7-14 days
Amy E. Lawrence	2019	Disposal Kit	ENT or Urology	154	No statistically significant difference between groups	No statistically significant difference between groups	Survey	2 & 4 weeks
Chad M. Brummett	2019	1.Education (Pamphlet) 2.Disposal Kit	Outpatient Surgical Procedures	208	No statistically significant difference between groups	No statistically significant difference between groups	Phone or email	4-6 weeks
Brandon C. Maughan	2016	Education	Dental	58	No statistically significant difference between groups	No statistically significant difference between groups	Text message	Postop days 1-7, 14, 21

*We eliminated patients who did not have left over opioids

Table 2. Average disposal rate in control, educational, and disposal kit intervention arms of included randomized controlled trials.

Study	Total Analyzed	Control				Educational Intervention				Disposal Kit Intervention				
		Patients Analyzed	Disposed	Proper Disposal	Improper Disposal	Patients Analyzed	Disposed	Proper Disposal	Improper Disposal	Patients Analyzed	Disposed	Proper Disposal		Improper Disposal
												Total	Disposal kit	
Brummett et al., 2019	208	63	28.57%	88.89%	11.11%	75	33.33%	96.00%	4.00%	70	57.14%	95.00%	87.50%	5.00%
Bicket et al., 2021	227	63	38.10%	41.67%	58.33%	91	25.27%	47.83%	52.17%	73	28.77%	66.67%	N/a	33.33%
Voepel-Lewis et al., 2020	368	122	18.85%	N/a	N/a	120	30.83%	N/a	N/a	126	34.13%	N/a	N/a	N/a
Lawrence et al., 2019	154	77	70.13%	92.59%	7.41%					77	87.01%	98.51%	89.55%	1.49%
Keyser et al., 2020	47	21	38.10%	100%	0%					26	84.62%	100%	100%	0%
Nahhas et al., 2020*	306	89	17.98%	50.00%	50.00%	217	21.20%	91.30%	8.70%					
Nahhas et al., 2020**	183					183	31.15%	84.21%	15.79%					
Buono et al., 2021	101	46	32.61%	93.33%	6.67%	55	63.64%	91.43%	8.57%					
Maughan et al., 2016	58	27	Intended ÷ Disposed n=8			31	Intended ÷ Disposed n=16							
Lam et al., 2021	162	83	16.87%	100%	0%	79	37.97%	100%	0%					
Total	**1814**	**591**	**30.50%**	**80.54%**	**21.48%**	**851**	**30.85%**	**86.57%**	**13.43%**	**372**	**51.88%**	**93.33%**	**90.70%**	**6.67%**
% Change from Control							**0.36%**	**6.04%**	**-8.06%**		**21.39%**	**62.84%**		**-14.81%**
% Change from Education											**21.03%**	**6.76%**		**-6.76%**

* = Pamphlet intervention, ** = Pamphlet + Text interventions; N/a = Data not reported

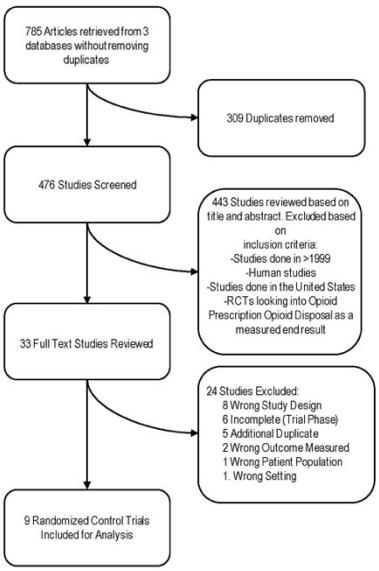

Figure 1. PRISMA flow chart of literature selection process

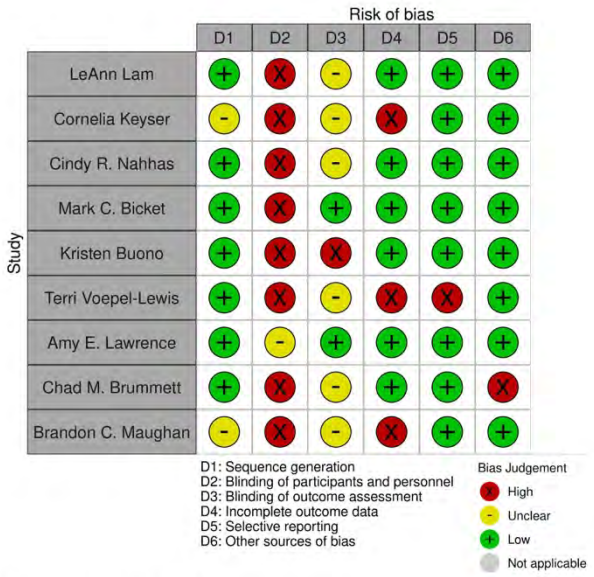

Figure 2. Risk of Bias Summary

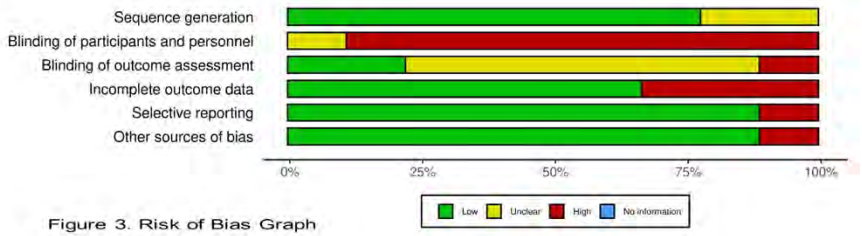

Figure 3. Risk of Bias Graph

Economics, Education and Policy - 17

Identifying residents with medical knowledge gaps pre-residency: Do we need test scores?

Merry Krueger[1], Annette Rebel[2], Robert Weaver[2], Melinda Eshelman[2], Aric Schadler[2], Amy DiLorenzo[2]

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Introduction: The majority of anesthesiology programs are using USMLE Step 1 scores during the applicant selection process to identify qualified applicants (1). Since USMLE 1 will be transitioned to pass/fail in Spring 2022, there are considerable concerns from residency programs about this change (2). Amongst the concerns, the reduction in test information may decrease awareness of knowledge gaps by medical students and prospective educators, while still holding residency programs responsible for board certification pass success. (3). Significant knowledge gaps may not be obvious in Step 2 or until later in the anesthesiology residency, creating a significant disadvantage for the learners. To prepare our program for the impending change, we investigated the use of a pre-residency medical knowledge test to indicate potential knowledge gaps allowing learners to address them as early as possible. We hypothesized that a post-match, pre-residency knowledge test, consisting of USMLE STEP1 questions will correlate with USMLE test scores taken during medical school and predict anesthesia knowledge learning success as quantified by Anesthesia Knowledge Test (AKT) scores.

Methods: Following IRB approval, we created a medical knowledge test, containing 100 multiple choice questions compiled from several USMLE Step 1 test preparation books. Three anesthesiologists identified anesthesiology relevant questions from the total content and created the test using the Delphi method. Following 2021 match, the incoming PGY-1 residents were invited to take the test ('UK Step1') before starting residency in July 2021. Test participation and results were processed independently from residency recruitment by the education specialist (AD). Data processing was handled by the education specialist until de-identification. All residents complete the 'AKTpre' at the beginning of the residency during orientation before July 1st, and on the last day of their first anesthesia month ('AKTpost', July 30th 2021). Data are shown as mean +/- SD. Linear correlations between all factors were calculated using Pearson's Correlation coefficient (IBM SPSS Statistics, version 27).

Results: Eleven residents participated in this study out of a total of 15 matched PGY-1 residents. The USMLE Step 1 score mean was 232 +/- 11, USMLE Step 2 score mean was 244.8 +/- 14.9 (Figure 1). The average increase from Step 1 to Step 2 was 12.82 +/- 15.52, with 2 students experiencing a drop in USMLE scores from Step 1 to Step 2. Using AKT scores as anesthesia related knowledge indicators, AKTpre scores showed a strong correlation with Step 2 scores but not with Step 1 (Table 1). There was also a strong correlation between USMLE score increase (Delta USMLE = USMLE 2- USMLE 1) with AKTpre and AKTpost scores. Neither standardized knowledge test (USMLE step 1 or 2, AKTpre and AKTpost) correlated with the UK Step 1 performance. The correlations between AKTpre and USMLE Step 2 ($r=0.844$, $p<0.01$) but not with USMLE Step 1 ($r=0.032$) are shown in Figure 2.

Conclusion: Our data indicate that the USMLE Step 2 performance correlates well with anesthesia knowledge tests, administered early on in the anesthesiology residency (first PGY1 month). Post medical school/pre-residency screening for USMLE Step 1 knowledge gaps does not correlate with standardized knowledge test performance during medical school or AKT. Our findings support several conclusions: 1) without a USMLE Step 1 score, the USMLE Step 2 score will be sufficient to assess anesthesia relevant medical knowledge status; 2) medical knowledge assessment at the beginning of anesthesiology residency is adequate to identify potential knowledge gaps; and 3) Screening for USMLE Step 1 knowledge appears unnecessary. Further directions are to use AKT pre /post for screening and offer additional educational tools/mentorship if indicated.

References: 1. National Resident Matching Program, Data Release and Research Committee: Results of the 2021 NRMP Program Director Survey. National Resident Matching Program, Washington, DC. 2021 2. Walsh DS (2020) USMLE Step 1 Scoring System Change to Pass/Fail - Perspective of a Program Director. JAMA Surg, 155(12):1094-96, 3. West CP, Durning SJ, O'Brien BC, Coverdale JH, Weiss Roberts L. (2020). The USMLE Step 1 Examination: Can Pass/Fail Make the Grade? Acad Med 95, 1287-89.

Figure 1 USMLE 1 and 2 (CK) scores

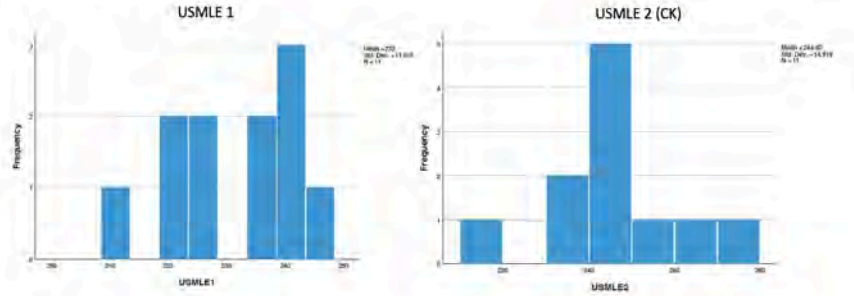
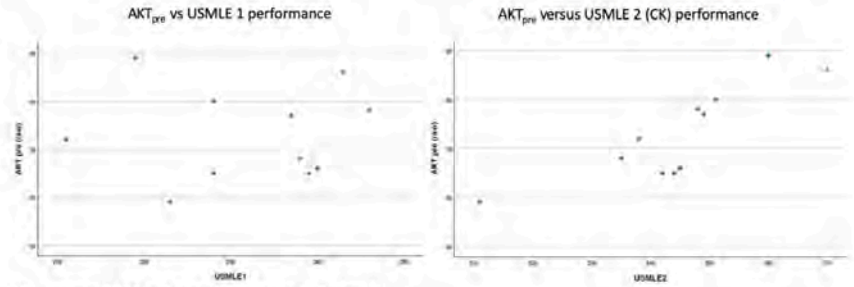


Figure 2
Correlation AKT pre versus USMLE



AKT_{pre} versus USMLE 1: Pearson coefficient r=0.032 (n=11)

AKT_{pre} versus USMLE 2: Pearson coefficient r=0.844 (n=11); p=0.001*

Table 1
Pearson Correlations (n=11)

		UK step 1	USMLE step 1	USMLE step 2	AKT pre	AKT post
USMLE step 1	Pearson correlation	- 0.025				
	P-value (2-tailed)	0.943				
USMLE step 2	Pearson correlation	0.052	0.314			
	P-value (2-tailed)	0.880	0.347			
AKT pre	Pearson correlation	0.191	0.032	0.844		
	P-value (2-tailed)	0.573	0.925	0.001*		
AKT post	Pearson correlation	0.108	- 0.313	0.647	0.684	
	P-value (2-tailed)	0.751	0.349	0.022*	0.020*	
Δ USMLE	Pearson correlation	0.067	- 0.408	0.739	0.788	0.873
	P-value (2-tailed)	0.844	0.213	0.009*	0.004*	0.001*

* P<0.05

Economics, Education and Policy - 18

Assessing Diversity among Full-Time Anesthesiology Faculty in United States Medical Schools, 1970-2019

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Introduction: Studies have shown improved outcomes in racially concordant physician-patient interactions and a greater success rate for pipeline and mentorship programs with racially or ethnically concordant mentors. Over the last 10 years or more, there has been an increased focus on promoting diversity in the healthcare workforce [1][2]. Despite such attention in the workforce diversity, the anesthesiology faculty at United States (U.S.) Medical Schools have been homogenous in areas of race, ethnicity and sex. Here we evaluated the diversity trends in anesthesiology faculty relative to the US census data.

Methods: This was a repeat cross-sectional study, based on the secondary analysis of data from the Association of American Medical Colleges (AAMC) Faculty Roster and United States Census data for the years between 1970 and 2019. We calculated the descriptive statistics of US allopathic medical school anesthesiology department faculty by sex, race, ethnicity and faculty rank.

Results: The overall number of U.S. medical school anesthesiology faculty increased from 850 in 1970 to 9168 in 2019. This increase appears to have primarily been due to a steady annual increase seen in the number of White and Asian faculty, as the absolute number of Black and Hispanic faculty has changed at a slower rate (Figure 1). Also, compared to White and Asian faculty, Black and Hispanic faculty of both sexes are disproportionately represented in the lower academic ranks (Figure 2). Finally, the proportion of underrepresented in medicine (URM) anesthesiologists does not reflect their representation in the US population (Figure 3).

Conclusion: The growth of faculty in U.S. anesthesiology departments over the last 50 years has led to greater representation of diverse groups, however, more work needs to be done to improve racial, ethnic, and sex diversity trends in U.S. anesthesiology departments to reflect the U.S. population. Addressing URM faculty's lagging representation in higher academic ranks requires attention to be paid to mentorship, recruitment, retention, and promotion. Additionally, collaboration with an existing, or creation of, a committee on Diversity, Equity, and Inclusion is invaluable.

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Fig. 1. Proportion (%) of Faculty by Race and Sex Between 1970 and 2019.

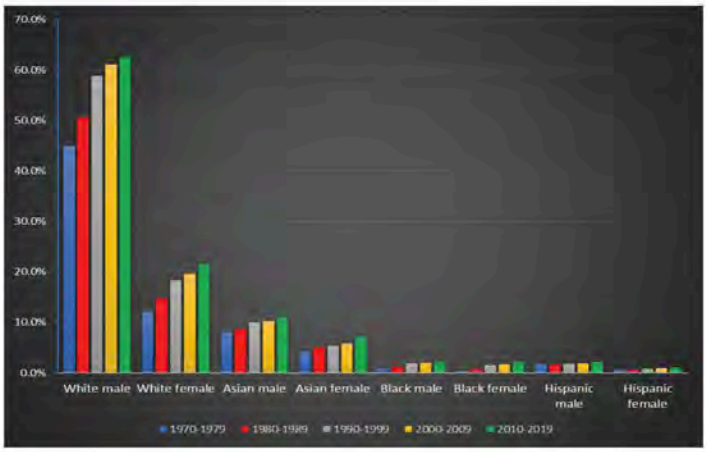


Fig. 2. Proportion (%) of Faculty by Race, Sex and Rank Between 1970 and 2019.

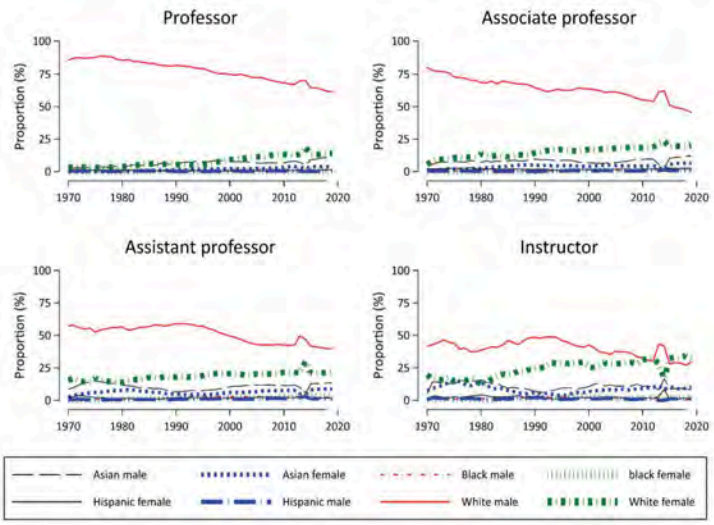
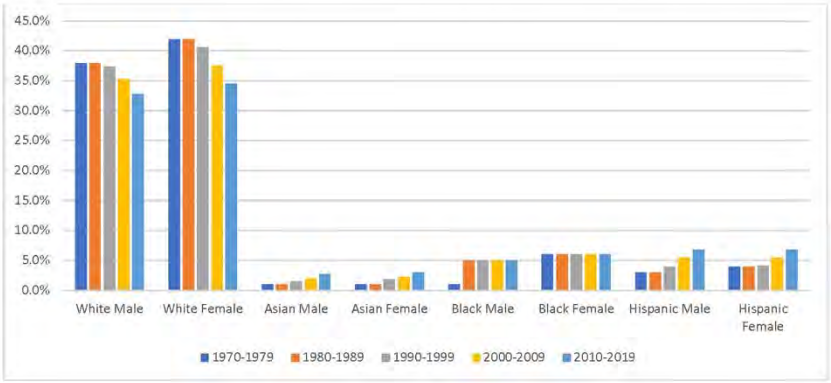


Fig. 3. Proportion (%) of United States Population by Race and Sex Between 1970 to 2019 (US Census Data).



Economics, Education and Policy - 19

Mentor-Mentee Program for Faculty Development at a Large Academic Department: The First-Year Survey

Tetsuro Sakai[1]

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Introduction: Mentorship is crucial for the development of academic faculty members. Effective mentorship to junior faculty members has resulted in faster academic promotion (1), increased confidence and academic retention (2), and improved academic performance (3). Many industries have implemented a company-led structured mentor-mentee (MM) program with success (4). Such a structured mentorship program, however, has rarely been adopted in academic institutions. In a large academic department, we launched a department-led Mentor-Mentee Program for academic anesthesiology faculty members. The first-year survey on both mentors and mentees was conducted.

Methods: Given the department chair's endorsement, the Vice-Chair of Faculty Development designed the MM Program in 2019. First, a MM program website (https://www.academicprofessionaldevelopment.org/) was created featuring 1) the goal and objective; 2) the basics of mentorship and its difference from coaching, sponsorship, or connecting; 3) a recommended method of MM meetings, and 4) the handbooks for mentor and mentee. Grand Rounds on the mentorship and faculty promotion process were provided to all faculty members in 2019, and they were uploaded on the web. Second, the e-mail invitation to the MM program was sent to junior faculty members (Assistant Professors and newly hired Clinical Assistant Professors), which prompted them to choose up to three faculty mentors. Upon acceptance by the mentor, we initiated the formal MM relationship. The MM program was officially launched in February 2020. In April 2021, the first-year mentor and mentee anonymous survey was administered using Microsoft software. Fifteen external mentors were not included in the department survey.

Results: The department has 211 anesthesiology physicians (76 academic faculty and 135 clinical faculty). Fifty-three mentees (39 Assistant Professors and 14 newly hired Clinical Assistant Professors) were invited as mentees, and 52 (98.1%) participated in the MM Program. Thirty-eight mentors [19 (50.0%) Associate/full Professors, 11 (28.9%) Assistant Professors, 8 (21.1%) Clinical Assistant/Associate Professors] were selected, and all agreed to serve as the mentor. Each mentor had a median of two (range 1-11) mentees. Forty-two (80.8%) mentees and 35 (92.1%) mentors completed the survey. 93% of mentees and 91% of mentors were satisfied with the current number of mentors/mentees. 83% of mentor-mentee pairs met at least bi-monthly. Overall satisfaction of the MM program was 76% (mentees) and 71.4% (mentors), while 21.4% (mentees) and 25.7% (mentors) were neutral. Perceived dissatisfaction for mentees was 1) lack of time or 2) misalignment of the mentor-mentee interest/stage/location/expertise. Perceived dissatisfiers for mentors were lack of mentee's proactiveness, time, and effectiveness. 91% of mentees and 100% of mentors felt mentorship was effective.

Conclusion: A department-led structured mentor-mentee program was initiated in a large academic department for junior faculty members. The first-year survey showed the majority of both mentees and mentors perceived the program as effective.

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Economics, Education and Policy - 20

Predicting Academic Success in Anesthesiology Residents - Will USMLE Step1 scores be missed?

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Introduction: USMLE Step 1 scores were utilized by 95.2% of the programs in the 2021 NRMP Program Director Survey with a mean importance score of 3.8/5 (4). This, however, will likely be changing as USMLE Step1 transitions to a pass/fail scoring system, thus eliminating a score that was previously ranked as high as 4.4/5 in 2018 (3). Studies in the past have suggested a high correlation between USMLE Step scores and in-service ITE exams and ABA exams (1,2). However, with introduction of the ABA Basic exam, it is unclear if learning behavior has changed due to the in-training placement of this high-stakes exam. Based on these prior studies, we hypothesize that USMLE STEP1 and STEP2 scores and/or Anesthesia Knowledge Test (AKT) scores (pre-residency, post first anesthesia clinical month, or change between pre/post scores) will predict the ability to improve anesthesia related medical knowledge as measured by a change in In-Training Examination (ITE) Scores.

Methods: Following IRB approval, a retrospective data analysis was performed on a de-identified data set from all anesthesiology residents at the University of Kentucky from 2013 to 2021. Data consisted of USMLE Step 1 and Step 2 scores, AKT exam scores (raw score) taken pre-residency and after first month of clinical anesthesiology rotation, and ITE exam scores taken every January during their four-year residency. The change between pre- and post- AKT exam scores and between yearly ITE exam scores was calculated. Linear correlations between all factors were calculated using Pearson's Correlation coefficient.

Results: Scores from a total of 136 residents were evaluated. All included residents obtained primary board certification. USMLE scores of the included residents were balanced distributed around national mean values during the study period (Figure 1). The raw test score data are shown in Table 1. USMLE Step1 scores had a statistically significant but weak positive correlation with ITE year 1-4 scores (r=.329, p<.001; r=.291, p=.001; r= 3.26, p = .001; r=2.76, p=.007) with no statistically significant correlation to ITE growth. USMLE Step2 scores showed similar results with a statistically significant and weak positive correlation to ITE year1-4 scores (r =.317, p<.01; r=.370, p<.01, r=.443, p<.01, r=.309, p=.02) and no correlation to ITE growth. AKT pre-test scores were most strongly correlated with ITE-1 scores (r=.409, p <.001) with strength of correlation decreasing through training. AKT post-anesthesia rotation scores showed statistically significant, weak positive correlation to ITE year 1-4 (r=.476, p<.01; r=.467, p<.01; r=.438; p<.01; r=.392, p<.01), with a statistically insignificant negative correlation to ITE growth. AKT growth showed no correlation to either ITE scores or ITE growth. It is important to note that none of the factors were associated with an r-value >0.5 suggesting they were moderate correlations.

Conclusion: Using a holistic recruitment and selection approach, recruiting residents with a broad range of academic performance, we made following observations: 1) Neither USMLE Step1 nor Step2 scores are predictive of trainees' ability to improve anesthesia related knowledge as measured by change in ITE scores over the course of training. 2) Neither AKT pre-residency score, AKT post-residency score, nor change in AKT pre/post scores are predictive of trainees' ability to improve anesthesia related knowledge. 3) Further research is needed to identify factors within an objective holistic selection approach to predict trainees' academic performance during anesthesia residency.

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3. National Resident Matching Program, Data Release and Research Committee: Results of the 2018 NRMP Program Director Survey. National Resident Matching Program, Washington, DC. 2018.
4. National Resident Matching Program, Data Release and Research Committee: Results of the 2021 NRMP Program Director Survey. National Resident Matching Program, Washington, DC. 2021

Figure 1 USMLE 1 and 2 (CK) scores

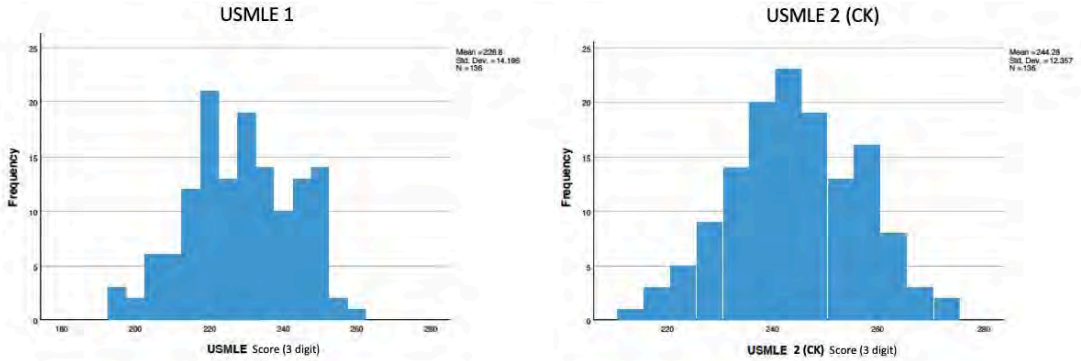

Table 1

Test	n	Test score (mean ± SD)
AKT pre [percentile]	134	43.97 ± 19.87
AKT post [percentile]	131	54.41 ± 21.33
AKT Δ pre-post [percentile]	131	10.52 ± 19.65
USMLE 1	136	228.80 ± 14.19
USMLE 2 (CK)	136	244.28 ± 12.36
ITE PGY1	126	26.63 ± 4.94
ITE CA1	123	34.72 ± 5.86
ITE CA2	107	39.50 ± 5.24
ITE CA3	94	40.20 ± 5.11
ITE Δ PGY1-CA1	123	10.36 ± 8.18
ITE Δ PGY1-CA2	107	15.20 ± 7.37
ITE Δ PGY1-CA3	94	16.23 ± 7.79

Economics, Education and Policy - 21

Race and Socioeconomic Status in Clinical Anesthesiology Research

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Introduction: Evidence Based Medicine (EBM), by definition, demands use of the best available evidence to make decisions about the care of individual patients. However, generalizability has been a long-standing concern when applying clinical research to real-world patients. Part of this discrepancy stems from recent research showing that racial/ethnic minorities and other disadvantaged populations bear a disproportionate burden of illness but are less likely to be included in clinical research samples. Recently, investigators have strived to better understand the impact of race and socioeconomic status (SES) on patient outcomes, but it is still unclear if these variables are consistently and effectively assessed. Specifically, there is a paucity of knowledge concerning the inclusion of race and SES in clinical anesthesiology research. Thus, we evaluated clinical anesthesiology publications to characterize the use of race and SES variables in anesthesiology research over a one-year period.

Methods: Ten major, high impact anesthesiology journals were selected to include major anesthesiology subspecialties from a wide geographic origin (U.S.-based and international journals). Journals included were: Anesthesiology, British Journal of Anesthesiology, Anesthesia, Journal of Clinical Anesthesia, Intensive Care Medicine, Journal of Cardiothoracic and Vascular Anesthesia, International Journal of Obstetrics, Journal of Pain, Pediatric Anesthesia, and Regional Anesthesia and Pain Medicine. All articles published in 2019 were queried for review. Upon review of full text, all original human-participant clinical research studies were included in the analyses. Each article was manually analyzed to assess 1) if race and SES variables were collected and reported, 2) how race and SES variables (if specified) were defined, and 3) the extent to which race and SES were analyzed or discussed as variables of interest. Analyses of Means for Proportions and œá¬≤ tests were performed to detect differences between different anesthesia subspecialties in the frequency of reporting, analysis, and discussion of race and SES. œá¬≤ tests and Fisher's Exact Tests were performed to detect differences between geographic origin of study (i.e. United States-based studies vs. international studies).

Results: Overall, 975 out of 3,090 (31.6%) articles met inclusion criteria. In total, 149 (15.3%) of studies specified race as a variable. Of the 149 studies that specified race, 29 (19.5%) defined race using racial and ethnic categories interchangeably. 143 (96.0%) reported data by race, 94 (63.1%) conducted analysis of race-based data, and 72 (48.3%) discussed race-based results. In total, 113 (11.6%) studies specified SES as a variable. Of the 113 studies that specified SES, 59 (52.2%) defined SES using education status, 31 (27.4%) using income level, 23 (20.4%) using health insurance (e.g. public vs. private), and 23 (20.4%) using employment status. 90 (79.6%) reported data by SES, 73 (64.6%) conducted analyses of SES-based data, and 65 (57.5%) discussed SES-based results. Lastly, sub-analysis by subspecialty revealed that compared to the average, 1) pain medicine articles reported/analyzed/discussed race ($p < 0.05$) and SES ($p < 0.05$) more, 2) cardiothoracic anesthesiology articles reported race ($p < 0.05$) and reported/analyzed/discussed SES ($p < 0.05$) less, 3) critical care anesthesiology articles analyzed race ($p < 0.05$) less, and 4) orthopedic/regional pain medicine articles analyzed SES ($p < 0.05$) more. Analysis of study location revealed that U.S.-based studies reported/analyzed/discussed race ($p < 0.05$) and SES ($p < 0.05$) more than international studies.

Conclusion: The inclusion of race and SES data in clinical anesthesiology research is low. Among studies that did specify race and SES data, the reporting and analyses of these data were even more limited. Although there was significant variation in rates of specification for race and SES data between different anesthesiology subspecialties, there remains a need to increase the specification of race and SES variables across all subspecialties. Thus, anesthesiology journals should emphasize increased reporting and analyses of race and SES data in order to improve the

quality of anesthesiology research and care for all patients.

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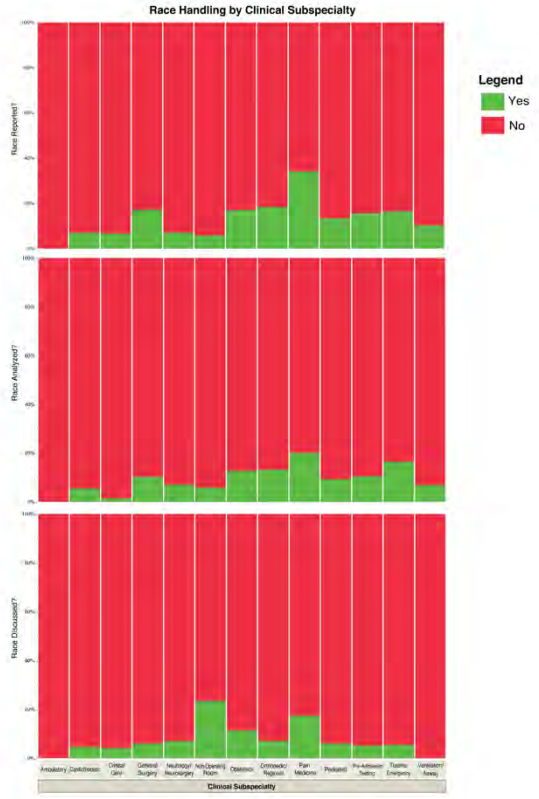

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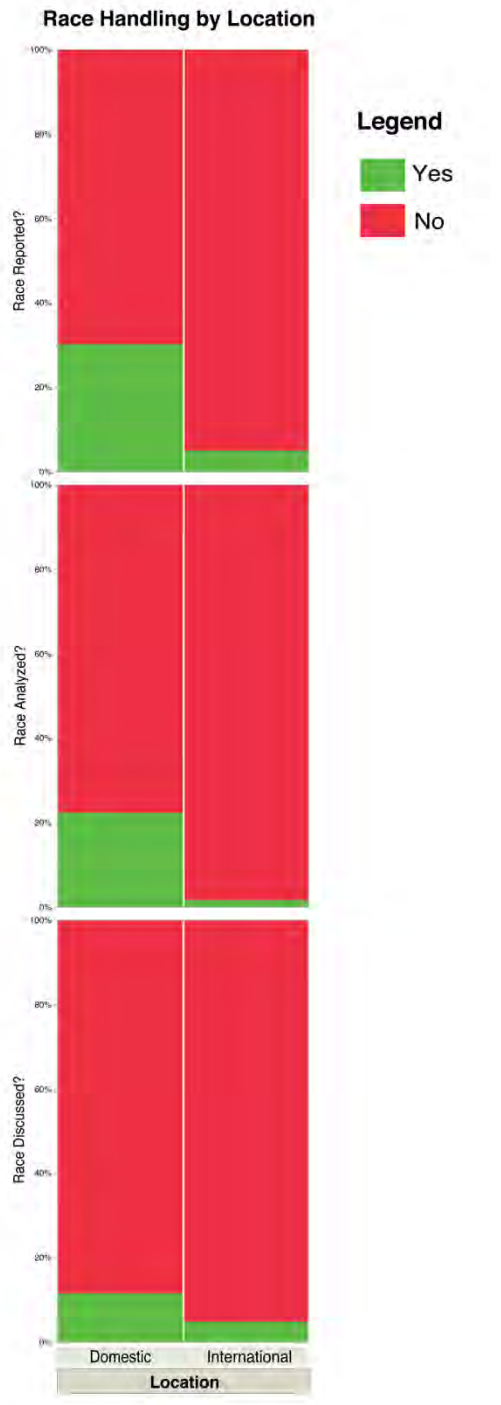
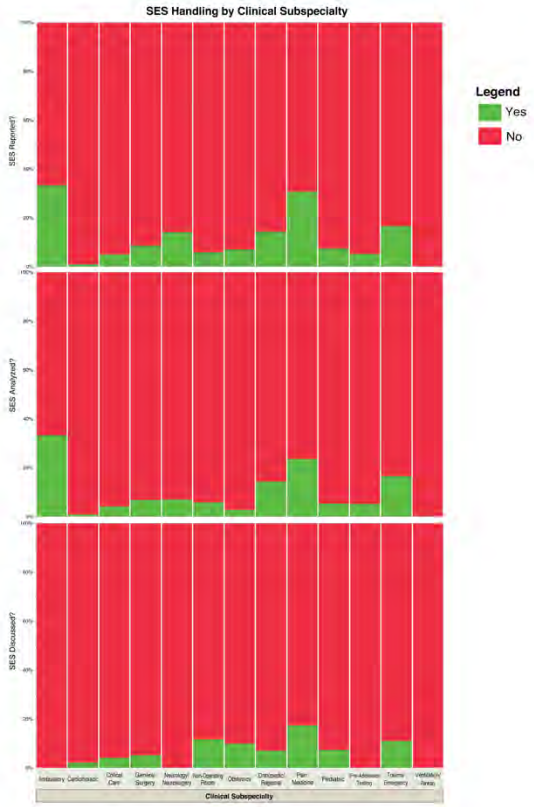
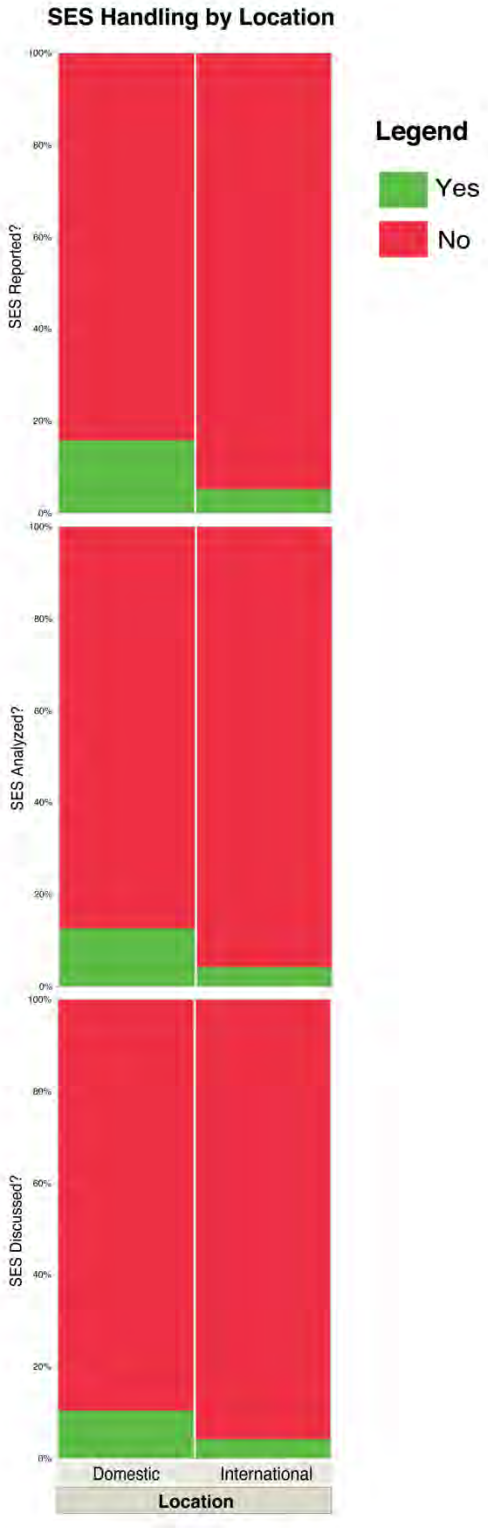



SES Handling by Clinical Subspecialty
Legend
Yes
No
SES Reported?
SES Analyzed?
SES Discussed?
Clinical Subspecialty


SES Handling by Location
Legend
Yes
No
SES Reported?
SES Analyzed?
SES Discussed?
100%
80%
60%
40%
20%
0%
Domestic
International
Location

Economics, Education and Policy - 22

The Individual Impact of Participation in a Diversity Curriculum Among Perioperative Residents

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Introduction: In recent years, equity and inclusion training in academic medicine broadly focused on providing foundational diversity knowledge. While faculty and emerging trainees confirm the ability to define diversity, equity, and inclusion (DEI) concepts, they also report difficulty in applying these insights throughout clinical, educational, and academic settings. For institutions to effectively engage anti-racist pedagogy, they must create space to discuss and address structural and interpersonal harm that occur in healthcare and academic medicine. Utilizing the framework of the Kirkpatrick Evaluation Model, this graduate medical education training series focuses on transferring DEI knowledge (level 2) into applied behaviors (level 3). The DEI curriculum centers around three core concepts including unconscious bias, microaggressions, and allyship. The series' objective is to curate facilitated spaces that will support faculty and residents in their ability to effectively engage in difficult dialogues and take action to support the lives of people who have long been marginalized within healthcare and society.

Methods: Using Kern's six steps, this study is a pretest-posttest design of a 4-series workshop utilizing activities to enhance competence and performance around unconscious bias, allyship, and microaggression. We administered a pre-workshop survey 6-8 weeks prior to the workshop series during an introduction session for first-year anesthesia residents that preceded this curriculum. The survey was also emailed out to all surgery and anesthesia residents at UCSF to capture a wider audience including those who were not able to attend the introduction session. This needs assessment captured what the residents felt were lacking in their education regarding DEI training and also their prior experiences with DEI training. Eighty-three percent (79/95) of participants stated that they have not previously received formal DEI training. Participants identified that actionable changes, tools, interactive activities to uncover biases, and small group discussions were important. The diversity curriculum included 2-hrs workshops on unconscious bias, allyship, and microaggression that encompassed pair-share, interactive exercises, role play in small breakout groups as well as evidence-based didactics on a virtual platform to 22 first-year clinical anesthesia residents and 15 senior general surgery residents (PGY-4 and PGY-5). The residents were selected based on available protected educational time with the least scheduling conflicts across the anesthesia and general surgery residency programs. Using Kirkpatrick's framework based on level 1 satisfaction and level 2 competency, the results were then measured using paired t-test analyses. The University of California San Francisco Institution Review Board deemed this study exempt from review (5/14/20).

Results: After participation in the Unconscious Bias workshop, 100% of Anesthesiology CA-1 survey responses and 63% of Surgery PGY-4 and PGY-5 survey responses were completed. On a 5-point Likert Scale, participants rated their agreement with 'I believe this unconscious bias workshop is relevant to my workplace' a mean of 4.70 (SD+/-0.54), 'I would recommend this unconscious bias workshop to my peers' a mean of 4.67 (SD+/-0.55), and 'this unconscious bias workshop has given me insight on biases I didn't know I had' a mean of 4.15 (SD+/-0.86). A total of 15 Anesthesia CA-1 participants who completed both the pre-workshop survey and post-workshop survey were matched to analyze their data using a paired T-Test. Fifteen paired participants increased their agreement with the statement 'I know how to define the term unconscious bias' from a pre-workshop mean of 4.1 (SD+/-0.59) to a mean of 4.8 (SD+/-0.41, $P<0.001$). They also self-reported increased agreement with the statement 'I have unconscious biases' from a pre-workshop mean of 4.3 (SDÔÇ±0.70) to a post-workshop mean of 4.8 (SD+/-0.41, $P=0.006$). 'My unconscious biases affect my clinical practice and/or interactions with others' mean agreement increased from 2.9 (SD+/-1.51) to 3.8 (SD+/-1.01, $P=0.021$).

Conclusion: The Unconscious Bias workshop filled an important need for DEI education for perioperative residents. With high response rates, the survey results demonstrated the residents' great satisfaction as well as increased awareness of their own implicit biases. This workshop also promoted active reflection on how these biases impact their interactions and clinical practice.

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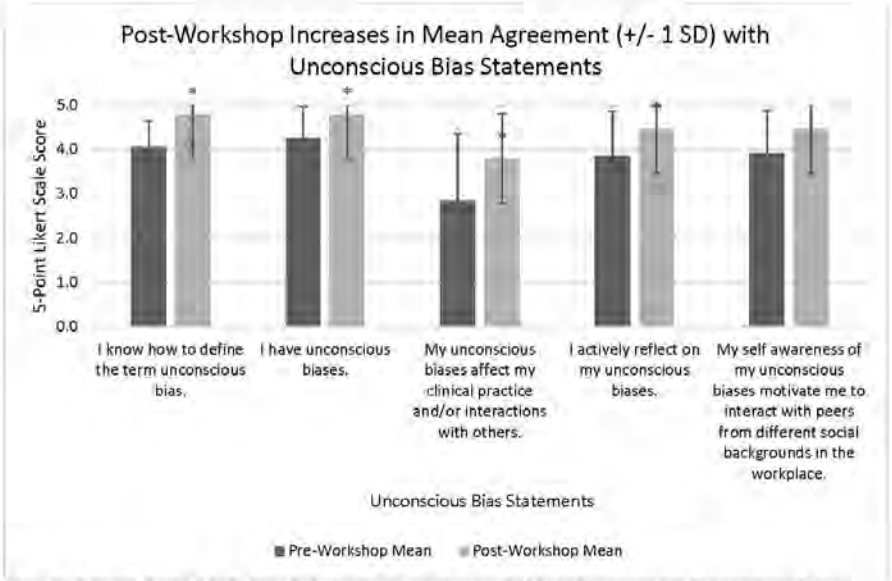

Figure 1. Paired T-Test Analysis Reveals Post-Workshop Increases in Mean Agreement with Unconscious Bias Statements. The * denotes $p<0.05$ for comparison between pre-workshop and post-workshop responses. The error bars represent the range of one standard deviation of the mean agreement. The statements were rated on a 5-point scale (1=*Strongly Disagree*, 5=*Strongly agree*).

Statement	Strongly disagree	Somewhat disagree	Neutral	Somewhat agree	Strongly agree
This unconscious bias workshop is important to my training	0%	0%	4%	26%	70%
I believe this unconscious bias workshop is relevant to my workplace	0%	0%	4%	22%	74%
I would recommend this unconscious bias workshop to my peers.	0%	0%	4%	26%	70%
This unconscious bias workshop has given me insight on biases I didn't know I had	0%	4%	19%	37%	41%

Table 2. Post-Workshop Student Evaluations of Workshop (N = 27).

Geriatric Anesthesia

Geriatric Anesthesia - 1 Preoperative factors predict neurocognitive disorder after CABG or PCI in a population-based cohort of older adults

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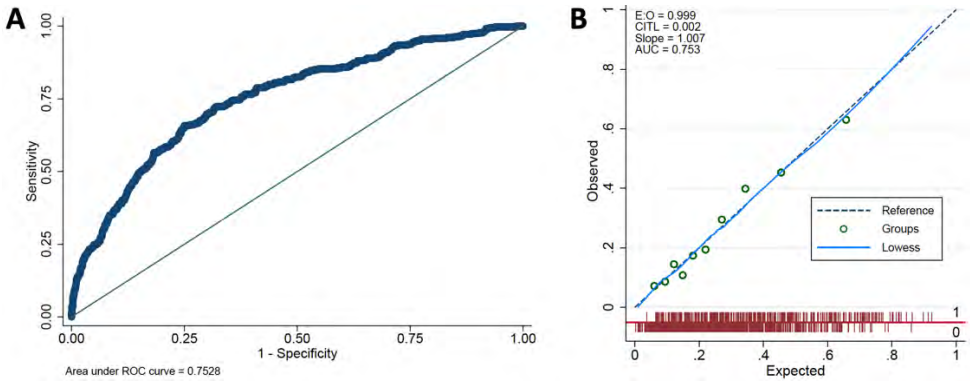
Introduction: We recently found no population-average difference in long-term cognitive outcomes after coronary revascularization by coronary artery bypass grafting (CABG; including off-pump CABG [OPCAB]) versus percutaneous coronary intervention (PCI).[1] However, durable postoperative neurocognitive disorder (PND) remains a feared outcome of medical care, and occurred in both CABG and PCI recipients in our study. It is currently unknown whether individual PND risk can be predicted. We analyzed the cohort of older adults from our published study[1] to establish whether preoperative factors predict PND at 0-2 years after coronary revascularization.

Methods: Older adults in the nationally-representative Health and Retirement Study (HRS) undergo biennial cognitive assessments throughout late life. We used Medicare billing records to identify 1,390 HRS participants (551 CABG, 839 PCI) who underwent CABG/PCI at age 65 or older between 1998 and 2015 and participated in at least one post-procedure HRS interview.[1] Using a summary measure of memory based on direct and proxy cognitive test responses,[2] we identified participants whose actual post-procedure memory performance was 1-2 ('mild NCD') or >2 ('major NCD') standard deviations lower than expected from pre-procedure memory assessment. After multiple imputation to address missing data, we modeled individual probability of mild or major NCD at the first postoperative cognition assessment using ordered logistic regression on a priori specified preoperatively-known factors including demographic and health factors, preoperative memory, and frailty.

Results: Participants underwent CABG/PCI at 75¬±6 years old; 39.7% were women, and 16.6% were of nonwhite race/ethnicity. At a median of 1.1 [interquartile range 0.6-1.6] years after procedure, 1,035 had no NCD, 267 (19%) had mild NCD, and 88 (6%) had major NCD. Risk factors predicting any NCD included older age, male gender, nonwhite race/ethnicity, frailty, OPCAB, and, counterintuitively, higher memory score at preprocedure. Obesity was protective. Participants meeting 'high risk' criteria (11% of the cohort) had a 59% rate of any NCD, and 21% rate of major NCD. In contrast, 78% of those at 'low risk' were free of any NCD; 96% had either no or mild NCD only. The area under the receiver operator characteristic curve for any NCD was 0.753, which remained stable when the model was applied to PCI-only or CABG-only recipients. Calibration was excellent (slope 1.007, with expected:observed 0.999) in the whole cohort and CABG and PCI subgroups.

Conclusion: A model using preoperatively-known factors predicted durable NCD with discrimination and calibration suitable for clinical use. Figure 1. Discrimination and calibration for the prediction model. A, receiver operator characteristic curve. B, calibration plot.

References: 1. JAMA 325(19):1955-64, 2021. 2. Alzheimer Dis Assoc Disord;27(3):207-12, 2013.


A
Sensitivity
0.00
0.25
0.50
0.75
1.00
1 - Specificity
Area under ROC curve = 0.7528
B
E:O = 0.999
CITL = 0.002
Slope = 1.007
AUC = 0.753
Observed
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Geriatric Anesthesia - 2 Perioperative neurocognitive and CSF Alzheimer's biomarker trajectories in older patients randomized to Isoflurane or Propofol for Anaesthetic Maintenance

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Introduction: Animal studies have suggested that isoflurane versus propofol have differential effects on Alzheimer's Disease (AD) - related neuropathological processes, such as amyloid beta [1] and tau pathology [2, 3], and on memory function [4]. Whether these drugs also have differential effects on cognition and AD neuropathology in actual patients is a clinically important question, since over 19 million older Americans undergo surgery each year [5] and are at risk for AD or other related dementias based on their age. [6]

Methods: Patients age ≥ 60 undergoing non-cardiac, non-neurologic surgery were prospectively enrolled and randomized to receive isoflurane (N=54) or propofol (N=52) for anesthetic maintenance. We collected CSF samples before, 24 hours and 6 weeks after surgery (via lumbar punctures performed for research), to measure CSF AD - related biomarker levels (ie, Aβ42, tau, and p-tau 181p) and performed cognitive testing to assess the effect of anesthetic choice on cognitive function. Wilcoxon rank sum tests were used to compare CSF AD-related biomarkers between groups; univariable and multivariable linear regression was used to evaluate the relationship between anesthetic treatment group and cognitive outcomes.

Results: There was no difference in the CSF tau/Aβ ratio between patients randomized to isoflurane vs propofol treatment groups before or 24 hrs after surgery (P = 0.186). All other CSF AD – related biomarkers (Aβ , tau, p-tau/ Aβ, and p-tau 181p) showed no significant difference between treatment groups before surgery, or 24 hours or 6 weeks after surgery. There was no significant difference in overall cognitive change from before to 6- weeks after surgery among propofol vs isoflurane treated patients (P = 0.881), nor were there any significant differences between anesthetic groups in individual cognitive domain changes over this time interval.

Conclusion: The results from this randomized controlled trial in over 100 older adults suggest that there is no reason to favor inhaled vs intravenous anesthesia for older adults concerned about their postoperative cognitive function and/or risk of developing Alzheimer's disease. These data suggest that the choice of anesthetic type (ie inhaled vs intravenous) should be made based on other patient, procedural or institutional factors.

References: 1. Anesthesia with isoflurane increases amyloid pathology in mice models of Alzheimer's disease. J Alzheimers Dis 2010;19(4):1245-57. 2. Tau phosphorylation and sevoflurane anesthesia: an association to postoperative cognitive impairment. Anesthesiology 2012;116(4):779-87. 3. Propofol directly increases tau phosphorylation. PLoS One 2011;6(1):e16648. 4. Brain and behavior changes in 12-month-old Tg2576 and nontransgenic mice exposed to anesthetics. Neurobiol Aging 2008;29(7):1002-10. 5. ASA geriatric Anesthesia Curriculum. 2007. www. asahq.org/For-Members/Clinical-Information/Geriatric-Curriculum. aspx. 6. Alzheimer's disease, anesthesia, and surgery: a clinically focused review. Journal of cardiothoracic and vascular anesthesia 2014;28(6):1609-23.

Of the 106 patients with complete cognitive data 14 (13.2%) were not treated as randomized. Hence, we conducted primary analysis according to the Intention To Treat principal. There was no evidence of a difference in rate of protocol deviations between groups (p=0.22).

Table 1

	Isoflurane (N=54)	Propofol (N=52)	p value
Age	67.5 [64, 71]	69.5 [64, 73]	0.502[1]
Race			0.079[2]
Black or African American	2 (3.7%)	8 (15.4%)	
Caucasian/White	51 (94.4%)	44 (84.6%)	
Not Reported/Declined	1 (1.9%)	0 (0.0%)	
GENDER (Male)	37 (68.5%)	29 (55.8%)	0.176[2]
BMI	28.0 [24.8, 31.3]	29.3 [24.5, 34]	0.259[1]
Years of Education	14.5 [12, 17.5]	16 [13.5, 18]	0.305[1]
Preop MMSE	29 [27, 29]	29 [28, 29]	0.122[1]
Pre-op Verbal Memory	0.40 (0.91)	0.60 (0.85)	0.248[3]
Pre-op Visual Memory	-0.10 (0.96)	0.07 (0.92)	0.365[3]
Pre-op Executive Function	0.02 (1.00)	0.30 (0.98)	0.155[3]
Pre-op Attention/Concentration	-0.17 (0.82)	-0.07 (0.80)	0.536[3]
PreOp Cognitive Index	0.04 (0.68)	0.22 (0.68)	0.167[3]
ASA			0.670[2]
1	1 (1.9%)	0 (0.0%)	
2	10 (18.5%)	13 (25.0%)	
3	42 (77.8%)	38 (73.1%)	
4	1 (1.9%)	1 (1.9%)	
SURGICAL SERVICE			0.598[2]
Thoracic	5 (9.3%)	5 (9.6%)	
General Surgery	14 (25.9%)	16 (30.8%)	
Gynecology	2 (3.7%)	0 (0.0%)	
Orthopedics	10 (18.5%)	9 (17.3%)	
Otolaryngology Head and Neck	0 (0.0%)	2 (3.8%)	
Plastic Surgery	2 (3.7%)	1 (1.9%)	
Urology	21 (38.9%)	19 (36.5%)	
Surgery duration (min)	131.5 [105, 191]	152 [92, 201]*	0.608[1]
CSF Biomarkers	N=48	N=49	
AB	358 [268.5, 399]	367 [298, 410]	0.521[1]
P-TAU 181P	27.5 [20.5, 30]	26.0 [21, 33]	0.989[1]
P-TAU/AB	0.08 [0.06, 0.10]	0.08 [0.06, 0.09]	0.711[1]
Tau	49.5 [44.5, 58.5]	47 [39, 59]	0.251[1]
TAU/AB	0.14 [0.12, 0.19]	0.13 [0.11, 0.18]	0.347[1]
Shaw Grouping			

[1]Wilcoxon [2]Chi-Square [3]Equal Variance T-Test [4]Unequal Variance T-Test
* Missing for 1

Table 2

CSF AD - related Biomarkers 24-hour change by treatment group

Grouping (N Iso/ N Prop)	Isoflurane median [Q1, Q3]	Propofol median [Q1, Q3]	Wilcoxon p-value
Intention To Treat (44/43)			
AB	-6 [-22, 18]	-1 [-25, 19]	0.879
P-TAU 181P	0 [-4, 6]	2 [-2, 6]	0.269
P-TAU/AB	0.00 [-0.01, 0.02]	0.01 [-0.01, 0.02]	0.339
Tau	-1 [-5, 2.5]	1 [-4, 4]	0.324
TAU/AB	-0.01 [-0.02, 0.02]	0.00 [-0.01, 0.02]	0.186

Table 3

CSF AD - related Biomarkers 6-Week change by treatment group

Grouping (N Iso/ N Prop)	Isoflurane median [Q1, Q3]	Propofol median [Q1, Q3]	Wilcoxon p-value
ITT (44/45)			
AB	-11 [-37, 18]	-3 [-13, 14]	0.512
P-TAU 181P	1 [-5, 6]	-2 [-7, 4]	0.248
P-TAU/AB	0.01 [-0.01, 0.02]	0.00 [-0.02, 0.02]	0.361
Tau	-2 [-4.5, 3.5]	-2 [-4, 3]	0.660
TAU/AB	0.00 [-0.02, 0.01]	0.00 [-0.01, 0.01]	0.575

Table 4

6-week Overall Cognitive Change

Domains	Isoflurane mean (SD)	Propofol mean (SD)	Univariable		Multivariable*	
			Mean Difference (95% CI)	p-value	Mean Difference (95% CI)	P-value
Overall	0.06 (0.27)	0.02 (0.34)	0.04 (-0.08, 0.16)	0.543	0.01 (-0.12, 0.13)	0.881

*Multivariable model adjusted for age, years education, APOE4 carrier, surgical service, surgery duration, baseline cognition

Table 5

6-week Cognitive Domain Change

Cognitive Domain	Univariable		Multivariable*	
	Mean Difference (95% CI)	p-value	Mean Difference (95% CI)	P-value
Verbal Memory	0.15 (-0.21, 0.51)	0.410	0.12 (-0.28, 0.52)	0.552
Visual Memory	-0.17 (-0.42, 0.07)	0.170	-0.25 (-0.50, 0.00)	0.051
Executive Function	0.09 (-0.07, 0.25)	0.257	0.08 (-0.08, 0.24)	0.318
Attention/Concentration	0.08 (-0.13, 0.28)	0.464	0.09 (-0.14, 0.31)	0.442

*Multivariable model adjusted for age, years education, APOE4 carrier, surgical service, surgery duration, baseline cognition

Geriatric Anesthesia - 3

Dexmedetomidine is associated with a reduced postoperative increase in plasma p-tau181 in older patients undergoing spine surgery

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Introduction: Perioperative acceleration of neurodegeneration is thought to be an important contributor to the development of perioperative neurocognitive disorders (PND). Biomarkers of neuroinflammation, neuronal injury, and Alzheimer's disease (AD) are increased in patients postoperatively; however, the contribution of specific anesthetic agents, such as inhalational or intravenous, remains unclear. In this study, we focus on plasma levels of phosphorylated tau 181 (p-tau181), a relatively specific and predictive biomarker of AD.[1,2 3] We recently published data showing significant increases in plasma p-tau181 in cardiac and hip surgery patients throughout the perioperative period from preinduction to postoperative day 2.[4] Here, we sought to determine whether patients having a predominantly inhalational anesthetic (GAS) compared to patients having a predominantly intravenous anesthetic (IV) would have differences in the change of plasma p-tau181 levels from preoperative baseline to 3-months postoperatively. We also examined whether there were differences in p-tau181 in patients who received dexmedetomidine intraoperatively.

Methods: In this prospective observational study of 70 patients (>= 65 years) having elective inpatient spine surgery under general anesthesia at a single academic center, we compared changes in plasma p-tau181 levels from preoperative baseline to 3-months postop in patients who received GAS (n=38) compared to IV (n=32). Plasma p-tau181 levels were measured using the fully automated immunoassay analyzer (Lumipulse G1200, Fujirebio) as previously described.[4] T-tests were used to compare 2 groups and 2-way ANOVA with Tukey's multiple comparisons test was used for dexmedetomidine analyses.

Results: Plasma analysis revealed that, on average, p-tau181 levels increased in the GAS group (n=38) and decreased in the IV group (n=32, mean ± SD; 0.64 ± 2.46 pg/mL vs. -1.06 ± 3.24 pg/mL; p=0.014). This was despite the IV group having increased duration of surgery, blood loss, and hospital length of stay (Table 1). Examination of plasma p-tau181 levels in relation to intraoperatively-administered sedative agents revealed a greater postop increase in plasma p-tau181 in patients not administered dexmedetomidine (p=0.002, Fig. 1a). Patients who were not administered dexmedetomidine had a greater increase in postop plasma p-tau181 in both the GAS and IV groups (main effect of Dexmedetomidine, $F(1, 66)=5.303$, p=0.02, Fig. 1b).

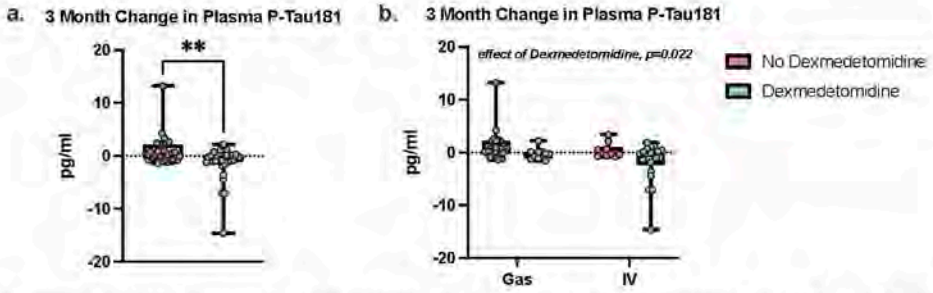
Conclusion: Changes in plasma p-tau181 levels from preoperative baseline to 3-months postop were greater in older surgical patients who had GAS compared to IV maintenance of general anesthesia. Importantly, patients not receiving dexmedetomidine had a greater increase in plasma p-tau181 levels regardless of anesthesia type. Biomarkers have the potential to identify individuals at risk for PND by allowing early and accurate postoperative diagnoses. Such tests have the potential to revolutionize perioperative research, clinical trials, and clinical practice.

References: 1. Plasma P-tau181 in Alzheimer's disease: relationship to other biomarkers, differential diagnosis, neuropathology and longitudinal progression to Alzheimer's dementia. Nature Medicine 26, 379-386 (2020). 2. Plasma phosphorylated tau 217 and phosphorylated tau 181 as biomarkers in Alzheimer's disease and frontotemporal lobar degeneration: a retrospective diagnostic performance study. Lancet Neurol 20, 739-752 (2021). 3. Longitudinal plasma phosphorylated tau 181 tracks disease progression in Alzheimer's disease. Transl Psychiatry 11, 356 (2021). 4. Plasma Biomarkers of Tau and Neurodegeneration During Major Cardiac and Noncardiac Surgery. JAMA Neurol (2021).

Table 1. Clinical characteristics IV vs. GAS

	IV n=32	GAS n=38	Difference
	Mean	Mean	95% CI
Anesthesia duration (min)	402	272.5	[54.1, 209.1]
Estimated blood loss (mL)	876.3	371.7	[165.5, 1034.4]
Length of Stay (Days)	4.3	3.1	[0.2, 2.3]

Figure 1. Change in plasma P-Tau181 levels



Changes in plasma p-tau181 levels from preoperative baseline to 3-months postoperatively. **a)** Patients had a greater increase in p-tau181 if they did not receive intraoperative dexmedetomidine (red) compared to those who received intraoperative dexmedetomidine (green). **b)** Patients who were not administered dexmedetomidine had a greater increase in postoperative plasma p-tau181 in both the GAS and IV groups. (main effect of Dexmedetomidine, $F_{(1, 65)}$=5.303, p=0.02)

Geriatric Anesthesia - 4 Multidisciplinary Geriatric Care in the PACU: A Quality Improvement Initiative

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Introduction: This pilot project seeks to develop and assess an intervention for management of frailty in older Americans undergoing elective surgery, with intent of future testing of the intervention in a large multicenter trial. Frailty is common in older surgical patients and is associated with higher rates of postoperative delirium. Hospital based multidisciplinary geriatric care (MGC) plans include simple non-pharmacologic approaches developed to decrease delirium in geriatric populations and have demonstrated success in diverse settings. In the surgical setting, MGC care plans have been instituted postoperatively on the ward following post-anesthesia care unit (PACU) transfer. However, onset of postoperative delirium primarily occurs within the first 24 hours. Thus, the PACU provides an opportunity for earlier MGC implementation during the time of highest cognitive risk in frail surgical patients. The purpose of this pilot is two- fold: to fine tune our protocol which incorporates elements of hospital based MGC into current post-anesthesia recovery room (PACU) practice; to obtain preliminary data for a multicenter trial to determine whether implementing a PACU based MGC model of care will decrease postoperative delirium in frail older surgical patients.

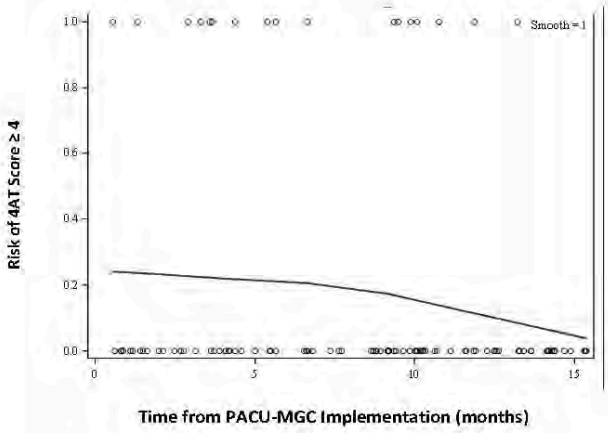
Methods: Following IRB approval, this performance improvement project occurred over 15 months and studied vulnerable subjects ≥ 65 years undergoing elective surgery not requiring ICU stay. Additional eligibility criteria included a preoperative Edmonton frailty score ≥ 6. The PACU-MGC model incorporates literature supported elements of hospital based MGC care for delirium prevention into current PACU practice (1). Nurses in the preoperative holding area, PACU, and the surgical ward were trained to screen all patients ≥65 years for delirium using the 4 A's test (4AT; www.the4at.com). A 4AT total score of 0 indicates that delirium or cognitive impairment is unlikely; a score between 1 and 3 indicates possible cognitive impairment, and a score ≥ 4 is suggestive of delirium. The 4AT has been validated on the hospital ward (2) and in the PACU (3) as an excellent screening instrument for delirium with high specificity and sensitivity.
The study took advantage of clinical data routinely collected through EPIC to provide necessary preliminary data and test out the feasibility of the proposed PACU-MGC intervention. The primary outcome was binary: 4AT score of ≥4 at any time postoperatively on the surgical wards or 4AT score <4 at all postoperative assessments. Lowess smoothing was used to examine changes in delirium risk as determined by postoperative 4AT scores with ongoing development and implementation of the PACU-MGC model of care.

Results: Current analysis included 99 patients studied from 7/20-10/21. Pertinent demographics are outlined in the table. During the 15 month study period the protocol was continuously developed and tweaked. Loess smoothing during that time period shows continuous improvement in delirium rates in this frail population. Postoperative delirium rates decreased from 14% during the first 5 months of the project to 5% in the last 6 months of instituting the PACU-MGC intervention (see figure)

Conclusion: Preliminary findings suggest that implementing a PACU-MGC program leads to a decrease in early postoperative 4AT scores. In addition, an MGC care program is feasible to implement in the PACU setting. Further study is warranted to determine the effects of the PACU-MGC program on outcomes in frail surgical patients.

References: 1. Cochrane Database Syst Rev. 2021;7:CD013307. 2. Age Ageing. 2014;43(4):496-502. 3. Anaesthesia. 2019;74(10):1260-1266.

Age	80 ± 9			
Gender	Female (66%)			
race	Black (22%)	Caucasian (73%)		
Surgical service	General (27%)	Neurosurgery (11%)	Orthopedics (25%)	Vascular (25%)
ASA	II (15%)	III (74%)	IV (11%)	
Anesthetic technique	General (67%)	Spinal/epidural (22%)	MAC/regional (11%)	
Discharge disposition	Home (74%)	skilled nursing (23%)		
death	In-hospital (1%)	Following discharge (8%)		



Geriatric Anesthesia - 5 Development and validation of a risk assessment model for postoperative delirium based on artificial intelligence

Nicolai Goettel[1], Nayeli Schmutz[2], Behnam Sadeghirad[3], Lawrence Mbuagbaw[3], Rick G Pleijhuis[4], Lisa Falco[5], Benjamin T Dodsworth[5]

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Introduction: Postoperative delirium (POD) is recognized as the most frequent postoperative complication in the elderly, occurring in 10 to 50% of older patients after major surgical procedures. It is associated with postoperative cognitive decline and long-term dementia, poor functional recovery, prolonged hospitalization, increased nursing home admission, and increased mortality. Early identification of patients at risk for delirium is paramount, because adequate well-timed interventions could reduce the occurrence of POD and the related detrimental outcome. We have developed a prognostic tool aiming at predicting the risk of a patient to develop postoperative delirium (POD) based on individual patient data.

Methods: This is an analysis of individual patient data originating from nine different observational cohort studies using systematic assessment of POD. The study met the criteria for waiver of ethical approval as defined by McMaster University Ethics Board as it used existing anonymized data. The dataset contained data from 2250 patients (1806 without POD, 444 with POD). The tool is based on statistical methods that avoid an overly optimistic estimation of the model performance.

Results: The final model contained nine variables: age, body mass index, ASA status, history of delirium, cognitive decline, medications, C-reactive protein, surgical risk, and type of surgery. The result on the training data was an area-under-the-curve (AUC) of 0.8255 with a 95% confidence interval (CI) of 0.796 - 0.854, with a cross-validation score AUC of 0.81. The test has been externally validated on a dataset from a ninth hospital with 293 patients (232 without POD, 61 POD). The validation data were missing two of the nine variables that had to be imputed. The performance on the external validation was an AUC of 0.75. Based on the predicted risk, patients can be divided into four sub-groups: low risk, medium risk, high risk, and very high risk. We propose three thresholds for this distinction based on sensitivity and specificity. The limit between low and medium risk is where we attain a 90% sensitivity. The limit between high risk and very high risk is where we attain 90% specificity, and the limit between medium and high risk is where sensitivity and specificity are equal.

Conclusion: We used individual patient data from different international studies to develop a robust test for predicting POD and performed an external validation of the model with good accuracy.

Global Health

Global Health - 1 Carbon pricing is an effective method to reduce environmental impact of the operating room

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Introduction: The World Health Organization has declared climate change as the greatest threat to global health in the 21st century.1 All physicians should consider reducing their carbon footprint in their clinical settings. It is well established that volatile anesthetics are potent greenhouse gases (GHG) and that desflurane is responsible for a significant portion of the carbon footprint of the operating theatre.2 We proposed to implement a strategy to make a tertiary care centre in Ontario (Health Sciences North [HSN], Sudbury, ON, Canada) desflurane-free to reduce the carbon footprint of the facility. We implemented an approach supporting the use of forcing functions according to a "hierarchy of effectiveness" as various studies have shown that relying on educational interventions to change clinicians' behaviours is predictably disappointing.3 We also calculated the effect of the Canadian Carbon pricing mechanism on the costs of sevoflurane and desflurane based on current pricing and future pricing declared at COP26.

Methods: The carbon footprint in CDE (carbon dioxide equivalents) was calculated using the Yale Gassing Greener program created by Yale Anesthesiology Media Lab.

Results: The implementation of these measures was associated with a significant drop in carbon dioxide equivalents (CDE) from the HSN volatile gases use. The 2016 CDE were: sevoflurane, 31 tonnes vs desflurane, 744 tonnes; the 2019 CDE were: sevoflurane, 66 tonnes vs desflurane, 140 tonnes; and the 2020 CDE were: sevoflurane, 52 tonnes vs desflurane, 0 tonnes. It should be noted that the number of anesthesia cases dropped in 2020 because of the COVID-19 pandemic. Using the existing Canadian carbon price of 30 CAD/tonne CDE (price in 2020 at the time of study completion)5 if applied to volatile anesthetic gases would increase prices by 1.48 CAD per bottle of sevoflurane and by 26.82 CAD per bottle of desflurane. In 2030, the projected carbon price of 170 CAD/tonne CDE would increase the price of sevoflurane by 8.39 CAD and the price of desflurane by 151.98 CAD in our Canadian institution.

Conclusion: We proposed to implement a strategy to make a tertiary care centre in Ontario (Health Sciences North [HSN], Sudbury, ON, Canada) desflurane-free to reduce the carbon footprint of the facility. We implemented an approach supporting the use of forcing functions according to a "hierarchy of effectiveness" as various studies have shown that relying on educational interventions to change clinicians' behaviours is predictably disappointing.3 This approach took years and significant effort from a few dedicated individuals. Interestingly, implementing carbon pricing is a well recognized effective strategy to reduce carbon pollution. We have calculated that applying the current Canadian pricing mechanism to the GHG emissions from volatile anesthetics would immediately make the purchase of desflurane difficult to justify and thus reduce the carbon footprint of the operating room as presented. Unfortunately, volatile anesthetics are currently not included in the GHG Canadian inventory and are not yet included in the carbon pricing. We have lobbied Canadian politicians to include volatile anesthetics in the inventory and pricing mechanism. Implementing a carbon price on anesthetic gases could be an immediate and effective strategy to further reduce the carbon footprint of operating rooms. An overwhelming message from the COP26 meetings was the need for urgency. A carbon price would be far more efficient in discouraging desflurane use than education and in-hospital advocacy.

References: 1. World Health Organization. COP24 Special Report Health & Climate Change; 2018: 1-74. Available from URL: https://apps.who.int/iris/bitstream/handle/10665/276405/9789241514972-eng. pdf?sequence=1&isAllowed=y (accessed September 2021). 2. Andersen MP, Nielsen OJ, Wallington TJ, Karpichev B, Sander S. Assessing the impact on global climate from general anesthetic gases. Anesth Analg 2012; 114: 1081-5. 3. Soong C, Shojania KG. Education as a low-value improvement

intervention: often necessary but rarely sufficient. BMJ Qual Saf 2020; 29: 353-7. 4. Caycedo-Marulanda, A, Caswell J, Mathur S. Comparing the environmental impact of anesthetic gases during transanal total mesorectal excision surgery at a tertiary healthcare centre. Can J Anesth 2020; 67: 607-8. 5. SawyerD, StiebertS, GignacR, CampneyA, BeuginD.2020Expert Assessment of Carbon Pricing Systems. Canadian Institute for Climate Choices. Environment and Climate Change Canada.

Global Health - 2 Peri-operative Anesthesia Research Output from Low- and Middle-Income Countries: A Systematic Review

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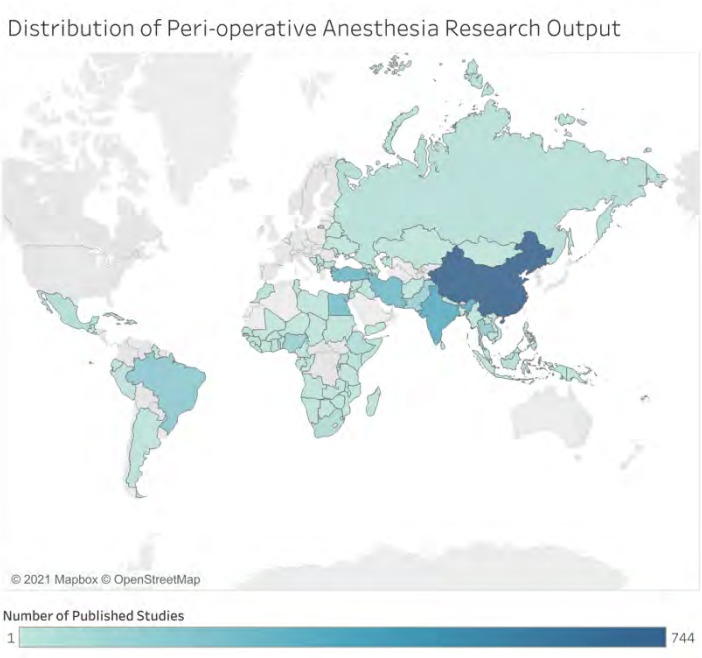
Introduction: Research infrastructure and capacity for anesthesia in low- and middle-income countries (LMICs) remain scarce. Promoting academic scholarship through research will increase the practice of evidence-based medicine in low resource settings. This systematic review examines the peer-reviewed research output for adult peri-operative anesthesia conducted in LMICs.

Methods: A systematic review of the medical literature was performed with search terms representing the following groups: 1) adult population aged ‚â•18 years, 2) peri-operative anesthesia (pre-, intra-, and post-operative anesthesia care), 3) LMICs as defined by the World Bank Atlas in 2020. The protocol included articles in all languages from journal inception to December 31, 2020 in the following databases: PubMed, CINAHL, Embase, Web of Science, PsycINFO, Cochrane and WHO Global Index Medicus. Non-human or basic science studies, studies of only pediatric subjects, dissertations and the grey literature were excluded. After export of citations and removal of duplicates via EndNote, articles titles and abstracts were screened using the Rayyan platform. Among the included studies, article title, year of publication, country of study, study design, journal of publication and impact factor were extracted. Temporal trend of publication counts globally and by WHO region, distribution of study designs, and impact factor of published journals were examined and analyzed in R. Geographical heat map for publication count based on study country was generated in Tableau Public.

Results: The search yielded 10,121 articles across the databases. We included 3105 studies and excluded 7016. Among the 132 LMICs, 89 countries published at least one peri-operative anesthesia study (67%). The top five countries with the highest research output were China (744), India (349), Turkey (283), Iran (269), and Egypt (242). Moreover, 62 of 89 (70%) published countries had fewer than 10 studies conducted locally, and only one published peri-operative anesthesia study was observed in 19 countries.

Conclusion: This is the first comprehensive systematic review examining peri-operative anesthesia research conducted in LMICs. The findings of our systematic review demonstrate the dearth of anesthesia research and disparity in research output among LMICs. Forty-three countries have been neglected with no anesthesia studies - a focus on these is needed. The double-screening to follow and final analyses will provide an updated overview of the landscape of anesthesia research conducted in LMICs.



Global Health - 3 Chronic pain and associated factors in Monrovia, Liberia

Zi Wei Liao[1], Isaac N Kaffey[2], Titus B Jerbo[2], Joseph N Siaway[2], Jonathan Niconchuk[3], J Matthew Kynes[3], Camila Walters[3]

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Introduction: Approximately one in three adults that live in low-and middle-income countries (LMICs) suffer from chronic pain(PMID: 27537761). Few studies characterized chronic pain in sub-Saharan Africa as a region, with the prevalence of chronic pain in Liberia being unknown.

Methods: Utilizing a structured household survey known the Vanderbilt Global Pain Survey (VGPS), this was a community-based, cross-sectional study that included adults aged ≥18 years old who live in Monrovia, Liberia. This survey tool was previously administered in Mozambique, India, and Nepal. The VGPS includes multiple validated surveys on pain and disability, including the Brief Pain Inventory, World Health Organization Disability Schedule (WHODAS 2.0), Post-traumatic distress disorder Checklist-Civilian Version (PLC-C), Pain Catastrophizing Scale (PCS), and Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) from the American College of Rheumatology 2010 Fibromyalgia diagnostic criteria.

Results: Of the 325 persons approached, a total of 309 eligible surveys were collected in Caldwell (24.3%), New Kru Town (27.8%), Sinkor (25.6%), and West Point (22.3%). Each community was randomly chosen to represent the four neighborhood classifications per the Liberia Housing Profile. Chronic pain, defined as recurrent or persistent pain ≥3months, was found to be 81.9%, which is significantly higher than described in other LMICs (P<0.05). Of these, 37.2% of whom reporting pain persisting for ≥1year. Although participants reported having mild pain with minimum interference with their daily lives on the BPI, 35.9% scored ≥10 on the WHODAS2.0, suggesting clinically significant disability. Approximately one in five (22%) respondents screened positive for post-traumatic stress disorder. One in three (38.5%) reported catastrophic thinking about pain on the PCS. In addition to taking medication, almost all respondents would be willing to undergo a procedure or participate in group therapy for pain management.

Conclusion: The burden of chronic pain amongst Liberians is substantial. Having chronic pain was associated with disability and catastrophic thinking about pain (P<.05). To improve Liberia's capacity for pain treatment, a first step is to understand the impact of chronic pain in Liberia as a country by including questions on chronic pain on national health surveys.

Liver

Liver - 1 An updated role of right heart echocardiography on early autograft dysfunction and other outcomes after orthotopic liver transplantation

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Introduction: Pre-operative testing is a vital component of patient risk evaluation prior to orthotopic liver transplantation. Since the incorporation of echocardiography, pre-operative assessments of the heart have focused on several key parameters, including ejection fracture, screening for pulmonary hypertension with pulmonary artery systolic pressure (PASP) estimation, valvular dysfunction, evidence of ischemia during dobutamine infusion, etc. Recently, researchers have looked at the role of the right heart in predicting outcomes after orthotopic liver transplantation (OLT) (1, 2). The goal of this presentation is to describe the experience and outcomes of several key right heart echocardiography variables at a single institution and their relationship with short-term and one-year outcomes of mortality and graft survival. A new area of research with this study incorporates the role of early allograft dysfunction, occurring seven days after OLT.

Methods: From a sample of 214 patients from 1/1/2019 through 6/30/2020, data were collected on patients undergoing liver transplantation. Pre-operative workup included echocardiography assessment of estimated pulmonary artery systolic pressure (PASP), left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), and severity of tricuspid regurgitation (TR). A multivariate analysis was conducted on early allograft dysfunction and patient survival at one-year or graft survival at one-year.

Results: From a sample of 214 patients, a multivariate analysis showed that MELD score at time of OLT, PASP, left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), and severity of tricuspid regurgitation (TR) with presence of tricuspid disease rated as mild or greater were not correlated with higher risk of patient survival at one-year or graft survival at one-year. With respect to early allograft dysfunction, PASP was shown to be a significant predictor of adverse outcomes ($p = 0.05$, OR = 1.05, 95 CI: 1.00 - 1.10) while other variables were not statistically significant predictors of adverse outcomes. On multivariate analysis, right heart echocardiography measurements were not statistically significant factors for length of stay (LOS).

Conclusion: On multivariate analysis, right heart echocardiography measurements were not statistically significant factors for length of stay (LOS), adding ambiguity to the discussion of PASP, TAPSE, or severity of TR in outcomes data (1,2). This presentation provides an update to the continued discussion regarding right heart echocardiography measurements and outcomes of liver transplantation patients and introduces the concept of early allograft dysfunction and its prediction from these measurements.

References: 1. Kia L, Shah SJ, Wang E, Sharma D, Selvaraj S, Medina C, Cahan J, Mahon H, Levitsky J. Role of pretransplant echocardiographic evaluation in predicting outcomes following liver transplantation. Am J Transplant. 2013 Sep;13(9):2395-401. doi: 10.1111/ajt.12385. Epub 2013 Aug 5. PMID: 23915391. 2. Leithead JA, Kandiah K, Steed H, Gunson BK, Steeds RP, Ferguson JW. Tricuspid regurgitation on echocardiography may not be a predictor of patient survival after liver transplantation. Am J Transplant. 2014 Sep;14(9):2192-3. doi: 10.1111/ajt.12821. Epub 2014 Jul 1. PMID: 24985366.

Liver - 2 Association of Right Ventricular TAPSE with increased length of stay after liver transplant surgery

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Introduction: To evaluate the association between Right ventricular TAPSE (Tricuspid Annular Plane Systolic Excursion) and length of stay after liver transplant surgery.

Methods: Retrospective cohort study accrued at the Johns Hopkins Hospital from July 1, 2016 through June 30, 2018. Patients who met the following criteria were eligible for inclusion: >18 yrs old, underwent liver transplant surgery with preoperative transthoracic echocardiography within 6 months of surgery.

Results: The study sample consisted of 74 patients with mean age 45 year, 47% female. Mortality was 8 % 6/74. After adjusting for MELD, baseline creatinine, and age, TAPSE was associated, in dose response fashion, with decreased hazard of prolonged hospital stay (HR 1.7, 1.07-2.3, $p < .023$).

Conclusion: Even though all transplant candidates must have normal left ventricular ejection fraction prior to transplant, heart failure and cirrhotic cardiomyopathy after transplant constitute significant amount of morbidity and mortality. Measures of right ventricular function may further elucidate this complex problem and provide further preoperative information for transplant candidacy. An increase in TAPSE may be a novel cardiovascular risk factor for bad outcome after liver transplant.

Neuroscience in Anesthesiology and Perioperative Medicine

Neuroscience in Anesthesiology and Perioperative Medicine - 1 A comparative study to evaluate the efficacy of IV dexmedetomidine and remifentanil to attenuate the hemodynamic response to skull pins during craniotomy

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Introduction: Skull pin application is intensely painful and is usually accompanied by wide fluctuations in hemodynamic parameters that influences cerebral blood flow and intra cranial pressure.[1] Several pharmacological methods have been tried to attenuate these responses including dexmedetomidine.[2-4] However, till date, literature does not show findings of any study using remifentanil as an attenuating agent. The aim of this study was to compare remifentanil with dexmedetomidine and observe the more superior agent in controlling hemodynamic fluctuations secondary to head pin application.

Methods: 40 patients undergoing elective craniotomy were randomized to either Remifentanil Group (RG: n=20) or Dexmedetomidine Group (DG: n-20) with each receiving 1 µg/kg remifentanil over 30-60 secs or dexmedetomidine in a similar dose but over 10 min starting after induction and tracheal intubation but immediately prior to pins application. Standard anesthetic regimen was used in both the groups. Patient's heart rate, blood pressure, adverse events were recorded at the following time intervals: pre induction (baseline), pre head pins insertion, post head pins application at 1, 5,10,15 min.

Results: We observed remifentanil to be superior in attenuating the hemodynamics after head pins insertion in craniotomy patients in comparison to dexmedetomidine. The heart rate was noted to be below the pre induction values in RG patients throughout the study period. In contrast, in the DG patients the heart rate marginally increased above the pre-induction value from a mean of 73.70 ±15.3 to 75.5±14.2 in the 1st minute after head pins insertion (p=0.546) The blood pressure (systolic and diastolic values) too remained below the pre induction values in RG patients throughout the study time intervals with mean arterial pressure ranging between 78.9-88.3 mmHg. In contrast, DG patients demonstrated a significant rise in systolic blood pressure at 1 min post pin placement from 132.8±26.5 to 157.2 ±35.0 mmHg (p=0.001) compared to pre-induction values.

Conclusion: Remifentanil offers a better attenuation of the hemodynamics after head pins insertion in patients undergoing elective craniotomy using a dose of 1mcg/kg over 30-60 secs before the insertion of pins compared to dexmedetomidine.

References: 1. J Neurosurg Anesthesiol 2008;20:174-9; 2. Ind J Anaesth 2015;59:785-8; 3. J Neurosurg Anesthesiol 2005;17:9-12; 4. J Neurosurg Anesthesiol 2011;23:110-7.

Neuroscience in Anesthesiology and Perioperative Medicine - 2 Phase-Locked Acoustic Stimulation Increases Human Thermal Arousal Thresholds during Dexmedetomidine Sedation

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Introduction: States of deep sedation and general anesthesia are characterized by slow-delta oscillations (0.1-4Hz) in the electroencephalogram (EEG), and the relative power of these oscillations correlates with depth of unconsciousness (1). Acoustic stimulation in-phase with the upslope of these slow oscillations enhances the expression of EEG slow waves during sleep states (2,3). It is unknown whether this technique induces similar phenomena during pharmacological sedation. Modulating EEG slow oscillations using non-invasive neurostimulation could provide clinicians with a targeted method to non-pharmacologically manipulate brain states during sedation and general anesthesia. We hypothesized that acoustic stimulation in-phase with the upslope of EEG slow oscillations during dexmedetomidine sedation would lead to 'deeper' sedation states, incurring higher thresholds for arousal during noxious thermal stimulation.

Methods: An interim analysis was performed on data acquired from healthy volunteers during the ongoing trial: Closed-Loop Acoustic Stimulation during Sedation with Dexmedetomidine (CLASS-D) (4). Thermal arousal thresholds are a pre-specified secondary outcome of this trial. Each participant received phase-locked acoustic stimulation (60 dB pink noise) while sedated with a target-controlled infusion (TCI) of dexmedetomidine titrated to induce both slow-delta oscillations and loss of responsiveness to a behavioral task. A custom-built device incorporating an endpoint-corrected Hilbert Transform (5) (Elemind Technologies, Inc., Cambridge, MA) was used to phase-lock auditory stimuli to a 1 Hz central frequency (Figure 1): in-phase stimuli were delivered shortly before slow wave peaks (0º) while anti-phase stimuli were delivered shortly before slow wave troughs (180º). A standard quantitative sensory testing (QST) protocol with a Thermal Sensory Analyzer (TSA-II, Medoc, Israel) was employed by applying a Peltier thermode to the non-dominant forearm and increasing its temperature at a rate of 1ºC per second (up to a maximum of 52ºC) until participants either opened their eyes or withdrew from the thermode (6). In this way, thresholds for behavioral arousals were determined at steady-state concentrations of dexmedetomidine across three conditions: in-phase, anti-phase and sham (silence). The order of in-phase, anti-phase and sham conditions was randomized across participants. For this preliminary analysis, paired parametric statistical testing was undertaken to compare arousal thresholds during in-phase and sham stimulation. A mixed effects model will be used to compare arousal thresholds across all three conditions at the conclusion of the trial.

Results: Data were analyzed from the first eight participants, one of which was withdrawn early precluding analysis. Target dexmedetomidine effect site concentrations required to induce slow-delta EEG oscillations and achieve a state of unresponsiveness ranged from 1.5 – 2.5 ng/ml. Approximately 1000 in-phase stimuli (median phase -5.7º, resultant 0.76) and 1000 anti-phase stimuli (median phase 169.7º, resultant 0.72) were delivered to each participant (Figure 2). Thus, phase-locking of stimuli relative to the peak and trough of slow EEG oscillations was effective. The mean temperature required to induce a behavioral arousal was 48.8ºC (95% CI, 47.8 – 49.8) during sham, 48.5ºC (95% CI, 47.0 – 50.0) during anti-phase stimulation, and 50.6ºC (95% CI, 49.9 – 51.3) during in-phase stimulation (Figure 3). Compared to the sham condition, thermal arousal thresholds were increased by 1.8ºC (95% CI, 0.6 – 3.0, p = 0.02) during in-phase stimulation. (Figure 4)

Conclusion: Preliminary data from this ongoing trial suggests that in-phase acoustic stimulation may increase thresholds for arousal to noxious stimulation during dexmedetomidine sedation. Non-invasive, phase-locked neurostimulation methods such as closed loop acoustic stimulation could allow clinicians to quickly modulate patients' sedation states without the adverse effects of traditional pharmacological interventions. Future studies should investigate the effect of in-phase acoustic stimulation on nociceptive processing and seek to translate these findings into clinical settings.

References: 1. Anesthesiology. 2018;129(1):22-36. 2. Nat Commun. 2017;8(1):1984. 3. Neuron. 2013;78(3):545-553. 4. Nat Sci Sleep. 2021;13:303-313. 5. Nat Commun. 2021;12(1):363. 6. Pain. 2006;123(3):231-243.

Figure 1. Schematic of phase-locked neurostimulation with inphase and antiphase conditions.

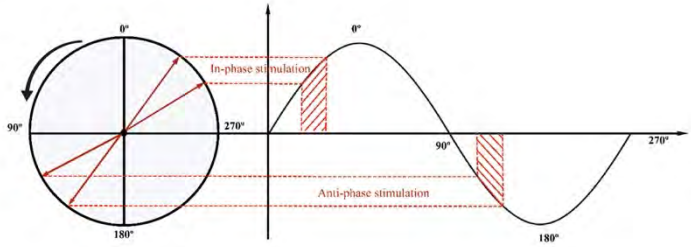


Figure 2. Phase histograms of inphase and antiphase stimulation, exhibiting accurate and precise phase-locking.

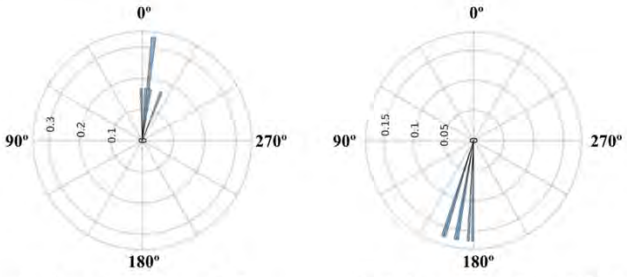


Figure 3. Thermal arousal thresholds during sham, antiphase and inphase stimulation. Markers denote means and error bars represent 95% confidence intervals.

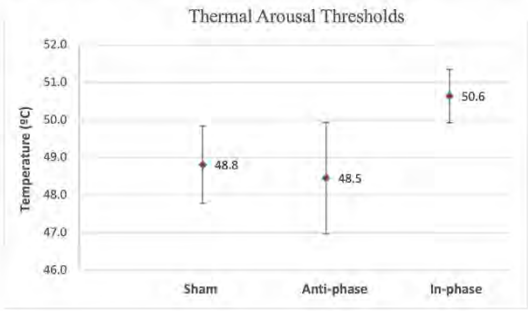
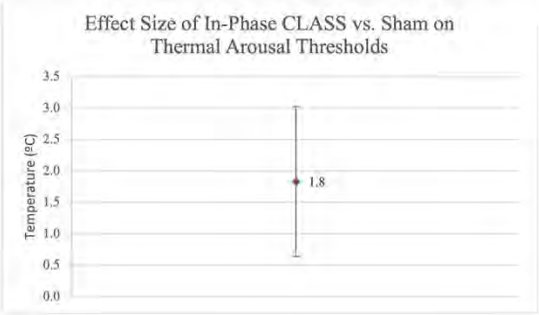


Figure 4. Effect sizes of inphase stimulation vs. sham on thermal arousal thresholds. Marker denotes mean effect size and error bars represent 95% confidence intervals.



Neuroscience in Anesthesiology and Perioperative Medicine - 3

Glutamatergic and Adrenergic Neurons Mediate Alpha-2-Agonist-Induced Sedation and Hypnosis in Mice

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Introduction: α2-adrenergic agonists induce hypnosis in part through their actions on the neural circuits regulating endogenous arousal (1,2) and produce a hypnotic state most similar to NREM sleep.(3) While downstream pathways involved in α2-agonist hypnosis have been characterized(4,5) the precise neuronal population(s) on which α2 agonists act to produce sedation and hypnosis are unknown.

Methods: We generated knock-in mice with LoxP sites flanking the Adra2a gene (Adra2af/f) and crossed them with tissue specific Cre recombinase (CRE) driver mice under the control of the Snap25 (n=10), Dbh (n=18), or Vglut2 (n=10) promoters to create cell-specific knockouts of Adra2a or controls (n=9). Cell specific deletion of Adra2a was assessed using fluorescent in-situ hybridization. Hypnotic, sedative, and physiologic actions of 0, 300, or 1000 µg/kg dexmedetomidine IP (Dex) were determined using the righting reflex, rotarod assay, and spontaneous locomotion, as well as core body temperature. To assess motor-independent measures of dexmedetomidine, a subset of mice from each genotype (n=5-7) was chronically implanted with EEG and EMG leads . Following recovery, EEG/EMG mice were challenged with Dex. Signals were band-pass filtered from 1-100 Hz. Spectral power estimation over M1 was computed over 5s non-overlapping windows using previously published code.(6) All analyses used Matlab 2021a or Prism 9.2.

Results: Adra2af/f controls showed expected changes in behavioral hypnosis (Fig 1), temperature (Fig 2), and sedation (rotarod distance and spontaneous movement, Fig 3) in response to Dex. The pan-neuronal knockout Adra2af/f:Snap25-Cre mice exhibited Dex resistance to all behavioral and physiologic endpoints. Mice with deletion of Adra2a in Vglut2 (primarily subcortical glutamatergic) and Dbh (adrenergic) neurons showed resistance to loss of righting equivalent to neuronal knockouts. While the Dbh-driven knockouts showed partial resistance to sedation and temperature change, mice missing Adra2a in Vglut2 neurons were indistinguishable from pan-neuronal knockouts. Spectral analysis of the EEG mirrored behavior, as Snap25-Cre and Vglut2-Cre showed high resistance to EEG changes and Dbh-Cre partial resistance to EEG changes after dexmedetomidine administration. (Fig 4, 5.)

Conclusion: The resistance to sedation and hypnosis shown by the glutamatergic and adrenergic Adra2a knockouts suggests that α2 agonists act through multiple neuronal subtypes to cause sedation and hypnosis. Additional glutamatergic sub-populations, beyond the previously-described NOS1 group, likely contribute to the sedative-hypnotic and theromregulatory actions of α2 adrenergic agonists. Adra2a knockout in adrenergic neurons produces a partial resistance to α2 sedative-hypnotic effects. Future studies will identify the glutamatergic population(s) responsible for sedation and whether and how adrenergic adrenergic neuronal pathways converge with those populations.

References: 1. Anesthesiology 98, 428-436 (2003). 2. Nat. Neurosci. 18, 553-561 (2015). 3. Front. Pharmacol. 9, 1196 (2018). 4. Curr. Biol. 28, 2263-2273.e4 (2018). 5. Curr. Biol. 29, 3315-3322.e3 (2019). 6. Proc. Natl. Acad. Sci. U. S. A. 111, 9283-9288 (2014).

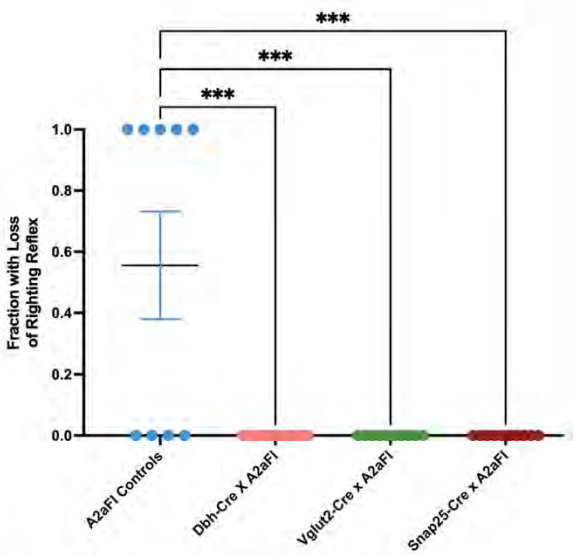

Figure 1. Behavioral Hypnosis Measured By Righting Reflex to IP Dexmedetomidine. Mice were given intraperitoneal saline, 0.3 mg/kg dexmedetomidine, or 1 mg/kg dexmedetomidine and righting reflex assessed 20 minutes after injection. No mice lost righting reflex at the 0.3 mg/kg dose, 1 mg/kg results shown here. Mean and SEM shown. One-way ANOVA. * p<0.05, ** p<0.01, *** p<0.001.

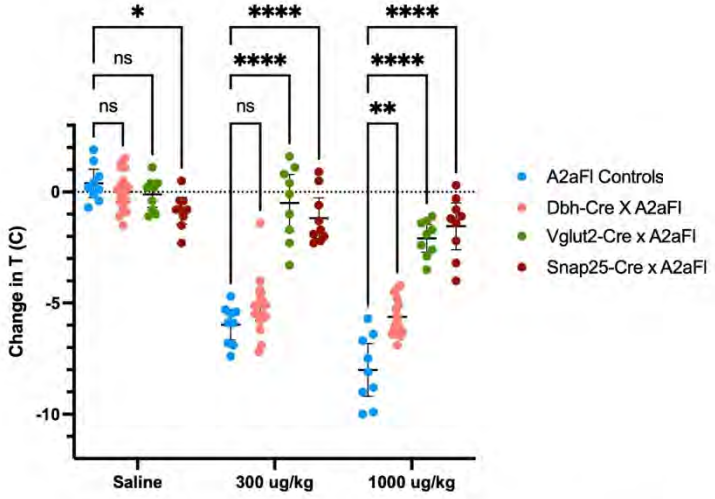

Figure 2. Temperature Change In Response to Dexmedetomidine. The Vglut2 cross and pan-neuronal knockout showed little temperature change 20 minutes after receiving dexmedetomidine, and significantly less change than controls. Adrenergic Adra2a knockouts show slightly less change than controls at the higest dose. 2-Way ANOVA with multiple comparrisons. * p<0.05, ** p<0.01, **** p<0.0001

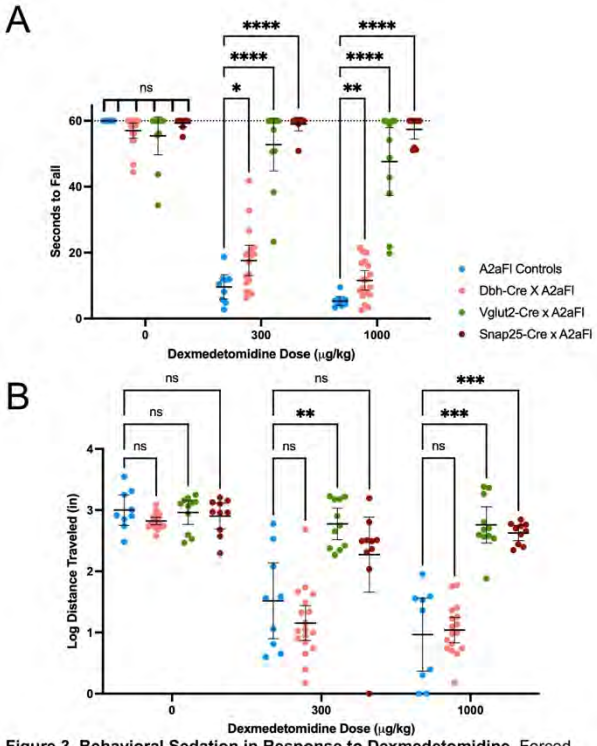

Figure 3. Behavioral Sedation in Response to Dexmedetomidine. Forced movement (rotarod, A) and spontaneous movement (beambreak measured over 1 hour, B) demonstrate profound resistance to sedation by pan-neuronal (Snap25) and Vglut2 Adra2a knockouts, while adrenergic (Dbh) Adra2a knockouts show partial resistance in the forced movement test. Individual values and means with 95% CI shown. 2-way ANOVA with multiple comparrisions, * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001.

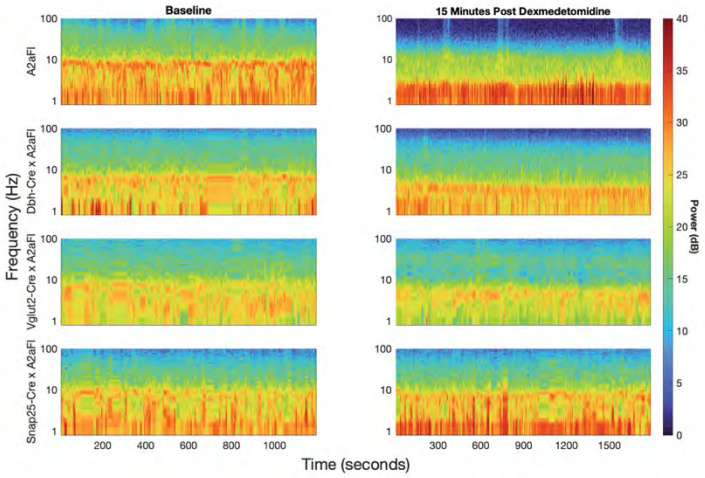

Figure 4. Representative Spectrograms of M1 Lead : 20 Minute Baseline and Minutes 15-45 Post 300 µg/kg IP Dexmedetomidine. Both pan-neuronal *Adra2a* knockouts (bottom) and Adra2a knockout in (the primarily subcortically-expressed) Vglut2 neurons produced profound resistance to spectral changes in EEG in response to dexmedetomidine. Adra2a deletion in adrenergic neurons produced a partial resistance to the effects of dexmedetomidine on EEG, with a decrease in alpha and high gamma power, as well as an increase in delta and theta power, though not to the degree seen in control animals.

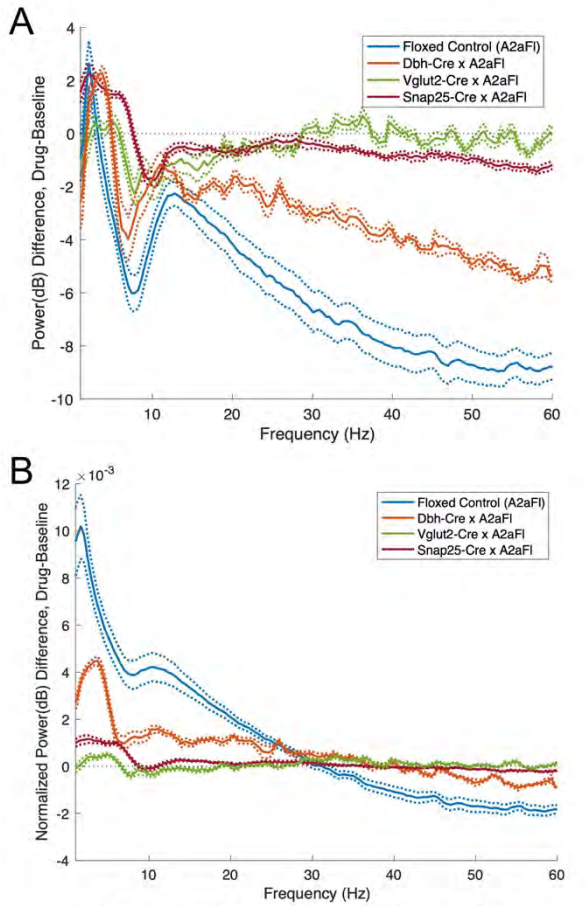

Figure 5. Mean Spectral Differences Between Pre- and Post-Dexmedetomidine Administration Mirror Degree of Sedation Seen in Behavior. The degree of difference from before to after dexmedetomidine in mean frontal spectra, non-normalized (A) and normalized to total power (B), corresponds to the relative level of sedation observed in each genotype. Floxed controls show the expected increase in delta power and supression of all other higher-frequency activity, while Vglut2 *Adra2a* knockouts and pan-neuronal *Adra2a* knockouts show only minor changes, and adrenergic *Adra2a* knockouts display intermediate changes between controls and pan-neuronal knockouts. Mean (solid) and 95% CI (dotted) spectra by genotype shown.

Neuroscience in Anesthesiology and Perioperative Medicine - 4

Dopaminergic activity during emergence from isoflurane anesthesia in mice

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Introduction: Mechanisms of emergence from general anesthesia are poorly understood, and patients emerge passively without the use of targeted interventions to promote arousal. The dopaminergic system plays an important role in both arousal and emergence from anesthesia. Here we take advantage of genetically encoded sensor technology to record dopamine activity during emergence from isoflurane in mice in order to develop a greater mechanistic understanding of neural circuits engaged in emergence.

Methods: The genetically encoded optical dopamine sensor dLight was expressed by stereotaxic viral delivery in nucleus accumbens of adult mice. Fiber photometry recording of dLight fluorescence was performed during restoration of the righting reflex (RORR), a behavioral marker of emergence in rodents, following isoflurane exposure.

Results: We find that dLight activity increases immediately preceding emergence from isoflurane anesthesia, reflecting an increase in dopamine levels in nucleus accumbens prior to restoration of the righting reflex. Optogenetic stimulation of ventral tegmental area dopamine terminals within nucleus accumbens increases dLight activity and plays a modulatory role in changing righting behavior.

Conclusion: These data align with published studies showing dopamine receptor agonism in nucleus accumbens accelerates emergence from general anesthesia. Further studies are aimed at using genetically encoded biosensors and chemogenetic approaches to dissect relative contributions of ventral tegmental area to nucleus accumbens projections in emergence.

Neuroscience in Anesthesiology and Perioperative Medicine - 5 Modulation of hippocampal contextual memory, place cells, and spatial engrams by (R)-CPP, a potent NMDAR antagonist

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Introduction: N-methyl-D-aspartate receptors (NMDARs) are strongly linked to memory, learning and other higher cognitive functions. We recently reported an interesting mismatch between the dose and brain concentration of CPP (a potent NMDAR antagonist) that suppresses contextual fear conditioning (IC50 = 2.3 mg/kg -> 53 nM) versus the concentration needed to block NMDARs and LTP in the hippocampus (361 - 464 nM)(1). To test whether this mismatch occurs because of CPP actions at extrahippocampal sites or within the hippocampus, we used a variant of fear conditioning that separates the contextual (hippocampal) and other (e.g. amygdaloid) components of learning temporally. We also imaged hippocampal CA1 pyramidal neuron activity in awake behaving mice to assess effects of CPP on place cell formation and spatial engram stability.

Methods: All experiments were carried out with institutional IACUC approval. CPFE - Context Preexposure Facilitation Effect: On day1 (context pre-exposure), mice (n=12/group) were placed explored a novel arena freely for 10 minutes. On day2 (aversive conditioning), mice were replaced into the arena and after 15sec administered foot shock. On day3 (recall), mice were placed in the same arena, and their freezing behavior (an innate fear response) was quantified. Saline or (R)-CPP (1mg/kg, 3mg/kg, and 10mg/kg IP) was administered on either day1 or day2. Ca2+ imaging: A miniature endoscopic camera (Inscopix nVoke) was used to capture the activity of underlying CA1 pyramidal neurons expressing GCaMP6f, in mice (n=4) repeatedly exposed to a novel context on day1, then the same or an alternate context on day2. Saline or (R)-CPP (1mg/kg, 3mg/kg, and 10mg/kg) was injected prior to day1 or day2 imaging.

Results: In CPFE experiments, CPP given before pre-exposure (day1) induced a dose-dependent reduction in fear memory, with IC50=3.2 mg/kg (Figure 1). CPP given pre-shock (day2) similarly blocked freezing (IC50 4.4mg/kg). In Ca2+imaging experiments, CPP given on day1 dose-dependently reduced place cell formation (Figure 2) and suppressed the formation of stable engrams (Figure 3), as shown by reduced rate map correlations between day1 and day2 (RMcorr:d1->d2). CPP given on day2 (pre-recall 10mg/kg (R)-CPP) did not significantly reduce RMcorr:d1->d2, showing that CPP blocked learning but not recall.

Conclusion: CPP suppresses hippocampus-specific memory (CPFE behavioral experiments) and the neural correlates of memory (place and engram cell formation) at doses that do not block LTP or NMDAR-mediated field potentials in brain slices. These findings indicate that CPP acts within the hippocampus to impair learning, but that acts on elements (e.g. interneurons) that are not reflected in commonly employed measures (i.e. LTP and EPSPs). The lack of effect of CPP on recall indicates that CPP also can suppress the association of context and shock by acting outside of the hippocampus.

References: 1. (authors redacted) (2021). CPP impairs contextual learning at concentrations below those that block pyramidal neuron NMDARs and LTP in the CA1 region of the hippocampus. Neuropharmacology, 202, 108846. https://doi.org/10.1016/j.neuropharm.2021.108846

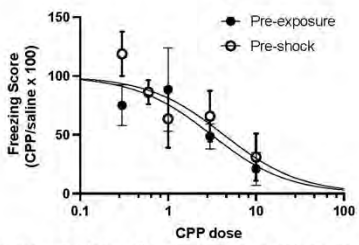

Figure 1. Dose-dependent reductions in fear memory expression by pre-exposure and pre-shock administration of (R)-CPP, as measured by CPFE learning paradigm.

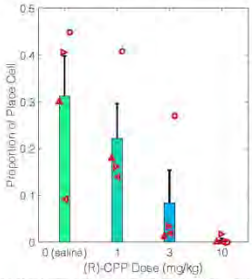

Figure 2. Dose-dependent reductions of hippocampal place cell formation, as measured by mutual information.

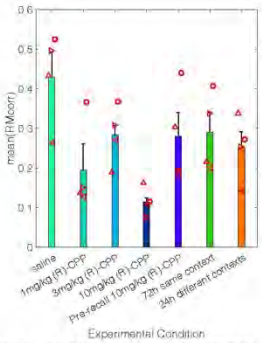

Figure 3. Dose-dependent reduction of rate-map (RM) correlation as a measure of spatial engram stability, as well as some control experiments.

Neuroscience in Anesthesiology and Perioperative Medicine - 6 Surgery, Anesthesia and Intensive Care Environment induce delirium-like disruption of sleep and circadian rhythm in aged mice

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[1]University of Virginia, Charlottesville, VA

Introduction: To date, the pathophysiology of postoperative Intensive Care Unit (ICU) delirium remains poorly understood. The lack of adequate experimental animal models is a major barrier to advancing the understanding of the neurobiological mechanisms underpinning delirium. Dysregulated sleep and circadian rhythm are a very common symptom in delirious ICU patients. Thus, we set out to test the face validity of our recently published mouse model of postoperative ICU delirium by assessing sleep quantity, fragmentation and circadian rhythm in aged mice subjected to anesthesia, surgery and ICU conditions (ASI). We hypothesized that ASI would induce disturbances in mouse sleep and circadian rhythm consistent with those of delirious patients and alter the expression of genes that are important for normal sleep-wake behavior and circadian function.

Methods: Eighteen-month-old C57BL/6J mice (N=31) were implanted with electroencephalographic (EEG) and electromyographic electrodes. After two weeks, they were randomized to insult (ASI) or control group. ASI mice received laparotomy under sevoflurane anesthesia (3 h), sedation with propofol (2 h) and ICU conditions, i.e., intermittent lights, sounds and cage shaking (12 h). Controls did not receive ASI. Twenty-eight hour-long EEG recordings were obtained at the end of ICU conditions. Mice hippocampi were collected upon completion of the EEG recordings and processed for gene and protein expression analysis of sleep and circadian markers by qPCR and western blot. Two-tailed unpaired t-test and repeated measures analysis of variance were used for statistical analysis. Sleep data are presented as mean ± S.D. Gene and protein data are expressed as fold change relative to controls and mean ± S.E.M, respectively.

Results: ASI significantly altered Rapid Eye Movement (REM) and Non-Rapid Eye Movement (NREM) sleep during the dark 1 (D1) and dark 2 (D2) phases (Fig.1, A REM: D1,**; D2,*; B NREM: D1, ***; D2,**) relative to controls. ASI mice spent more time asleep during dark, at a time when they should be more awake (Fig. 1C,**), and experienced greater numbers of wake bouts in between sleep, and shorter wake bout duration, compared to controls (Fig.2, A,*; B,**). ASI impaired gene expression of Cry 1 (-1.495 fold change), Cry 2 (-1.200), Per 1 (-1.250), Per 2 (-1.412) and Per 3 (-1.369) (Fig.3). Additionally, protein levels of BMAL1 and CLOCK were down-regulated (Fig. 4, A: 25.7 ± 9.1%,*; B: 28.9 ± 9.1%,*) in ASI mice relative to controls.

Conclusion: ASI caused sleep fragmentation and impaired sleep quantity and circadian rhythm in aged mice. Mice with ASI-induced sleep-wake disruption exhibited decreased expression of key genes that regulate sleep-wake activity and circadian function. The sleep and circadian rhythm changes evoked by ASI in aged mice closely recapitulate those of delirious human subjects and thus support the use of our preclinical model for future mechanistic studies of postoperative delirium.

References: 1.Nat Rev Dis Primers 6(1):90 (2020) 2. Sci Rep 6:29874 (2016) 3. Intensive Care Med 30(2):197-206 (2004) 4. Crit Care 13(6):234 (2009) 5. Front Aging Neurosci 12:542421 (2020)

Fig. 1

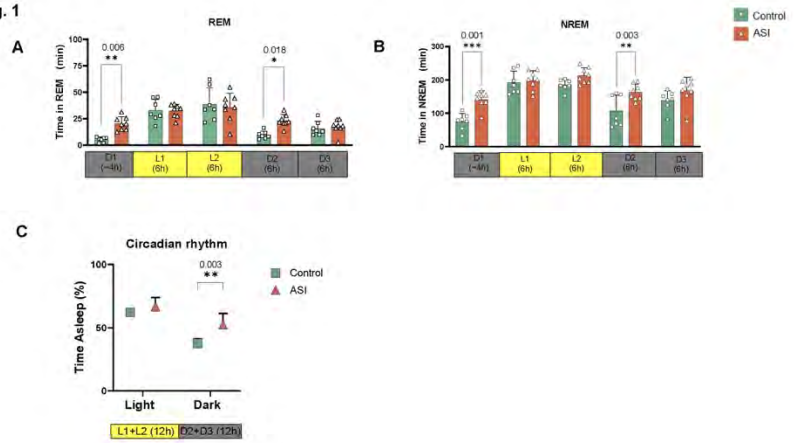


Fig. 2

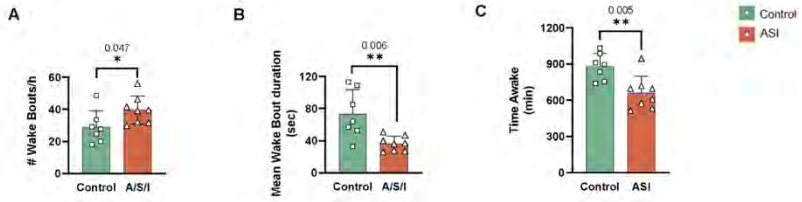


Fig. 3

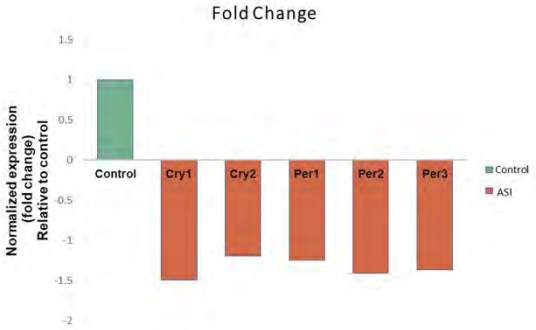
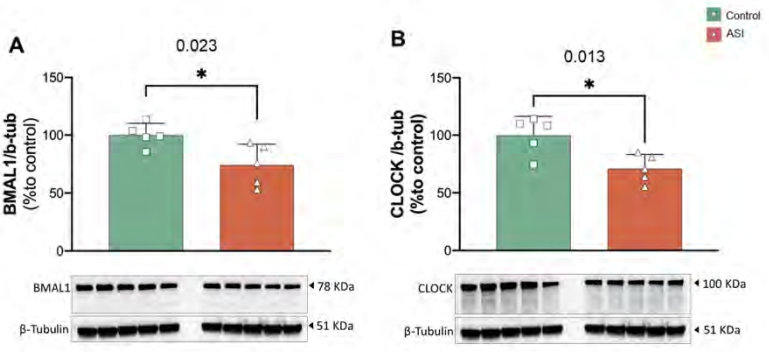


Fig. 4



Neuroscience in Anesthesiology and Perioperative Medicine - 7 Anesthesia, Surgery and Intensive Care environment impair hippocampal BDNF-Arc signaling and dendritic arborization in aged mice

Nadia Lunardi[1], Hari Prasad Osuru[1], Elzbieta Dulko[1], Meghana Illendula[1], Joanna Klos[1], Tam Le[1], NAVYA ATLURI[1]

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Introduction: Background: We recently reported impaired expression of brain-derived neurotrophic factor (BDNF)-dependent proteins critical for synaptic plasticity in aged mice with delirium like-behaviors induced by anesthesia, surgery and Intensive Care environment (A/S/I). Importantly, it has been shown that BDNF activates the tyrosine kinase B (TrkB) receptor, which in turn phosphorylates extracellular kinases (Erk 1/2), activating cAMP responsive element-binding protein (CREB) and ultimately promoting expression of Arc, an activity-regulated cytoskeleton-associated protein that is a master regulator of dendritic development, synaptic plasticity and memory consolidation. In light of this, we aimed to test whether BDNF-Arc signaling plays a role in A/S/I-induced delirium-like cognitive dysfunction. Our hypothesis was that A/S/I would impair the hippocampal BDNF-Arc pathway, as well as hippocampal dendritic arborization, in aged mice.

Methods: Methods: Eighteen-month-old C57BL/6J mice were randomized to insult (A/S/I) or control group. A/S/I mice received laparotomy under sevoflurane anesthesia (3 h), sedation with propofol (2 h) and Intensive Care Unit (ICU) conditions, i.e., intermittent lights, sounds and cage shaking (12 h). Controls did not receive A/S/I. Mouse hippocampi were collected at the end of ICU conditions for gene and protein expression studies and for rapid Golgi staining. This study was approved by the Institutional Animal Care and Use Committee at the University of Virginia.

Results: Expression of several BDNF gene exons was differentially regulated in A/S/I mice compared to controls (fold change 'F'=1) (Fig.1: BDNF-I (0.69 F, *p=0.01), BDNF-IIa (0.57 F, p=0.001**), BDNF-IIb (0.84 F, p=0.01*), BDNF-IV (0.84 F, p=0.006**), BDNF-VI (1.24 F, p=0.005**), BDNF-VII (0.78 F, p=0.004**)). BDNF exons IIc, III, V, VIII, IXA, and nerve growth factor (NGF) gene expression levels were not significantly modulated by A/S/I. Protein expression of total BDNF (-22.1± 8.1%, p=0.02*), TrkB (-24.4± 7.9%, p= 0.01*), Erk1/2 (-5.8 ± 3.0%, p= 0.09), pErk1/2 (-33.8± 9.5%, p= 0.007**), Elk1 (-28.2± 11.9%, p=0.04*), pElk1 (-42.6± 11.6%, p=0.007**), CREB (-13.1± 3.7%, p=0.007**), pCREB (-35.1± 14.2%, p=0.03*) and Arc (-33.1± 8.1%, p=0.003**) were also decreased in A/S/I mice, relative to controls (Fig.2). A/S/I mice displayed impaired dendritic arborization, as measured by a decrease in the mean length of the longest dendrite originating from CA-1 neurons (-82.0±17.1, p=0.0002***) and the number of its branches (-1.69±0.4, p=0.0010**), compared to controls (Fig.3 a,b).

Conclusion: Conclusions: Surgery, Anesthesia and Intensive Care environment impair BDNF-induced expression of Arc and dendritic arborization in the hippocampus of aged mice. Given Arc's critical role for synaptic plasticity, memory and cognitive function, BDNF-mediated decrease in Arc expression may be important in triggering and supporting cognitive impairment in delirium evoked by anesthesia, surgery and ICU environment.

References: 1. Front Aging Neurosci 12:542421 (2020) 2. J Neurosci 28:2589-600 (2008) 3. Exp Brain Res 200:125-40 (2010)

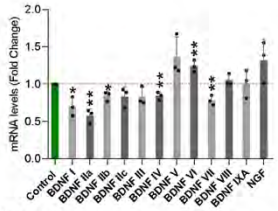


Fig 1. mRNA expression levels of Brain Derived Neurotrophic Factor (BDNF exons I-IXA) and Nerve Growth Factor (NGF) profiling in mouse hippocampus of control vs ASI (N=3). Two-tailed unpaired t-test *P < 0.05 and **P < 0.01, respectively and data represented as mean ± SEM.

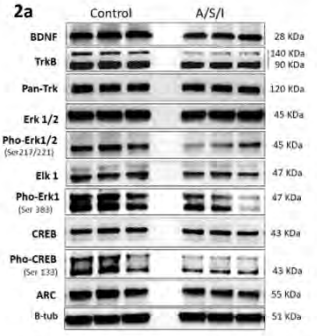
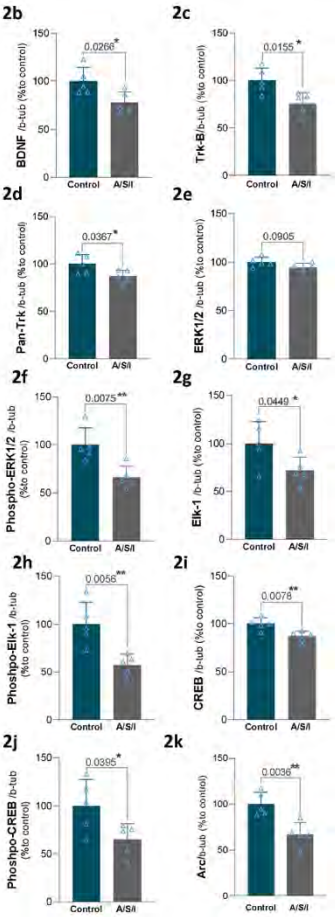


Fig 2. (2a) Representative immunoblots displaying protein expression patterns and β-tubulin (loading control). The quantified protein expression levels shown in graphs are (2b) BDNF, (2c) TrkB, (2d) Pan-Trk, (2e) Erk1/2, (2f) phospho-Erk1/2, (2g) Elk1, (2h) phospho-Elk1, (2i) CREB, (2j) phospho-CREB and (2k) Arc. Protein densities were quantified using Syngene – Gene Tools analysis software and expression levels were normalized with β-tubulin. Data is presented as percent change to controls. N=5 Control and 5 A/S/I mice. Two-tailed unpaired t-test *P < 0.05 and **P < 0.01, respectively and data represented as mean ± SEM.



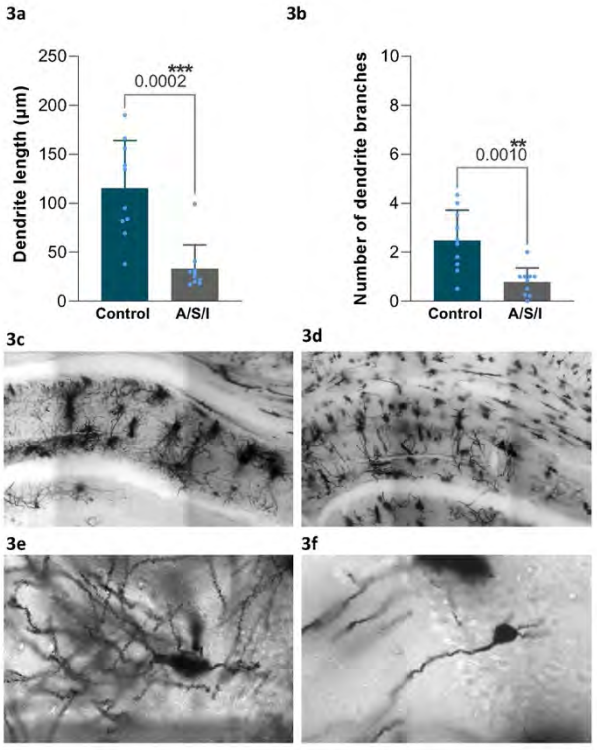


Fig 3. (3a) Mean length of the longest dendrite originating from CA-1 neurons and (3b) average number of its branches. Representative microscopy images from one control (3c, 10X magnification and 3e, 63X magnification) and one A/S/I (3d, 10X magnification and 3f, 63X magnification) animal. N=10 neurons/group. Two-tailed unpaired t-test ***P < 0.001 and **P < 0.01, respectively and data represented as mean ± SEM.

Neuroscience in Anesthesiology and Perioperative Medicine - 8

Chemogenetic activation of GABAergic neurons in the rostromedial tegmental nucleus reduces arousal and increases sensitivity to general anesthetics in mice

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Introduction: The rostromedial tegmental nucleus (RMTg) in the midbrain sends inhibitory GABAergic projections to the ventral tegmental area (VTA) to inhibit wakefulness and increase non-rapid eye movement (NREM) sleep.1,2 We hypothesized that activating GABAergic neurons in the RMTg decreases wakefulness and increases sensitivity to anesthetic-induced unconsciousness. In this study, designer receptors exclusively activated by designer drugs (DREADDs) were used to selectively activate GABAergic RMTg neurons in transgenic Vgat-ires-cre mice. The behavioral effects on arousal and sensitivity to anesthetic-induced unconsciousness were measured.

Methods: All experiments were approved by our Institutional Animal Care and Use Committee. Adult Vgat-ires-cre mice (4 males and 4 females) were used for all experiments. These mice express Cre recombinase under the transcriptional control of the vesicular GABA transporter (Vgat), thus limiting expression to GABAergic neurons. Stereotaxic surgery was performed to inject AAV2-hSyn-DIO-M3Dq-mCherry bilaterally (60 nL/side) into the RMTg (AP: -3.8 mm, ML: +/- 0.55 mm, DV: -4.8 mm). This adeno-associated virus (AAV) induces Cre-dependent expression of the excitatory DREADD M3Dq, which is a modified M3 muscarinic receptor that has low affinity for the native ligand acetylcholine, and high affinity for the synthetic ligand clozapine-N-oxide (CNO). On the day of behavioral experiments, mice were injected intraperitoneally (IP) with 3 mg/kg clozapine-N-oxide hydrochloride (CNO-HCl) or saline (vehicle) 30-45 minutes prior to conducting the open field test. The order of CNO-HCl and saline was randomized, and the experimenter was blinded to the condition. For the open field test, mice were placed in a 40 cm x 40 cm opaque box for 5 minutes. Activity was recorded by video and analyzed using ANY-maze software (Stoelting). To measure the effect of activating GABAergic RMTg neurons on anesthetic sensitivity, mice were anesthetized with isoflurane (2.5% for 50 minutes) or propofol (100 mg/kg, IP) and placed in the supine position. Return of the righting reflex (RORR), defined as returning to the prone position, was used as a surrogate measure for return of consciousness.

Results: When GABAergic neurons of the RMTg were activated using excitatory DREADDs, mice travelled significantly shorter distances (CNO-HCl: 10.1 ± 9.5 m; Saline: 17.1 ± 4.0 m) and spent more time immobile (CNO-HCl: 126.0 ± 72.1 s; Saline: 27.3 ± 12.3 s) in the open field test after receiving CNO-HCl compared to saline ($p < 0.05$, n=8). These mice also showed a trend of taking more time for RORR after 2.5% isoflurane after receiving CNO-HCl (12.3 ± 4.9 min) compared to saline (5.6 ± 2.5 min). After propofol, mice showed a trend of increased time to return of righting with CNO-HCl (55.4 ± 27.8 min) compared to saline (8.6 ± 17.3 min). Four mice that did not lose the righting reflex after saline + propofol, did lose righting for over 50 minutes after receiving CNO-HCl + propofol.

Conclusion: These results suggest that activating GABAergic RMTg neurons reduces overall motor activity and makes the brain more susceptible to isoflurane- and propofol-induced unconsciousness. The RMTg may play an important role in actively suppressing arousal during states of unconsciousness induced by general anesthetics that potentiate GABAA receptors such as halogenated ethers and propofol.

References: 1PLoS Biol. 2018;16(4):e2002909.
2Anesth Analg. 2021;132(4): e50-e55

Neuroscience in Anesthesiology and Perioperative Medicine - 9 Performance in distinct domains of cognition may be differentially impacted by light sedation with diverse anesthetics

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Introduction: The effect of sedation with distinct anesthetics on specific cognitive domains has not been rigorously studied. Prior studies have demonstrated that different aspects of cognition may be impaired during sedation [1, 2] or emergence from general anesthesia [3]. Understanding the changes in arousal and memory formation under anesthesia is important for tailoring sedation to patient needs. To further investigate, we developed a short battery of cognitive tasks to quantify performance in the cognitive domains of attention, executive function, and memory, with motor responses. These tasks were deployed in a larger functional neuroimaging trial comparing 3 anesthetics. Results from a preliminary cohort are presented.

Methods: Data was collected from healthy volunteers during a randomized saline-controlled, parallel-arm within-subject study (NCT04062123) comparing propofol, dexmedetomidine, and fentanyl (IRB #19030183). Three tasks were included in a 3.5 min battery. First was a psychomotor vigilance task, for which subjects were asked to respond as quickly as possible to a series of unpredictable tones, measuring motor response and attention. A serial object recognition paradigm (Fig. 1) then employed a 3-back task (measuring attention and executive function) and also assessed long-term memory [1,4]. The proportion of correct recognitions and false-positive identifications were calculated, separately, for the 3-back and memory tasks. The difference in Z-scores for correct vs. false identifications were used to quantify performance in standard deviation units. The task battery was repeated 3 times with unique images, under steady-state drug concentrations.

Results: Data from 21 subjects (10 male) were analyzed; age (mean, SD) was (24.2, 5.7), drug-group sample sizes are listed in Figures 2 & 3. Small cohorts in this preliminary dataset precluded formal statistical comparisons between drug conditions. Response times to the psychomotor vigilance task are displayed in Fig. 2, with an indication that dexmedetomidine resulted in slower responses. Performance on the 2 tasks in the object recognition paradigm are shown in Fig. 3. Different profiles suggest that the drugs have distinct cognitive effects on each performance metric relative to saline.

Conclusion: We have successfully implemented a brief testing battery that can be used to periodically profile distinct cognitive impairments in studies of anesthetic action. Our preliminary findings suggest that dexmedetomidine may cause more pronounced slowing of motor response to auditory stimuli. Early data also suggest that propofol and dexmedetomidine may have a greater impact on attention, executive function, and memory than fentanyl. We plan to confirm if these preliminary trends persist in the full study cohort.

References: [1] Anesthesiology, 2009.110(2):295-312. [2] Anesthesiology, 1997. 87:749-764. [3] eLife, 2021.10:e59525. [4] Learn Mem, 2012. 19(1):15-25.

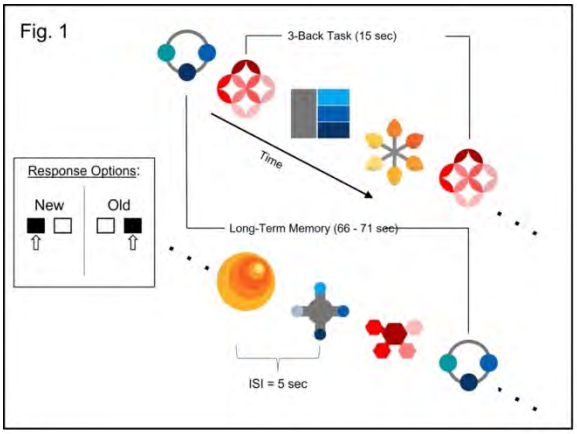


Fig. 2

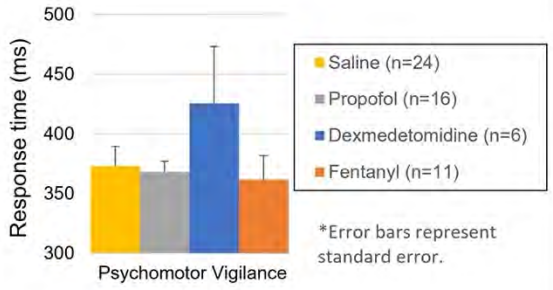
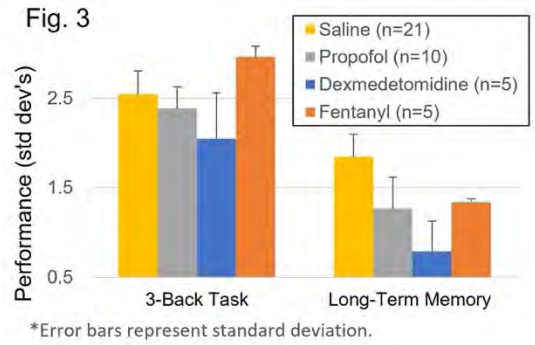

500
450
400
350
300
Response time (ms)
Saline (n=24)
Propofol (n=16)
Dexmedetomidine (n=6)
Fentanyl (n=11)
*Error bars represent standard error.
Psychomotor Vigilance

Fig. 3


Saline (n=21)
Propofol (n=10)
Dexmedetomidine (n=5)
Fentanyl (n=5)
2.5
1.5
0.5
Performance (std dev's)
3-Back Task
Long-Term Memory
*Error bars represent standard deviation.

Neuroscience in Anesthesiology and Perioperative Medicine - 10 Distinct neural firing patterns are observed in unit recordings from the rat prefrontal cortex during anesthetic-induced unconsciousness

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Introduction: The prefrontal cortex (PFC) is thought to be critically involved in the regulation of consciousness. It has been reported that administering a cholinergic agonist in the PFC restores consciousness during continuous sevoflurane anesthesia in rats.1 Furthermore, the medial PFC is involved in thalamocortical and corticocortical interactions that modulate both induction and emergence from propofol anesthesia.2 However, it is not known how various anesthetics and sedatives with distinct molecular targets modulate single unit activities in the rat PFC during the transition into unconsciousness and subsequent recovery.

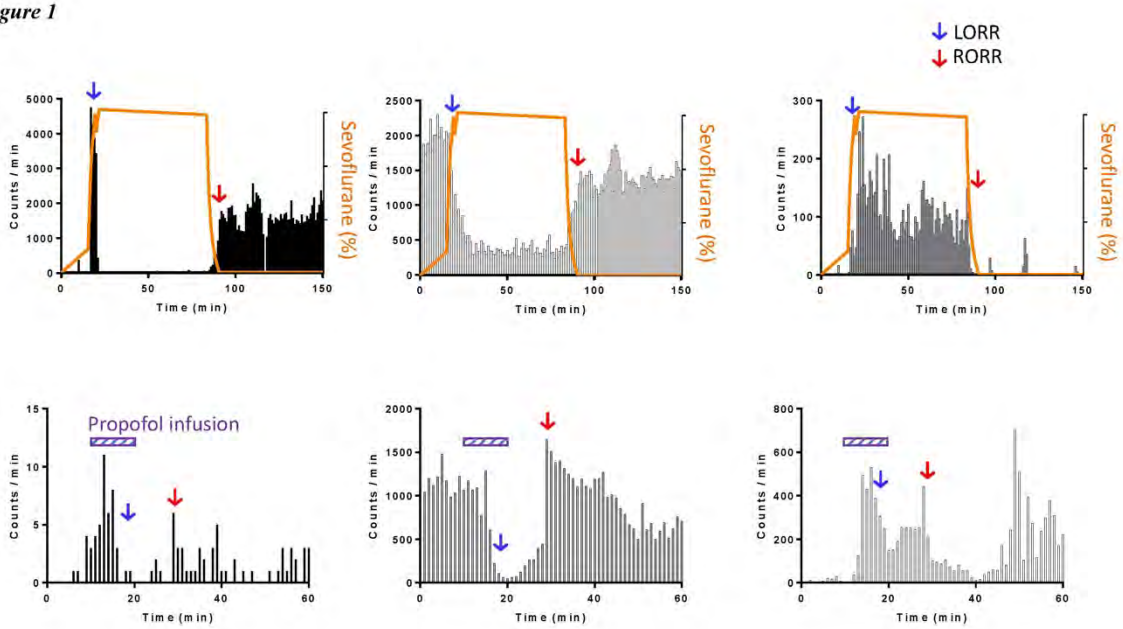
Methods: All experiments were approved by our Institutional Animal Care and Use Committee. One female Sprague Dawley rat (29 weeks old) was used for this pilot study, and experiments were conducted between 9am to 5pm. A central venous catheter was surgically placed in the femoral vein by Charles River Laboratory prior to arrival in our animal housing facility. The rat underwent stereotaxic neurosurgery under isoflurane anesthesia to implant a 64-channel Neuronexus microelectrode in the PFC. The 4-shank microelectrode contains 16 channels in each shank separated by 50 µm spaces. Analgesia was provided with ketoprofen after surgery, and the animal recovered for at least one week before conducting the following experiments. IV anesthetics (Propofol: 1.6mg/kg/min over 10 min; Dexmedetomidine (DEX): 3.0 µg/kg/min over 10 min; Ketamine: 5 mg/kg/min over 10 min; or Fentanyl: 3.67 µg/kg/min over 15 min) were administered via the central venous catheter. At least three days of rest were provided between experiments. After all IV anesthetic experiments were completed, additional experiments were performed with volatile anesthetics (2% isoflurane over 60 min; 3% sevoflurane over 60 min). Neural activity was continuously recorded during the awake state (before anesthetic administration), anesthetized state, and recovery state. These states were behaviorally defined by loss and recovery of the righting reflex (LORR and RORR, respectively). The neural firing frequencies were compared with the awake state, and if the firing frequency was higher or lower than the mean ±2 standard deviations, the neural firing frequencies were defined as significantly increased or decreased, respectively.

Results: Three distinct neural firing patterns were identified with propofol, isoflurane, and sevoflurane. The first type exhibited a brief increase in firing frequency immediately before LORR (Figure 1). The second type exhibited a decrease in firing frequency during the anesthetized state and recovered to baseline after RORR. The third type exhibited an increase in firing frequency during the anesthetized state which decreased after RORR. DEX, ketamine and fentanyl did not significantly change the neural firing frequencies despite inducing LORR.

Conclusion: Three distinct firing patterns were identified in the rat PFC during propofol, isoflurane, and sevoflurane anesthesia. The neurons that increased their firing frequency immediately before LORR may be involved in producing paradoxical brain excitation during the transition to unconsciousness with these drugs. However, these changes were not observed with DEX, ketamine, or fentanyl despite inducing LORR, suggesting that anesthetics and sedatives with distinct molecular targets produce unconsciousness by distinct neural circuit mechanisms. These results encourage additional experiments to confirm these findings, and additional analysis to characterize the specific neuron types that exhibit these distinct firing patterns.

References: 1. Current Biology 2018;28:2145.
2. Proc Natl Acad Sci USA 2017;114:E6660.

Figure 1



Neuroscience in Anesthesiology and Perioperative Medicine - 11 Mdivi-1 Post-treatment Decreases Rat Neonatal Hypoxia-Ischemia-induced Neuroinflammatory Gene Expression Changes and the Incidence of Severe Brain Lesions

Brian M Polster[1], Ayodele Jaiyesimi[1], Hyehyun Hwang[1], Nagendra Yadava[1], David Loane[2], Jaylyn Waddell[1]

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Introduction: Hypoxic-ischemic encephalopathy (HIE) is a leading cause of death and disability in preterm and term infants (1,2). Oxidative stress and neuroinflammation contribute to HIE. Literature suggests that the blood-brain barrier permeable compound mdivi-1 can suppress both these injury mechanisms, potentially by limiting reactive oxygen species production from mitochondrial Complex I (3). We hypothesized that mdivi-1 protects against rat neonatal hypoxic-ischemic (HI) brain injury by reducing oxidative stress-dependent neuroinflammation. In this study, we tested the predictions that mdivi-1 post-treatment significantly reduces the severity of HI-induced brain lesions and decreases oxidative stress and neuroinflammatory gene expression changes in the hippocampus.

Methods: The study was approved by the University of Maryland Institutional Animal Care and Use Committee. Three cohorts of male and female Sprague-Dawley rats were subjected to HI on postnatal day 10 using the Rice-Vannucci HIE model (4). A unilateral carotid artery ligation was followed by a one-hour exposure to 8% oxygen. Mdivi-1 (2 mg/kg) or vehicle was given at two and 24 hours after HI. Hippocampal oxidative stress was evaluated at 25 hours post-injury by staining for 3-nitrotyrosine (3-NT) (5). The NanoString nCounter® Neuroinflammation panel was used to quantify the neuroinflammatory gene signature at 12 hours post-HI. Brain lesion size was quantified at 72 hours after HI. The ipsilateral brain lesion volume was expressed as a percentage of the contralateral hemisphere volume. Two-way ANOVA was used to analyze 3-NT staining, followed by Bonferroni post-hoc analysis to compare individual groups. Gene set enrichment analysis was done on housekeeping gene-normalized NanoString mRNA data using ROSALIND® software. Brain lesion size was analyzed by the nonparametric Mann-Whitney U test. A p value of less than 0.05 was considered significant. For pathway analysis, the p value was adjusted using a false discovery rate of 0.05.

Results: Mdivi-1 post-treatment significantly shifted the brain lesion size distribution toward less severe injury. Brain lesions of ≥30% of the contralateral hemisphere size were observed in six of 12 vehicle-treated pups, but only in one of 15 mdivi-1-treated pups. Mdivi-1 post-treatment significantly reduced 3-NT staining in the ipsilateral hippocampus CA1 region and blunted the neuroinflammatory gene signature after HI. The top pathway altered by HI in the drug vehicle-treated group, TRAF6-mediated NF-κB activation ($p<0.0005$), was not significantly altered when mdivi-1 was administered after HI ($p=0.3142$).

Conclusion: Initial results are consistent with the hypothesis that mdivi-1 is neuroprotective following HI by reducing oxidative stress and neuroinflammation. Further experiments are necessary to determine whether either oxidative stress or neuroinflammation depend on the other or causatively contribute to brain injury.

References: 1. Hypoxic-ischemic encephalopathy in the term infant. Perinatol. 2009;36:835-858. 2. A systematic review of the role of intrapartum hypoxia-ischemia in the causation of neonatal encephalopathy. Am J Obstet Gynecol. 2008;199:587-595. 3. The Putative Drp1 Inhibitor mdivi-1 Is a Reversible Mitochondrial Complex I Inhibitor that Modulates Reactive Oxygen Species. Dev Cell. 2017;40:583-594. 4. The influence of immaturity on hypoxic-ischemic brain damage in the rat. Ann Neurol. 1981;9:131-141. 5. 3-Nitrotyrosine: a versatile oxidative stress biomarker for major neurodegenerative diseases. Int J Neurosci. 2020;130:1047-1062.

Neuroscience in Anesthesiology and Perioperative Medicine - 12 Weak, layer- and region-dependent pairwise coupling of cortical sites underlies globally synchronous state transitions during fixed isoflurane in rats.

Ethan B Blackwood[1], Brenna P Shortal[1], Alexander Proekt[2]

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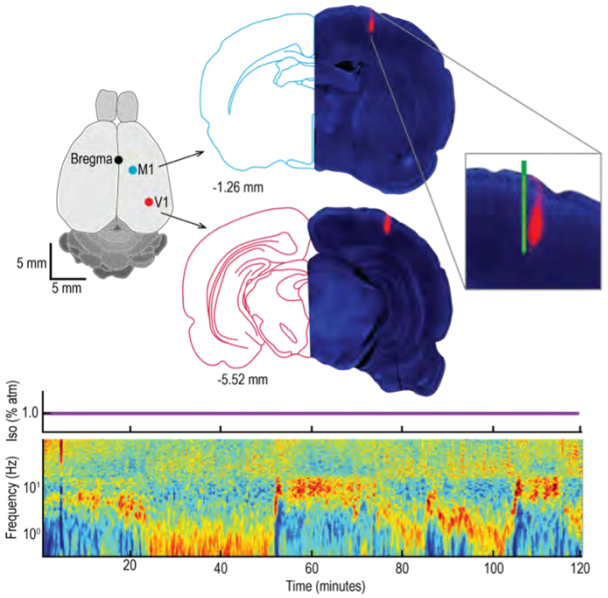
Introduction: During recovery from anesthesia, cortical activity states defined by the power spectra of electrophysiological recordings have been observed to transition abruptly between several characteristic patterns in rodents (1), non-human primates (2), and humans (3). These transitions often appear synchronized between regions; furthermore, the full state obtained by combining the time-frequency spectrograms of several regions is low-dimensional (1). The circuit mechanism that produces such state transitions is unknown. Modulation from the brainstem and basal forebrain is known to coordinate uniform changes in oscillatory activity across the thalamocortical network (4), but changes in activity may also propagate through the network in a decentralized manner. To test the uniformity of transitions and distinguish these possibilities, we directly measure transition synchrony and state correspondence between cortical sites.

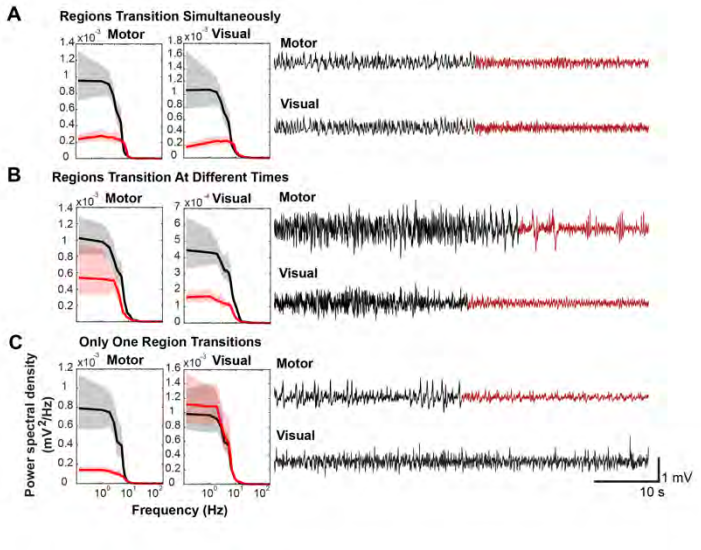
Methods: Rats were implanted with linear silicon probes in either visual (V1) and motor (M1) cortices or left and right V1. They were held at 1% isoflurane while local field potential (LFP) was recorded for up to 7 hours. Spectrograms were created by the multitaper method. Nonnegative matrix factorization (NMF) was used to compress each spectrogram, and discrete state labels were assigned based on the NMF component with the largest loading at each time. For each pair of recording sites, state transitions, normalized mutual information (NMI) of states, and canonical correlation (CC) of NMF scores were computed. Each of these measures was compared to a null model that shuffled each site's transitions using a Markov chain, with Bonferroni correction over pairs. Coupling measures for different groups of site pairs were compared using permutation tests.

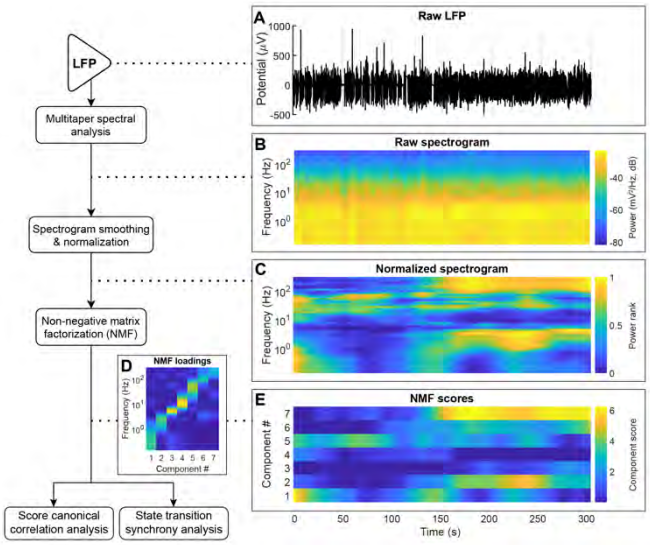
Results: Three M1/V1 and 4 bilateral V1 rats were included. Transitions were more synchronized than chance in 57.0% of site pairs in M1/V1 recordings and 80.2% of pairs in bilateral V1 recordings. Discrete state NMI was greater than chance in 81.9% and 96.9% of pairs in the two recording types respectively, and NMF score CC was greater than chance for all pairs in all recordings. Within-region site pairs had higher coupling by all three measures than across-region pairs ($p < 10^6$, permutation tests). In V1 recordings, site pairs that included a channel in layer 4 (L4) had lower coupling by all measures than those that did not ($p < 0.05$, permutation tests).

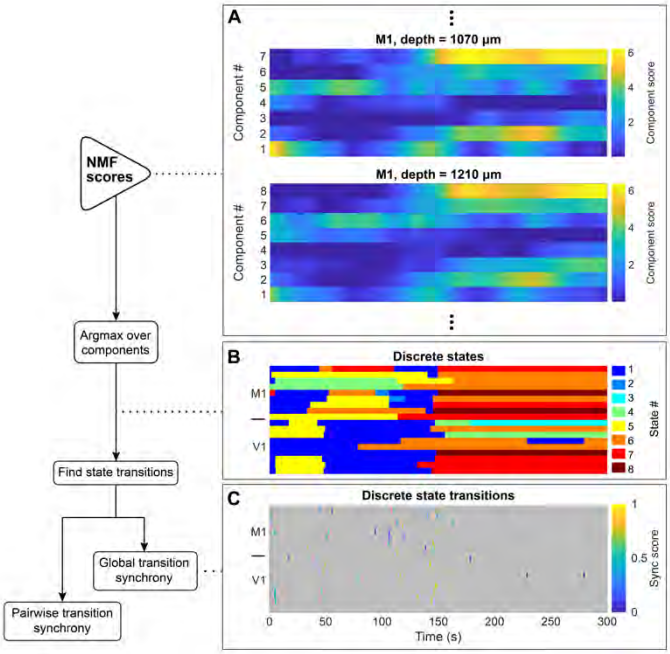
Conclusion: Pairs of recording sites in M1 and V1 did not consistently transition synchronously. Also, both transition synchrony and state correspondence varied depending on whether the pair mixed brain regions and whether one of the sites was in L4; sites that are expected to receive more differing input had less coupling. While the global synchrony of state transitions may emerge even from weak pairwise coupling (5), these results suggest that modulation from subcortical structures may not be responsible for synchrony.

References: 1. P Natl Acad Sci USA, 2014, 111, 9283-88. 2. Brain, 2020, 143, 833-43. 3. PLOS One, 2014, 9, e106291. 4. Science, 1993, 262, 679-85. 5. Nature, 2006, 440, 1007-12.


Bregma
M1
V1
-1.26 mm
-5.52 mm
5 mm
5 mm
Iso (% atm)
1.0
Frequency (Hz)
Time (minutes)


A
Regions Transition Simultaneously
Motor
Visual
B
Regions Transition At Different Times
C
Only One Region Transitions
Power spectral density (mV²/Hz)
Frequency (Hz)
1 mV
10 s


LFP
Multitaper spectral analysis
Spectrogram smoothing & normalization
Non-negative matrix factorization (NMF)
Score canonical correlation analysis
State transition synchrony analysis
Raw LFP
Raw spectrogram
Normalized spectrogram
NMF loadings
NMF scores
Time (s)


NMF scores
Argmax over components
Find state transitions
Global transition synchrony
Pairwise transition synchrony
M1, depth = 1070 µm
M1, depth = 1210 µm
Discrete states
Discrete state transitions
Time (s)

Neuroscience in Anesthesiology and Perioperative Medicine - 13 The Mu opioid receptor gene does not impact survival in the MLL-AF9 murine model of acute myelogenous leukemia

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Introduction: The anesthetic care of cancer patients would benefit from further mechanistic understanding of cancer related perioperative processes. Preclinical and clinical studies have suggested opioids impair functions of immune cells, which could disrupt immune mediated clearance of cancer. However, in human cancer surgery, opioid dosing is confounded by tumor stage and burden, and retrospective studies are insufficient for justifying witholding of opioids during cancer surgery at this time. Indeed, retrospective studies have emerged suggesting that some cancer surgery patients may actually benefit from liberal opioid administration, while other patients may be negatively impacted by higher intraoperative opioid doses. Esophageal squamous cell carcinoma surgery patients given higher fentanyl doses enjoyed improved recurrence free survival (RFS) and overall survival (OS), though adenocarcinnoma patients did not (ref1). We also recently reported significantly improved RFS of triple negative breast cancer patients with higher opioid doses (ref2). In contrast, our lung adenocarcinoma cohort suffered worse OS with higher intraoperative opioid doses, though patients with genetic alterations in the Wnt and Hippo signaling pathways received RFS benefit from higher intraoperative opioid doses (ref3). Understanding the molecular mechanisms underlying these observations could greatly improve preoperative determinations of anesthetic and analgesic strategies for cancer surgery, and preclinical modeling of these processes could be an important tool to such insights. Opioid effects on cancer could be mediated by neural control of immune system (ref4), through opioid effects on immune cells (ref5), or through opioid effects on cancer cells themselves (ref6). Genetics represent a powerful way to disentangle these mechanisms (ref7). We modeled acute myelogenous leukemia (AML) using wildtype versus opioid receptor (Oprm1) knockout lineage negative, Sca-1 positive, C-Kit positive (LSK) cells as the basis, usings the mixed lineage leukemia (MLL)-Af9 fusion oncogene model. Our investigations were motivated by the previous observation that bone marrow of Oprm1 KO mice are hyperproliferative and that proliferative hematopoietic progenitor cells are permissive for MLL-Af9 transformation.

Methods: Lentivirus expressing the MLL-Af9 fusion protein and green fluorescent protein (GFP) was generated in HEK-293T cells, and viral supernatant used to transduce bone marrow progenitor cells enriched for lineage negative, Sca-1 positive, C-Kit positive (LSK) cells. Transduced progenitor cells were expanded ex vivo, then purified for GFP(+) cells by fluorescence activated cell sorting (FACS), and GFP(+) cells were transplanted into lethally irradiated CD45.1 congenic mice. These cohorts of mice were followed for cell-autonomous survival differences, analyzed by Log-rank (Mantel-Cox) testing with Prism. The bone marrow of a moribund Oprm1 KO derived MLL-Af9 AML was harvested, and transplanted into a secondary transplant into wt versus Oprm1 KO mice and followed for surivival differences, analyzed by Log-rank (Mantel-Cox) testing.

Results: Figure 1: The survival analysis of female CD45.1 congenic mice transplanted with MLL-Af9 leukemia derived from LSK cells of female wt versus Oprm1 KO mice did not evidence survival differences (p=0.858). Figure 2: To examine whether MLL-Af9 AML generated in LSK cells of Oprm1 KO would demonstrate differences in AML kinetics, we subsequently transplanted MLL-Af9 Oprm1 KO AML into female wt versus Oprm1 KO recipient mice. MLL-Af9 Oprm1 KO AML did not demonstrate signifficant differences in growth in wt versus Oprm1 KO recipients (p=0.2687).

Conclusion: Though others have previously shown that Oprm1 KO mice have hyperproliferative hematopoietic progenitor cells in bone marrow, and that MLL-Af9 AML is reportedly licensed by

proliferative status, our experiments indicate that the MLL-Af9 AML model is insensitive to Oprm1 genotype in cell autonomous (mutation in the leukemia) and cell-non-autonomous (mutation in the somatic tissues) contexts. We provide a model for the study of opioid receptor genetics and tumors, by independently mutating Oprm1 in tumor versus host. Future studies will examine drug effects.

References: 1. Du et al. Anesth Analgesia 2018 PMID 29757780 2. Montagna et al. BJA 2021 PMID 33220939 3. Connolly et al. BJA 2021 PMID 34147159 4. Weber and Pert. Science 1989 PMID 2749256 5. McCarthy et al. J Neuroimmunol 2001 PMID 11240029 6. Mathew et al. Anesth Analg 2011 PMID 21156980 7. Gav√©riaux-Ruff et al. PNAS 1998 PMID 9600964

Figure 1

Survival kinetics of murine MLL-Af9 AML derived from wt vs *Oprm1* KO LSK cells in CD45.1 congenic transplant recipients

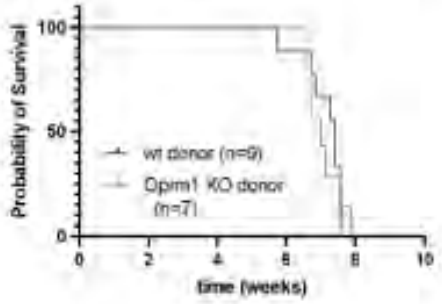
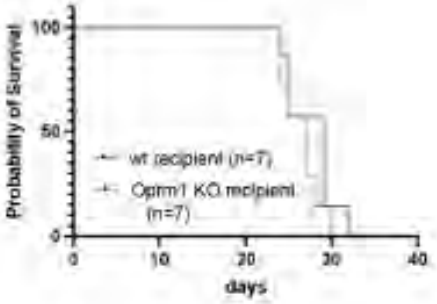


Figure 2

Survival kinetics of murine MLL-Af9 AML derived from *Oprm1* KO LSK cells in wt vs Oprm1 KO transplant recipients



Neuroscience in Anesthesiology and Perioperative Medicine - 14 An immune signature of postoperative cognitive dysfunction (POCD)

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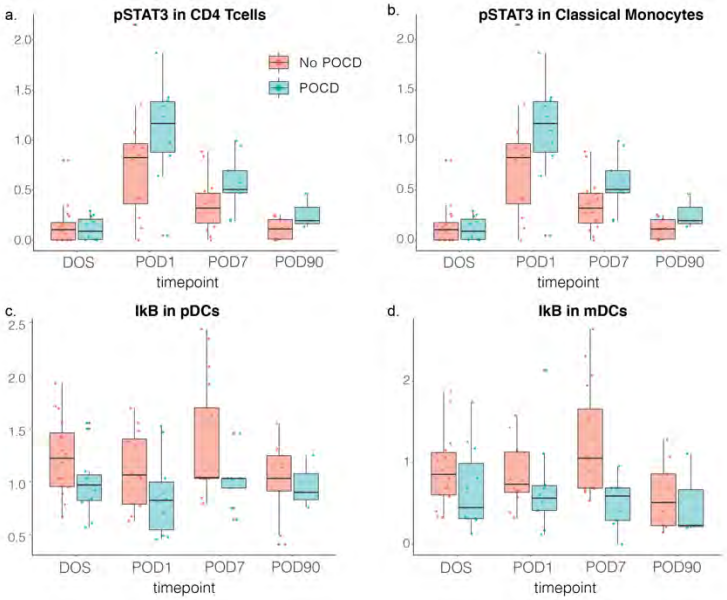
[1]Stanford University, Stanford, United States of America, [2]UC Davis School of Medicine, Sacramento, CA, [3]Stanford University School of Medicine, Palo Alto, CA, [4]Telecom Paris, Paris, France, [5]Universit√© de Paris, Paris, France, [6]Institut Pasteur, Paris, France, [7]Universit√© Jean Monnet Saint-Etienne, Saint-Etienne, France, [8]Stanford University School of Medicine, Stanford, CA, [9]Stanford University, Palo Alto, CA, [10]Stanford University School of Medicine, Stanford, California

Introduction: Postoperative cognitive dysfunction (POCD) is a keystone complication of major surgeries and affects up to 41% of surgical patients aged over 60 years. POCD is associated with earlier retirement, greater use of social financial assistance, higher risk of developing dementia and higher mortality. However, there is no therapy to prevent or treat these cognitive disorders. A precise understanding of the complex neuro-immune mechanisms implicated in the pathophysiology of POCD is integral towards the development of targeted interventions to prevent POCD. We employed an integrated single-cell and plasma proteomic approach to comprehensively characterize immune system trajectories after major orthopedic surgery in patients with and without POCD. We hypothesized that 1) postoperative immune trajectories differ between patients with and without POCD and 2) that patient-specific preoperative immune states are predictive of POCD.

Methods: 102 whole blood samples were obtained from a unique biobank of human perioperative samples collected over four time points before and after major orthopedic surgery: day of surgery (DOS) and postoperative days (POD) one, seven, and ninety. Samples were processed and analyzed using suspension mass cytometry (CyTOF) and plasma proteomics aptamer assays. The goal of this study was to identify inflammatory biomarkers associated with the occurrence of postoperative cognitive dysfunction defined as an absolute difference in Z-score ,â• 1 in at least one cognitive test (Montreal Cognitive Assessment (MoCA) or Trail Making Test A and B) between the presurgical (DOS) and postsurgical POD7 or POD90 timepoints. We employed a statistical framework to characterize the difference in the postoperative immune signature associated with the onset of POCD disorders using one-way ANOVA.

Results: The high-dimensional analysis of the combined single-cell and plasma proteomic data identified a distinct immune signature of POCD. Examination of the most informative immune trajectories of the multivariate model revealed upregulated STAT3 response in CD4 T-cells (p=8e-3, Fig. 1a) and classical monocytes (p=1e-2, Fig. 1b) at postoperatively in patients with POCD. In addition, preoperative expressions of IkB in pDCs (p=4e-3, Fig. 1c) and mDCs (p=4e-3, Fig. 1d) differed between patients who developed POCD and those who did not.

Conclusion: Immunological trajectories differentiate patients who develop POCD from patients who do not highlight a key role of the peripheral immune system in the pathophysiology of POCD. The resulting immune signature of POCD points at cell-specific immune dysfunctions in patients with POCD (including JAK/STAT3 and NFŒ∫B signaling responses) and provides the basis for the development of a predictive test that may assist in the perioperative management of patients at risk for POCD.


a.
pSTAT3 in CD4 Tcells
No POCD
POCD
2.0
1.5
1.0
0.5
0.0
DOS
POD1
POD7
POD90
timepoint
b.
pSTAT3 in Classical Monocytes
2.0
1.5
1.0
0.5
0.0
DOS
POD1
POD7
POD90
timepoint
c.
IkB in pDCs
2.5
2.0
1.5
1.0
0.5
DOS
POD1
POD7
POD90
timepoint
d.
IkB in mDCs
2
1
0
DOS
POD1
POD7
POD90
timepoint

Neuroscience in Anesthesiology and Perioperative Medicine - 15 Inhaled anesthetics for hypnosis in critical care patients: Evaluating neurocognitive and mental health outcomes.

Sean Cuninghame[1], Marat Slessarev[1], Asaanth Sivajohan[1], kevin gorsky[2], Brian H Cuthbertson[3], Boris Yakubov[4], Martin Chapman[3], Beverley A Orser[5], Adrian M Owen[6], Conall Francoeur[7], Davinia Withington[8], Lisa Burry[9], Angela Jerath[10]

[1]London Health Sciences Centre, London, Canada, [2]University of Toronto, Toronto, Ontario, [3]University of Toronto, Toronto, Canada, [4]Sunnybrook Research Institute, Toronto, Canada, [5]University of Toronto Faculty of Medicine, Toronto, Ontario, [6]Western University, London, Canada, [7]Universit√© Laval, Quebec City, , Canada, [8]McGill University, Montreal, Canada, [9]Lunenfeld-Tanenbaum Research Institute, Toronto, Canada, [10]Sunnybrook Health Sciences Centre, Toronto, Canada

Introduction: The use of inhaled volatile anesthetic agents to provide sedation and hypnosis in critically ill general medical and postoperative patients who require invasive ventilation has been well described.1-3 Available evidence suggests there may be potential benefits on neuropsychiatric outcomes after discontinuation of drug delivery, but the study of cognitive and mental health outcomes remains understudied. We conducted a systematic review and meta-analysis to assimilate studies that evaluated the short-term in-hospital and longer-term post-hospital discharge neurological outcomes in adult mechanically ventilated intensive care unit (ICU) patients.

Methods: We searched key databases MEDLINE, EMBASE, and PsychINFO between the time period of 1970 to 2021 for case series reports, observational studies and prospective clinical trials of postoperative and general medical-surgical patients who received inhaled anesthetic drugs in the ICU. We studied cognitive (i.e., delirium) and psychiatric (i.e., anxiety, depression, posttraumatic stress disorder) neurocognitive outcomes.

Results: We identified 5 postoperative and 3 general medical-surgical ICU studies that included a total of 564 patients. The studies included 5 single centre trials, 1 multicentre trial and 2 cohort studies that compared the effect of inhaled (sevoflurane, isoflurane or desflurane) to intravenous sedative drugs (propofol or midazolam). Variation in the parameters of patient outcome assessments, measurement tools and quality of the data limited metanalytic-review. Delirium was reported by 5/8 (63%) studies (n=344) during ICU or hospital stay using varied tools. Pooling of 4 trials (n=258) showed no difference in delirium (risk ratio 0.90, 95% CI 0.5-1.56). A single trial (n=60) assessed attention and concentration using psychometric tests in ICU and showed no significant difference. One trial (n=40) evaluated anxiety/depression (using Hospital Anxiety and Depression Scale) and post-traumatic stress disorder (using Impact Event Scale) at 6-months and showed no significant difference (60% volatile vs. 33% IV). One trial evaluated cognition at 3-months using a telephone interview (TICS) assessment and showed no difference in sedation arms (78% volatile vs. 67% IV).

Conclusion: The study of neurocognitive recovery among mechanically ventilated ICU patients who received inhaled general anesthetic drugs for hypnosis and sedation is limited. Current data are suggestive of equivalent cognitive and psychiatric outcomes between inhaled and injectable sedative and anesthetic drugs, but further in-depth and adequately powered studies using standardized measurement tools are needed.

References: 1. Jerath A, Ferguson ND, Cuthbertson BH. ICM 2020;46:1563 2. Jerath A, Wong K, Wasowicz M et al. CCE Nov 2020;2(11):e0281 3. Jerath A, Parotto M, Wasowicz et al. AJRCCM 2016;193(11):1202

Neuroscience in Anesthesiology and Perioperative Medicine - 16 Inter-patient vs intra-patient variability in spectral EEG information during critical illness

Brian A Chang[1], Tuan Cassim[2], Matthias Kreuzer[3], Aaron Mittel[2], Paul S Garcia[4]

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Introduction: Bifrontal electroencephalography (EEG) montages are commonly used intraoperatively to observe spectral EEG changes during transitions in consciousness. They are placed easily and facilitate timely interventions, such as the modification of sedation strategies (1,2). Despite the routine use of analgosedation regimens among mechanically ventilated patients, bifrontal EEG monitoring is not commonly used in the critical care setting. It is well understood that the complexity of EEG signals is associated with varying anesthetic states (3), thus, the goal of this study was to describe the variability in EEG waveforms among mechanically ventilated, critically ill, adult patients receiving intravenous analgosedation.

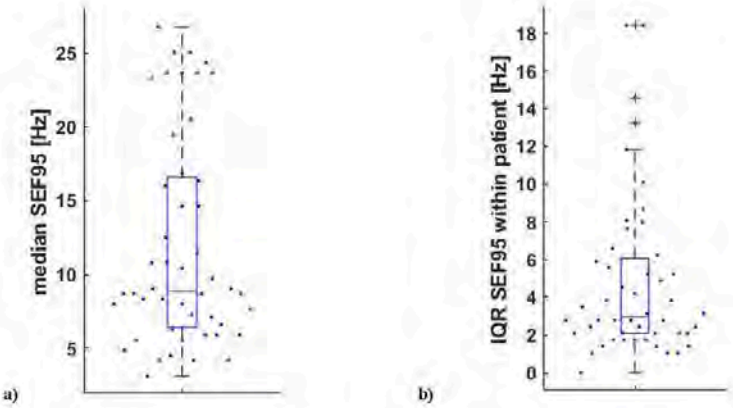
Methods: Eligible patients underwent EEG monitoring via Sedline Root™ (Masimo Corp., Irvine, CA). Four channels of EEG information were obtained through adhesive electrodes configured on a disposable sensor applied across the forehead (electrodes Fp1/2,F7/8, common reference, Fz). Daily sensor checks were conducted to ensure integrity and appropriate impedance. MATLAB (Mathworks, Inc. Natick, MA) was used to calculate the 95th percentile of spectral edge frequency (SEF95) and relative logarithmic β-ratio-degree of high frequency activation-for each patient. The first 6 hours of continuous EEG data (free from artifacts) was used for analysis. Patient demographics and factors that could influence the patients' EEG findings were collected via retrospective chart review.

Results: Forty-eight patients were enrolled over the course of the study. At time of EEG placement, the majority of patients (45/48) were receiving intravenous analgosedation and most (34/48) had a RASS (Richmond Agitation Sedation Scale) score of -4, or lower (Table 1). The interquartile range for the SEF95 varied from 6.3 – 16.7 Hz (median 8.9 Hz), suggesting heterogeneity in traditional α band activity in this population (Figure 1a). The median logarithmic β ratio was -3.2 (IQR: -3.6 – -2.6), which is consistent with reduced activity at cortical synapses. The intra-patient median interquartile range for SEF95 only varied by 4.1 Hz (IQR: 2.1 – 6.2, median variability, 3.0 Hz) (Figure 1b).

Conclusion: Over the course of a six-hour monitoring period, most critically ill patients exhibit EEG patterns dominated by low-moderate frequency activity, which could be explained by the patients' illness, excessive sedation drug effect, or poor pre-existing neurologic substrate. There was a wide-range of interpatient variability when compared with intra-patient variability, suggesting that the underlying patients' underlying neurologic function could be more relevant than differences in analgosedative regimens. Ongoing studies will focus on the relationship between the quantitative EEG parameters derived from these abbreviated montages and critically ill patient outcomes.

References: 1) Anesthesiology, 125, 861-72, 2016. 2) Proc Natl Acad Sci, 108, 8832-37, 2011. 3) Anesthesiology, 132, 1003-16, 2020.

Figure 1: Inter-patient and intra-patient variability of median SEF95 over a 6-hour monitoring in period in critically ill patients



Legend:

SEF95: 95th percentile of spectral edge frequency

Figure a: The interquartile range for the SEF95 in the entire study population varied from 6.3 – 16.7 Hz (median: 8.9 Hz).

Figure b: The intra-patient median interquartile range for SEF95 varied from 2.1 – 6.2 Hz (median: 3.0 Hz)

Table 1. Patient Charactertistics

	N = 48
Age (y)	59.6 ± 16
Sex (%)	
M	38 (77.6)
F	11 (22.4)
RASS Score (IQR)*	-4 (-3 to -4)
Patient Comorbidities	
Neurologic history‡	
Y	10 (20.8)
N	38 (79.2)
Uremia†	
Y	20 (40.8)
N	28 (59.2)
Requiring dialysis	
Y	7 (14.6)
N	41 (85.4)
Liver dysfunction‖	
Y	15 (31.3)
N	33 (68.7)
Cardiac arrest	
Y	7 (14.6)
N	41 (85.4)
Drug Exposure	
Analgosedation†	
Y	45 (93.7)
N	3 (6.3)
Fentanyl (mcg/hr)	105.5 ± 93.1
Propofol (mcg/kg/min)	34.9 ± 21.7

*Richmond Agitation Sedation Scale score at time of Sedline placement

‡Neurologic history included: history of stroke, seizures, and dementia

†Uremia: BUN >30mg/dL

‖Liver failure: AST > 80U/L and ALT > 110U/L

†Analgosedation: Any documentation of patients receiving continuous infusions of opioids, propofol, midazolam, dexmedetomidine, or ketamine

Neuroscience in Anesthesiology and Perioperative Medicine - 17 Assessing the Analgesic Properties of Volatile Anesthetics Using High-Power Infrared Lasers in Mice

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Introduction: Many volatile general anesthetics (VGA) block the experience of pain by inducing unconsciousness, however, a select few can provide analgesia in responsive patients. What makes one VGA analgesic, and another non-analgesic, is currently unknown. As the ongoing inhalation of VGAs in awake, freely moving mice precludes the use of most widely used nociceptive sensory tests, it is technically challenging to quantitatively assess the analgesic properties of VGAs. Here, we develop a methodology for that allows for simultaneously assessing both the reflexive and non-reflexive measures of pain during inhalation of subanesthetic concentrations of VGAs in awake, freely moving mice. To demonstrate the utility of this method, we investigated the influence of non-analgesic (isoflurane [ISO]) and analgesic (nitrous oxide [N2O]) anesthetics on thermal sensory thresholds and on noxious stimulus-evoked behavioral responses.

Methods: In adult mice, we monitored thermal noxious stimulus-evoked responses during inhalation of VGAs. Stimuli were generated by a high-power infrared laser (LASMED Inc.) targeted to the hindpaw. The Dixon Up/Down method was used to document thermal stimulus-response thresholds, and behavioral responses (no response, withdrawal, shake, lick) were recorded after each stimulus. Testing occurred within a modified anesthetic chamber with a high-transmittance glass floor. Mice were tested during inhalation of medical air, or equipotent, subhypnotic concentrations of ISO (0.26%) or N2O (60%), with equivalent concentrations of oxygen throughout (~21%).

Results: We found that laser-evoked 50% response thresholds increase under ISO (+18%) and N2O (+28%) compared to air. Interestingly, however, ISO and N2O differentially alter laser-evoked behavioral responses. Thus, laser-evoked licking of the stimulated hindpaw was reduced by N2O (-75%), but not ISO, compared to air. In contrast, under ISO, but not N2O, laser-evoked hindpaw shaking increased (+37%), whereas hindpaw withdrawals decreased (-64%), compared to air.

Conclusion: We conclude that analgesic and non-analgesic VGAs differentially alter behavioral responses to noxious stimuli. In rodents, licking of the hindpaw following a noxious stimulus is indicative of the experience of pain; not merely a reflexive response. Therefore, our finding that N2O, but not ISO, decreases laser-evoked licking of the hindpaw is of particular interest, and indicates that N2O, but not ISO, provides relief from laser-evoked pain (i.e., analgesia). In fact, as ISO, but not N2O, increased the severity of laser-evoked behavioral responses (increasing shaking at the expense of withdrawals), our findings confirm that ISO is not analgesic at subhypnotic concentrations. In the future, to develop a circuit level understanding of the analgesic properties of VGAs, we plan to simultaneously monitor laser-evoked behavioral responses and record neural activity from pain processing regions of the brain.

Neuroscience in Anesthesiology and Perioperative Medicine - 18 The Incidence of Post-Intubation Awareness in Young People: An International Multicenter Cohort Study

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Introduction: Intraoperative awareness, assessed by response to command, occurs in at least 5% of surgeries. Age is believed to be an important risk factor; in a subgroup analysis of our prior study 12% of 18-40 year olds experienced unintended awareness during general anesthesia. The primary objective was to establish the incidence of awareness after intubation in young people, age 18-40 years old. Secondary objectives were to assess the nature of these responses and identify relevant risk factors.

Methods: This was an international, multicentre prospective cohort study using the isolated forearm technique to assess responsiveness shortly after intubation. Each subject was read a randomized sequence of verbal commands and nonsense statements. A priori, we planned to identify risk factors for awareness: we included age, sex, exposure to continuous anaesthesia prior to laryngoscopy, and site (random effect).

Results: Of 344 enrolled subjects, 338 completed the study (mean age, 30 years; 232 female). Responsiveness following intubation occurred in 37/338 subjects (11%). Females (13%, 31/232) responded more often than males (6%, 6/106). In logistic regression, the risk of responsiveness was increased with female sex (ORadjusted = 2.7, 95% CI [1.1, 7.6], p=0.022) and was decreased with continuous anaesthesia prior to laryngoscopy (ORadjusted = 0.43, 95% CI [0.20, 0.96], p=0.041). Responses were more likely to occur after a command to respond (20/338) than after a nonsense statement (11/338, p=0.049).

Conclusion: Intraoperative awareness may occur following intubation in 11% of young adults, with females at increased risk. Continuous exposure to anaesthesia between induction and intubation is a simple approach and should be considered to reduce awareness. Further research is required to understand the sex-related differences in risk of awareness, which may be related to biological mechanisms or an unappreciated practice bias.

Neuroscience in Anesthesiology and Perioperative Medicine - 19

Characterizing ketamine-induced dissociation using human intracranial neurophysiology: brain dynamics, network activity, and interactions with propofol

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Introduction: Ketamine is a widely used anesthetic. At higher doses, ketamine induces unconsciousness and immobility, whereas at lower or subanesthetic doses, it produces a dissociative state, which includes altered sensory perception and a sense of disembodiment. The mechanism whereby a subanesthetic dose of ketamine disrupts normal brain activity to produce the dissociated state remains unclear. It is also unknown how ketamine-induced EEG power changes relate to ketamine's actions at the receptor level. It is believed that at subanesthetic doses, ketamine has a more pronounced effect on NMDA receptors on GABAergic interneurons, leading to disinhibition of the downstream excitatory neurons. The objective of this study was to investigate in humans the effects of subanesthetic doses of ketamine on brain dynamics and network activity, as well as its interactions with a GABAa receptor agonist propofol. We hypothesized that ketamine would increase high-beta and gamma oscillations in prefrontal cortical structures, decrease alpha power in posterior cortical sensory areas, and that some subset of these effects would be reversed by propofol.

Methods: Ten epilepsy patients were implanted with intracranial depth electrodes for detection of seizure foci. We recorded intracranial EEG (iEEG) during a ketamine infusion administered just prior to the electrode removal surgery. We recorded baseline signals for 5 minutes. We then administered an infusion of a subanesthetic dose of ketamine (0.5 mg/kg over 14 minutes). Patients completed an abbreviated version of the Clinician-Administered Dissociative States Scale (CADSS) questionnaire at the conclusion of the ketamine infusion. Propofol bolus was given to the patients to induce general anesthesia. Structural and functional network mapping analysis was conducted to investigate the iEEG power changes after ketamine and propofol.

Results: The responses on the CADSS questionnaire confirmed that our subanesthetic ketamine administration paradigm induced a dissociative state. This state was associated with a remarkable increase of gamma power (25-55Hz) in frontal region of the brain, which includes superior frontal, middle frontal, orbitofrontal, and inferior frontal regions, as well as anterior and posterior cingulate cortex (Figure 1). While parietal and temporal cortices showed mild increase of gamma power, a decrease in gamma power was observed in occipital regions. A global reduction of iEEG power was detected at low frequency oscillations (0-25Hz) for nearly all brain regions studied. The presence of propofol largely reversed the iEEG power changes induced by ketamine (Figure 2). Meanwhile, propofol further intensified the alpha power (8-15Hz) decrease at occipital cortex and the gamma power increase at precentral, postcentral, isthmus cingulate, hippocampal, amygdala, and insula regions of the brain.

Conclusion: These results suggest that a subanesthetic dose of ketamine may induce dissociative states in distinct ways, first by disrupting posterior cortical alpha networks involved in sensory processing, and second by disrupting prefrontal gamma networks involved in arousal and attention. The iEEG power changes that could be reversed by

propofol may be related to the NMDA antagonism of ketamine and the GABAa agonism of propofol. The additive effects of propofol on ketamine may be accounted by their shared inhibition at the hyperpolarization-activated cyclic nucleotide-gated potassium channel 1 (HCN1). This study could provide important insights into the neurophysiological mechanism of the subanesthetic ketamine-induced dissociative state.

Figure 1. Structural mapping (DKT40 atlas) for intracranial EEG power changes after ketamine infusion.

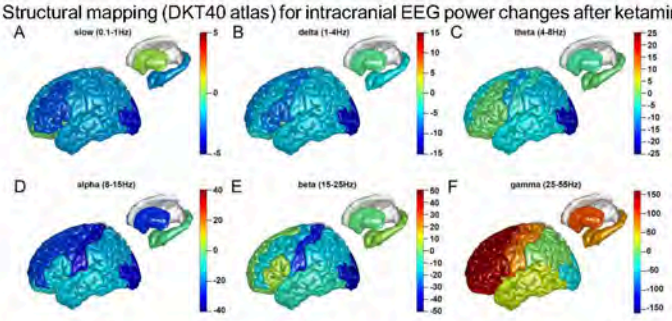
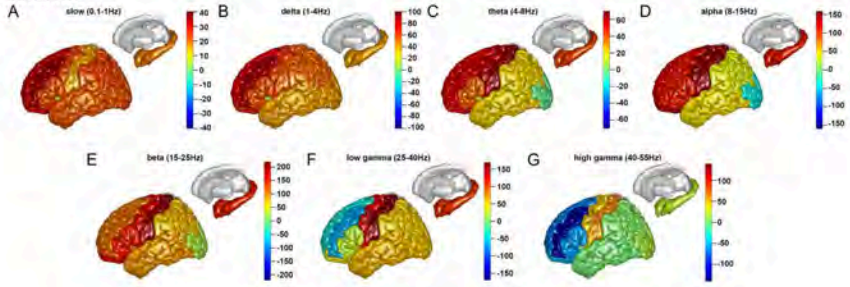


Figure 2. Structural mapping (DKT40 atlas) for intracranial EEG power changes after propofol infusion.



Neuroscience in Anesthesiology and Perioperative Medicine - 20

Electroencephalographic features in the cardiothoracic intensive care unit following intraoperative aminocaproic acid administration

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Introduction: Tranexamic acid (TXA) and the less-potent[1] aminocaproic acid (ACA) are commonly used antifibrinolytic agents in the perioperative setting to reduce allogenic transfusion and decrease hemorrhage-associated mortality.[2] Despite potential benefits, there is concern that antifibrinolytic administration may confer an increased risk of convulsive seizures in humans,[3] which is corroborated by animal data.[4] These studies point to a potential mechanism for cortical hyperexcitability as TXA and ACA can antagonize both gamma-aminobutyric acid (GABA) and glycine receptors.[5] Indeed, recent large human trials studying TXA have shown a strong association with postoperative seizures.[3,6] However, meta-analyses have not corroborated this finding.[7,8] This may be partially because seizure is not a consistent secondary outcome in many studies, and when seizure is reported, it is largely based on the clinical presentation and not electrographic findings. Moreover, the potential association between ACA and seizure activity is not well-studied. This gap in knowledge is underscored in cardiothoracic (CT) surgery patients who are routinely administered antifibrinolytics and at high seizure risk from neurological complications. Here, we performed a retrospective analysis of electrographic findings of patients receiving continuous electroencephalographic (EEG) monitoring in our hospital's CT surgery intensive care unit (CT-ICU). Our primary outcome was electrographic evidence of seizure activity in patients receiving ACA.

Methods: After Institutional Review Board approval, we obtained electronic medical records of patients admitted to our hospital's CT-ICU who underwent continuous EEG (cEEG) monitoring from January 01, 2015 to December 31, 2019. Demographic information, diagnosis and procedure codes, operation type, dose history, laboratory results, and cEEG reports were collected. We included patients with a cEEG monitoring start date within seven days of their date of surgery or CT-ICU admission (Figure 1). We compared demographic characteristics, cEEG findings, and dose dependency with respect to ACA administration. Categorical variables were compared via Fisher's Exact test. Continuous variables were compared via Student's t, Welch's t, and Mann-Whitney U tests where appropriate. P-value < 0.05 was considered significant.

Results: Of 124 patients with cEEG monitoring in the CT-ICU, 83 met inclusion criteria. 41 received ACA; 42 did not receive antifibrinolytic (AF). Within the non-AF group, 21 underwent surgery prior to admission to the CT-ICU. There were no significant differences in demographics between the ACA and non-AF groups (Table 1). However, there was a significant association between surgery and ACA administration ($p < 0.001$), reflecting perioperative AF administration practices. There was a significant association between ACA administration and electrographic seizure on cEEG monitoring (Table 2, $p = 0.006$). Among those with seizures on cEEG, the majority were subclinical (not associated with motoric activity). Moreover, a greater proportion of patients receiving ACA exhibited generalized seizures (Table 2, $p = 0.03$) and markers of cortical hyperexcitability (Table 2, $p = 0.0486$). We further observed a trend toward electrographic seizure and markers of cortical hyperexcitability with increasing ACA dose (Figure 2, $p = 0.1$). Patients with seizures on cEEG monitoring had significant associations with advanced age, CT surgery, cardiopulmonary bypass, and acute neurologic injury (Table 3).

Conclusion: We found an increased incidence of electrographic seizure and markers of cortical excitability in patients receiving ACA, and a trend toward seizure and markers of cortical excitability with increasing ACA dose. Our results suggest that patients receiving ACA, known to be less potent for anti-fibrinolysis than TXA, may still be vulnerable to hyperexcitable cortical states. Thus, patients receiving

AF therapy may warrant a lower threshold for cEEG monitoring during and after AF administration. However, the retrospective and exploratory nature of this study posits limitations, including a lack of a control group, a small sample size, and selection bias, as most patients undergoing cEEG monitoring had a witnessed clinical event suspicious for seizure. Future prospective studies should be designed to more fully elucidate the relationship of ACA administration and hyperexcitable cortical states.

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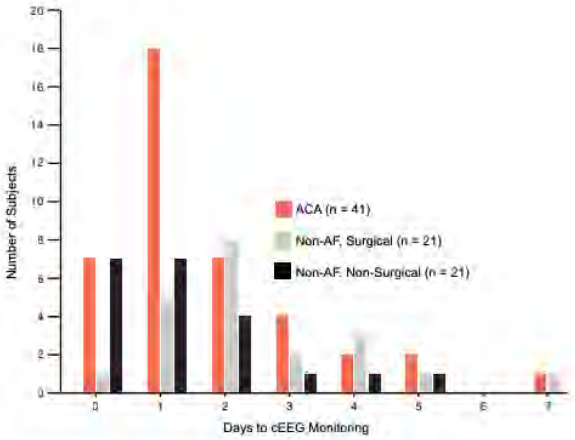
Figure 1. Histogram of patients undergoing cEEG monitoring with respect to surgery or CT-ICU admission



Abbreviations: ACA, aminocaproic acid; AF, antifibrinolytics.

Table 1. Baseline characteristics of patients undergoing cEEG

	Total (n = 83)	Non-AF (n = 42)	ACA (n = 41)	P
Demographics				
Mean age – years	65.4	64.0	66.9	0.2
Female gender – no. (%)	34 (41)	14 (33)	20 (49)	0.2
History of epilepsy – no. (%)	3 (4)	2 (5)	1 (2)	1.0
Primary Operation Type – no. (%)				
Valvular repair	28 (34)	5 (12)	23 (56)	**< 0.001**
CABG	3 (4)	0 (0)	3 (7)	0.1
CABG + valvular repair	7 (8)	0 (0)	7 (17)	**0.005**
Great vessel repair	11 (13)	6 (14)	5 (12)	1.0
LVAD/device placement	4 (5)	2 (5)	2 (5)	1.0
ECMO cannulation	2 (2)	2 (5)	0 (0)	0.5
Non-cardiac	28 (35)	27 (64)	1 (2)	**< 0.001**
Thoracic	4 (5)	3 (7)	1 (2)	
Neuro	2 (2)	2 (5)	0 (0)	
General	1 (1)	1 (2)	0 (0)	
N/A	21 (25)	21 (50)	0 (0)	
Reason for cEEG – no. (%)				
Witnessed event suspicious for seizure*	39 (47)	17 (40)	22 (54)	0.3
Unexplained encephalopathy**	32 (39)	16 (38)	16 (39)	1.0
Other***	12 (14)	9 (21)	3 (7)	0.1

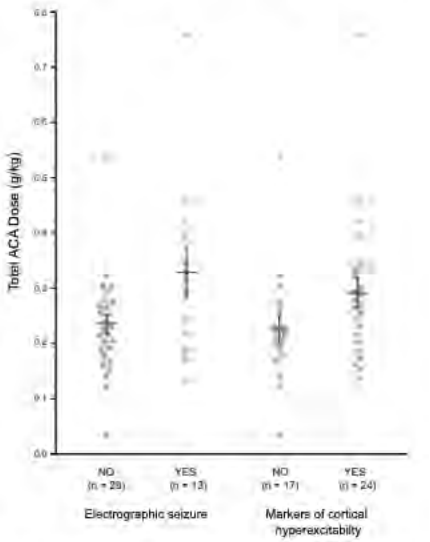
Percentages reported are proportion of total number of patients in group. *Witnessed event suspicious for seizure defined as clinically witnessed convulsion, twitching, and abnormal, involuntary body movement. **Unexplained encephalopathy defined as clinically witnessed altered mental status, unresponsiveness, aphasia, weakness, and dysconjugate gaze. ***Other defined as prognostication status post pulseless electrical activity (PEA) arrest, prognostication status post cardiac arrest, safety of discontinuation of automated external defibrillator (AED), and subarachnoid hemorrhage (SAH) management. Abbreviations: ACA: aminocaproic acid; AF: antifibrinolytics; CABG, coronary artery bypass surgery; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; N/A, not applicable.

Table 2. Electrographic findings among patients undergoing cEEG monitoring

	Total (n = 83)	Non-AF (n = 42)	ACA (n = 41)	P
Electrographic seizure (any type) – no. (%)	16 (19)	3 (7)	13 (32)	**0.006**
Subclinical seizure	12 (14)	3 (7)	9 (22)	0.07
Status epilepticus (any type)	4 (5)	0 (0)	4 (10)	0.06
Subclinical status	3 (4)	0 (0)	3 (7)	0.1
Onset location – no. (%)				
Generalized/non-localizing	5 (6)	0 (0)	5 (12)	**0.03**
Focal	3 (4)	1 (2)	2 (5)	0.6
Unknown/undocumented	9 (11)	2 (5)	7 (17)	0.09
Epileptiform and/or periodic discharges – no. (%)	39 (47)	15 (36)	24 (59)	**0.0486**
Sporadic (sharp waves, spikes)	37 (45)	15 (36)	22 (54)	0.1
Periodic discharges	9 (11)	4 (10)	5 (12)	0.7
Lateralized (LPDs)	5 (6)	2 (5)	3 (7)	0.7
Generalized (GPDs)	4 (5)	2 (5)	2 (5)	1.0
Bilateral independent (BIPDs)	2 (2)	0 (0)	2 (5)	0.2

Subclinical seizure defined as electrographic seizures not associated with witnessed evidence of convulsions or rhythmic motor activity. Epileptiform discharges defined as generalized spike-and-wave complexes, lateralized spike-and-wave complexes, bilateral independent spike-and-wave complexes, multifocal spike-and-wave complexes, and triphasic waves. Periodic discharges defined as generalized periodic discharges, lateralized periodic discharges, and bilateral independent discharges. Abbreviations: ACA, aminocaproic acid; AF, antifibrinolytics.

Figure 2. Effect of aminocaproic acid dose on electrographic seizure and markers of cortical hyperexcitability



Dots represent individual patients with weight-normalized aminocaproid acid dose. Crosshairs represent mean and standard error. Markers of cortical hyperexcitability include sporadic discharges, generalized spike-and-wave complexes, lateralized spike-and-wave complexes, bilateral independent spike-and-wave complexes, multifocal spike-and-wave complexes, triphasic waves, generalized periodic discharges, lateralized periodic discharges, and bilateral independent discharges. Abbreviations: ACA, aminocaproic acid; g, gram; kg, kilogram.

Table 3. Risk factors associated with electrographic seizure on cEEG monitoring

	Total (n = 83)	Electrographic Seizure (n = 16)	No Electrographic Seizure (n = 67)	P
Baseline characteristics				
Age ≥ 65	52 (63)	14 (88)	38 (57)	**0.02**
Female gender	34 (41)	9 (56)	25 (37)	0.26
History of epilepsy	3 (4)	0 (0)	3 (4)	1.0
Clinical course				
Cardiothoracic surgery	59 (71)	15 (94)	44 (66)	**0.03**
Cardiopulmonary bypass	44 (53)	15 (94)	29 (43)	**0.0002**
Induced circulatory arrest	6 (7)	2 (13)	4 (6)	0.3
ACA use	41 (49)	13 (81)	28 (42)	**0.006**
Reason for monitoring				
Witnessed event suspicious for seizure	39 (47)	13 (81)	26 (39)	**0.004**
Unexplained encephalopathy	32 (39)	3 (19)	29 (43)	0.09
Other	12 (14)	0 (0)	12 (18)	0.1
In-hospital Diagnoses				
Acute renal injury	39 (47)	8 (50)	31 (46)	0.8
Acute hepatic failure	6 (7)	1 (6)	5 (7)	1.0
Acute myocardial infarction	9 (11)	1 (6)	8 (12)	1.0
Acute neurologic injury*	47 (57)	12 (75)	25 (37)	**0.01**
Lab Values				
Peak AST (U/L), mean	672.8	495.5	718.5	0.5
Peak AST (U/L), median	167.5	184	152	0.9
Peak ALT (U/L), mean	414.2	236.6	460.0	0.3
Peak ALT (U/L), median	81.5	119.5	76	0.6
Peak Creatinine (mg/dL), mean	2.5	2.1	2.7	0.2
Peak Creatinine (mg/dL), median	1.8	1.5	1.8	0.3
Markers of cortical Hyperexcitability				
Epileptiform and/or periodic discharges	39 (47)	15 (94)	24 (36)	**< 0.001**
Sporadic discharges	32 (39)	14 (88)	18 (27)	**< 0.001**
Periodic discharges	9 (11)	2 (13)	7 (10)	1.0
Lateralized (LPDs)	5 (6)	1 (6)	4 (6)	1.0
Generalized (GPDs)	4 (5)	0 (0)	4 (6)	1.0
Bilateral independent (BiPDs)	2 (2)	1 (6)	1 (1)	0.3

*Acute brain injury was determined by review of neuroimaging reports and is defined as cerebral infarcts, intracerebral brain hemorrhage, restriction diffusion, stroke, posterior reversible encephalopathy syndrome (PRES), air emboli, ischemia, diffuse loss of cerebral gray-white differentiation, severe global anoxic brain injury, hypodensities, and aneurysm. Epileptiform discharges defined as generalized spike-and-wave complexes, lateralized spike-and-wave complexes, bilateral independent spike-and-wave complexes, multifocal spike-and-wave complexes, and triphasic waves. Periodic discharges defined as generalized periodic discharges, lateralized periodic discharges, and bilateral independent discharges. Abbreviations: ACA, aminocaproic acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; dL, deciliter; mg, milligram; L, liter; U, units.

Neuroscience in Anesthesiology and Perioperative Medicine - 21 Frontal Electrocortical Activity and Respiratory Dynamics After Administration of Fentanyl in Humans

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Introduction: Opioid drugs are double-edged swords in medicine: They are an essential tool for pain management, yet their side effects are profound, difficult to manage, and potentially deadly [1,2]. Although it is well-known that opioid drugs influence multiple brain circuits to produce analgesia as well as its side effects[3,4], we are unable to directly measure how opioid drugs affect the brain in a clinical setting[5]. Here describe the results of a human study in which patients were administered increasing doses of fentanyl prior to induction of general anesthesia for surgery while measuring EEG, respiration, and reaction time in response to an auditory task. We report here a noninvasive EEG-based brain biomarker that is highly correlated with opioid predicted effect site concentration (ESC) and with opioid induced respiratory depression.

Methods: The protocol consisted of recording EEG, respiratory inductance plethysmography (RIP) and sedation state during administration of fentanyl prior to induction of general anesthesia. We administered fentanyl gradually over a 4-minute period in doses of 2 µg/Kg of ideal body weight (IBW) every 2 minutes with a maximum dose of 6 µg/Kg IBW according to patient tolerance and level of consciousness. Subjects were administered oxygen and vital signs were closely monitored by the research anesthesiologist, keeping oxygen saturation above 95%. We collected data from a 4-channel SEDLine® frontal EEG sensor. RIP was measured using inductive elastic bands placed across each subject's chest and abdomen. The data from the RIP sensor was captured using a Neuroelectrics® NIC2 device. The auditory behavioral task was administered using a computer-driven script. The subjects were asked to listen to a series of sounds played every 4 seconds, and to respond via button press to identify the sound as either a train of clicks, or verbal stimuli. Auditory stimuli were delivered using Etymotic® ER-3C earphones. Button presses were recorded using a computer mouse strapped to the subject's hand. To analyze changes in respiration, we used a neural oscillator state-space model to estimate instantaneous time-varying respiratory amplitudes and frequencies, and derived an expression for an instantaneous minute ventilation index (MVI) based on those values. We estimated fentanyl effect site concentrations (ESC) using Stanpump in R. We analyzed relationships between the EEG and fentanyl ESC, MVI, and reaction time (RT) using mixed-effects models. We calculated the time lag between decreases in MVI and increases in RT using cross correlation and the bootstrap, and estimated the relative potency of fentanyl for respiratory depression compared to sedation based on these time lags.

Results: We completed 25 data sets out of 31 subjects enrolled. From these participants 13 were female (52%), with a mean age of 54.4 years (range: 31 - 64 years) and a mean weight of 78.76 Kg (SD = 22.6). The mixed-effects analyses showed a strong positive association between EEG theta power and fentanyl ESC (Slope: 0.55 (0.25, 0.86), Marginal R^2 = 0.151, Conditional R^2 = 0.744; Fig. 1D) and a strong negative association between EEG theta power and MVI (Fig 2; Slope: -1.62 (-2.51, -0.73), Marginal R^2 = 0.054, Conditional R^2 = 0.248).The mean lag between changes in MVI and RT was 277 seconds (95% CI: 219.5 sec. - 332.5 sec)(Fig. 3 A and B). We also observed that MVI would decline by 51.4% (95% CI: 30.9 – 80.4 %) before noticeable increases in reaction time occurred (Fig. 3C). Finally, we estimated that the predicted ESC of fentanyl needed to induce a 10% drop in the MVI is roughly 1750-fold lower than the concentration present upon RT changes (95% CI: 839-2854-fold) (Fig. 3D).

Conclusion: The specific EEG signature of fentanyl we describe here and its unique associations with respiration, sedation, and unconsciousness have not, to our knowledge, been previously reported. We found that respiratory decline induced by fentanyl far outpaces any behavioral change, suggesting that in non-medical settings, fentanyl would induce apnea before any behavioral effects, and would be dangerous in any quantity. This novel biomarker of fentanyl drug effect could provide real-time feedback to enable opioid titration in the operating room, post-anesthesia care unit, intensive care unit and beyond.

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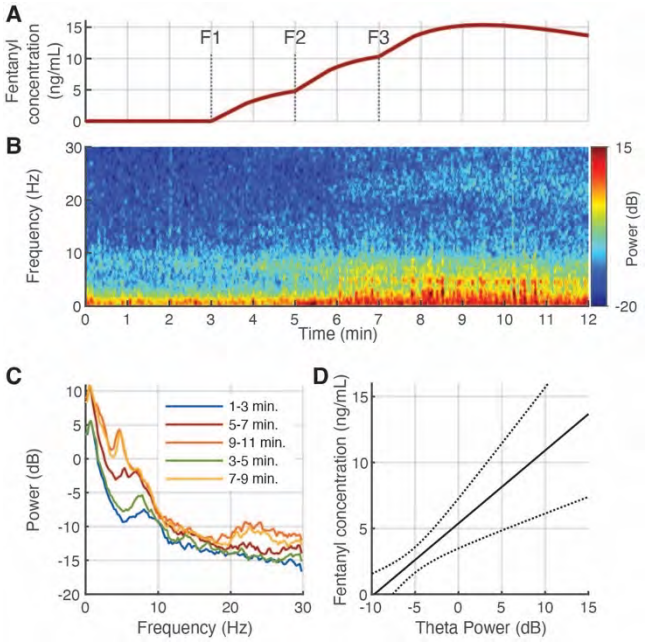

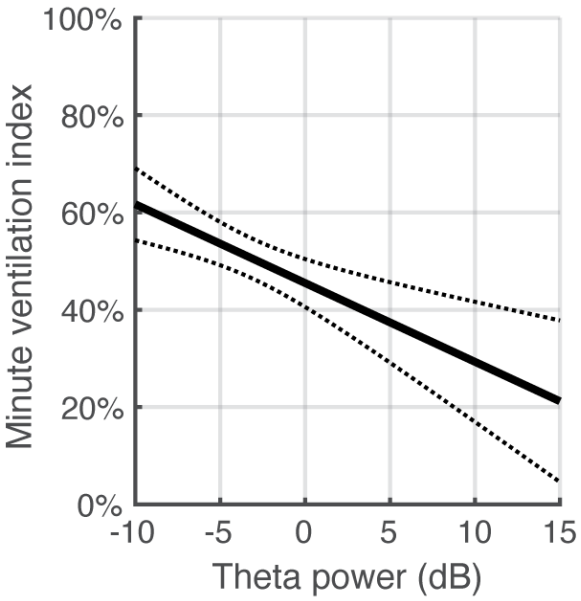

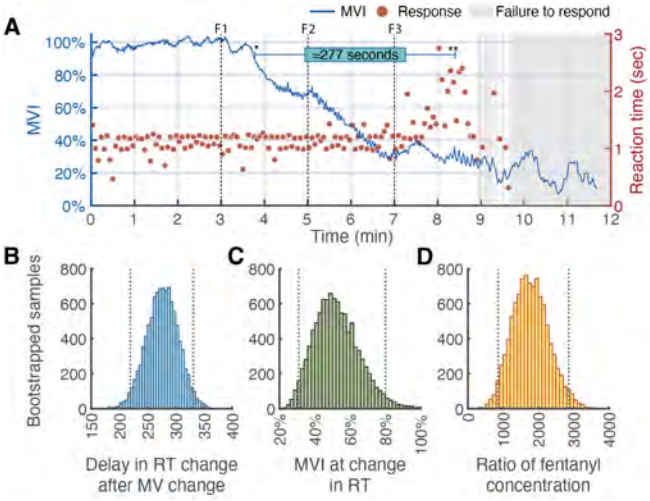

Neuroscience in Anesthesiology and Perioperative Medicine - 22 A genetic variant causing alcohol intolerance leads to impaired recovery from propofol-induced general anesthesia in rodents

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Introduction: Alcohol has a major impact on an individual's sensitivity to general anesthetics. Chronic alcoholics require higher doses of general anesthetic agents, whereas acute intoxication increases sensitivity to anesthetics1. Over half a billion people are alcohol intolerant due to a genetic variant in the mitochondrial enzyme, aldehyde dehydrogenase 2 (ALDH2*2)2. This alcohol intolerance is due to the ALDH2*2 inactivating variant limiting the metabolism of the product of alcohol, acetaldehyde to acetic acid. However, little is known whether an intolerance to alcohol will alter general anesthetic sensitivity. Here we hypothesize that an inactivating genetic variant in ALDH2, known as ALDH2*2, will delay recovery from general anesthesia due to an alteration in the redox state at the mitochondria.

Methods: ALDH2*2 knock-in mice are heterozygous for targeted insertion of the inactivating human ALDH2 point mutation into the native ALDH2 locus on a C57/BL6 background, which mimics the human phenotype3. Wild-type (WT) ALDH2 and ALDH2*2 male and female 12-18 week old mice were pair-wise placed in individual cages on heating pads. Baseline activity was recorded for 15 minutes followed by induction of general anesthesia by either propofol (200mg/kg, intraperitoneal) or 1.5% isoflurane in room air for 40 minutes. Open field activity was analyzed with Biobserve software by a blinded observer as an objective measure of recovery from general anesthesia. Primary astrocytes were cultured from the cerebellum of adult mice to assess mitochondrial function. The basal respiration, ATP-linked respiration, maximal and reserve capacities and non-mitochondrial respiration were measured using the Seahorse XF96 (Agilent). WT ALDH2 and ALDH2*2 primary astrocytes were incubated with 10 μM propofol for 60 minutes and cells were washed 3 times with assay medium prior to the assay. Liver homogenates from WT and ALDH2*2 mice and ALDH2 recombinant protein were used to quantify ALDH activity at baseline and in the presence of propofol or isoflurane. A two-way ANOVA with Bonferroni correction was used for multiple comparisons between WT and ALDH2*2 with statistical significance defined as p-value <0.05.

Results: Representative open-field tracking images of WT ALDH2 and ALDH2*2 mice from the first 2.5 minutes following the return of the righting reflex (RR) from propofol-induced (Fig A) and isoflurane (Fig B) general anesthesia are shown. There was no significant difference between the two groups in the time to loss of RR (WT 177±17sec; ALDH2*2 234±22sec, n=8/group) or the duration of general anesthesia (WT 57±10min; ALDH2*2 75±15min, n=8/group). Importantly, there was a significant decrease in activity following the return of the RR in the ALDH2*2 compared to WT mice (Fig A, 53±7% vs 26±4%, respectively, n=8/group, p=0.03) that was specific to propofol. There was no significant difference in activity between WT and ALDH2*2 following emergence from isoflurane anesthesia (Fig B). At baseline, there was decreased ALDH2 activity from the liver of ALDH2*2 mice compared to WT ALDH2 mice (Fig E, 14.51±1.0, n=6 vs 26.4±1.8, n=4 [NADH] μM/μg/min, respectively, p=0.01). Isoflurane increased ALDH2 activity in WT recombinant protein (Fig D), as opposed to propofol which did not alter ALDH2 activity. Baseline cerebellar mitochondrial respiration was not different between WT and ALDH2*2, however, there was an increase in reserve capacity with and without propofol in the mitochondria of ALDH2*2 astrocytes (Fig E).

Conclusion: The ALDH2*2 genetic variant mice have delayed recovery from propofol-induced general anesthesia without altering emergence from isoflurane. Our results suggest that the mitochondrial activity of ALDH2 may impact the bioenergetic profile in the brain following general anesthesia. As isoflurane induces ALDH2 activity, this increased activity may compensate for the reduced activity of ALDH2*2, however this does not occur with propofol. Future work will delineate the differential bioenergetic profiles with

altered aldehyde metabolism following post-operative recovery from isoflurane and propofol. In addition to mechanistic insights underlying general anesthetics, this work offers an opportunity to implement precision anesthetics for the growing East Asian population. Understanding the neurobiological effects of general anesthesia in ALDH2*2 variant patients will improve anesthetic management and unlock potential targets to accelerate recovery from general anesthesia.

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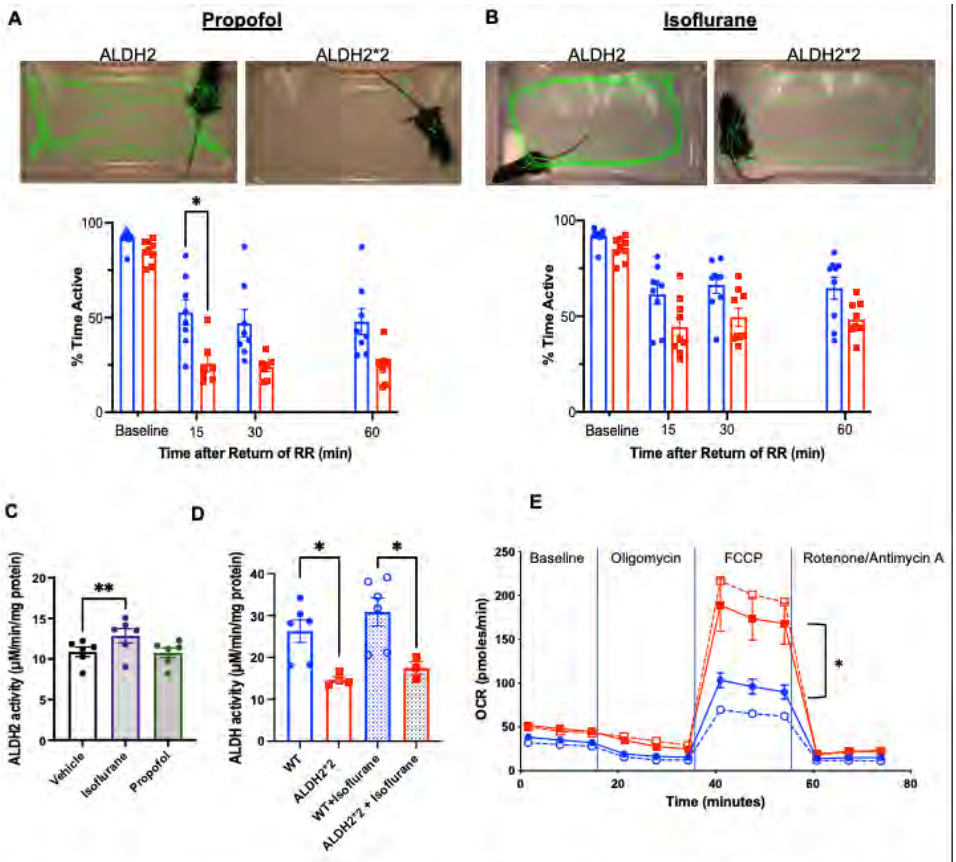

Figure. (A-B) Representative mouse tracking image for the first 2.5 minutes following return of the righting reflex (RR) after 200mg/kg intraperitoneal propofol (A) and 40 minutes 1.5% isoflurane (B) in WT (left) and ALDH2*2 mice (right). The percent time active in the one hour following return of the RR after propofol (A) and isoflurane (B) in WT (blue) and ALDH2*2 (red). (C) Quantification of ALDH2 activity from WT recombinant ALDH2 protein in the presence of DMSO vehicle (black), isoflurane (purple), and propofol (green). (D) ALDH activity at baseline in WT (blue, closed circles) and ALDH2*2 (red, closed squares) liver homogenates and in 1mM isoflurane in WT (blue, open circles) and ALDH2*2 (red, open squares). (E) Oxygen consumption rate (OCR) in primary cerebellar astrocytes in WT (solid, blue) and ALDH2*2 (solid, red) and following administration of 2µM oligomycin (ATP-linked respiration), 2µM FCCP (maximal respiration), and 0.5µM rotenone/antimycin A (non-mitochondrial). OCR following incubation for one hour in 10µM propofol in WT (dotted blue) and ALDH2*2 (dotted red). *p<0.05 WT vs ALDH2*2, **p<0.05 vehicle vs isoflurane.

Neuroscience in Anesthesiology and Perioperative Medicine - 23 Effect of deep versus light general anesthesia on postoperative pain and cognitive function: a meta-analysis with trial sequential analysis of randomized controlled trials

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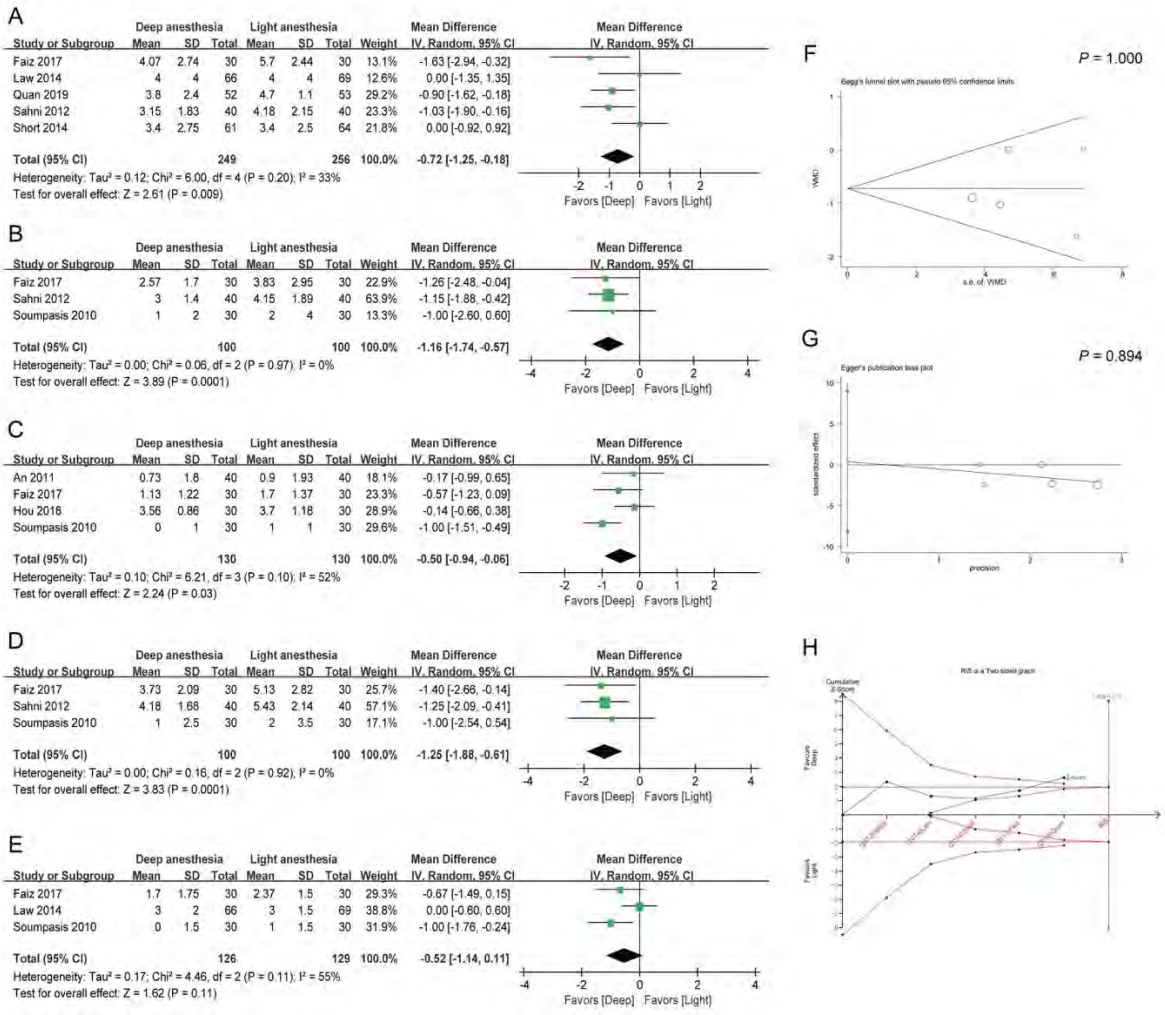
Introduction: The association between the depth of general anesthesia and postoperative outcomes remains controversial. This meta-analysis was conducted to determine the effects of deep vs. light anesthesia on postoperative pain, cognitive function, recovery from anesthesia, and postoperative complications (1-4).

Methods: Methods: PubMed, EMBASE, and Cochrane library databases were searched until February 20, 2021 for eligible randomized controlled trials. The co-primary outcomes were postoperative visual analog scale (VAS, 0-10) pain scores and the incidence of postoperative cognition dysfunction (POCD). Meta-analyses were performed using a random-effect model. Publication bias was assessed using Egger's and Begg's tests. Trial sequential analysis (TSA) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) were utilized to assess the reliability and level of evidence.

Results: Results: A total of 23 trials with 10262 patients were included. Deep anesthesia was associated with lower VAS pain scores at rest within 1 hour postoperatively (weighted mean difference = -0.72 points, 95%CI = -1.25 to -0.18 points, P = 0.009, I2 = 33%) and at 8 and 24 hours postoperatively, as well as on movement at 8 hours postoperatively. The incidence of POCD during 1-7 days (risk ratio = 1.37, 95%CI = 0.82 to 2.28, P = 0.23, I2 = 65%) or 1-3 months postoperatively did not differ between the two groups. No publication bias was detected. The TSA suggested sufficient evidence for VAS pain scores, but not for the incidence of POCD. The GRADE level of evidence was rated as moderate to low for the primary outcomes. In addition, deep anesthesia was associated a delayed recovery profile, without affecting postoperative complications or 1-year mortality.

Conclusion: Conclusion: Deep anesthesia was associated with reduced postoperative pain during the first 24 hours after surgery. The depth of general anesthesia itself may not influence cognitive function, postoperative complications, or long-term mortality.

References: J Clin Anesth 2018; 45:55-59. PLoS ONE 2020; 15(2). Minerva Anestesiol 2020; 86(9):965-973. Lancet 2019; 394(10212):1907-1914.


A
Deep anesthesia
Light anesthesia
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Faiz 2017 4.07 2.74 30 5.7 2.44 30 13.1% -1.63 [-2.94, -0.32]
Law 2014 4 4 66 4 4 69 12.6% 0.00 [-1.35, 1.35]
Quan 2019 3.8 2.4 52 4.7 1.1 53 29.2% -0.90 [-1.62, -0.18]
Sahni 2012 3.15 1.83 40 4.18 2.15 40 23.3% -1.03 [-1.90, -0.16]
Short 2014 3.4 2.75 61 3.4 2.5 64 21.8% 0.00 [-0.92, 0.92]
Total (95% CI) 249 256 100.0% -0.72 [-1.25, -0.18]
Heterogeneity: Tau² = 0.12; Chi² = 6.00, df = 4 (P = 0.20); I² = 33%
Test for overall effect: Z = 2.61 (P = 0.009)
-2 -1 0 1 2
Favors [Deep] Favors [Light]
B
Deep anesthesia
Light anesthesia
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Faiz 2017 2.57 1.7 30 3.83 2.95 30 22.9% -1.26 [-2.48, -0.04]
Sahni 2012 3 1.4 40 4.15 1.89 40 63.9% -1.15 [-1.88, -0.42]
Soumpasis 2010 1 2 30 2 4 30 13.3% -1.00 [-2.60, 0.60]
Total (95% CI) 100 100 100.0% -1.16 [-1.74, -0.57]
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 2 (P = 0.97); I² = 0%
Test for overall effect: Z = 3.89 (P = 0.0001)
-4 -2 0 2 4
Favors [Deep] Favors [Light]
C
Deep anesthesia
Light anesthesia
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
An 2011 0.73 1.8 40 0.9 1.93 40 18.1% -0.17 [-0.99, 0.65]
Faiz 2017 1.13 1.22 30 1.7 1.37 30 23.3% -0.57 [-1.23, 0.09]
Hou 2018 3.56 0.86 30 3.7 1.18 30 28.9% -0.14 [-0.66, 0.38]
Soumpasis 2010 0 1 30 1 1 30 29.6% -1.00 [-1.51, -0.49]
Total (95% CI) 130 130 100.0% -0.50 [-0.94, -0.06]
Heterogeneity: Tau² = 0.10; Chi² = 6.21, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 2.24 (P = 0.03)
-2 -1 0 1 2
Favors [Deep] Favors [Light]
D
Deep anesthesia
Light anesthesia
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Faiz 2017 3.73 2.09 30 5.13 2.82 30 25.7% -1.40 [-2.66, -0.14]
Sahni 2012 4.18 1.68 40 5.43 2.14 40 57.1% -1.25 [-2.09, -0.41]
Soumpasis 2010 1 2.5 30 2 3.5 30 17.1% -1.00 [-2.54, 0.54]
Total (95% CI) 100 100 100.0% -1.25 [-1.88, -0.61]
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 2 (P = 0.92); I² = 0%
Test for overall effect: Z = 3.83 (P = 0.0001)
-4 -2 0 2 4
Favors [Deep] Favors [Light]
E
Deep anesthesia
Light anesthesia
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Faiz 2017 1.7 1.75 30 2.37 1.5 30 29.3% -0.67 [-1.49, 0.15]
Law 2014 3 2 66 3 1.5 69 38.8% 0.00 [-0.60, 0.60]
Soumpasis 2010 0 1.5 30 1 1.5 30 31.9% -1.00 [-1.76, -0.24]
Total (95% CI) 126 129 100.0% -0.52 [-1.14, 0.11]
Heterogeneity: Tau² = 0.17; Chi² = 4.46, df = 2 (P = 0.11); I² = 55%
Test for overall effect: Z = 1.62 (P = 0.11)
-4 -2 0 2 4
Favors [Deep] Favors [Light]
F
P = 1.000
Begg's funnel plot with pseudo 95% confidence limits
(WMD)
s.e. of WMD
G
P = 0.894
Egger's publication bias plot
standardized effect
precision
H
RIS of a Two-sided graph
Cumulative Z-Score
Favors Deep
Favors Light

Neuroscience in Anesthesiology and Perioperative Medicine - 24 Gut microbiota is critical for postoperative delirium in mice

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Introduction: Postoperative delirium (POD) occurs in 9-50% older patients undergoing surgery and anesthesia, leading to worse clinical outcomes. Emerging evidence supports a role of gut microbiota in the pathogenesis of POD. Gut microbiota is composed a diverse consortium of microorganisms residing in the gastrointestinal tract with signature metabolites released to the blood stream. Interrogating these metabolites provides great opportunities in capturing microbiota-related changes which lead to mechanistic insights into the host-microbiota interactions.

Methods: We collect blood sample from mice with and without POD, and conducted targeted metabolites profiling using a panel of ~500 molecules. Using rigourous analytic pipeline including random forest-based machine learning algorithm, key features of metabolomic changes were extracted. These key features were then calidated in human blood samples from patients with POD or without POD.

Results: Using an experimental paradigm to induce POD, we were able to collect blood samples from mice with POD and samples from mice without POD. These samples were analyzed using targeted metabolomic study to identify key differences between these two groups. Using a 3-fold change and t test p value of 0.01 as cutoff, several metabolites were associated with POD status.

To validate these metabolites, we collected human samples from patients who underwent orthopedic surgeries. One gut microbiota associated metabolite was found to be statistically different betweeen patients with and those without POD.

Conclusion: Metabolomic tools (LC-MS/MS) provide efficient high throughput identification of a large number of metabolites which could be used for phenotypical analysis of preclinical and clinical samples. Using these tools, we identified a gut microbiota derived molecule that was associated with POD development in both mice and humans.

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Neuroscience in Anesthesiology and Perioperative Medicine - 25 Reactive astrocytes contribute to post surgical cognitive decline via release of Complement C3 in young WT mouse.

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Introduction: Functioning astrocytes are crucial in the CNS and are involved in neuroinflammation but can become pathologically reactive and contribute to cognitive deficits by releasing complement factors[1]. Complement C3 is an essential component for the complement pathway and its excessive levels in adult brains correlates with cognitive dysfunction in neurodegenerative diseases. However, whether reactive astrocytes and C3 contribute to post-operative cognitive decline remains unknown. Here, we investigate the role of reactive astrocytes and complement C3 in post-operative cognitive decline using a murine WT mouse surgical model.

Methods: Adult male C57BL/6N mice were subjected a laparotomy under sevoflurane anesthesia. Novel objective recognition and forced Y-maze tests were used to assess cognitive function. Expression of cytokines and activation of astrocyte in the hippocampus were evaluated by immunofluorescent staining and RT-PCR. Astrocytes from post-surgical hippocampi samples were extracted and purified by FACS, followed by RNA-seq. Cerebral C3 was knocked down by administration of AAV9-C3shRNA in the lateral ventricle

Results: We showed a significant decline in postoperative cognitive performance, along with increase in neuroinflammatory markers as well as A1 reactive astrocyte. Furthermore, astrocytes extracted from post-operative hippocampal samples were subjected to transcriptomal profiling. The enrichment of KEGG pathway analysis indicated complement system is elevated by surgical stimuli and C3 is the central molecule in the complement activation. Finally, cerebral C3 knocked down by AAV9-C3shRNA was able to alleviate post-operative cognitive impairment.

Conclusion: Our study demonstrated that surgery induced increase of reactive astrocyte and its C3 are associated with cognitive deficits, which could be alleviated by knockdown of C3. It indicates the potential of C3 to be one of therapeutic target of for post-operative cognitive decline.

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Neuroscience in Anesthesiology and Perioperative Medicine - 26 Altered complexity and network integration during anesthesia and sleep

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Introduction: We seek to understand the neural correlates of loss and recovery of consciousness by exploring common mechanisms during anesthesia and sleep [0]. Leading theories of consciousness predict that loss of consciousness (LOC) during anesthesia and sleep is precipitated by reorganization of brain networks critical for consciousness [1]. We used an analysis of resting state functional connectivity called diffusion map embedding (DME; [2]) to identify these organizational changes. DME maps data into a space in which distance represents similarity in connectivity to the rest of the sampled network, and has been used previously to demonstrate the hierarchical structure of cortical networks [3] and to track changes in that structure in response to treatments, disorders, and aging [4]. We investigated changes in cortical networks across arousal state using DME applied to functional connectivity derived from resting state intracranial electroencephalography (iEEG) recordings in neurosurgical patients.

Methods: Resting state intracranial recordings were obtained during induction of propofol anesthesia or during sleep from adult neurosurgical patients implanted with electrodes (propofol: n = 15 total; sleep: n = 13 total) in temporal, parietal, and frontal cortex to identify epileptic foci. Three arousal states were compared during anesthesia [pre-drug wake (WA), sedated/responsive (S) and unresponsive (U), determined by OAA/S] and five in sleep [wake (WS), N1, N2, N3, and REM, determined by standard polysomnography]. During pre-processing, channels in the white matter or seizure foci were excluded, and artifact rejection used to excluded interictal spikes. Channel-by-channel adjacency matrices were computed as pairwise gamma (30-70Hz) orthogonalized power envelope correlations [5]. Adjacency matrices were thresholded (top 33%) and normalized to yield the transition probability matrix P, which was analyzed using DME. The eigenvalue spectrum of P ($|\lambda_i|$) was used to calculate effective dimensionality (estimated as the quadratic entropy: $(\Sigma \lambda_i)^2/(\Sigma \lambda_i^2)$), a measure of network redundancy. Pairwise distances in the embedding space, a measure of network integration, were calculated and compared across states.

Results: Embeddings in states involving reduced consciousness (U, N2, N3) had lower mean effective dimensionality but higher variability over time compared to corresponding states (S/WA and N1/WS). REM sleep had similar effective dimensionality to WS. The increased variability in U, N2 , and N3 was especially evident when the time resolution of the analysis was increased (using 10-sec rather than 60-sec data segments). In this case, some data segments exhibited 'wake-like' effective dimensionality while others had reduced values, suggesting fluctuating arousal or awareness states. No individual brain region was responsible for these changes, suggesting a global rather than centralized functional reorganization with LOC. However, specific inter-ROI embedding distances (PFC-auditory cortex; PFC-limbic) increased in U compared to WA/S, and in N2/N3 compared to WS/N1/REM, consistent with reduced network integration upon LOC.

Conclusion: Decreases in effective dimensionality reflect decreased network complexity (increased redundancy) associated with states of reduced levels of arousal and awareness (U, N2, N3). Increased variability may reflect behavioral state changes between dreaming (disconnected consciousness) and unconsciousness. Increases in inter-ROI distances in these states reflect impaired integration and information sharing that may be critical to normal waking consciousness.

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Neuroscience in Anesthesiology and Perioperative Medicine - 27 Propofol Modulates the Stemness and Migration of Cancer Stem Cells Derived from Lung Tumor-Derived Brain Metastases and their Interaction with Glial Cells

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Introduction: Recent studies demonstrated the effects of anesthesia on tumor progression and patient survival in solid tumors. (1) Various mechanisms have been proposed, including direct effects on tumor cells and indirect effects via activation of the immune system. (2) However, there is less information on anesthetic effects in brain tumor patients. While some reports are conflicting or inconclusive, there is also evidence that propofol is beneficial in certain brain tumors. (3) Brain metastases (BM) are the most common brain tumors in adults and a major cause of cancer morbidity and mortality. Metastatic tumors develop following infiltration of the brain through the blood brain barrier of cells from primary tumors such as lung, breast, melanoma, and colorectal cancers. BM are treated with combination therapies, including surgery, radiotherapy, chemotherapy, and immunotherapy, however the prognosis of patients with BM remains dismal. In this report we investigated the effects of propofol on cancer stem cells derived from human lung cancer brain metastases and crosstalk with microglia.

Methods: In this study we employed cancer stem cells derived from lung tumor-derived brain metastases (BM-CSCs) and analyzed the effects of propofol on the apoptosis, self-renewal, mesenchymal transition, and migration of these cells. Cell apoptosis was determined using LDH assay and caspase 3 activation; expression of mesenchymal transition was analyzed using qRT-PCR mesenchymal and cell migration by a transwell assay. One of the major factors that determine the establishment of new metastases depends on a complex interaction of the tumor and the microenvironment niche. We therefore also analyzed these effects of propofol on cancer stem cell self-renewal and apoptosis in co-culture with human microglia cells. We further examined the effects of propofol on the activation/polarization of microglia in co-culture with CSCs using qRT-PCR.

Results: We found that propofol exerted a dose-dependent inhibitory effect on BM-CSCs self-renewal and proliferation. These effects were already observed at 25 microM propofol. At concentrations higher than 100 microM, propofol exerted a large degree of cell death (Figure). In addition, propofol decreased the expression of the stemness markers SOX2 and Nanog and those of mesenchymal transit, CD44 and ZEB1. At lower concentrations, propofol decreased BM-CSC migration. Co-culturing BM-CSCs with microglia increased the self-renewal and stemness of the CSCs, and propofol treatment abrogated this increase as well. Propofol also promoted the M1 phenotypes of co-cultured microglial cells and decreased the expression of TGF-beta, while increasing that of IL-1 beta.

Conclusion: Propofol exerted anti-tumor effects on BM-CSCs ranging from inhibition of cell renewal, proliferation, mesenchymal transition, and cell death. In addition, propofol abrogated the pro-tumor interaction of BM-CSCs and microglia. Inhibition of stemness and mesenchymal transit decreases the oncogenic phenotypes of the CSCs and is expected to inhibit tumor progression. The activation of microglia M1 phenotype promotes anti-tumor effects via activation of the immune system and by inhibiting tumor growth. The propofol effects we observed were obtained in a range of concentrations suggesting that its effects could be exploited as a GA of choice during tumor resection. Further studies are planned using tumor xenografts in mice to explore if propofol (in the correct dosage and interval) could be effective as an anti-tumor agent in sub-anesthetic doses, either alone or in combination with radiation or other treatments.

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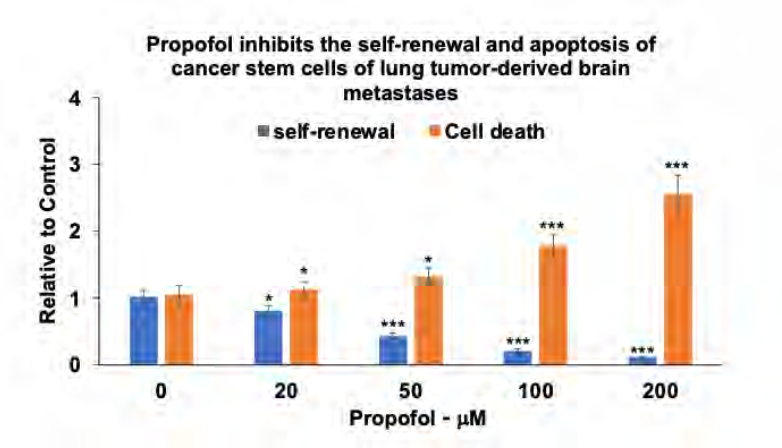

Neuroscience in Anesthesiology and Perioperative Medicine - 28 Exposure to Preeclampsia In Utero Leads to Cerebrovascular Dysfunction in Offspring

Emmett Whitaker[1], Abbie Johnson[1], Sarah Tremble[1], Marilyn Cipolla[1]

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Introduction: Preeclampsia (PE) is a devastating hypertensive disorder that affects 5-10% of pregnancies worldwide. [1] Aside from its acute effects during pregnancy, PE is known to have long-term effects on both the mother and baby. [3-5] While considerable research has focused on the maternal brain in PE, relatively little is known about how preeclampsia affects offspring, particularly with respect to cerebrovascular function and brain perfusion. In addition, though it is known that the cerebrovasculature matures over time in the developing brain, the effect of PE on cerebrovascular maturation is not known. The purpose of this study was to determine if in utero exposure to experimental PE (ePE) would lead to abnormal cerebrovascular maturation and if this would be associated with impaired cerebral blood flow autoregulation (CBFAR) in juvenile and/or adult offspring.

Methods: To induce ePE, pregnant rats were fed a high-cholesterol diet from day 7 - day 20 of a 22 day gestation. Mothers were maintained on the high cholesterol diet until offspring were weaned. Offspring from ePE and normal pregnant (NP) rats were studied at p30 (postnatal day 30, approximating a 2-year-old child; n=9-11/group) or at 18-22 weeks of age (adult; n=5-7/group). To assess CBFAR, offspring were anesthetized with 3% isoflurane in oxygen, intubated, and mechanically ventilated on room air to maintain normoxia and normocarbia. Femoral arterial and venous catheters were placed to measure continuous arterial blood pressure (ABP) and administer compounds. A laser Doppler probe was placed on the skull in the territory of the middle cerebral artery (MCA) to measure relative cerebral blood flow (rCBF). Animals were transitioned to IV chloral hydrate to minimize the effects of vasodilating anesthesia on CBF. Then, ABP was increased in 10 mmHg increments via IV infusion of norepinephrine (NE) to assess the upper range of CBFAR and controlled hemorrhage was used decrease ABP and determine the lower range of CBFAR. Change in CBFAR at each pressure was calculated as % change from baseline. The amount of blood required to cause hypotension was also measured. Continuous recordings of blood pressure and heart rate were measured in separate groups of unanesthetized, freely moving adult rats using radio telemetry.

Results: CBFAR curves were similar between p30 NP and ePE offspring, showing no difference in the upper or lower limits (Figure 1). However, in adult offspring from ePE animals, the upper limit of the CBFAR curve was shifted to the right compared to NP (Figure 1). The rightward shift was found to be significant at 130, 140, and 150 mmHg ($p<0.05$). When compared to p30 offspring, all adult offspring had CBFAR curves that were shifted to the right regardless of PE exposure in utero, demonstrating…. The total volume of hemorrhage required to decrease the blood pressure from baseline to 20 mmHg was significantly higher in the ePE group at p30 (1.44±0.2 vs. 2.25±0.16 mL, $p<0.01$), but not in adult animals (6.43±2.1 vs. 8.15±1.7 mL, $p<0.01$). Average diurnal heart rate (305±3 vs 349±4, $p<0.01$) and nocturnal heart rate (373±7 vs 417±5, $p<0.01$) were significantly higher in adult ePE offspring (Figure 2) without a difference in ABP (data not shown).

Conclusion: Our results showed no difference in CBFAR curves between NP and ePE offspring at a young age of p30. However, we found maturation was associated with a rightward shift in the upper limit of the CBFAR curve in adults from both groups that was more pronounced in offspring from ePE dams. We also found a resistance to hemorrhagic hypotension ePE p30 offspring and persistent tachycardia in adult offspring exposed to ePE, suggesting ePE offspring had enhanced sympathetic tone. Understanding how ePE affects CBFAR in offspring may be important when considering the effect of anesthesia on blood pressure and CBF.

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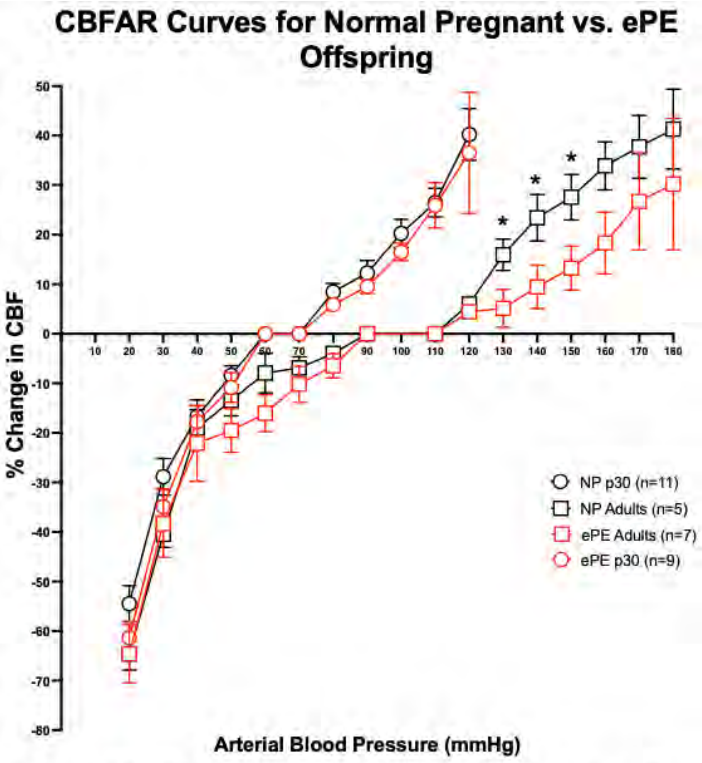

Figure 1. CBFAR curves for p30 (open circles) and adult (open squares) offspring of NP vs. ePE rats. CBFAR in p30 offspring CBFAR curves were found to be similar in both groups. In contrast, the CBFAR curve was shifted to the right in adult animals, and was significantly so at 130, 140, and 150 mmHg. *p<0.05, Student's t-test.

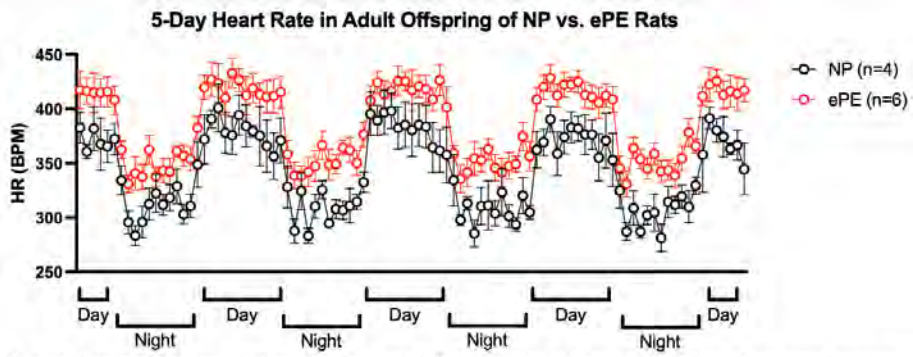

Figure 2. Implanted telemeter data from adult offspring of NP vs. ePE rats. This figure shows 5 days of continuous telemeter data in which each data point represents one hour of averaged data.

Neuroscience in Anesthesiology and Perioperative Medicine - 29 Cathepsin B Knockout Offers Brain Protection in the Mouse Model of Stroke

Bingren Hu[1], Chunli Liu[2], Hiro Teramoto[3], Kurt Hu[4]

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Introduction: The N-ethylmaleimide sensitive fusion protein (NSF) is the sole ATPase for controlling endolysosomal trafficking. Disruption of the endolysosomal trafficking leads to CTSB release and cell death. The objective of this study is to investigate the role of the endolysosomal trafficking and CTSB release in stroke brain injury.

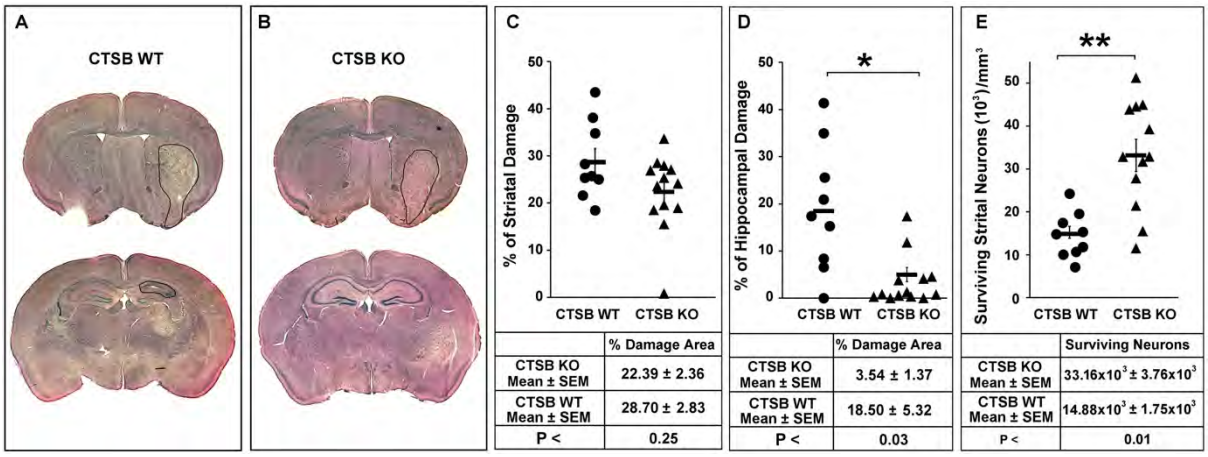
Methods: A total of 72 mice were randomly assigned into four experimental groups: (i) wt sham; (ii) wt stroke; (iii) CTSB knockout (KO) sham; and (iv) CTSB KO stroke. Mice were subjected either to 0 min (sham) or 40 min of middle cerebral artery occlusion (MCAO), followed by 4 and 24 h, and 7 days of reperfusion. After stroke, mice underwent physical and behavioral examinations until the day-7 endpoint.

Confocal microscopy and Western blot analysis were utilized to analyze the levels, redistribution, and co-localization of key marker proteins of the NSF, autophagosome and endosomes, and auto/endolysosomes. Light and electron microscopy were used to examine the histopathology and endolysosomal ultrastructures.

Results: Confocal or electron microscopy showed that, relative to those in sham, NSF was irreversibly depleted, autophagosomal and endolysosomal structures were significantly accumulated, and CTSB was leaked out into extracellular space in post-ischemic penumbral neurons.

Furthermore, CTSB distribution was changed from small puncta to the diffused pattern in the cytoplasm and extracellular space, indicating the CTSB release from post-ischemic neurons. Relative to the wt mice, CTSB knockout (KO) mice showed a significantly smaller hippocampal injury area and more survival neurons in the striatal core (Fig. 1), and a significant improvement in the physical and functional performance (Fig. 2).

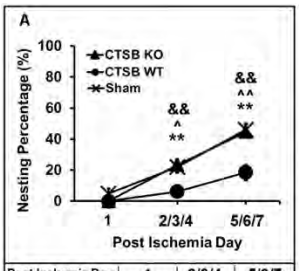
Conclusion: Stroke inactivates NSF, resulting in the disruption of the endocytic and autophagic pathways, endolysosomal structural damage, and the release of CTSB from post-ischemic neurons. CTSB KO mice showed impressive protection against stroke brain injury.



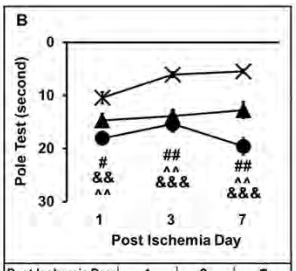
	% Damage Area
CTSB KO Mean ± SEM	22.39 ± 2.36
CTSB WT Mean ± SEM	28.70 ± 2.83
P <	0.25

	% Damage Area
CTSB KO Mean ± SEM	3.54 ± 1.37
CTSB WT Mean ± SEM	18.50 ± 5.32
P <	0.03

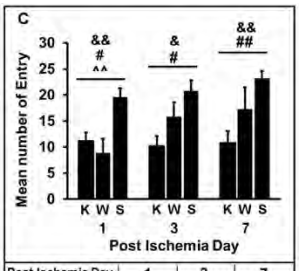
	Surviving Neurons
CTSB KO Mean ± SEM	$33.16 \times 10^3 \pm 3.76 \times 10^3$
CTSB WT Mean ± SEM	$14.88 \times 10^3 \pm 1.75 \times 10^3$
P <	0.01



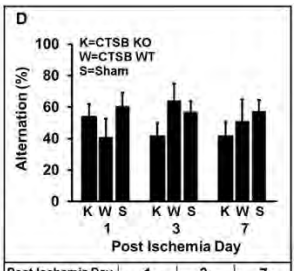
Post Ischemia Day	1	2/3/4	5/6/7
CTSB KO mean±SEM	0.00 ±0.00	23.36 ± 3.80	44.52 ±4.54
CTSB WT mean±SEM	0.00 ±0.00	6.19 ± 2.95	18.43 ± 4.95
Sham mean±SEM	4.80 ± 3.41	22.13 ± 3.86	46.13 ± 3.98
KO vs WT P<		0.01	0.01
KO vs Sham P<		1.00	1.00
WT vs Sham P<		0.02	0.01
KO vs WT vs Sham P<		0.01	0.01



Post Ischemia Day	1	3	7
CTSB KO mean±SEM	14.69 ± 1.23	13.87 ±1.18	12.74 ±1.52
CTSB WT mean±SEM	18.06 ±1.22	15.38 ± 1.48	19.57 ±1.65
Sham mean±SEM	10.45 ± 1.10	6.10 ±0.50	5.45 ± 0.34
KO vs WT P<	0.35	1.00	0.11
KO vs Sham P<	0.03	0.01	0.01
WT vs Sham P<	0.01	0.01	0.01
KO vs WT vs Sham P<	0.01	0.00	0.00



Post Ischemia Day	1	3	7
CTSB KO mean±SEM	11.15 ±1.64	10.15 ±1.99	10.79 ±2.29
CTSB WT mean±SEM	8.88 ± 2.76	15.88 ± 2.75	17.25 ± 4.20
Sham mean±SEM	19.60 ± 1.50	20.80 ± 1.72	23.20 ± 1.40
KO vs WT P<	1.00	0.63	0.25
KO vs Sham P<	0.02	0.02	0.01
WT vs Sham P<	0.01	0.56	0.95
KO vs WT vs Sham P<	0.01	0.02	0.01



Post Ischemia Day	1	3	7
CTSB KO mean±SEM	53.85 ± 8.18	41.31 ± 8.57	41.31 ± 9.63
CTSB WT mean±SEM	40.90 ±11.60	64.07 ±11.02	51.15 ±13.90
Sham mean±SEM	60.65 ± 3.83	57.25 ± 3.06	57.47 ± 6.56
KO vs WT P<	1.00	0.64	1.00
KO vs Sham P<	1.00	1.00	1.00
WT vs Sham P<	1.00	1.00	1.00
KO vs WT vs Sham P<	0.65	0.46	0.62

Neuroscience in Anesthesiology and Perioperative Medicine - 30 Estrous cycle affects emergence latency from dexmedetomidine but not propofol, isoflurane, nor sevoflurane anesthesia in rats

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Introduction: While sex differences in anesthetic sensitivity have been reported in both human and animal studies, little is known about the mechanisms underlying these differences. It has been previously found that female rats show greater delay and variability in return of right reflex (RORR) latency following anesthetic doses of dexmedetomidine [1]. A commonly cited source of female variability is the estrous cycle, the reproductive cycle in rodents analogous to the menstrual cycle in humans. In rats, the cycle repeats every four to six days and includes four stages: proestrus (Pro), estrus (Est), metestrus or early diestrus (Di-I), and late diestrus (Di-II) [2]. During these stages, hormonal fluctuations impart broad physiological and neurochemical changes in the rat. To establish whether the changes associated with the estrous cycle impact sensitivity to commonly used general anesthetic agents, we measured RORR latency, gonadal hormone serum concentration, total body weight, and frontal electroencephalographic (EEG) signatures in female rats under multiple anesthetic agents across each of the four stages. We hypothesized that variability in RORR latency within female rats following general anesthesia is attributable to physiological fluctuations that occur across the estrous cycle.

Methods: Sixteen female Sprague Dawley rats underwent stereotaxic surgery for intracranial EEG electrode placement. After a one-week postoperative recovery period, rats were divided into cohorts that received inhalational anesthesia (N=8) and intravenous anesthesia (N=8). The inhalational cohort was tested under isoflurane (2% for 1 hour, ISO) and sevoflurane (3% for 20 minutes, SEVO). RORR latency was measured as the time taken to flip from a supine to a prone position following their removal from the induction chamber. The intravenous cohort was tested under dexmedetomidine (50 µg/kg, infused over 10 minutes, DEX) and propofol (10 mg/kg, bolus, PROP). RORR latency was measured as the time taken to return to the prone position following the end of drug infusion. All rats were tested under the respective agents once per estrous stage with at least 72 hours between testing sessions. The estrous cycle was tracked by daily vaginal lavage for cytology assessment (Figure 1)[3]. Serum concentration of progesterone and 17β-estradiol was measured by enzyme linked immunosorbent assay (ELISA) from blood collected on each test day. The effect of estrous cycle stage on RORR latency was assessed by repeated measures ANOVA. The association between RORR latency and total weight and serum hormone concentration was tested by linear regression. Power spectral densities measured from frontal EEG electrodes were analyzed across estrous stages by repeated measures ANOVA.

Results: Rat estrous cycle does not affect RORR latency following ISO, SEVO, or PROP (Figure 2A). When in the Di-I stage, rats emerge more rapidly from DEX than when in the Pro or Di-II stage (Fig 2A). Independent of estrous cycle, greater total body weight was associated with longer emergence latencies from PROP and DEX in female rats (Figure 2B). Surprisingly, 17β-estradiol and progesterone serum concentrations were unrelated to RORR latency for the anesthetics tested. Finally, frontal EEG spectral analysis revealed significantly reduced power under DEX anesthesia at both early (30 min, Fig. 2C) and late (90 min, Fig. 2D) time periods when rats were in Di-I compared with Pro and Di-II.

Conclusion: Overall, our data suggest that the effects of the estrous cycle on anesthetic sensitivity are anesthetic-dependent. Importantly, at high doses of dexmedetomidine sufficient to induce loss of righting,

the rat estrous cycle significantly affects both RORR latency and anesthetic depth, but this effect is through an estradiol- and progesterone-independent mechanism. In contrast, sensitivity to isoflurane, sevoflurane, and propofol is not affected by the estrous cycle, though greater total body weight does contribute to prolonged RORR latency for propofol in female rats. By identifying when and how sex-specific biophysiological processes interact with general anesthetics, better guidelines for patient care can be established.

Figure 1

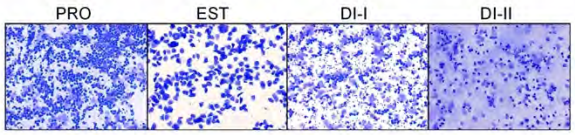
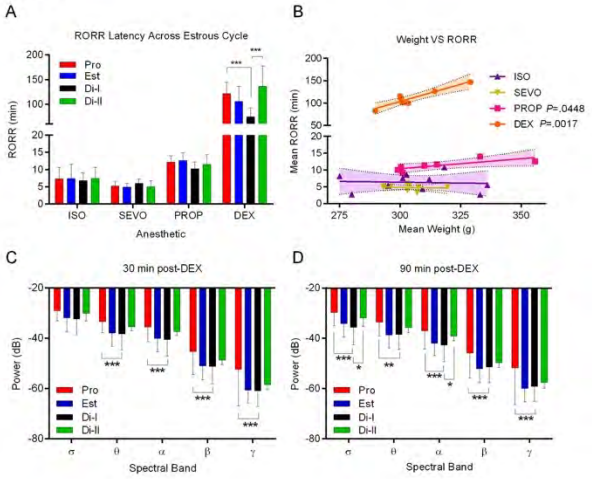


Figure 2



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Neuroscience in Anesthesiology and Perioperative Medicine - 31 Effect of mitochondrial SIRT3 inhibition on mouse brain glucose metabolism

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Introduction: Mitochondrial protein acetylation is controlled by NAD+-dependent class III histone deacetylase SIRT3. Pathologic conditions, including acute brain injury or neurodegenerative disease, lead to depletion of cellular and mitochondrial NAD+ pools. This is reflected in the increased acetylation of mitochondrial proteins. Although the SIRT3 target proteins in mitochondria have been identified, the effect of SIRT3 activity on overall glucose metabolism in the brain remains elusive.

Methods: To examine the effect of mitochondrial protein hyperacetylation on brain glucose metabolism mice were injected with [1,6-13C]glucose and ex vivo 13C-NMR spectroscopy was used to analyze brain tissue samples. Adult, 3 months old C57Bl6 wild type and SIRT3 KO male and female mice were used. The deletion of the SIRT3 gene was confirmed by genotyping and only WT and homozygous SIRT3 KO animals showing complete absence of SIRT3 in brain tissue were used for the experiments. Changes in mitochondrial protein acetylation were determined by western blots using isolated mitochondria from WT and SIRT3 KO brains. After the mice were weighed, they received intraperitoneal injection of [1,6-13C]glucose (543mg/kg) and euthanized by decapitation 15 min post-injection. Brains were removed rapidly and snap-frozen in liquid nitrogen in under 30 seconds. Frozen tissue samples were homogenized in ice-cold 7% perchloric acid (PCA) and extracted. Neutralized samples were lyophilized, and extracts stored at -80 C. The 13C-NMR spectra were obtained on Bruker AVANCE III 950 MHz spectrometer.

Results: The 1H-NMR spectra and amino acid analysis showed no differences in the concentration of lactate, glutamate, alanine, succinate, or aspartate between SIRT3 KO and WT mice. However, glutamine, total creatine (Cr), and GABA were lower in the SIRT3 KO brain. Incorporation of a label from [1,6-13C]glucose metabolism into lactate or alanine was not affected in SIRT3 KO brain. However, the incorporation of the label into all isotopomers of glutamate, glutamine, GABA, and aspartate was lower in the SIRT3 KO brain, reflecting decreased activity of mitochondrial and TCA cycle metabolism in both neurons and astrocytes. The acetylation levels of mitochondrial protein in SIRT3 KO animals were previously confirmed to be three-fold higher when compared to wild type mice

Conclusion: Our data show that hyperacetylation of mitochondrial enzymes due to suppressed SIRT3 activity in the brain of SIRT3 KO mice results in impaired mitochondrial oxidative energy metabolism and neurotransmitter synthesis in the brain. Since the SIRT3 activity is NAD+ dependent, these results might parallel changes in glucose metabolism under pathologic reduction in mitochondrial NAD+ pools. This research was funded by Veteran's Affairs Merit Review Award BX004895 and NIH NINDS R01NS119275 to T.K. and NIH NICHD P01 HD085928 to M.C.M.

Neuroscience in Anesthesiology and Perioperative Medicine - 32

Chemogenetic activation of dopaminergic midbrain neurons accelerates cognitive recovery following dexmedetomidine- but not ketamine-induced loss of consciousness in rats

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Introduction: Dopaminergic midbrain neurons, specifically those in the ventral tegmental area, are likely involved in restoring consciousness following general anesthesia [1,2]. However, it is unknown whether these circuits contribute to cognitive recovery following emergence. Recently, a novel cognitive recovery testing paradigm for rodents using an adapted version of the 5-Choice Serial Reaction Time Task (5CSRTT) has been developed. In it, higher order neurocognitive processes, such as attention and working memory, are tracked in real-time following emergence to establish neurocognitive recovery trajectories. Importantly, young, healthy rats recover cognitive function rapidly following isoflurane, sevoflurane, and propofol, but have delayed cognitive recovery following dexmedetomidine- and ketamine-induced loss of consciousness (LOC). To assess whether neural circuits involved in re-establishing consciousness can be similarly exploited to hasten cognitive recovery, we employed chemogenetic techniques to activate midbrain dopaminergic neurons in rats following dexmedetomidine and ketamine-induced LOC. It has been previously reported that pharmacologic activation of dopaminergic neurotransmission with d-amphetamine hastens emergence from dexmedetomidine, but not ketamine-induced LOC [3]. Therefore we hypothesized that activating dopaminergic midbrain neurons would differentially affect cognitive recovery following dexmedetomidine and ketamine exposure.

Methods: Eight adult Sprague Dawley rats (4 male, 4 female) were trained on the 5CSRTT until they achieved high accuracy (>80%) and low omissions (<20%). Once trained, midbrain neurons were targeted using a combinatorial adeno-associated viral (AAV) strategy to drive selective expression of Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in dopaminergic neurons. The targeting virus, AAV9-rTH-Cre, induces expression of Cre recombinase in dopaminergic neurons that express tyrosine hydroxylase (TH). This was co-injected with an AAV that induces Cre-dependent expression of the excitatory DREADD, AAV2-DIO-hM3DGq-mCherry, into the midbrain (+/-0.9ML, -4.8AP, -8.3DV). After waiting three weeks for DREADDs expression, rats received dexmedetomidine (20 µg/kg, i.v. infused over 10 min) or ketamine (50 mg/kg, i.v. infused over 10 min). Following the anesthetic infusion, rats were administered either saline (control) or clozapine-N-oxide (CNO, 3mg/kg, i.p.), the designer ligand used to activate the excitatory DREADD, in a randomized order. Rats were placed supine in the testing chamber to recover. Following the return of the righting reflex (RORR), rats had three hours to perform the task. Recovery of working memory was measured as the time taken following RORR to achieve ≥80% accuracy in five consecutive trials. Recovery of attention was measured as the time taken following RORR to achieve ≤20% omissions in five consecutive trials. After all testing was completed, histological analysis was performed to confirm DREADDs expression in the targeted brain region. Recovery latency was compared between CNO and saline conditions by Mantel-Cox comparison.

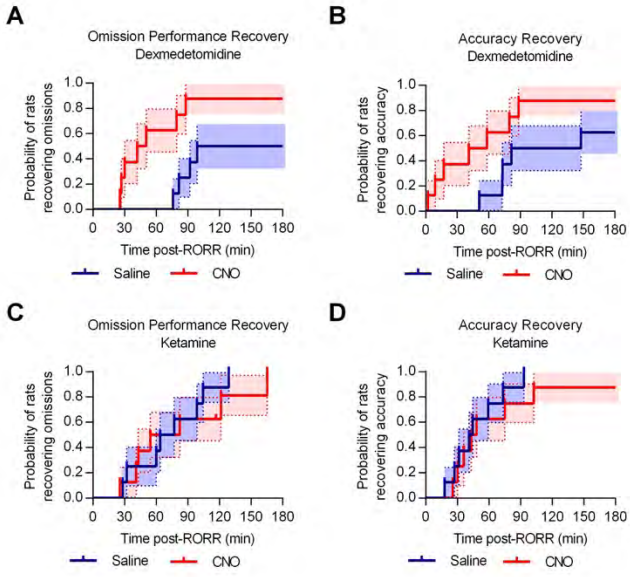
Results: DREADDs expression in the midbrain was confirmed by mCherry fluorescence (Fig 1). Recovery of a low omission rate, a metric of sustained attention, following dexmedetomidine was significantly faster in the CNO condition ($\chi2=5.588$, P=.0104) (Fig 2A). Following RORR from dexmedetomidine, the median latency to recover high accuracy, a metric of working memory, was 114.7 minutes with saline and 49.7 minutes with CNO, but this was not significantly different ($\chi2=2.705$, P=.1001) (Fig 2B). In contrast, CNO had no impact on cognitive performance following ketamine. Median recovery of low omissions was 70.5 min with saline and 68.5 min with CNO ($\chi2=0.3793$, P=.5380)(Fig 2C). Median recovery of high accuracy was 42.9 min with saline and 45.6 min with CNO ($\chi2=0.9155$, P=.3387)(Fig 2D).

Conclusion: Selective activation of midbrain dopaminergic neurons hastens neurocognitive recovery following dexmedetomidine-induced LOC in rats. Interestingly, activating these neural circuits has no impact on cognitive function following ketamine. These data suggest there are distinct mechanisms by which the brain recovers cognitive function following anesthetic-induced breaks in consciousness. Identifying these mechanisms will be key to designing effective strategies for facilitating neurocognitive recovery.

References: 1. Anesthesiology 121, 311-319, (2014). 2. Proc Natl Acad Sci U S A 113, 12826-12831,(2016). 3. Front Pharmacol 12:668285, (2021).

Figure 1

Figure 2



Neuroscience in Anesthesiology and Perioperative Medicine - 33 Comparison of three anesthetic techniques on emergence and recovery profile in patients undergoing supratentorial craniotomy

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Introduction: Smooth emergence and early extubation are important goals of neurosurgical procedures. It prevents occurrence of hypertension and raised intracranial pressure, thereby helping in prevention of complications like intracranial haematoma and cerebral edema. Various drugs like fentanyl have been used in studies to achieve this goal and recently dexmedetomidine has also been tried for this purpose. We carried out this study using these agents, to compare three anaesthetic techniques on emergence and recovery profile in patients undergoing supratentorial craniectomy.

1.The primary objective of our study is to compare the extubation time with use of three different anaesthetic techniques. 2.Secondary objectives:

a) Severity of coughing on emergence
b) Time to attain Modified Aldrete Score (MAS) ≥ 9
c) Hypertensive response and need of antihypertensive therapy.
d) Assessment of cognitive function(short orientation memory concentration test), postoperative pain
e) Time to first analgesic requirement in the postoperative period
f) Incidence of postoperative complications including nausea, vomiting, shivering, and respiratory depression.

Methods: A total of 54 adult patients of american society of anaesthesiologists grade 1 and 2, divided into three groups (F,D and P) of 18 patients each, were studied while undergoing surgery for supratentorial craniotomy. Patients were explained short orientation memory concentration test (SOMCT) in the preoperative visit 1 day prior to the surgery. Exclusion criteria was preexisting bradycardia (HR < 50/min) or hypotension (systolic arterial pressure less than 100 mm Hg); planned elective ventilation in the postoperative period; poor respiratory reserve and poor cough reflex, active smokers, intracranial hypertension, gross cerebral edema on CT scan, GCS <15, intracranial aneurysm or arterioveinous malformation, cognitive impairment; pregnancy or breast feeding; known allergy to α2-agonists; and use of β-blockers, cimetidine, digoxin, α2-agonists or psychotropic medications. As per randomization and double blinding observed, towards the closure of dura, the patients of group F received fentanyl 1 µg/kg/hr, group D received dexmedetomidine 0.2 µg/kg/hr and group P received 0.9% normal saline till the time closure of skin was complete. All three groups had similar anaesthesia technique as maintenance using sevoflurane. The study period was segregated into three phases: closure and pre-extubation (beginning of closure of dura to the time of giving neuromuscular blockade reversal), extubation (from giving reversal to 5 minutes after extubation) and ICU phase (first recording after shifting to ICU and then for the next 4 hours). For statistical analysis, a comparison of parametric variables was done with student t test. For non-paramateric variables. Nonparametric data were compared using Pearson's $\chi 2$ or Kruskal–Wallis test. Categorical data were analyzed with the Fisher's exact test. A p-value of less than 0.05 was taken as significant. Data was analysed using STATA statistical software.

Results: Group F and D had less hypertensive episodes compared to group P (p 0.00) (Table 4, Fig 1) and also the requirement of labetalol was less in both group F and D (p 0.00). The extubation quality score was also significantly better in group F and D (p 0.00) (Table 5). There was no difference in the emergence time, extubation time and recovery time between these three groups. All three group had similar time taken to achieve baseline SOMCT score. Time to reach a modified aldrete score (MAS) of atleast 9 was similar among three groups. The mean time interval when patients required 1st analgesic postoperatively was similar in all the three groups. All three groups had

similar occurrences of complications in postoperative period of study in the intensive care unit. All three groups were comparable demographically (Table 2) and on baseline characteristics (Table 3). Two patients in Group P and 3 patients in Group F were excluded from final statistical analysis as they were not extubated in the operating room.

Conclusion: Fentanyl infusion and dexmedetomidine infusion started at the time of closure of dura till the skin closure starts, provides smooth emergence, with less hypertensive response as compared to placebo in craniotomy patients. Use of fentanyl and dexmedetomidine in this fashion does not delays the emergence, extuabtion and recovery times. Emergence characteristics of fentanyl and dexmedetomidine infusion are comparable.

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Table 1: Study drug methodology

	GROUP P (placebo)	GROUP D (dexmedetomidine)	GROUP F (fentanyl)
Dural closure start	**Loading**- 0.9% normal saline 10 ml over 10 minutes **Maintenance-** 0.9% normal saline	**Loading**-dexmedetomidiine 0.5 microgm/kg in 10 ml 0.9% normal saline over 10 minutes **Maintenance-** dexmedetomidiine 0.2 microgm/kg/hr.	**Loading-** 10 ml 0.9% normal saline over 10 min **Maintenace-**1.5 microgm/kg/hr.
	sevoflurane at an inspired concentration of 0.6 %	sevoflurane at an inspired concentration of 0.6 %	sevoflurane at an inspired concentration of 0.6 %
Skin closure start	0.9% normal saline off, sevoflurane reduced to inspired concentration of 0.4%	dexmedetomidine off, sevoflurane reduced to inspired concentration of 0.4%	fentanyl off, sevoflurane reudced to inspired concentration of 0.4%
Skin closure end	sevoflurane switched off	sevoflurane switched off	sevoflurane switched off
Head dressing complete	N2O switched off	N2O switched off	N2O switched off

Table 4: Recovery characteristics of the patients

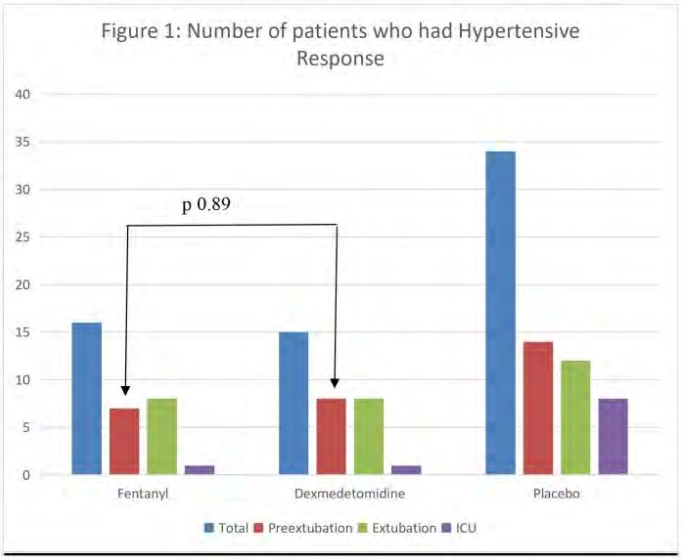
Parameters	Group F (n=15)	Group D (n=18)	Group P (n=16)	P Value
Emergence time (minutes)	3.4 ±2.6	4.0 ±2.0	3.8 ±1.7	0.65
Extubation time (minutes)	5.6 ±2.7	6.7 ±3.9	6 ±2.8	0.28
Recovery time (minutes)	7.6 ±3.2	9.2 ±4.7	8.5 ±3.2	0.50
t-SOMCT (minutes)	44.3 ±19.5	42.1 ±27.8	40.3 ±24.4	0.90
HTR - Pre extubation*	7	6	14	0.00
HTR- Extubation*	8	8	12	0.19
HTR- ICU*	1	0	2	0.92
Labetalol use*	7	5	15	0.00
HTRB*	14	17	8	0.00
t MAS atleast 9 (min)	12 ±3.5	11 ±4.7	13 ±4.1	0.46
Time of first analgesia in icu (min)	54.9 ±9.34	58 ±10.3	52.5 ±10.8	0.29

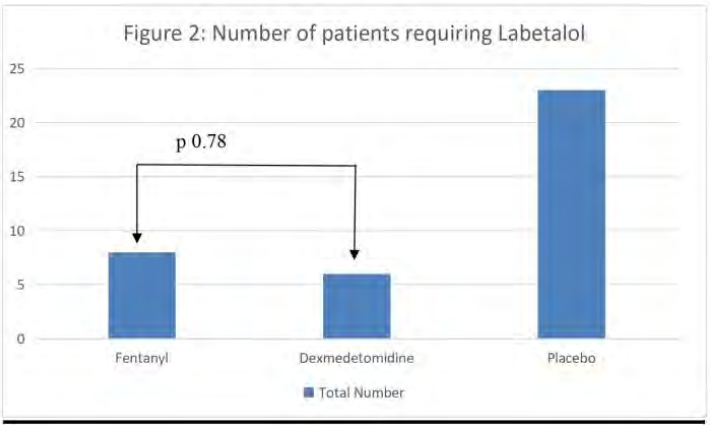
*n=number of patients
t SOMCT: Time to baseline Short Orientation Memory Concentration Test
HTR: hypertensive response
HTRB: Hypertension return to baseline
t MAS; time to achieve Modified aldrete score ≥ 9

Table 5: Extubation Quality Score (EQS)

EQS	1	2	3	4	5	P value
Group F (n=15)	14	0	1	0	0	0.000
Group D (n=18)	14	4	0	0	0	
Group P (n=16)	4	3	7	1	1	

EQS: Extubation Quality Score





Obstetric Anesthesiology

Obstetric Anesthesiology - 1 Acute Postpartum Pain and Anxiety Influence Long-term Postpartum Pain, Maternal-Infant Attachment and Parenting Self-Efficacy

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Introduction: Pain and depression are bi-directionally related in chronic pain settings, and worse labor pain has been linked to postpartum depression symptoms1-3. These findings raise questions about whether improving pain and mood after delivery can improve maternal parenting function. However, few studies have examined relationships between postpartum pain and negative mood, and their effects on parent-infant relationship outcomes. We aimed to assess the relationships between postpartum pain, depression, parent-infant attachment, and parenting self-efficacy.

Methods: This was a prospective longitudinal observational study of healthy, adult, nulliparous women, at term gestation presenting for labor and delivery at ≥38 weeks gestational age. Baseline self-reported outcome assessments included validated inventories of depression (Edinburgh postnatal depression screen, EPDS), anxiety (state trait inventory, STAI), pain (brief pain inventory short, BPI). Demographic and labor variables were recorded. At 6 weeks and 3 months postpartum, self-reported assessments included EPDS, STAI, BPI, maternal infant attachment (MPAS), and parenting self-efficacy (PMPSE). Pain severity scores were calculated as the average of items 2-5 on the BPI and pain interference scores were averaged on items 8-14 from the BPI. Linear regression was used to estimate the effects of 6-week pain scores on 3-month pain scores. A P-value less than 0.05 was considered statistically significant.

Results: 187 subjects participated; 87 subjects had complete data on parent-infant attachment and 85 had complete parenting self-efficacy data. Cohort demographic and labor and delivery characteristics are in Table 1. Worse postpartum anxiety scores were associated with lower parenting self-efficacy scores (Table 2). Higher pain severity at 3 months was associated with lower parent-infant attachment and parenting self-efficacy scores (Table 3) Pain severity scores at 6 weeks postpartum were significantly associated with pain severity at 3 months (Parameter Estimate 0.25, 95% CI 0.07 to 0.43, P=0.01) (Table 4). The potential strength and dose-responsiveness of these relationships will be assessed and reported.

Conclusion: We observe trends that associate worse postpartum anxiety and pain with worse parenting outcomes. The potential relationships between postpartum anxiety, pain, and parenting self-efficacy deserve scrutiny, because reducing both postpartum pain and improving mood can potentially improve long-term postpartum parenting outcomes.

References: 1. Depression and pain comorbidity: a literature review. 163: 2433-45 (2003) 2. Obstetric pain correlates with postpartum depression symptoms: a pilot prospective observational study 20:240 (2020) 3. Labor Analgesia as a Predictor for Reduced Postpartum Depression Scores: A Retrospective Observational Study. 126:1598-1605 (2018)

Tables

Table 1. Demographic Labor & Delivery Characteristics among the cohort.

Characteristic	Result (N = 187)
Epidural labor analgesia utilization rate – no./total no. (%)	116/187 (62.0%)
Race – no./total no. (%)	
White	142/187 (75.9%)
Black/African American	41/187 (21.9%)
Asian	14/187 (7.4%)
Hawaiian	1/187 (0.5%)
American Indian/Alaskan	4/187 (2.13%)
Other	2/187 (1%)
Ethnicity – no./total no. (%)	
Hispanic	179/187 (95.7%)
Non-Hispanic	8/187 (4.3%)
Outcome of labor (n=147)	
NSVD	103/144(71.5%)
Cesarean delivery – Arrest of dilation or descent	15/144(10.4%)
Cesarean delivery – other reason	9/144(6.25%)
Cesarean delivery – non-reassuring fetal status	7/144(4.8%)
Assisted vaginal delivery	5/144(3.74%)

Data are presented as mean (SD), median (IQR), frequency (percentage)
NSVD, normal spontaneous vaginal delivery.

Table 2. Parent survey responses by depression (EPDS) and anxiety (STAI) measures.

	MPAS (N=87)	*P*-value	Parent self-efficacy (N=85)	*P*-value
EPDS < 25	34.9 ± 2.6 (N=38)	0.11	32.6 ± 5.9 (N=36)	0.35
EPDS ≥ 25	35.8 ± 2.6 (N=49)		33.9 ± 5.9 (N=49)	
STAI state < 69	35.2 ± 2.6 (N=46)	0.35	31.8 ± 5.6 (N=44)	**0.01 ***
STAI state ≥ 69	35.7 ± 2.7 (N=41)		35.0 ± 5.4 (N=41)	
STAI trait < 69	35.3 ± 2.8 (N=42)	0.63	31.8 ± 6.4 (N=40)	**0.03 ***
STAI trait ≥ 69	35.5 ± 2.4 (N=45)		34.7 ± 5.2 (N=45)	

** P < 0.05*
MPAS, maternal parent infant attachment scale. STAI, state trait anxiety inventory. EPDS, Edinburgh postnatal depression scale.
Results reflect T-test statistic. EPDS score calculated by summing responses to 10 EPDS items. Score ranged from 16-29, with median score of 25 which was used to categorize into low and high values. The 40 item STAI questionnaire assesses State and Trait anxiety. Median scores for both State and Trait were 69.0 which was used to categorize patients into lo/hi categories (State: range 11.0-80.0 and mean 66.8 ± 10.4; Trait: 24.0-80.0 and mean 67.1 ± 9.6).

Table 3. Parent survey responses by postpartum Pain Severity and Pain Interference.

BPI: postpartum (N=78)	MPAS (N=87)	*P*-value	Parent self-efficacy (N=85)	*P*-value
Pain Severity: mild	35.8 ± 2.4 (N=43)	0.40	33.7 ± 5.5 (N=43)	0.68
Pain Severity: moderate-severe	35.3 ± 2.9 (N=35)		33.1 ± 6.3 (N=35)	
Pain Interference: mild	35.4 ± 2.2 (N=40)	0.64	33.2 ± 5.8 (N=40)	0.73
Pain Interference: moderate-severe	35.7 ± 3.0 (N=38)		33.7 ± 6.0 (N=38)	

Results reflect T-test statistic. Note: Pain Severity score = average of items 2-5 and Pain Interference score = average of items 8-14 from the Brief Pain Inventory short form.

Table 4. Unadjusted linear regression models estimating the effect of postpartum pain score on 6-week pain score and on 3-month pain score (postpartum pain severity score used to predict pain severity; postpartum pain interference score used to predict pain interference).

Outcome	Parameter estimate of postpartum pain score	95% confidence interval	*P*-value
Pain Severity 6 week	0.19	-0.002 – 0.38	0.06
Pain Interference 6 week	0.12	-0.03 – 0.26	0.13
Pain Severity 3 months	0.25	0.07 – 0.43	**0.01** *
Pain Interference 3 months	0.12	-0.03 – 0.26	0.12

* *P < 0.05*

Note: Pain Severity score = average of items 2-5 and Pain Interference score = average of items 8-14 from the Brief Pain Inventory short form.

Obstetric Anesthesiology - 2 Assessment of benefits and accuracy of a handheld ultrasound device for neuraxial placement

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Introduction: Background: Although the use of ultrasound (US) guided neuraxial anesthesia was described over two decades ago, its use remains scarce. The lack of adoption of this non-invasive technique persists despite its known benefits of better identification of the lumbar interspace level, optimal needle insertion site, diagnosis of associated scoliosis and estimated depth of epidural space. The causes for its limited use may relate to cost, technical expertise, difficulty interpreting images, access to, and space for storage of ultrasound equipment.(1,2)

Methods: Methods: After institutional review board approval, we have started this prospective observational study for epidural placement utilizing handheld US (Butterfly iQ+) guidance and landmark technique. We evaluated time to perform epidural placement (the time from needle insertion till loss of resistance), number of insertion attempts (needle in and out of skin), number of needle redirections (needle adjustments without removal of needle from insertion point), and -for cases in which US was utilized we compared the estimated depth by US and actual depth of epidural space. Intergroup differences were assessed for significance using Mann-Whitney test. Values are presented as mean and standard deviation (SD)

Results: Results: A total of 125 of epidural placement were evaluated, 82 of which were placed with US guidance. The average number of needle insertion attempts [US 1.0 (0.6) versus landmark 2(1.3); p = 0.29[and number of needle redirection [US 1.0 (0.8) versus landmark 3.0 (1.3); p < 0.001[was lower in the US group. The duration of the procedure was also lower in the US groups versus the landmark groups with average duration of 3.1 min (3.2) versus 6.3 (7.5); p = 0.009, respectively. In terms of accuracy, our handheld US underestimated measurements by -0.15 (0.37) 95% confidence interval [-0.07, -0.23].

Conclusion: Conclusion: In a cohort of patients with a mean (SD) body mass of 33.3 (6.9), the use of US helped reducing the number of needle insertion attempts and adjustments in a statistically significant manner when compared to landmark-guided technique. Our results are in agreement with previously reported accuracy, with some authors reporting an accuracy within 0.8 cm. The use of the portable Butterfly iQ+, obviates some of the limitations related to cost and real state. More importantly, the use of this device resulted in procedure performance in half the time when compared to a landmark technique. the authors think that the additional information obtained improves patient satisfaction and may potentially decrease the risk of complications, such as accidental dural puncture.

References: 1. Seligman KM, Weiniger CF, Carvalho B. The Accuracy of a Handheld Ultrasound Device for Neuraxial Depth and Landmark Assessment. Anesthesia Analgesia. 2018 Jun;126(6):1995 1998. 2. Lee A. Ultrasound in obstetric anesthesia. Semin Perinatol. 2014 Oct;38(6):349 358.

Obstetric Anesthesiology - 3 The Effect of Obesity on Opioid Consumption Following Quadratus Lumborum Block After Cesarean Delivery: A Retrospective Review

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Introduction: Obesity plays a significant role in anesthetic management during the peri-operative period. Specifically, it has been shown to be related to complications of regional anesthesia, with reports suggesting that obesity results in reduced ultrasound visibility of target structures, inadequate needle positioning, and altered drug distribution.[1,2] Such difficulties may lead to increased failure rates of multiple regional anesthetic blocks.[3] However, studies analyzing the impact of obesity on quadratus lumborum block (QLB) after cesarean delivery is lacking, in part because trials of QLBs exclude patients with higher body mass indexes (BMI). The purpose of this study is to analyze the effect of obesity on opioid consumption following QLB after cesarean delivery.

Methods: Charts of patients who received a QLB after cesarean delivery during 2017-2021 were reviewed. Patients were divided into a control group with BMI < 30 kg/m^2 and a study group with BMI ≥ 30 kg/m^2. In addition to baseline demographics, outcome variables studied were opioid request rate, time to first rescue opioid analgesia, and opioid consumption measured as morphine milligram equivalents (MME). Statistical analysis was performed using ANOVA, Fischer's exact test, or χ^2 test when appropriate. P< 0.05 was considered significant.

Results: Of the 175 patients who received a QLB after cesarean delivery, 144 patients (82.3%) met inclusion criteria. Exclusion criteria included patients who were < 16 years old, received intrathecal morphine intraoperatively, or continuous epidural postoperatively. 45 patients (31.2%) had a BMI < 30 kg/m^2 and 99 patients (68.8%) had a BMI ≥ 30 kg/m^2. Patient demographics were comparable between the two groups, except for age (29.7 ± 6.3 vs. 31.9 ± 4.8, p=0.022) and duration of cesarean delivery, in min (60.6 ± 19.6 vs. 71.5 ± 27.0, p=0.017) between patients with a BMI < 30 kg/m^2 and BMI ≥ 30 kg/m^2, respectively. There was no significant difference in the opioid request rate between the control and study groups (84.4 % vs. 83.8 %, p=0.93) after receiving a QLB. Additionally, the difference between median time to rescue opioid analgesia (376.5 [178.75 – 1137.25] min in women with a BMI < 30 vs. 512 [177.0 – 1485.0] min in women with a BMI ≥ 30) was not statistically significant (p = 0.232). Analysis of median MME consumed within the first 24hrs of receiving a QLB revealed no significant difference between the control and study groups (15.0 [7.5 – 30.0] vs. 15.0 [0.0 – 30.0], p=0.445). No difference was also observed between 24-48hrs and 48hrs+.

Conclusion: Our results suggest that obesity does not result in significantly increased opioid consumption following QLB for women who have undergone cesarean delivery. Quadratus lumborum blocks should be encouraged in obese patients and future clinical trials studying QLB should include patients with greater BMI.

References: 1. Regional anesthesia and obesity. 2009;22(5):683-686. 2. The perioperative effect of increased body mass index on peripheral nerve blockade: an analysis of 528 ultrasound guided interscalene blocks. 2012;62(1):28-38. 3. Increased body mass index and ASA physical status IV are risk factors for block failure in ambulatory surgery - an analysis of 9,342 blocks. 2004;51(8):810-816.

Table 1. Baseline demographics of patients who received quadratus lumborum block after cesarean delivery.

Characteristic	BMI < 30 kg/m^2 (n=45)	BMI ≥ 30 kg/m^2 (n=99)	*p*-value
Age (years)	29.7 ± 6.3	31.9 ± 4.8	0.022*
Race			0.691
Black/African American	40 (88.9)	92 (92.9)	
Caucasian	4 (8.9)	6 (6.1)	
Undisclosed	1 (2.2)	1 (1.0)	
Hypertension			0.272
Yes	8 (17.8)	23 (23.2)	
Prior pregnancies	2 (4.4)	11 (11.1)	
No	35 (77.8)	65 (65.7)	
Diabetes			0.320
Yes	6 (13.3)	19 (19.2)	
Prior Pregnancies	0 (0)	3 (3.0)	
No	39 (86.7)	77 (77.8)	
ASA Class			0.155
I	0 (0)	2 (2.0)	
II	39 (86.7)	72 (72.7)	
III	6 (13.3)	25 (25.3)	
Prior Cesareans	0.98 ± 0.8	0.86 ± 0.8	0.907
Current Cesarean Type			0.846
Elective	32 (71.1)	67 (67.7)	
Emergent	12 (28.9)	32 (32.3)	
Anesthetic Technique			0.476
Combined Spinal Epidural	44 (97.8)	93 (93.9)	
Spinal	1 (2.2)	3 (3.0)	
General	0 (0)	3 (3.0)	
Operative Duration (min)	60.6 ± 19.6	71.5 ± 27.0	0.017*
Sedative Prior to QLB			0.354
Yes	14 (31.1)	40 (40.4)	
No	31 (68.9)	59 (59.6)	

Data is expressed as mean ± SD or n (%)

Table 2. Post-QLB opioid request rates and use measured in oral milligram morphine equivalents (MME).

	BMI < 30 kg/m^2 (n=45)	BMI ≥ 30 kg/m^2 (n=99)	*p*-value
Opioid Requested			0.93
Yes	38 (84.4)	83 (83.8)	
No	7 (15.6)	16 (16.2)	
Time to first rescue analgesia (min)	376.5 [178.75 – 1137.25]	512 [177.0 – 1485.0]	0.232
MME Consumed			
0-24hrs	15.0 [7.5 – 30.0]	15.0 [0.0 – 30.0]	0.445
24-48hrs	15.0 [0.0 – 31.875]	15.0 [7.5 – 30.0]	0.489
48hrs +	7.5 [0.0 – 22.5]	7.5 [0.0 – 22.5]	0.677

Data is expressed as n (%) or median [interquartile range]

Obstetric Anesthesiology - 4 Baseline parameters for rotational thromboelastometry in healthy pregnant American women Population: a retrospective study

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Introduction: The early recognition of hypofibrinogenemia is critical to minimize bleeding during postpartum hemorrhage (PPH).1 Unfortunately, the gold standard reading of Clauss fibrinogen takes an hour to obtain. Research in pursuit of new technology for the early detection and correction of hypofibrinogenemia highlights the benefits of Point of Care Viscoelastic Testing (POCVT) for PPH management due to its rapid run time (10 minutes).2 Baseline parameters must be established to identify treatment triggers as recommended by both the manufacturer and by the International Federation of Clinical Chemistry.3 While baseline studies using rotational thromboelastrometry (ROTEM¬Æ) has been conducted 3,4, there is a lack of literature representing our United States obstetric population. When comparing baseline parameters, some variations are expected secondary to sample size, genetic composition, and geographic differences. For instance, some studies have excluded patients with a body mass index (BMI) >30 kg/m2. Such exclusion criterion would misrepresent our U.S. population. Our primary aim is to create a representative baseline ROTEM parameters. A secondary aim is to evaluate the effect of obesity on ROTEM parameters.

Methods: After institutional review board approval, we obtained data from 681 patients presenting for labor at Yale New Haven Hospital from 2017 - 2021. All charts were reviewed by two obstetric anesthesiologists, with any discrepancies resolved by a third. Exclusion criteria included receiving medications affecting coagulation, tranexamic acid, or blood products before conduction of ROTEM and having inherited or acquired thrombophilia. Patients were sorted into 4 groups by BMI and age-adjusted mean differences of all ROTEM parameters were found for the BMI cutoff of 30 kg/m2. (Table 1and 2)

Results: A total of 466 charts were reviewed. FIBTEM A10 by BMI is summarized in Table 1. After adjusting for age, patients with a BMI >30 kg/m2 demonstrated higher ROTEM parameters, when compared to their counterparts as shown in Table 2. The average values of ROTEM parameters by BMI group are presented in Table 3.

Conclusion: Our study demonstrates that patients with BMI ≥30 kg/m2 exhibit a hypercoagulable profile. These alterations in addition to venous stasis, may result in an increased risk of postpartum hemorrhage5 and clotting disorders such as venous thromboembolism (VTE) 6 . As the most common comorbidity in women of reproductive age, 7 obesity is known to increase thromboembolism risk, potentially due to increased factors like adipokines, fibrinogen, factor VII, plasminogen activator inhibitor,8 and LDL-C.9 Given these pathophysiologic risk factors in obese patients, consideration of this baseline state is essential for proper coagulation assessment and hemorrhage management with the ROTEM. Particularly, given the postpartum risk of VTE in the obese patient, should the American College of Obstetricians and Gynecologists consider pregnancy BMI >30 kg/m2 as an important determinant for thromboprophylaxis?

References: 1. J Thromb Haemost. 2006;5(2):266-73. 2. Am J Obstet Gynecol. 2014;210(4): 323.e1-323.e7. 3. BJOG. 2020;127(7):820-7. 4. Int J Obstet Anesth.2011;20(4):293-8. 5. Obstet Gynecol.2011;118(3):561-8. 6. J Matern Fetal Neonatal Med.2013;26(6):547-51. 7. BMJ. 2017;356. 8. Clin Exp Pharmacol Physiol.2011;38(12):864-71. 9. Lipids Health Dis.2016; 15:95.

Obstetric Anesthesiology - 5 Decision Analysis for Evaluating Ante-Partum Risk Prediction of Pre-Eclampsia: Minimum Test Tradeoff

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Introduction: Pre-eclampsia complicates 2-8% of pregnancies worldwide, and in the US such hypertensive disorders are associated with 16% of maternal deaths. The prevalence of pre-eclampsia is higher at centers specializing in the care of high-risk patients and significantly influences anesthetic management. As anesthesiologists become increasingly involved in prenatal care of obstetric patients, it is important to recognize the potential value of pre-eclampsia screening. Because accurate early prediction of the later development of pre-eclampsia leads to changes in obstetrical management, a number of studies have evaluated biomarkers, clinical factors, and other tests by using receiver-operating characteristic curve analysis and area under the curve (AUC). A recent study(1) compared a model that included clinical factors plus the biochemical marker Inhibin-A with a model adding the biophysical parameter of uterine artery pulsatility index (UtA PI) to the first model. The results showed an improvement (higher AUC) with the latter. That study, as well as numerous other studies in this area, failed to consider the costs of data acquisition to improve the model. We therefore questioned whether the addition of the UtA PI was worthwhile to improve risk prediction. We investigated the cost of UtA PI measurement to decide whether improvements in risk prediction are sufficient to justify data collection costs.

Methods: We used decision analysis to compare two models predicting in early (12-14 weeks) pregnancy the risk of late-onset (>34 weeks gestation) pre-eclampsia (LO PE), based on published data (1). The methodology is based on recent work by Baker (2,3), who developed a useful decision-analytic metric, the test tradeoff, and a simple approximation of its minimum value. For a given ratio of the benefit of a true positive to the cost of a false positive, the test tradeoff is the minimum number of data collections per true positive to yield a positive net benefit. Data were not available for a detailed test tradeoff analysis. We used Baker's formula applied to model comparisons to compute an approximate minimum test tradeoff (over benefit-cost ratios) for an added predictor, MTT. Formula for MTT is in Figure. Formula inputs included published AUC's (1) that used models incorporating clinical background factors plus measurements of inhibin A with (AUC 0.824) or without (AUC 0.815) the addition of uterine artery pulsatility index (UtA PI). The formula also includes the probability of developing LO PE disease. We compared the MTT for the general US population (5% prevalence) with the MTT for a high risk group of subjects with a history of PE (40% prevalence). We obtained cost data from CPT codes used at our institution. For UtA PI, we assumed that patients already undergo screening doppler studies in the first trimester, and therefore the additional cost of UtA PI would not include the doppler cost.

Results: For the low risk, general US population, we found that MTT = 1250 for comparing a model using clinical background factors plus Inhibin A with a second model using clinical background factors plus Inhibin A and UtA PI. For the high risk group, MTT = 156. There were no costs of data collection of clinical background factors, as this information was included in each patient's history and physical exam. Cost per measurement of Inhibin-A (CPT 86336) is $53.00. UtA PI (CPT93976) costs $1395.30 ($720.30 facility fee + $675 pro fee) per measurement.

Conclusion: A recent study (1) evaluated two models to predict the development of LO by comparing AUC's, without considering whether additional costs of UtA PI data collection for improved risk prediction were worthwhile. In this study, we found that for a positive net benefit, we would need to trade 1250 UtA PI measurements for every true positive prediction of LO PE in the general US obstetrical population. This number is significantly lower (156) in women with PE in the past. Data collection costs are low for the model that incorporates baseline clinical data with Inhibin-A levels. Based on MTT, costs of adding UtA PI are relatively high compared to the anticipated benefit of a true positive that prompts intervention, especially in the general US group. Implications of a true positive include prophylactic administration of aspirin and

frequent monitoring of maternal blood pressure and fetal condition. In summary, MTT can assist with medical decision-making when risk prediction alters clinical management.

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MTT = minimum test tradeoff

AUC_1 = AUC for Model 1 (clinical risk factors with inhibin A)

AUC_2 = AUC for Model 2 (clinical risk factors with inhibin A and UtA PI)

P = probability of developing late onset pre-eclampsia (LO PE) in the population

$$\text{MTT} = \frac{1}{\{(h(\text{AUC}_2) - h(\text{AUC}_1)\} \text{ x P}}$$

$$h(\text{AUC}) = \text{AUC} - \sqrt{\frac{1-\text{AUC}}{2}}$$

Pain Mechanisms

Pain Mechanisms - 1 Association between aesthetic satisfaction and chronic postsurgical pain in breast cancer patients treated with one stage prosthesis implantation

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Introduction: Chronic post-surgical pain (CPSP) is reported to be one of the most serious problems for patients who have survived breast cancer. Post-mastectomy pain has been estimated to affect 20-50% of patients. In our previous study, we found that the rate of chronic pain after mastectomy is about 40-50%. It was reported that for patients receiving single-stage implant-based breast reconstruction (IBBR), no more incidence of CPSP was found. However, studies on CPSP in patients with single-stage IBBR have often had a very small sample size, and there has been no separate analysis of patients who received a tissue expander and those who had an implant. Apparently, it is not precise to calculate the incidence of CPSP of these two different surgical procedures together. This study retrospectively studied the incidence of CPSP following single-stage IBBR and evaluated the possible risk factors.

Methods: This was a retrospective cohort study, involving all patients who underwent single-stage IBBR between January and December 2019. The female patients, aged between 18 and 60, were identified for inclusion in the study and attended follow-ups between January and March 2021. Patients' details were collected, including history of psychological disorders, history of preoperative chronic pain, the severity of postoperative pain (PP), type of surgery, whether a biological matrix was used, and the size of implant. The scores for satisfaction (SS) were based on the BREAST-Q, while the pain burden index (PBI) was used to assess the degree of CPSP. Statistical analysis was performed using SPSS version 21.0. Risk factors for the development of CPSP were compared using logistic regression. Patients were divided into the SS ≥12 vs SS< 12 groups, the unilateral vs bilateral groups, the severe acute PP vs non-severe acute PP groups, and the history of chronic pain vs no history of chronic pain groups. The PBIs of those subgroups was compared using a Mann–Whitney U test.

Results: The study involved 182 patients. One patient, who died from metastasis, was excluded from the final analysis. The questionnaires were completed by 159 patients, where there were 2 cases of metastasis, 2 cases of local relapse, and 13 cases of postoperative complications, including 3 cases of nipple necrosis, 8 cases of implant retraction due to infection, and 2 cases of implant displacement. 9 of them received bilateral single-stage IBBR plus a mastectomy. CPSP occurred in 48.43% of the patients, 2.52% of them being severe cases. Significant predictors for the development of CPSP in the univariate analysis included severe acute PP, a history of preoperative chronic pain, psychological disorders, SS with the reconstructed breasts, and whether there were any regrets about having had the reconstruction. Multivariate analysis identified severe acute PP (odds ratio (OR) = 2.80, 95 % confidence interval (CI) = 1.16-6.79, p = 0.023), a history of preoperative chronic pain (OR = 3.39, 95 % CI = 1.42-8.10, p = 0.006), and the SS (OR =0.86, 95 % CI = 0.75-0.99, p = 0.034) as being independently associated with the development of CPSP. In subgroup analysis, the PBI of the patients in the SS <12 group (p <0.001), the bilateral group (p <0.01), and the severe acute PP group (p <0.005) was significantly higher than the PBI of those in the control groups.

Conclusion: This study demonstrated a significant incidence of CPSP following single-stage IBBR. It was possible to identify patient-specific characteristics associated with an increased risk of CPSP. Patients who have a lower SS developed more CPSP, and it is clear that lower SS, bilateral procedures, and severe acute PP are predictors of higher PBI. Although nearly half of the patients in this study experienced CPSP, none of them had ever pursued treatment. Both anesthesiologists and surgeons should be encouraged to counsel patients on the course and risks of CPSP following single-stage IBBR, and they should be made more aware of the potential need to solicit aggressive CPSP management for symptomatic women.

Table 1. The incidence of CPSP, the amount of pain originating from different locations, and the different PBI levels and VAS scores.

The total incidence of CPSP	48.43% (77/159)
Location (n, %)	
Breast	48 (30.19%)
Chest wall	34 (21.38%)
Axillary	26 (16.35%)
Arm	11 (6.92%)
Intensity (n, %)	
VAS 0	82 (51.57%)
VAS 1–3	37 (23.27%)
VAS 4–6	36 (22.64%)
VAS 7–10	4 (2.52%)
PBI (n, %)	
0	82 (51.57%)
1–20	55 (34.59%)
21–50	19 (11.95%)
51–100	2 (1.26%)
>100	1 (0.63%)

CPSP chronic post-surgical pain; VAS visual analogue scale; PBI Pain Burden Index.

Table 2. The univariate analysis of risk factors for CPSP.

Variables	CPSP	No CPSP	Odds ratio (95 % CI)	P value
Age (years)	40.7 ± 6.4	41.4 ± 7.5	0.99（0.95–1.04）	0.560
Type of surgery				0.104
With SLNB	55	53	0.84（0.69–1.03）	
With ALND	15	27	1.58（0.92–2.71）	
Biological matrix				1.000
Yes	62	65	0.98 (0.84–1.15)	
No	15	17	1.06 (0.57–1.98)	
Unilateral or bilateral				0.091
Unilateral	70	80	1.07 (0.99–1.16)	
Bilateral	7	2	0.27 (0.06–1.25)	
Psychological problems				0.027
Yes	44	32	0.68 (0.49–0.95)	
No	33	50	1.42 (1.04–1.94)	
History of preoperative chronic pain				0.002
Yes	25	10	0.38 (0.19–0.73)	
No	52	72	1.30 (1.09–1.55)	
Acute PP				0.004
Non-severe	53	72	1.28 (1.08–1.51)	
Severe	24	10	0.39 (0.20–0.76)	
Postoperative complications				0.392
Yes	8	5	0.59 (0.20–1.72)	
No	69	77	1.05 (0.95–1.15)	
Regretted having single-stage IBBR				0.034
Yes	12	4	0.31 (0.11–0.93)	
No	65	78	1.13 (1.01–1.26)	
The size of implant	222.4 ± 51.8	232.7 ± 57.9	1.0（0.99–1.0）	0.238
SS	11.0 ± 2.7	12.5 ± 2.7	0.8（0.71–0.91）	0.001

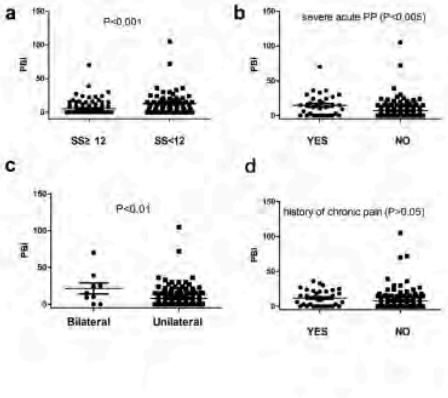
CPSP chronic post-surgical pain; ALND axillary lymph node dissection; SNLB sentinel lymph node biopsy; PP postoperative pain; IBBR implant-based breast reconstruction; SS satisfaction score.

Table 3. The multivariate analysis of risk factors for CPSP.

Variables	Odds ratio (95 % CI)	P value
Psychological disorders	1.70 (0.85–3.40)	0.135
History of preoperative chronic pain	3.39 (1.42–8.10)	0.006
Severe acute PP	2.80 (1.16–6.79)	0.023
SS	0.86 (0.75–0.99)	0.034
Regretted having single-stage IBBR	3.20 (0.90–11.43)	0.073

PP postoperative pain; IBBR implant-based breast reconstruction; SS satisfaction score.

Fig 1



Pain Mechanisms - 2 The encoding of peripheral stimuli by superficial dorsal horn excitatory and inhibitory networks in vivo

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Introduction: The superficial dorsal horn (SDH) of the spinal cord represents the first site of integration between innocuous and noxious somatosensory stimuli. According to gate control theory, diverse populations of excitatory and inhibitory interneurons within the SDH are activated by distinct sensory afferents, and their interplay determines the net nociceptive output projecting to higher pain centers. Although specific SDH cell- types are ill-defined, numerous classifications schemes find that excitatory and inhibitory neurons fundamentally differ in their morphology, electrophysiology, neuropeptides, and pain-associated plasticity; yet little is known about how these neurons respond over a range of 'natural' innocuous and noxious stimuli.

Methods: We applied an in vivo imaging approach where the genetically encoded calcium indicator GCaMP6s was expressed either in vGluT2-positive excitatory or vIAAT-positive inhibitory neurons. Neuronal activity was imaged in vivo, using a custom-made imaging window. Fluorescence traces were analyzed offline and inferred spiking rates were deconvolved using CaImAn, an established image analysis software.

Results: We found that inhibitory neurons were markedly more sensitive to innocuous touch than excitatory neurons but still responded dynamically over a wide range of noxious mechanical stimuli. In a capsaicin model of acute pain sensitization, the responses of excitatory neurons were significantly potentiated to innocuous and noxious mechanical stimuli, whereas inhibitory neurons were only depressed to noxious stimuli.

Conclusion: Our in vivo studies in anesthetized animals suggest that excitatory and inhibitory superficial dorsal horn neurons are activated by fundamentally different stimuli, and therefore inhibition may serve to contrast between somatosensory channels rather than sharpen the resolution within- contrary to what is typically observed in other sensory systems. Future in vivo studies characterizing more refined neural subtypes and their responses to natural stimuli will aid in identifying dorsal horn cell- types based on their function, in addition to their variety of forms.

Pain Medicine

Pain Medicine - 1 IARS General Abstract Submission - 0779

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Introduction: Ultrasound lumbar sympathectomy block (ULS) is not described extensively in literature due to deep location of lumbar sympathetic chain. (1-3). Here we describe a new technique. The primary objective was to study the feasibility of ULS with an electrical stimulation needle. Secondary objectives were: needle attempts, vertebral level, Pain Numeric rating scale (NRS), temperature rise and any other complications.

Methods: After Clinical Trial Registry, institutional ethics committee approval (CTRI/2018/09/015681/ IECPG-636/31.01.2018, RT-24/28.02.2018) and patient consent, recruited patients were patients with Peripheral arterial disease (PAD) with rest pain (NRS) ≥ 3. Exclusion criteria were more than one gangrene in the affected limb, deranged coagulation parameters, diabetes mellitus and BMI ≥ 35 kg/m2. Baseline investigations of hemogram, renal and kidney function tests and coagulation tests were determined. Antiplatelet therapy was discontinued, and procedure undertaken with normal coagulation parameters (4). Description of the technique: In the block room, baseline pain NRS at rest was assessed, intravenous canula inserted and monitors of pulse oximeter, electrocardiography, non-invasive blood pressure, surface temperature probe (on affected limb) and surface electrode (for electrical stimulation) were attached. Patient was positioned laterally with affected limb non-dependent (Figure 1). A cloth roll was placed under the flank to expand space between lower ribs and iliac crest. Under standard aseptic precautions, a low frequency curved probe (FUJIFILM SonoSite Edge, 2-5 MHz) was placed transversely at the highest part of the iliac crest in abdomen mode. The lower border of kidney moving with respiration and the adjacent vertebral body and its transverse process were ascertained (Figure 2a). Colour doppler confirmed aorta and IVC anterior to the vertebral body (Figure 2b). 10 ml injection tubing with 10 ml saline syringe was attached to 15cm 22 G current stimulating needle (Stimuplex ,B. Braun) and de-aired. Needle tip was inserted in out of plane needle trajectory at the highest point of the iliac crest, between the lower pole of kidneys and the adjacent transverse process, directed towards the anterior part of the vertebral body (Figure 3). If needle tip was not visible, current of 2.0 Hz at 2A was applied to the needle. Thigh and knee of affected limb were left uncovered to view quadriceps contractions. Needle path was guided as below : a) Quadriceps contractions in patient and psoas muscle contractions on ultrasound; stimulation of lumbar plexus; needle tip at posterior part of psoas muscle; incorrect location. b) No quadriceps contraction in patient and psoas muscle contractions on ultrasound; needle tip lateral to vertebral body anterior to location A; incorrect location c) No quadriceps contractions in patient, no psoas muscle contractions on ultrasound and needle contact with bone; needle tip anterolateral to vertebral body anterior to location A and B; incorrect location d) No quadriceps contractions in patient, no psoas muscle contractions on ultrasound and no needle tip contact with bone; needle tip anterior to location A, B and C; correct location

Results: Of the 30 recruited patients, needle tip placement at location D was possible in all patients In 12 patients (40%), location D was reached in single needle attempt. In one patient, blood was aspirated at location D, needle tip was withdrawn and after negative blood aspiration and dye confirmation, local anaesthetic mixture was injected with no untoward complications. Ultrasonic landmarks of the block (lower pole of kidneys and transverse process of the vertebral body below the kidney) were identified in all patients. In 22 patients (73.3 %), fluoroscopic confirmation revealed needle tip at L3. NRS significantly decreased from pre-procedure baseline values at one week post-procedure till two weeks. All patients demonstrated an increase in temperature of 20 C or more in the affected limb, at 30 minutes post procedure. Lower limb ulcer, present in three patients, decreased in all by more than 35% at end of two weeks post procedure. All Patients remained hemodynamically stable.

Conclusion: ULS can be performed with an electrical stimulation needle , in out of plane needle trajectory.

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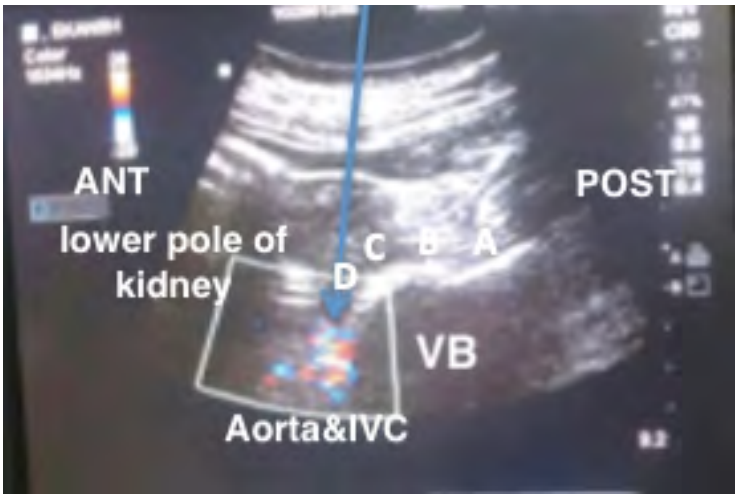

Pain Medicine - 2 Potential Value of a Survey of Treatment Expectations on Patient Satisfaction with Chronic Pain Management: Preliminary Results from a Prospective Study

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Introduction: Patient satisfaction improves patient adherence to treatment and is needed for quality improvement in healthcare. [1] It can be defined in context of the degree of congruency between the individual's expectations and actual clinical experiences. [2] Prior studies in the Pain Medicine literature have focused on identifying factors associated with patient satisfaction, such as the level of provider engagement. [3] The objective of this study is to determine if an expectation survey, administered prior to initial clinical evaluation, would lead to enhanced patient satisfaction regarding treatment planning and outcomes within the scope of chronic pain management.

Methods: This was an IRB-approved, prospective study at an outpatient chronic pain management clinic at an academic teaching hospital. 66 patients na√Øve to the Pain Medicine Department at the Multidisciplinary Pain Center were enrolled into the study. Participants were administered questionnaires in the waiting room prior to first visit with the provider. Primary outcome measures were pain rating and locations, prior treatments, expected degree of functionality, expected quality of life, opioid misuse and willingness to participate in treatment planning. Secondary outcome measures were satisfaction with treatment, satisfaction with meeting goals and expectations and satisfaction with overall experience. Statistical analysis was done using two tailed t-tests and ANOVA to define patient improvement.

Results: 66 patients, ages ranging from 21 to 87, naïve to the Pain Medicine Center were each administered a survey prior to the first visit with the provider. Based on a numerical pain rating scale of 0-10, the participants reporting pain rating > 0 were divided into three categories, participants with pain rating of 1-3 (n=4), participants with pain rating of 4-6 (n=5), and participants with pain rating of 7-10 (n=57) (Tables 1 & 2). Participants with a pain rating of 7-10 reported that improvement in Quality of Life (QoL) was extremely important in treatment planning compared to participants with pain ratings of 1-3 and 4-6 (65% vs 60% vs 50%) (Table 3). Participants with a pain rating of 4-6 reported that they expected QoL to be significantly improved compared to participants with pain ratings of 1-3 and 7-10 (60% vs 25% vs 56%) (Table 4).

Conclusion: Based on initial surveys, expectations of participants with a pain rating of 7-10 were that it was extremely important to have most significant improvement in QoL compared to expectations of participants with pain ratings of 1-3 and 4-6. The participants with a pain rating of 7-10 had the highest expectations for some sort of improvement in QoL, when compared to the other participants with pain ratings of 1-3 and 4-6. This study presents some preliminary results on expectations from participants undergoing initial evaluations in a Pain Management Clinic. Further data must be collected to determine true improvement in outcomes correlating with initial survey results.

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Table 1. Pain categories based on patient-reported numerical pain rating of 0-10

Average Pain Rating	Pain Category (Based on Average Pain in past 30 days)
0	0
1 to 3	1
4 to 6	2
7 to 10	3

Table 2. Number of patients in each pain category

Pain Category	Number of patients
0	0
1	4
2	5
3	57

Table 3. Number (percentage) of patients by degree of importance of quality of life improvement

Pain Category	Improvement of QoL not at all important	Improvement of QoL is not so important	Improvement of QoL is somewhat important	Improvement of QoL is very important	Improvement of QoL is extremely important
1	0	0	0	2 (50.0%)	2 (50.0%)
2	0	0	1 (20.0%)	1 (20.0%)	3 (60.0%)
3	1 (1.8%)	1 (1.8%)	7 (12.3%)	11 (19.3%)	37 (64.9%)

Table 4. Number (percentage) of patients by degree of expectations of quality of life improvement

Pain Category	Expect QoL to be mildly improved	Expect QoL to be moderately improved	Expect QoL to be fully improved
1	0	3 (75.0%)	1 (25.0)
2	1 (20.0%)	1 (20.0%)	3 (60.0%)
3	11 (19.3%)	14 (24.6%)	32 (56.1%)

Pain Medicine - 3 Improving Anesthesia Resident Knowledge of the Preoperative Management of Buprenorphine/Naloxone Therapy Through the Use of OSCE Teaching

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Introduction: Buprenorphine has been available since the 1970s and after passage of DATA 2000 it has been utilized for outpatient detoxification, addiction therapy and chronic pain treatment (1). Buprenorphine prescriptions in Kentucky increased from the first quarter of 2015 to the fourth quarter of 2017 from 30.8 to 46.6 per 1000 persons (2). Clearly, there is a growing need to address the specialized needs of patients on a Buprenorphine/Naloxone regimen. Buprenorphine/Naloxone contains a combination of buprenorphine and naloxone in different doses depending upon the prescription. Naloxone, an opioid antagonist, is added to the drug compound to ensure the drug is not abused by intravenous means. Managing intraoperative and postoperative pain in patients on a Buprenorphine/Naloxone regimen is complicated due to the complex pharmacology of the medication. All of these factors contribute to the complexity of developing a safe and effective treatment plan for patients on a Buprenorphine/Naloxone regimen. Given the increasing number of patients on Buprenorphine/Naloxone therapy, as well as the complexity of the medication, there is a clear need for further education on the perioperative management of patients on this medicateon in residency training programs. Simulation training has shown to be useful tool for the evaluation of resident performance within training programs (3). In this study, we attempted to develop an OSCE scenario to focus on this need for further education in the perioperative management of Buprenorphine/Naloxone in our anesthesia residents. The overall aim of this study is to evaluate the University of Kentucky Anesthesiology residency program training in intraoperative and postoperative pain management for patients with a history of Buprenorphine/Naloxone use by comparing OSCE scores each year of training.

Methods: This is a prospective study of the University of Kentucky Anesthesia residents from their PGY1 year through the PGY4 year of training. It is a cross-over study in that PGY-1 residents are fairly na√Øve to opioid management in patients undergoing treatment for opioid addiction, whereas, the same residents, in their third year, will be expected to have experienced some intervention for opioid management techniques for patients with opioid use disorder in the pain clinic, CAS, and inpatient surgical rotations. We did this by creating several OSCE stems. A case script was developed for each standardized patient that highlighted the major aspects of patient discussion including the anesthesia plan, patient's beliefs regarding pain, patient's coping strategies, post procedure pain control, and details regarding possible effects to their Buprenorphine/Naloxone therapy. A 20 point grading rubric was then developed to evaluate each anesthesia resident. After each OSCE session, a debriefing and teaching session was conducted. Scores from each year were then compared to each other to evaluate the effectiveness of OSCE teaching.

Results: Through this study, a 30% improvement was seen in overall OSCE scores from the PGY1 year to the PGY4 year.

Conclusion: Through this study, we found that PGY1 anesthesia residents had a limited knowledge base of the management of Buprenorphine/Naloxone therapy in the preoperative period. Our initial results show an overall improvement in OSCE scores over the residency training period. Limiting factors in this study include: multiple evaluators, the inability of certain residents to participate due to clinical responsibilities, and the inability to evaluate Group E in the 2020 period due to the COVID 19 Pandemic. Our future plans include development of a more complex OSCE scenarios to continue to present to the University of Kentucky residents. Further data points are needed to clearly show the relationship between OSCE teaching and anesthesia resident education.

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Pain Medicine - 4 Inpatient Opioid Stewardship Program Results in Fewer *Patients of Concern* at Discharge

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Introduction: The opioid epidemic remains a national public health crisis throughout the United States. In response, several institutions have implemented various programs to curtail adverse consequences from the use and prescribing of opioids. Evidence regarding the effectiveness of these programs is limited. Here we report a new post-implementation outcome associated with our institution's Opioid Stewardship Program: a reduction in the fraction of patients with escalating opioid demand immediately prior to discharge.

Methods: The Opioid Stewardship Program (OSP), an institution-wide quality improvement campaign, was launched in June 2019. It consisted of educational and informatics components. Daily opioid utilization was calculated for each inpatient as oral morphine equivalents (OME) and real-time data related to OME and pain scores were made readily available to treating physicians. Daily OME data was obtained for patients admitted to medical and/or surgical services for at least five days between January 2019 and June 2021. We defined opioid trajectories as a patient's total daily OME 1 day before discharge minus the total daily OME 4 days before discharge. We compared OME trajectories pre- and post- OSP implementation using Pearson's Chi-squared test with Yates' continuity correction. We also stratified these comparisons by surgical vs. non-surgical visits. Odds ratios for a positive trajectory post-OSP campaign were estimated via logistic regression. The Benjamini-Hochberg method for controlling the false discovery rate (FDR<0.05) was used to adjust for multiple comparisons.

Results: Of the 31,083 patients included in this analysis, the proportion of patients of concern, defined as those with positive OME trajectories (increasing opioid use immediately prior to discharge), was significantly lower after implementation of the OSP. Prior to OSP implementation, 32% of patients had a positive MME trajectory, compared to 30% afterward ($p<0.05$). Furthermore, after stratifying the data by surgical vs. non-surgical visits, we continued to observe a decrease in patients with positive OME trajectories in both groups following implementation of the OSP. For the surgical group, 31% had a positive MME trajectory before the OSP campaign, whereas 29% had one afterward ($p<0.05$, OR 0.92 [0.840, 0.998]). For the non-surgical group, 34% had a positive MME trajectory prior to OSP implementation, compared to 30% after ($p<0.05$, OR 0.83 [0.75,0.91]). All comparisons were significant when using the Benjamini-Hochberg FDR control method ($p<0.05$, FDR<0.05).

Conclusion: Following implementation of the OSP, there was a significantly reduced proportion of patients who had an escalating use of opioid medications prior to discharge. Future studies will define whether changes in OME trajectories correlate with improved long-term outcomes.

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Pain Medicine - 5 Identification of Foramen Ovale with H-figure Fluoroscopic Landmark Improves Treatment Outcomes in Idiopathic Trigeminal Neuralgia

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Introduction: Radiofrequency thermocoagulation (RFT) of trigeminal ganglion through foramen oval (FO) is an effective way to manage idiopathic trigeminal neuralgia (ITN),1, 2 one of the most common causes of persistent intense orofacial pain with an incidence of 12.6 per 100,000 persons per year.3 However, the ambiguous fluoroscopic visualization of FO by existing approaches often lead to prolonged procedure time and suboptimal distance between the active RFT needle tip and target branches of trigeminal ganglion. This ambiguity can also lead to inadvertent puncture of the jugular foramen and/or foramen spinosum that causes injury to the internal carotid artery or middle meningeal artery - both can be fatal complications.4-6 Recently, we developed the 'H-figure' approach as a novel and easily-recognizable fluoroscopic landmark that significantly facilitates the visualization of FO with less fluoroscopic shots and shorter procedure time.7, 8 The H-figure landmark composes of two vertical lines from the medial border of mandible and lateral edge of maxilla, and one horizontal line from the Superior line of Petrous ridge of Temporal bone (S-P-T line). With H-figure fluoroscopic landmark, the FO fluoroscopic view can be easily optimized above the S-P-T line at the center of the H-figure when the medial end of the temporomandibular joint is located midpoint between the lateral and medial borders of mandible.7 Compared to the classical approach, RFT needle inserted by H-figure method required lower electrical stimulation to elicit paresthesia in affected area after FO puncture,7 suggesting that the needle tip from H-figure approach is closer to the target trigeminal ganglion branches. However, it remains unclear if RFT performed with H-figure has better clinical outcomes. We now report a 12-month follow-up retrospective cohort study to show that RFT with H-figure fluoroscopic approach is associated with better long-term therapeutic efficacy in managing idiopathic trigeminal neuralgia than the classical approach.

Methods: In a 12-month follow-up retrospective cohort study, patients with ITN had fluoroscopy-guided RFT of trigeminal ganglion via either classical approach (n=100) or H-figure approach (n=136) to identify FO. The primary outcome was the facial pain measured by Visual Analogue Scale (VAS) at one year after the treatment. The secondary outcomes included the quality of the fluoroscopic FO views, the threshold voltage to provoke paresthesia, the procedure time, the number of fluoroscopic images, and the facial numbness VAS.

Results: Compared with the classical approach group, the H-figure approach group was associated with better long-term pain relief after the procedure, with significantly lower pain VAS scores at 6 months (0.5±0.1 vs. 1.3±0.2, p=0.029) and 12 months (1.0±0.2 vs. 2.0±0.3, p<0.0001). Importantly by 12 months, while the analgesic effect from RFT in the classical group started to wear off (1.1±0.2 at 1 week vs. 2.0 ±0.3 at 12 months, p=0.0013), the analgesic effect was sustained in H-figure group (0.7±0.1 at 1 week vs. 1.0 ±0.2 at 12 months, p=0.5670). Moreover, compared to the classical approach, the H-figure approach provided better fluoroscopic view of FO, lower threshold voltage to elicit paresthesia (0.23±0.01 vs. 0.46±0.01 V, p<0.0001), with shorter procedure time (7.8±0.2 vs. 14.7±0.5 min, p<0.0001), and required less number of fluoroscopic images (4.2 ±0.1 vs. 8.0±0.3 p<0.0001).

Conclusion: RFT of the trigeminal ganglion using the H-figure approach is associated with superior longer term clinical pain relief than the classical approach in treating ITN.

References: 1. Pain Pract. 2021;21(1):26-36. 2. Clin J Pain. 2019;35(12):958-966. 3. Pain. 2011;152(3):507-13. 4. J Neurosurg. 2009;110(4):638-41. 5. J Clin Neurosci. 2007;14(6):563-8. 6. Neurosurgery. 2004;54(6):1522-4. 7. Reg Anesth Pain Med. 2021;46(4):350-353. 8. Reg Anesth Pain Med. 2021.

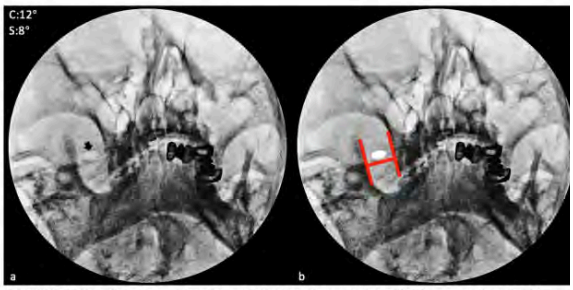

FIGURE 1. The fluoroscopic landmark of the H-figure to identify foramen ovale (FO).

a. The fluoroscopic view of FO, which is indicated by the black arrow. **b.** The H-figure composes of two vertical lines which are the medial border of mandible and lateral edge of maxilla, and one horizontal line which is the Superior line of Petrous ridge of Temporal bone (S-P-T line). The FO marked by the white ovale. C: coronal angle; S: sagittal angle.

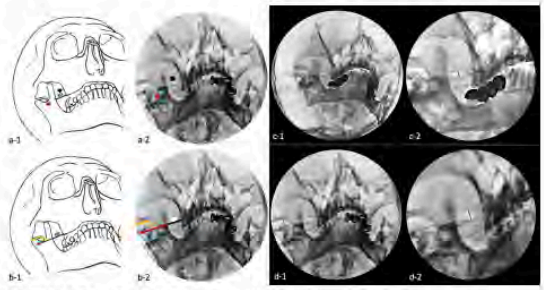

FIGURE 2. Identification of foramen ovale (FO) with medial end of temporomandibular joint and S-P-T line and the grades of FO view with different width to length ratio.

a-1 and a-2 FO is at the center between the medial border of mandible and lateral edge of maxilla when the medial end of temporomandibular joint at the midpoint between lateral and medial borders of mandibular ramus. The red arrow indicates the medial end of temporomandibular joint, the black arrow indicates FO. **b-1 and b-2** The medial end of the temporomandibular joint is on the on the lateral extension of S-P-T line. The red arrow indicates the lateral extension of S-P-T line, the yellow arc marked the medial end of temporomandibular joint, and the white ovale marked FO. **c.** Grade 1 FO view (**c-1**) with width to length ratio of 1/3, and **c-2** is the amplified image of red circle in **c-1**. **d.** Grade 2 FO view (**d-1**) with width to length ratio of 2/3, and **d-2** is the amplified image of red circle in **d-1**. The black line indicates width, and the grey line indicates length.

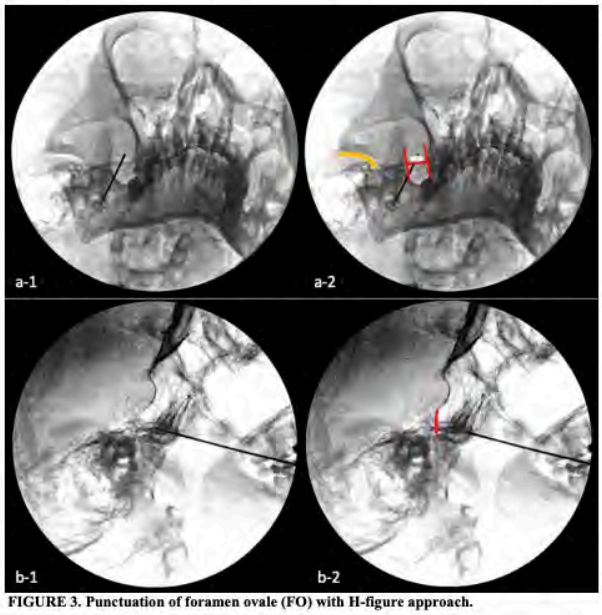

FIGURE 3. Punctuation of foramen ovale (FO) with H-figure approach.

a. The image of FO punctuation (**a-1**) with highlighted H-figure (**a-2**) in oblique projection. The white ovale marked FO, the yellow arc shape indicates the temporomandibular joint, and the red arrow indicates the midpoint between lateral and medial borders of mandibular ramus. **b.** The image showing the position of the needle tip (**b-1**) with highlighted clivus (**b-2**) in lateral projection. The red vertical line indicates the clivus.

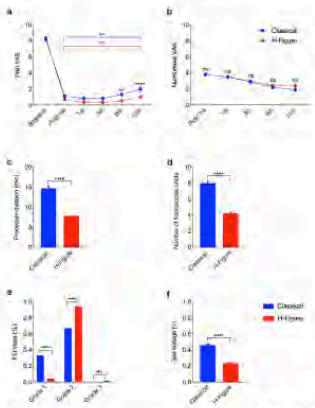

FIGURE 4. H-figure method is superior to classical method in treating ITN with RFT.

Compared with to the classical method, H-figure method provided better long-term facial pain alleviation (**a**) without significant difference in facial numbness (b) through taking about half the procedure time (**c**), with approximately half number of fluoroscopic shots (**d**), better view of FO (**e**), and roughly half testing voltage to evoke paresthesia (**f**). Data were presented as mean ± SEM. Analyses were performed using two-way ANOVA with post-hoc Sidak's multiple comparison test (**a-b**), unpaired two-tailed Student's *t* tests (**c, d, f**), and two-tailed Chi-square test (**e**). $^{**}p<0.01$, $^{****}p<0.0001$. FO: foramen ovale, RFT: Radiofrequency thermocoagulation, ITN: idiopathic trigeminal neuralgia

Pain Medicine - 6 Machine Learning Can Identify Geographic Disparities in Opioid Overdose Before and After the COVID-19 Pandemic

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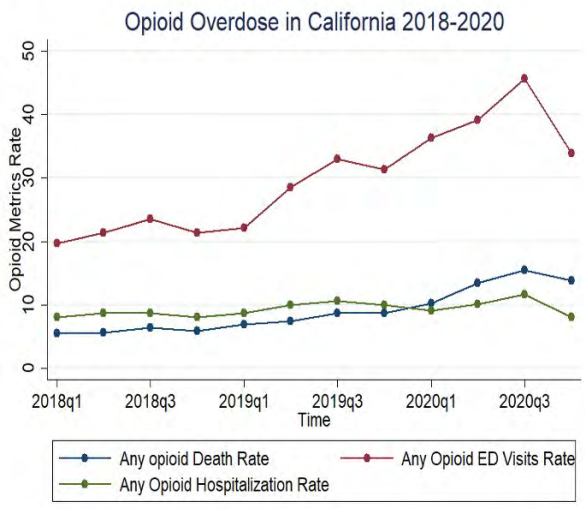
Introduction: New data suggest that COVID-19 has exacerbated the opioid epidemic. 1 Unexpected increases in overdose mortality have highlighted potential weaknesses in our nation's approach to prevention and treatment of opioid related adverse outcomes. California, with its robust data collection history in this domain, may provide helpful insights on the geographical patterns and potential associations between the opioid epidemic and COVID-19 pandemic. The objective of this study was to compare the opioid overdose risks in different rural/urban regions within California before and after the start of the COVID-19 pandemic and identify sociodemographic risk factors

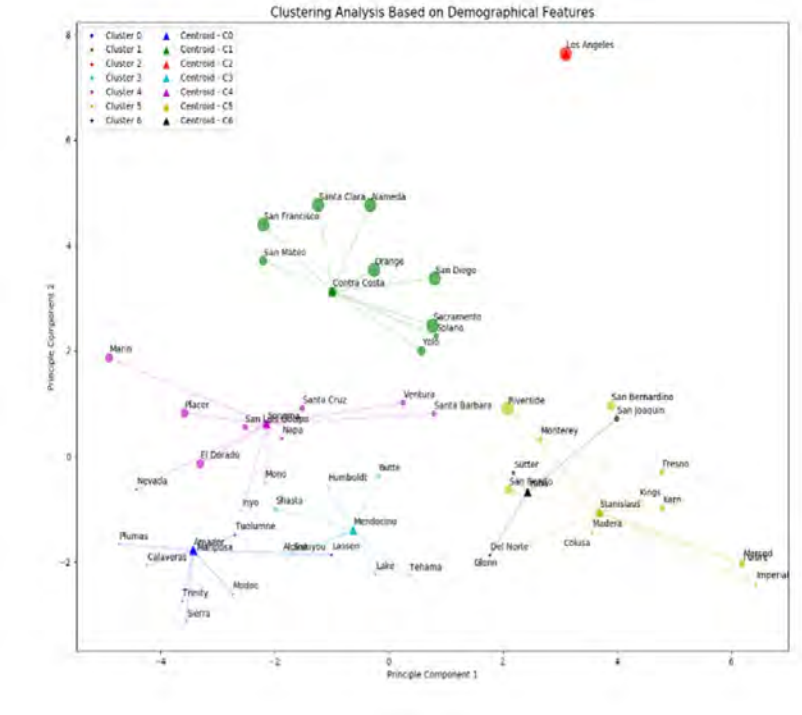
Methods: This study used publicly available, deidentified data and was exempt from IRB review. We included cross-sectional data from 2018 to Dec. 2020 from 1) the California Opioid Overdose Surveillance Dashboard that integrates metrics for thirty opioid-related adverse outcomes (including overdoses and deaths) across California's 58 counties; 2) demographic variables (age, race, gender, socioeconomic status, education, county) from the University of California San Francisco Health Atlas; and 3) urban-rural classifications at the county level from the National Center for Health Statistics (large central metropolitan, large fringe metropolitan, medium metropolitan, small metropolitan, micropolitan, noncore region). The period prior to March 2020 (statewide shelter in place order in effect) was designated as the pre-Covid era. Our statistical analysis involved several steps. First, we evaluated trends in overall opioid adverse outcomes from 2019-2020 within California and studied the opioid overdose risks across all counties within California. Second, we used affinity propagation clustering techniques to group the counties a) based on their sociodemographic and geographic features; and b) based on thirty opioid-related adverse outcomes between the pre-Covid and Covid eras. Features were selected after testing to build models. We used Python (version 3.10.0, Python Software Foundation) and Stata (version 17, Stata Corp.) for the statistical analyses. For all analyses, two-tailed nominal P-values of < 0.05 were considered significant.

Results: From 2019 to 2020, California experienced increases across 3 key opioid-related adverse outcomes: deaths, emergency department visits, and hospitalizations (Fig. 1). Large central metropolitan counties experienced the largest absolute increase in any opioid-related death rate (median 7.76 to 13.76 deaths/100,000). The six-level urban-rural classifications (e.g., large central metropolitan, micropolitan,.) were strongly associated with clustering labels based on the various opioid overdose metrics, the Pearson Chi-2 statistic is 77.79($p<0.001$) (Fig 2). Clustering results show that after the pandemic started, opioid-related deaths and emergency department admission risks were higher in the micropolitan counties relative to small metropolitan and non-core counties.

Conclusion: After the COVID-19 pandemic began, many regions in California experienced increases in opioid-related adverse outcomes. Micropolitan counties (geographic areas of 10-50,000 people) experienced disproportionate increases in opioid-related deaths and emergency department risks relative to their opioid prescription rates. These data suggest a worsening of healthcare disparities regarding the opioid response in micropolitan areas compared to larger cities, and additional resources may be needed in these areas to mitigate opioid deaths as the pandemic continues.

References: 1. Provisional drug overdose death counts. National Center for Health Statistics. 2021. 2. https://covidactnow.org/data-api





Pain Medicine - 7 Liposomal bupivacaine compared to conventional bupivacaine in transversus abdominis plane blocks for elective lower abdominal surgery

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Introduction: Transversus abdominis plane (TAP) blocks, using local anesthetic infiltration, are an established method for providing postoperative analgesia for abdominopelvic surgeries.1-6 Liposomal bupivacaine (LB) is an extended-release formulation of bupivacaine reported to provide up to 72 hours of analgesia, significantly longer than conventional bupivacaine (CB).7 The purpose of our study is to examine institutional experience of liposomal bupivacaine for TAP blocks in patients undergoing elective lower abdominal surgery. We investigated if LB was associated with reduced opioid consumption and pain scores compared to CB.

Methods: This is a retrospective cohort study of patients who underwent TAP blocks with either LB or CB for post-surgical anesthesia following elective lower abdominal surgery between 12/1/2020 and 8/31/21 at a single institution. Patients who had a second surgery within 48 hours of the original surgery were excluded from analysis. After institutional review board approval, data was collected on demographic information, surgical type, average and maximum pain scores and total opioid consumption in Morphine Milligram Equivalent (MME). Data presented as means (SD), medians [IQR], or frequency counts (%) as appropriate; $p < 0.05$ considered significant.

Results: A total of 144 patients were included in our analysis: 81% (117) were female and 95.1% (137) white. The most common procedures involved were hysterectomy 37.5 % (54), pelvic mass resection 20.1% (29), ileostomy closure 12.5% (18), nephrectomy 11.1% (16), cesarean section 6.9% (10), and herniorrhaphy 6.3 (9). Most of the procedures, 92.4% (133), were performed under general anesthesia. There was no statistically significant difference in average dose of opioid consumption on postoperative days (POD) 0, 1, 2 in LB TAP block compared to CB TAP block (Table 1). Additionally, there was no statistically significant difference between the average pain scores and maximum pain scores between LB and CB TAP block groups. Patients who underwent TAP block with LB received opioids less frequently than those with CB TAP block, but this did not reach statistical significance.

Conclusion: LB TAP block following lower abdominal surgeries did not show a statistically significant difference in opioid consumption or pain scores compared to conventional bupivacaine, however our findings were limited by a small sample size in the LB TAP group. There were no differences in pain scores at the time points investigated. A larger sample size may be required to detect significant differences in these outcomes.

References: 1. Anesth Analg. 2008;107(6):2056-2060. 2. Surg Endosc. 2010;24(10):2480-2484. 3. J Pain Res. 2014;7:477-482. 4. Dis Colon Rectum. 2014;57(11):1290-1297. 5. J Surg Res. 2015;195(1):61-66. 6. Anaesthesia. 2001;56(10):1024-1026. 7. J Pain Res. 2012;5:107-116.

Table 1: Patient outcome measures, stratified by use of TAP block with liposomal bupivacaine

Variable	TAP block with liposomal bupivacaine			
	Yes		No	
	Measurement		Measurement	p-value
N	32		112	
Local anesthetic dose (mg)	-		106	120 [88.5-120.0]
MME				
POD 0	40.5 [23.1-79.9]		63.0 [27.0-107.5]	0.26
POD 1	16.0 [10.0-67.5]		38.8 [18.4-60.0]	0.15
POD 2	74.4 [61.9-273.8]		56.0 [22.5-101.7]	0.35
Average pain score				
POD 0	4.7± 1.9		5.2 ± 1.7	0.15
POD 1	4.7 ± 1.6		4.9 ± 1.4	0.38
POD 2	4.6 ± 2.5		4.3 ± 1.5	0.79
Maximum pain score				
POD 0	7.1 ± 1.8		7.7 ± 1.8	0.15
POD 1	6.6 ± 1.9		7.0 ± 1.7	0.48
POD 2	5.4 ± 3.4		5.9 ± 2.7	0.68

Abbreviations: POD, post-operative day; calculated as 24-hour periods after anesthesia stop time
Data are shown as mean ± standard deviation or as median [interquartile range]

Pain Medicine - 8 Pain on top of pain: The impact of longstanding chronic non-cancer pain on the management of acute pain in patients with cancer

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Introduction: Pain is a central symptom for postsurgical patients who present to the emergency department (ED) after cancer surgery. Acute pain exacerbation is often even more complex and challenging to manage among those with a history of chronic pain (CP). The current study aimed to compare pain-related outcomes and ED and hospital length of stay, between cancer patients with and without a history of chronic pain.

Methods: Methods: Cancer patients presenting to the ED with a complaint of acute pain (> 4/10 NRS) completed validated self-report measures assessing socio-demographics, cancer diagnosis and treatment, pain severity (BPI-SF), medication use, and psychosocial wellbeing (depression, anxiety, pain catastrophizing, sleep disturbance), as well as length of time since most recent surgery. Pain scores, opioid administration, length of stay were abstracted from the medical record. Groups were defined according to whether they endorsed having other chronic pain (>3 months) prior to cancer diagnosis. Mann-Whitney U, t-tests, and chi-square tests were used to compare groups on several pain-related outcomes.

Results: Results: About 30% (50/173) of the participants reported having chronic pain before cancer. Metastatic disease was common (76%), and 42% were using opioids, which did not differ between groups(p=0.40). However, patients with historical CP were more likely to receive opioids in the ED (70% vs 53%) and as inpatient (97% vs 71%) compared to those without historic CP. Similarly, patients with historical CP received a higher total dose of opioids (Morphine Mg Equivalents, MMEs) during their ED stay (27.0±40.1 vs 20.4±48.8, p=0.034) and during their inpatient stays (m=446.8± 655.3 vs 263.2±604.1, p=0.006; also when normalized per hour of admission (3.4±3.3 vs 1.5±2.2, p<0.001). Despite receiving more opioids, patients with historical CP had higher average pain scores in the ED (6.1±1.9 vs 5.1±2.1, p=0.003) and during their inpatient stay (4.6±1.9 vs 3.0±1.8, p<0.001). However, there was no difference in stay duration in ED (12.5 ±13.3 vs 10.5±9.2 hours, p=0.17) or hospital (146.4± 151.9 vs 148.6±157.4, p=0.65), or differences in psychological well-being.

Conclusion: Pain and opioid consumption during ED stay and hospital admission were higher in cancer patients with a history of other CP. These findings underscore the challenge of managing pain while preventing post-discharge dose escalation in cancer patients who has a history of chronic pain, and highlight the importance of implementing multimodal pain management strategies.

References: Azizoddin DR, Schreiber KL, Beck MR, Enzinger AC, Hruschak V, Darnall BD, Edwards RR, Allsop MJ, Tulsky JA, Boyer E, Mackey S.Chronic pain severity, impact, and opioid use among patients with cancer: An analysis of biopsychosocial factors using the CHOIR learning health care system. Cancer. 2021 Sep 1;127(17):3254-3263. PMID: 34061975

Pain Medicine - 9 Buprenorphine ordering patterns during and after critical illness

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Introduction: Buprenorphine (BUP) is a partial opioid agonist administered for induction and maintenance treatment of opioid use disorder (OUD).1 The 2018 PADIS clinical practice guideline did not include recommendations for managing prior to admission (PTA) BUP use during critical illness.2 The objectives of this study were to describe the clinical characteristics of patients receiving BUP prior to intensive care unit (ICU) admission, characterize BUP and opioid dosing patterns during critical illness, and to evaluate the incidence of BUP prescribing upon hospital discharge and at 3 and 12 months post-hospital discharge.

Methods: We performed a retrospective electronic medical record review of all patients requiring ICU admission between December 1, 2014 and May 1, 2019 at a single institution after obtaining Institutional Review Board approval. Patients were included if they were ,â•18 years of age and were receiving BUP prior to hospital admission. Patients were excluded if they transferred to a different hospital, had a hospital length of stay <24 hours, did not survive to hospital discharge, or were prescribed BUP for chronic pain. Only the first ICU admission for each patient was used. Opioid dosing in the ICU and post-ICU was obtained from a computer-generated report and post-hospital discharge opioid data came from the state-maintained Prescription Monitoring Program. Opioid doses were converted to fentanyl-equivalents (FE). Data are reported as median (IQR) or frequency (%).

Results: A total of 34 patients were included with a median age of 38 [32-46] years and an ICU length of stay of 3 [2-6] days. Most patients (23/34, 68%) required invasive mechanical ventilation for 2 [1-7] days and were admitted to the trauma service (15/44, 44%). The median PTA BUP dose was 16 (12-16) mg/day. BUP was ordered in the ICU for 12/34 (35%) patients who received it PTA, increasing to 24/34 (70%) after transfer to a non-ICU floor. BUP patients received 921 [329-1469] FE/day while in the ICU, decreasing to 168 [19-278] FE/day after ICU discharge to a non-ICU floor. A total of 56% patients were discharged from the hospital on their PTA BUP, while 29% received opioids other than BUP. Among patients receiving an opioid prescription post-hospital discharge, BUP use was 27/30 (87%) at 3 months and 25/26 (96%) at 12 months.

Conclusion: 35% of ICU patients prescribed BUP prior to admission received it during their ICU course. Approximately half of patients received a BUP prescription for upon hospital discharge and 25/26 (96%) of patients receiving an opioid prescription were using BUP again at 12 months. Further study is needed to determine the clinical implications of continuing or withholding premorbid buprenorphine in the ICU and to determine the rationale for doing so for differing patient characteristics.

References: References 1. Medications for Opioid Use Disorder. 2021; Treatment Improvement Protocol 63. 2. Crit Care Med. 2018;46(9):e825-e873

Table 1. Demographics and ICU Characteristics

Variable	N=34
Age, years	37.5 [32.3-45.8]
Male, no. (%)	17 (50.0)
Race	
White	30 (88.2)
African American	1 (2.9)
Asian	2 (5.9)
Other	1 (2.9)
BMI (kg/m^2)	25.6 [22.9-29.2]
Reason for admission	
Trauma	15 (44.2)
Sepsis	6 (17.6)
Respiratory failure	5 (14.7)
Endocarditis/soft tissue infection/ osteomyelitis	4 (11.8)
Cardiac arrest	2 (5.9)
Overdose	2(5.9)
Home buprenorphine dose (mg)	16 [12-16]
ICU LOS, days	3.0 [2.0-6.2]
Hospital LOS, days	14.0 [6-34.7]
Mechanical ventilation, n (%)	23 (67.6)
Mechanical ventilation, days	2.2 [1.0-6.6]
Discharge disposition, n (%)	
Home or self-care	26 (76.5)
Acute rehabilitation facility	6 (17.6)
Skilled nursing, intermediate care, long-term care	2 (5.9)
Self directed discharge	1 (2.9)

Continuous variables reported as median (IQR) and proportions as number (%)

BMI= body mass index ICU = intensive care unit; LOS = length of stay

Table 2: ICU, Post-ICU, Hospital and Post-discharge Opioid Exposure Data

Variable	N=34
ICU opioid fent equiv (mcg)	2173 [689-8471]
ICU fent equiv/day (mcg)	921 [329-1469]
ICU buprenorphine given n(%)	12/34 (35%)
ICU buprenorphine (mg)	7.5 [3.2-25]
ICU methadone given n(%)	10 (29%)
ICU methadone (mg)	132.5 [31.2-262.5]
post ICU opioid fent equiv	1345 [166-3430]
post ICU fent equiv/day	168 [19.4-277.8]
post ICU buprenorphine given n(%)	24/34 (70%)
post ICU buprenorphine (mg)	16.5 [6.0-75.2]
Post ICU methadone given n(%)	12(35%)
post ICU methadone (mg)	213.8 [160-392.5]
Hospital total fent equiv, mcg	5062 [2192-13,208]
Hosp total buprenorphine (mg)	14.5 [6.2-67.0]
Hosp total methadone (mg)	437.5 [236.2-572.5]
Survival at 3 months	34 (100.0)
Opioid at 3 months post-discharge, n (%)	30 (88.2)[c]
% receiving buprenorphine	26/30 (86.7)
Survival at 6 months	33 (97.1)
Opioid at 6 months post-discharge, n (%)	30/33 (90.9)
% receiving buprenorphine	27/30 (90.0)
Survival at 12 months	33 (97.1)
Opioid at 12 months post-discharge, n (%)	26/33 (78.8)
% receiving buprenorphine	25/26 (96.2)

Continuous variables reported as median (IQR) and proportions as number (%)

Fent equiv =fentanyl equivalents

Pain Medicine - 10 Gender Distribution of Editorial Members of Pain Medicine Journals

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Introduction: The purpose of this study was to characterize the gender distribution among pain medicine editorial boards.

Methods: This study represents a cross-sectional analysis. Selection Criteria: Active pain medicine journals with titles that included any English or non-English iteration of the word 'pain,' pain-related therapies, or focused on pain management were selected from the SCImago Journal & Country Rank list in 2021.1 Data collection: Editorial board member information was parsed from journal websites and editors were categorized into three groups: editors-in-chief, executive/section/senior editors, and editors/associate editors. Gender was assigned according to member profiles from the journal website, as well as from other works denoting their pronoun. Available photographs were used to further confirm gender. The Genderize program2 was used twice, when gender could not be determined otherwise.

Results: Of 126 journals, 38 met inclusion criteria and 2146 editors were categorized. Men comprised the majority across all categories, representing 75.5% (1620/2146) of all editorial board members. Of 50 editors-in-chief, 47 (94%) were men. For executive/section/senior editors, 156/203 (76.8%) were men. The editor/associate editor category showed the smallest disparity, with men numbering 1417/1893 (74.9%).

Conclusion: Women are disproportionately underrepresented in the higher ranks of editorial boards. The magnitude in gender disparity was directly related to editorial rank. The gender distribution of authorship in pain publications, leadership positions in medicine, graduating pain medicine fellows, and practicing pain physicians has historically skewed male. Although women accounted for 45.1% of the 144988 active residents in US programs for the 2019-2020 academic year, they made up only 22.8% of pain medicine fellows and 19% of practicing pain management physicians.3,4 Disproportionate gender distribution in pain journal editorial boards may lead to bias in pain literature and subsequently clinical practice. Despite this, women represented 40% of authors in all positions of authorship in pain publications.5 Similar trends have been identified in editorial boards of other specialties. A 2020 study of emergency medicine journals, for example, found that only 8.7% of editors-in-chief and 16.3% of total editorial board members were women.6 Academic productivity is critical for career advancement. Disproportionate access to these career-advancing distinctions may in turn increase the opportunity for further gender bias to develop within medicine

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Pain Medicine - 11 Do Mechanically Ventilated Covid-19 Patients on Prolonged Opioid Infusions Require Opioids upon Hospital Discharge?

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Introduction: Intubated COVID-19 patients often require opioid infusions to combat pain and facilitate synchronization with mechanical ventilation. In addition, chronic pain can develop after both surgical and medical ICU care, with one study showing 44% of patients reporting chronic pain 6 months to 1 year after ICU stay [1-6]. Therefore, critically ill COVID-19 patients are at a theoretical risk of developing chronic pain and opioid dependence. We evaluated a cohort of COVID-19 intubated patients treated with opioid infusions to compare those who were discharged with opioids to those who were not.

Methods: A retrospective case control analysis was performed on 42 COVID-19 intubated patients treated with opioid infusions from February 1, 2020 to May 1, 2020 at a large New York City hospital. The electronic medical record was queried to identify 56 patients who were discharged with opioids after COVID-19 intubation. Of those, 21 were selected at random for chart review and compared to 21 controls. Variables included duration of ventilator use and opioid infusion, opioid dosages, history of substance abuse and basic demographics such as gender, age, and comorbidities. Data was analyzed using Stata v17. Descriptive statistics were calculated, and continuous variables were evaluated using students t-test. Logistic regression was used to look for covariables associated with the use of opioids at discharge.

Results: There were no significant differences in the demographic data and baseline clinical characteristics between the cases (patients discharged with opioid) and controls (patients not discharged with opioid) (Table 1). The mean age of the cases and control groups were 55.8 and 58, respectively. There was no significant differences between the cases and controls for mean number of days on the ventilator (26.6 and 16.6, respectively), number of days on opioid infusions (10.16 and 5.16, respectively), or maximum dosages of fentanyl (150 mcg/hr and 137 mcg/hr, respectively) and hydromorphone (0.87 mg/hr and 1.7 mg/hr, respectively) (Table 2). None of the variables evaluated were significantly associated with opioid use at discharge (Table 3).

Conclusion: In a small study of 42 intubated COVID-19 patients, there was no statistically significant association between the duration or dose of opioid administration while mechanically ventilated and the incidence of opioid use at discharge. This finding is consistent with other recent studies [7- 13]. Although this study is limited by a small sample size, the results add to the evidence that in COVID-19 intubated patients, high dose opioid infusions may not increase the risk of later opioid use.

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Demographic Categories		CASES	CONTROLS	P Value
Gender				
	Male	7	10	
	Female	8	17	NS
Age				
	25-34	2	5	
	35-44	3	1	
	45-54	3	4	
	55-64	2	4	
	>64	5	13	NS
	(Mean ± SD)	55.9 ± 17.6	58. ± 16.3	NS
Clinical Characteristics		N		
	Hx of Pulm Dz	3/15	10/25	NS
	Hx CV Dz	6/15	7/25	NS
	HTN	5/15	16/25	NS
	DM	2/15	9/25	NS
	Tobacco	0/15	4/25	NS
	Alcohol	0/15	5/25	NS
	Illicit Drug Use	3/15	3/25	NS
	Prior Opioid Use	2/15	2/25	NS

Table 1. Clinical Characteristics between Cases and Controls: Percent of patients based on gender, age, and clinical characteristics or comorbidities. Hx (History), Pulm (pulmonary), CV (cardiovascular), Dz (disease), HTN (hypertension), DM (diabetes), NS (not significant).

Results		CASES	CONTROLS	P Value
Days on Vent	(Mean ± SD)	26.6 ± 37.6	16.6 ± 24.6	0.84
Days on Opioids	(Mean ± SD)	10.16 ± 15.3	5.16 ± 9.6	0.89
Max Dose of Fentanyl (mcg/hr)	(Mean ± SD)	150.0 ± 198.2	137.0 ± 192.5	0.58
Hydromorphone (mg/hr)		.87 ± 2.9	1.7 ± 3.3	0.18

Table 2. P-Value > 0.05, No Statistical Significant Difference in Days on Ventilator, Days on Opioids, and Maximum dosages on Fentanyl and Hydromorphone Between Cases and Controls.

Discharged with opioids	Odds ratio	Std. err.	z	P>|z|	[95% conf.	interval]
Ventilator days	1.007697	.021169	0.37	0.715	.9670496	1.050054
Opioid days	1.045182	.0526096	0.88	0.380	.9469918	1.153552
Fentanyl	0.9935767	.0083709	-0.76	0.444	.9773048	1.01012
Hydromorphone	.8771579	.1202525	-0.96	0.339	.6704767	1.147551
Fentanyl by dosage	2.211459	3.085065	0.57	0.569	.1436223	34.05146

Table 3. Logistics Regression Model: P-Value > 0.05, Odds Ratio of Different Independent Predictors (i.e. ventilator days, opioid days, fentanyl infusion only, hydromorphone infusion only, fentanyl by dosage) Versus Dependent Binary variable (i.e. Discharged with Opioids). Std. err. (standard error), Z (z- score), P (p-value), 95% conf. interval (95% confidence interval).

Pain Medicine - 12 It's lonely at the top (of the pandemic): Depression mediates the impact of loneliness on pain-related catastrophizing during COVID-19

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Introduction: Feelings of loneliness increased during the pandemic-related social distancing, potentially exacerbating negative cognitions about pain. Individuals with chronic pain may have been more at risk of isolation as a result of social distancing guidelines, and consequently worsen pain. Chronic pain is often comorbid with depression, and thus, depression may link feelings of loneliness and negative cognitions about pain. Because pain catastrophizing is a modifiable risk factor, it is important to identify factors related to increased catastrophic pain-related cognitions as a means of indirectly reducing pain.

Methods: Participants (n=93) living with chronic pain (pain for ≥3 months) completed two sets of electronic questionnaires. The initial set of questionnaires was completed from April 28-June 17, 2020 (Time 1, T1) and the follow-up survey a year later from May 21-June 7, 2021 (Time 2, T2). The 3-item UCLA Loneliness Scale Version 3 assessed feelings of loneliness at T1. The 13-item Pain Catastrophizing Scale assessed negative cognitions about pain at T1 and T2. The 8-item depression short form from the Patient Reported Outcome Measurement Information System was used to measure depressive symptoms at T2. Spearman correlations and Mann-Whitney U test were used to explore associations between psychosocial, pain, and demographic characteristics. A mediation analysis investigated whether depression (T2) mediated the relation between loneliness (T1) and pain catastrophizing (T2). Covariates from T1 included average pain intensity and pain interference, pain medication use, (patients indicated whether or not ('yes' or 'no') they typically take any medications for their pain),and baseline pain catastrophizing.

Results: Greater feelings of loneliness (T1) were associated with higher levels of pain catastrophizing (T2) (Figure 1). Pain catastrophizing (T2) was associated with greater depression, pain severity and pain interference, pain medication use, and baseline catastrophizing (T1). A mediation analysis investigated whether depression (T2) mediated the relation between loneliness (T1) and pain catastrophizing (T2). The model was significant, $F(6, 85) = 18.85$, $p < 0.001$, $R2 = 0.562$, and there was a significant indirect effect of loneliness on pain catastrophizing through depression ($b = 0.57$, 95% CI [0.15, 1.31]). This mediation analysis demonstrated that there was a significant indirect effect of loneliness on pain catastrophizing through depression. The direct effect of loneliness on pain catastrophizing was no longer significant when depression was included in the model.

Conclusion: The longitudinal design of this study allowed identification of early loneliness as a unique predictor of subsequent pain catastrophizing. Greater severity of depression during the pandemic year partially mediated this relationship. Findings suggest feeling lonely may contribute to depressed mood, leading to more maladaptive cognitions about pain. Future studies may benefit from investigating the temporal associations among these variables over the course of empirically-supported treatments that can improve cognitive and affective outcomes.

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Pain Medicine - 13 Dysfunction of the descending pain-modulation system is involved in the augmented pain response after traumatic brain injury

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Introduction: Individuals with histories of traumatic brain injury (TBI) exhibit high rates of acute and chronic pain. Such patients may be susceptible to persistent pain after peripheral injuries. Recent laboratory and clinical data suggest dysregulated endogenous pain-modulating circuits could also be involved. Brainstem output nodes of this pain-modulating system, such as rostral ventromedial medulla (RVM) and locus coeruleus (LC), play an important role in regulating pain-related behaviors and nociceptive processing via their projections to the dorsal horn. The pain-modulating function of these descending projections can be controlled by the endogenous opioid tone in the brainstem. Interestingly, endogenous opioid concentration in brainstem regions is altered after TBI, rising the possibility that the dysfunction of brainstem pain-modulating system after TBI is opioid-mediated.

Methods: These studies employed a recently developed mouse closed head model of TBI and a well-established model of incisional pain. Pain sensitization was quantified using mechanical pain thresholds in cohorts of mice from 1 to 100 days after injuries. Immunohistochemical staining of c-fos was used to identify nuclei involved in the observed pain-related behaviors after naloxone administration

Results: We observed pain sensitization bilaterally in the hindpaws of mice with TBI lasting up to 10 days. When hindpaw incisions were made in control and TBI mice after recovery of normal pain thresholds, mechanical thresholds in control mice returned to baseline after 7 days, while those animals with prior TBI experienced prolonged sensitization lasting up to 38 days. Furthermore, blockade of central but not peripheral mu opioid receptors (MORs) led to mechanical sensitization in both hindpaws in animals recovered from TBI. Control animals and those with incision alone did not experience changes in their pain thresholds after MOR blockade. Increased neuronal activation, marked by c-Fos staining, was observed in brain regions important for descending pain-modulation, such as rostral ventrolateral medulla and locus coeruleus, in animals recovered from TBI after MOR blockade.

Conclusion: Collectively, these data suggest that dysfunctional descending pain-modulation is responsible for the slow resolution of pain after peripheral injury in the setting of TBI. The endogenous opioid system is important for the subsequent recovery of pain sensitivity after TBI but not after peripheral injury alone. Identifying ways to enhance endogenous pain control mechanisms may help those with pain after TBI.

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Patient Safety

Patient Safety - 1 The Trainee Experience with Quality Improvement: Standardization Of OR To ICU Handoff (SOOTH)

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[1]University of Utah, Salt Lake City, UT, [2]University of Utah, salt lake city, United States of America

Introduction: The ACGME outlines expectations for residents to participate in activities that address patient safety and specifically participating in Quality Improvement (QI) activities(1). Published attitudes on QI participation in a small cohort of residents found that the generally negative trainee perspectives could impede the future of the learning health care system(2). Further, there is a large body of evidence promoting resident involvement in QI as well as implementing a QI curriculum(3). However, the experience of trainees in QI projects has not been well described and the aim of this paper is to share the experience of a trainee in developing and implementing a QI initiative.

Methods: As part of the University of Utah Department of Anesthesiology's QI training, the CA-1 residents participate in an online 6 week QI primer course through the University of Minnesota. QI principles are taught through modules with weekly assignments wherein faculty facilitate discussions among learners as they define a problem, detail specific measurement tools and interpret data. Additionally, there is a dedicated 4 week QI rotation away from clinical responsibilities which has a structured curriculum including: literature search, faculty mentorship matching, weekly meeting with value engineer and faculty mentor(s), project planning, and a project presentation at the monthly research meeting to solicit feedback. This resident QI experience is focused on the standardization of OR to ICU Handoff.

Results: PROBLEM DEFINITION After the online primer course the first week of the QI month is focused on problem definition. A fishbone analysis of current workflow and thorough literature search for precedent and the salient data points in a handoff were conducted. It quickly became clear that understanding of implementing lasting cultural change in a healthcare system was requisite to the project's success. The in-depth publication and availability of resources from the HATRICC(4) trial, including speaking with primary investigator Dr Meghan Lane-Fall, proved to be invaluable to the development of the project plan. STRATEGIC PLANNING Through combining previously acquired healthcare strategy training along with the peer-reviewed published processes(5) to implement healthcare change, an effective strategic analysis of the ICU handoff was performed. This analysis demonstrated a need for project champions from several departments and involvement of high-level stakeholders such as departmental chairs, ICU nursing administrators, ICU directors, and program directors. It was also evident from the analysis that this was a longitudinal project and early recruitment of additional residents and medical students would improve success. Three aims of the project were then defined: Needs Assessment, Implementation of Handoff and Evaluation of Implementation and Effectiveness. NEEDS ASSESSMENT During the needs assessment, observations of handoffs were used to collect pre-intervention data and stakeholders' feedback were used to gauge feasibility and appropriateness of a new protocol. IMPLEMENTATION Several planning meetings were held with relevant stakeholders and the multidisciplinary champions to refine the workflow and protocol. Educational and promotional presentations were held in department M&M conferences, resident didactics and nursing in-service trainings. Implementation also included re-structuring the environment through visual aids and bedside forms created to streamline the workflow and communication of salient info during handoff. Input from project champions facilitated strategic placement of the visual aids as well as bedside forms to enhance buy-in of the protocol. EVALUATION Effectiveness will be evaluated through handoff observations post intervention for 1 month to be compared to pre-intervention data. The observations will then continue for the period of one year to evaluate the longevity of the change.

Conclusion: QI training is an excellent way to empower trainees to enact change and further the learning health care system. Providing trainees with foundational QI training in addition to structured and

supported time away from clinical responsibilities led to a constructive and efficacious experience developing and implementing a QI project. Moreover, early recruitment of additional residents and medical students facilitated project progress as the developing resident returned to clinical responsibilities.

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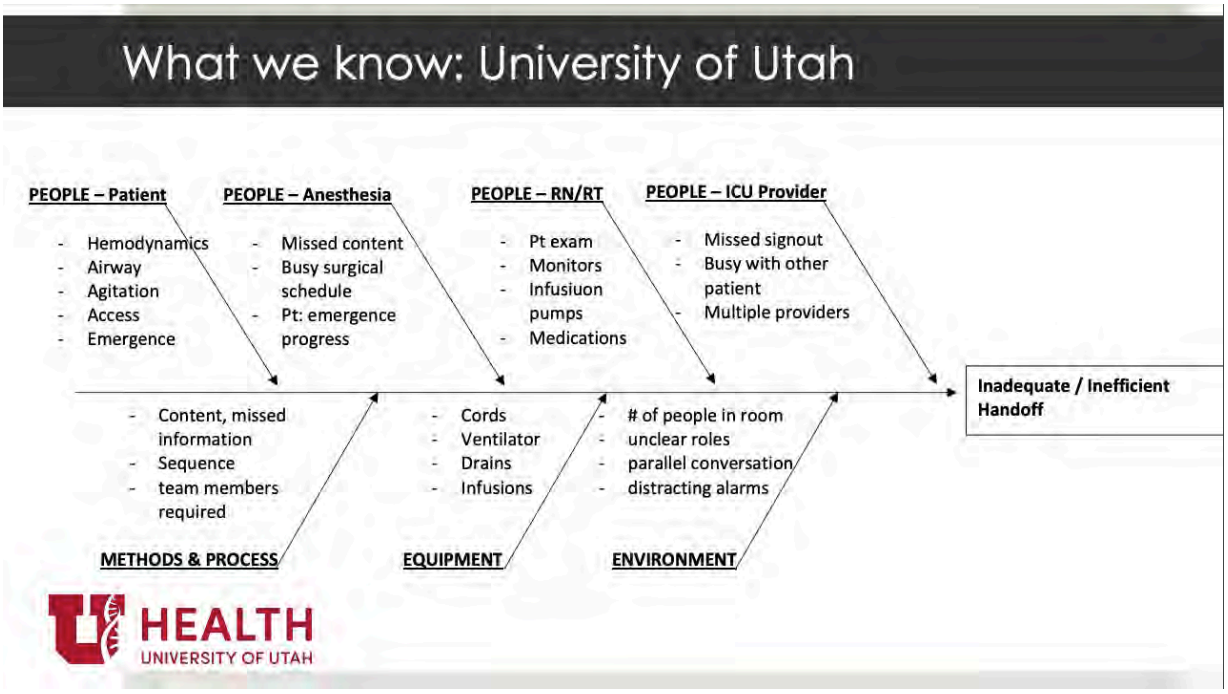
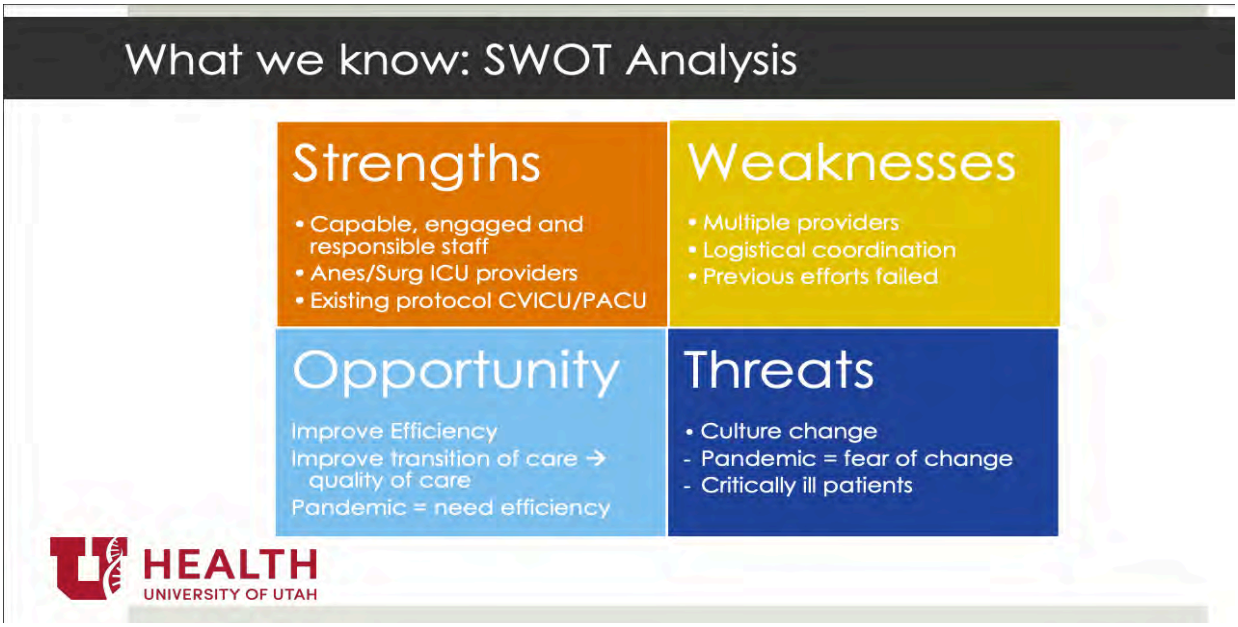




Pt Name:_____ Time: arrive_____ start_____ complete_____

MRN:_____ RN ☐ Anesthesia ☐ Surgery ☐ ICU ☐

HANDOFF CONTENT				
Hands on exam by receiving team?	Y ☐	N ☐	UNK ☐	Exam
Past Medical history	Y ☐	N ☐	UNK ☐	PHist
Reason for ICU admission	Y ☐	N ☐	UNK ☐	HPI
Allergies	Y ☐	N ☐	UNK ☐	Allergies
Airway	Y ☐	N ☐	UNK ☐	Airway
Breathing	Y ☐	N ☐	UNK ☐	Breathing
Circulation	Y ☐	N ☐	UNK ☐	Circulation
Inputs	Y ☐	N ☐	UNK ☐	Ins
Outputs	Y ☐	N ☐	UNK ☐	Outs
Drains/lines	Y ☐	N ☐	UNK ☐	lines
Complications (or absence of)	Y ☐	N ☐	UNK ☐	Course/Comps
Plan	Y ☐	N ☐	UNK ☐	Plan
Team Contact Info	Y ☐	N ☐	UNK ☐	Contact

Exam: including alaris pump sign out

PHist: Medical history

HPI: Name • Diagnosis • Procedure • Reason for ICU admit

Allergies

Airway: (Difficult, Easy, Fiberoptic, Glidescope)

Breathing: vent settings • neuromuscular blockade (blocker: rocuronium, succinylcholine, cisatracurium; reversal agents: sugammadex, neostigmine, glycopyrrolate)

Circulation: hemodynamic stability • Vasoactives (levophed, nor-epi, epi, vaso, phenylephrine)

Ins: IV fluids administered • Blood products (type and amount)

Outs: Estimated blood loss • Urine output • drain output

Drains/Lines: IV, arterial lines, central lines, surgical drains, chest tubes, NG, dobhoff

Course/Comps:
Type of anesthesia • Anesthesia complications • Intraoperative & transport medications, including dose • Surgical complications and interventions • Surgical course

Plan: Anticipated recovery and problems • Clear postoperative management plan • Postoperative orders and investigations • Monitoring plan and range for physiological variables

Observer Name _____

ICU Hand-off Checklist

I. Intraoperative Report — Circulator name: _____

Name _____ DOB ___/___/___ Wt _____kg PMH _____

ICU admit reason _____ Procedure _____

Allergies _____ COVID Status _____ (PCR/rapid) ☐ Intubated ☐ Vasopressor infusions

PIV x ____, Arterial Line Central Line Chest Tubes x_____ Drains x_____

II. Anesthesia Sign Out — Anesthesia Attending/Resident

Diagnosis _____ Procedure _____

Relevant PMH: _____

Anesthetic: ___GETA ___TIVA ___Regional

Meds: Fent _____ (mcg) Paralytic: _____ Ancef _____(g)/_____(time)

Dilaudid _____ (mg) Last dose: _____ (mg) _____

Midaz _____ (mg) _____ (time) _____

_____ ☐ Reversal _____

Prop _____ mcg/kg/min Epi _____mcg/kg/min

Fent _____mcg/kg/min Norepi _____mcg/kg/min

Insulin _____unit/hr Vaso _____unit/hr

_____ Phenyl _____mcg/kg/min

Access: PIV_____(g)/_____(site) A-line _____(site)

PIV_____(g)/_____(site) Central _____(fr)/_____(lumen)/_____site

_____ _____

Airway: ☐ Easy ☐ Difficult: _____ ETT size _____ Vent Settings _____

I/O: Crystalloid _____mL Colloid_____mL UOP_____mL EBL_____mL

Transfusions: ____ Units PRBC ___Units FFP ___Units Platelets ___Units Cryo

☐ TXA ☐ Amicar

Most Recent labs: ☐ Blood Gas ☐ Rotem Complications:

III. Surgery Sign Out — Surgical Attending/Resident

Surgical site: Tubes_____ drains_____

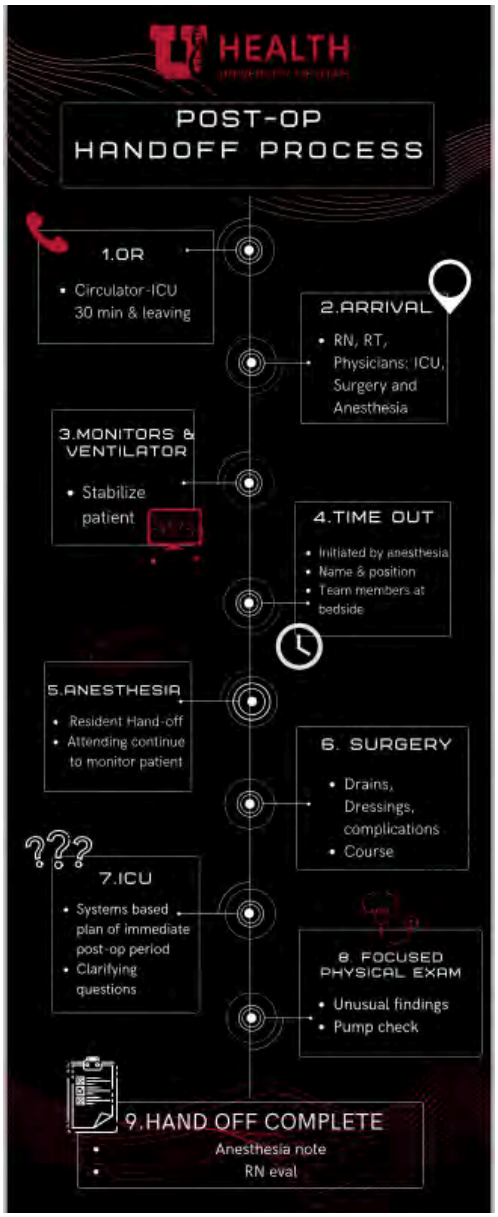
Dressing _____ packing_____

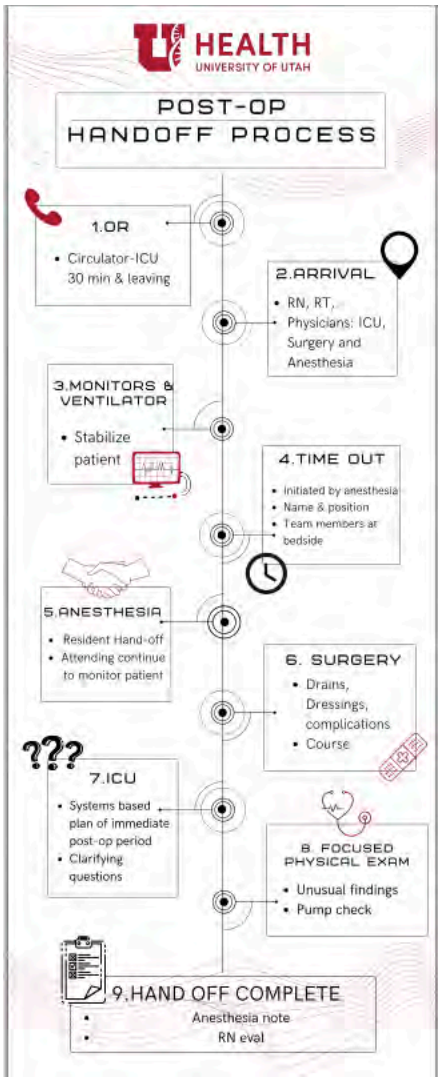
Surgical complications _____ ☐ Bowel discontinuous

Operative Plan: _____

IV. Patient-specific Concerns/Treatment Goals — ICU Attending/Resident

☐ **Family Contacted**


HEALTH
POST-OP
HANDOFF PROCESS
1.OR
• Circulator-ICU 30 min & leaving
2.ARRIVAL
• RN, RT, Physicians: ICU, Surgery and Anesthesia
3.MONITORS & VENTILATOR
• Stabilize patient
4.TIME OUT
• Initiated by anesthesia
• Name & position
• Team members at bedside
5.ANESTHESIA
• Resident Hand-off
• Attending continue to monitor patient
6. SURGERY
• Drains, Dressings, complications
• Course
7.ICU
• Systems based plan of immediate post-op period
• Clarifying questions
8. FOCUSED PHYSICAL EXAM
• Unusual findings
• Pump check
9.HAND OFF COMPLETE
Anesthesia note
RN eval


HEALTH
UNIVERSITY OF UTAH
POST-OP
HANDOFF PROCESS
1.OR
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2.ARRIVAL
• RN, RT, Physicians: ICU, Surgery and Anesthesia
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???
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• Systems based plan of immediate post-op period
• Clarifying questions
8. FOCUSED PHYSICAL EXAM
• Unusual findings
• Pump check
9.HAND OFF COMPLETE
• Anesthesia note
• RN eval

Patient Safety - 2 Continuous Operating Room Patient Vital Signs Enhance the Prediction Power for Postoperative Complications

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Introduction: An improved ability to predict postoperative complications (POC) would allow clinicians to target interventions to improve outcomes. Machine-learning methods using high fidelity intraoperative vital signs (VS) might facilitate development of robust predictive analytics. The authors hypothesized that VS analysis would enhance prediction of the risk of POC.

Methods: The University of Maryland Department of Anesthesiology maintains a 'Perioperative Data Warehouse (PDW)' that contains anesthesia-specific data, relevant data from patients' electronic patient record, and high fidelity VS. After IRB approval, data from the PDW was extracted for adult patients undergoing surgery at the University of Maryland Medical Center from 2016-19 with admission on day of procedure, excluding cardiac and liver transplant surgery. We analyzed the last hour of operating room high-resolution VS (VS: HR, SpO2, RR, BP collected at a rate of 0.5Hz and ECG, PPG waveform collected at 240Hz), patient demographics, and preoperative laboratory values (DEMO: age, ASA class, BMI, albumin, bilirubin, and creatinine). Models were developed for prediction of POC using VS and DEMO and the Gradient Boosting Tree technique. POCs included: 7-day post OR Mortality (MORT); postoperative Ventilation Support (VENT); postoperative acute kidney injury (AKI), anemia (ANEM) and return to the OR (RtOR). Highly linearly correlated variables were removed. 10-fold cross-validation and the area under the receiver operating characteristic curve (AUROC) with a 95% confidence interval (CI) were used to assess a model's performance. The SHAP (SHapley Additive exPlanations) value was used to quantify variables' importance in models.

Results: The rate of POCs were (%=Incident/Total): MORT (0.11%=15/14,100), VENT (0.4%=51/12,838), AKI (5.2%=156/3,019) ANEM (1.77%=120/6795) and RtOR (0.32%=45/14,100). AUROCs of three types of models (DEMO, VS, DEMO+VS) were MORT (0.65, 0.87, 0.89), VENT (0.76, 0.87, 0.90), AKI (0.95, 0.78, 0.94), ANEM (0.73, 0.66, 0.77) and RtOR (0.56, 0.68, 0.69) respectively (Table 1). The SHAP values show that VS variables rank top contributions in those predictions. For example, higher entropy (instability) of pulse pressure has a higher impact on the odds of VENT than other DEMO variables such as ASA class (Figures 1 and 2). In general, for VS models, more than 400 VS related features were evaluated and 20-30 variables were selected in the final model.

Conclusion: High fidelity analysis of VS can enhance the prediction of POCs. For some outcomes (MORT, VENT and RtOR), the high resolution VS model achieved a better prediction power than the DEMO only model, which shows the feasibility of real-time machine-learning models for predictive analytics in the field of anesthesiology. Some complications, such as ANEM, are better predicted by DEMO+VS than by either set alone. Heterogeneity of etiology for some complications, such as for RtOR, may limit predictability as a single outcome.

Table 1. AUROCs with 95% CI of models using variables from DEMO, VS and DEMO+VS for five outcomes. * Indicate the significant difference between VS and Demo based model AUROCs and + indicate the significant difference between Demo + VS and Demo based model AUROC results

	DEMO	VS	DEMO+VS
MORT	0.65 (0.59-0.70)	0.87 (0.82-0.92)*	0.89 (0.86-0.92)+
VENT	0.76 (0.73-0.79)	0.87 (0.84-0.89)*	0.90 (0.88-0.91)+
AKI	0.95 (0.94-0.96)	0.78 (0.76-0.80)	0.94 (0.93-0.96)
ANEM	0.73 (0.71-0.75)	0.66 (0.63-0.69)	0.77 (0.75-0.80)
RtOR	0.56 (0.51-0.60)	0.68 (0.63-0.72)*	0.69 (0.65-0.73)+

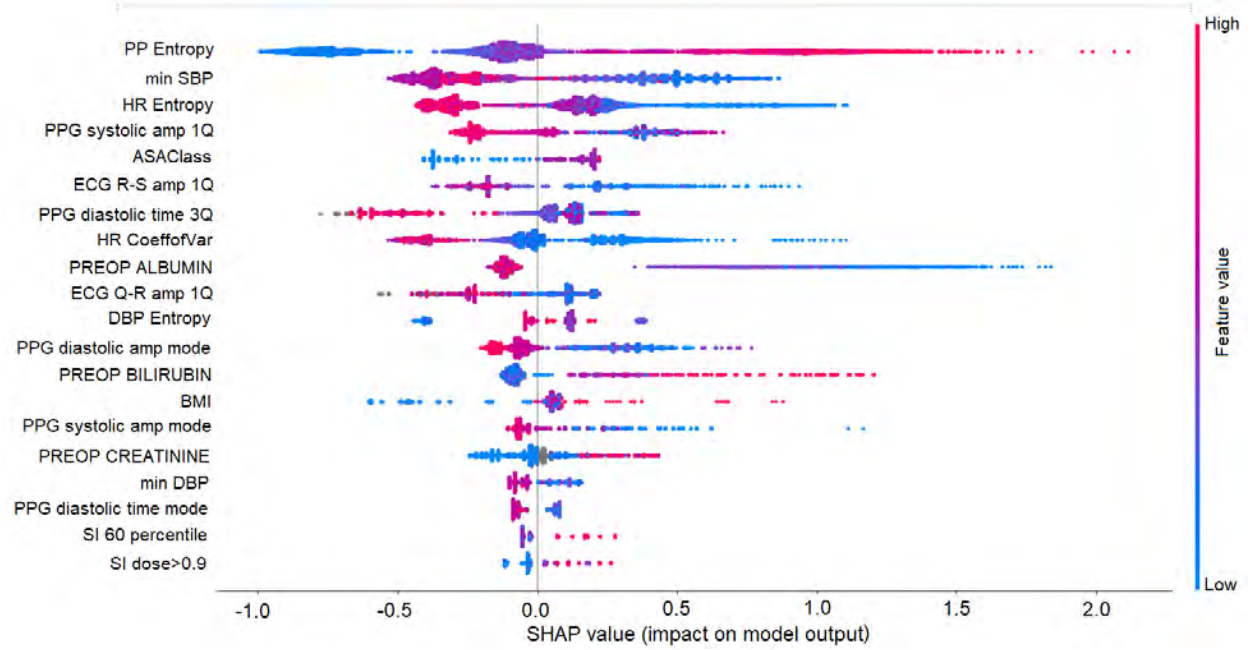

Figure 1. Rank of DEMO and VS variables showing their impact on the model output in predicting VENT. Each feature's values are represented in color ranging from red to blue (high to low). The x axis shows their corresponding SHAP values. A larger SHAP value stands for higher log odds ratio that a variable's value added to the prediction.

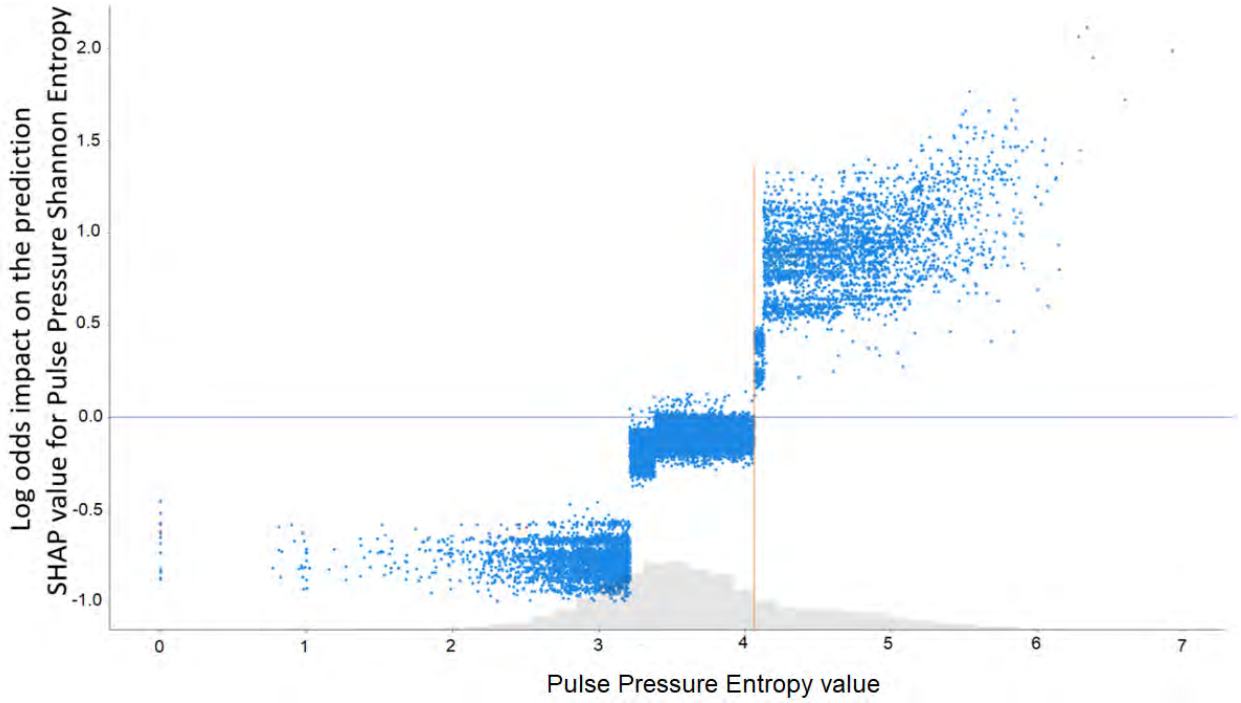

Figure 2. Scatter plot of each pulse pressure entropy value and its impact on the prediction of VENT. Higher PP entropy has higher impact in predicting positive VENT outcome.

Patient Safety - 3 A Pragmatic Pilot for Improving Teamwork: What Do I Need to Know About What You Do?

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Introduction: Mutual performance monitoring, back-up behavior and a team orientation are key dimensions of an effective team. These require team shared mental models, mutual trust, and closed-loop communication. (Salas, 2005) To improve clinical teamwork, we instituted a pilot program to encourage anesthesiologists to learn about the work and priorities of other role groups on their teams, and to translate this information into actionable teamwork behaviors.

Methods: We created this pilot program within our required training for anesthesiologists to maintain lower malpractice premiums through our insurer. The goal of the program was to improve teamwork by learning about the work of other role groups and undertaking actions to support that work. Participants watched a 10-minute presentation describing the program, including a recorded, simulated example with some modeled wording to facilitate the exercise. Our intention was for each participating anesthesiologist to ask someone in a different clinical role group to tell them something that anesthesiologists may not appreciate about their work, and the effect of this knowledge gap on the ease and safety of their work. Participants reported what they learned via survey (RedCap) and then participated in a virtual group discussion for sharing and reflection.1-2 weeks after the group discussion, a second survey link was sent asking participants what action(s) they had trialed. We performed a qualitative content analysis to identify categories of actions. Each response was initially coded independently by groups of 2 authors; consensus was reached through team discussion.

Results: From August to November, 2021, 60 attending anesthesiologists completed all steps of the training. 87 individuals from different role groups were engaged in discussion to learn about their work (Table 1). From the anesthesiologists' reports (see Table 2 for examples), we identified 62 different actions in support of their teammates; we grouped these into 21 codes (Table 3). 38% percent of actions had more than one code. We classified 7 (12%) as non-responsive; i.e., the reported actions did not reflect learning about what would help another role group, but instead focused on ways other role groups could help anesthesiologists.

Conclusion: This piloted pragmatic approach engaged licensed professionals in cross-professional discussion to develop their knowledge of each other's needs in an effort to build mutual trust and improve cross-monitoring and supportive team behaviors. We plan to expand this program to include other role groups in the training, to decrease the rate of non- and partial responses by improving the clarity of our intentions, and to help build a toolbox of supportive team behaviors applicable to others in the perioperative environment.

References: SMALL GROUP RESEARCH, Vol. 36 No. 5, pp. 555-599, 2005

Table 1: Participants engaged in discussion with the following role groups during this training:

Role group engaged in discussion	Number	%
Surgeon	16	18%
Nurse (including preoperative, operating room and post-operative care unit)	36	41%
Anesthesia Technician	15	17%
Scrub Technician	2	2%
Pharmacy	4	5%
Other	14	16%
Total	**87**	**100%**

Table 2: Illustrative examples of anesthesiologists' reported actions

Anesthesiologist-reported actions based on their learning from the program
I was doing a post-op epidural in the PACU (never the easiest thing) and it made me think about what [one co-participant] shared in our [virtual group discussion] about how disruptive to the nurses the epidurals can be on [Labor and Delivery]. I made sure to communicate with the nurse and ask her input on a lot of my decisions (like how should we position and support the patient, how did she want monitors, etc). These were little things that didn't impact my workflow but made a big difference to her ability to settle the patient after placement.
Instead of bugging the circulators about when I could bring the patient back, I just went to coffee central and bought a coffee and sat next to the pre-op bay enjoying it until they were ready for me to [bring the patient into the operating room]. It was win-win. And we all had a lovely day working together. I think it actually helped us have quicker turnovers later in the day because they knew I was pretty flexible.
I spoke with pre-op nurses … and told them the information obtained during [the] preop visit was important and valuable for patient safety in the OR. I learned their EPIC template so pre-op information could be obtained together in order to save time. Worked out well.

Table 3: Anesthesiologists supported colleagues in other role groups through the following categories of actions or behaviors

Category	Number	%
Improving communication	19	20
Reducing burden for other role groups	13	14
Providing time to complete a task	10	11
Respecting the workflow of other role groups	8	9
Seeking input to collaborate effectively	6	6
Cross monitoring for patient safety	5	5
Recognizing other role groups' needs	5	5
Offering to help another provider	4	4
Supporting the learning of a teammate in another role	3	3
Being more patient with other role groups	3	3
Helping another to complete their required task	3	3
Increasing mutual understanding of conflicting interests	2	2
Acknowledging contributions to team	2	2
Increasing mutual understanding of conflicting interests	2	2
Being aware of how actions affect other role groups	2	2
Building rapport	1	1
Speaking up to help another role group clarify	1	1
Being aware of the impact of my noise level on others	1	1
Exhibiting empathy for and to another role group	1	1
Escalating another role group's concern for action	1	1
Learning about the communication preferences of another role group	1	1
Total	**93**	**100**

Patient Safety - 4 Crisis training in non-operating room anesthesia (NORA) locations: What do front-line staff need?

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Introduction: More than 30% of anesthetic cases take place in non-operating room anesthesia (NORA) settings,[1,2] which are often managed by interprofessional care teams with highly specialized roles (e.g., radiology technicians, anesthesia clinicians). Lack of familiarity between teams and diverging expectations about roles and responsibilities can make the management of adverse events and crises especially challenging in NORA.[3,4] Following an adverse event involving a pediatric patient undergoing a computed tomography (CT) scan, our institution recognized the need for urgent intervention, and interprofessional education on emergency preparedness was requested by the hospital safety leadership. This needs-assessment was developed to encourage front-line staff to weigh in on needs and preferences prior to designing a team training module.

Methods: A questionnaire was developed in an iterative process by anesthesia providers with expertise in NORA. We asked about respondents' personal experience with adverse events affecting NORA patients and preferences for education relevant to NORA events. The final questionnaire contained eight closed questions and two free-text questions. It was distributed via email to the Anesthesiology and Radiology departments at Dartmouth-Hitchcock Medical Center. A descriptive analysis of the data collected was performed.

Results: A total of 64 responses were received (36 anesthesia, 28 radiology, see Table 1). The most witnessed adverse events affecting NORA patients involved airway/ventilation problems (56%) and cardiac arrest/hemodynamic instability (28%). Only 21 (33%) respondents had not experienced an adverse event. Airway/ventilation adverse events were reported as the most worrisome by both types of providers. The most frequently cited challenges of NORA reported by anesthesia clinicians were remote location (42%), infrequent exposure and unfamiliarity (31%), and lack of NORA staff support (25%) (Figure 1). When asked what resources and/or curricula would be most helpful in improving safety of anesthetized patients in non-OR locations, on-site crisis simulation was favored by respondents (44%) over cognitive aids (38%), written hand-outs (33%) and video tutorials (31%). The preferred way of learning differed by department, with radiology personnel most often choosing simulation (50%) and anesthesia clinicians most often choosing cognitive aids (50%). Very few participants were in favor of no changes needed (11%). Eighteen (28%) of respondents provided additional comments, which provided further insight into preferred educational content (Table 1).

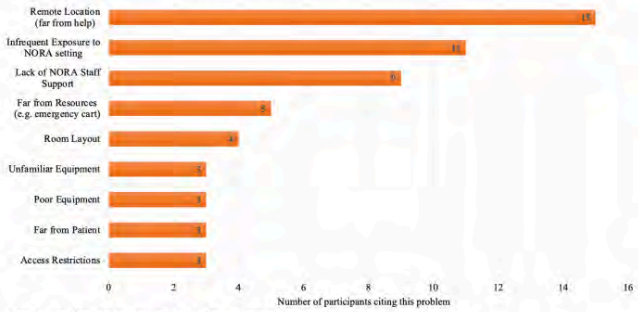
Conclusion: ···Results from this survey support a need to train healthcare personnel in NORA crisis management, especially for airway events. Given an overall favorable view of simulations at our institution and recent evidence supporting their effectiveness,[5] we prioritized creation of a "lost airway" scenario for in situ simulation training. Taking into consideration that the preferred mode of learning differed among groups, we are simultaneously developing cognitive aids and a tutorial video. With NORA procedures becoming more prevalent and increasingly complex,[4] interprofessional team education and collaboration is important to proactively address common crisis scenarios and to achieve the best possible outcomes for our patients.

References: 1. Anesth Analg, Vol. 124, 1261 - 1267, 2017. 2. J Patient Saf, Vol. 14, 9-16, 2018 3. Anesthesiol Clin, Vol. 34, 223 - 240, 2016. 4. APSF Newsletter, Vol. 34, 3-21, 2019 5. Int J Qual Health Care, Vol 33, mzaa148 (1-7), 2021

Table 1: Cross-departmental questionnaire results

	Anesthesia N = 36	Radiology N = 28	Total N = 64
Adverse Event Experienced in NORA			
Airway/ventilation	23 (64%)	13 (46%)	36 (56%)
Cardiac arrest, hemodynamic instability	12 (33%)	6 (21%)	18 (28%)
Anaphylaxis, allergy, drug reaction	2 (6%)	1 (4%)	3 (5%)
Other	3 (8%)	3 (11%)	6 (9%)
None	11 (31%)	10 (36%)	21 (33%)
Most worrisome adverse event in NORA			
Airway/ventilation	24 (67%)	9 (32%)	33 (52%)
Cardiac arrest, hemodynamic instability	9 (25%)	7 (25%)	16 (25%)
Anaphylaxis, allergy drug reaction	1 (3%)	3 (11%)	4 (6%)
Other	1 (3%)	1 (4%)	2 (3%)
None	2 (6%)	9 (32%)	11 (17%)
Preferences for new curriculum			
1–2-page written summary	11 (31%)	10 (36%)	21 (33%)
5-minute video orientation	7 (19%)	13 (46%)	20 (31%)
On-site crisis simulation	14 (39%)	14 (50%)	28 (44%)
Cognitive aids	18 (50%)	6 (21%)	24 (38%)
No change	4 (11%)	3 (11%)	7 (11%)
Example quotes from respondents	"It's imperative for the staff in all NORA locations to be educated in anesthesia emergencies" - Anesthesia		
	"As non-anesthesia providers/non-RN's in during a crisis, it would be good to know how we can help (run for supplies, call for help) or just get out of the way" - Radiology		
	"Having a dedicated NORA team for various sites and requiring mock codes every few months would be best" - Anesthesia		
	"The more frequently we can run scenarios in NORA locations, the better! There are many unique things about each department that are useful to know" - Anesthesia		
	Most MRI/CT Techs get minimal training on airway issues when anesthesia is involved. [Provide] training on basic airway management more than every two years" - Radiology		

Figure 1: Factors that make NORA locations stressful for Anesthesia clinicians



*Answers from free response questions were assigned to appropriate categories, listed above

Patient Safety - 5 Focused financial incentives to drive quality improvement amongst anesthesiologists: a report on 15 years' experience

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Introduction: Implementation of best practices to improve quality and safety (Q&S) remains a challenge in healthcare. Focused financial incentives are one approach to nudge clinicians into desired behavior changes, when combined with physicians' professionalism and internal drive to 'do the right thing.' They have been shown to decrease testing in ICUs,[1] increase trainee engagement with quality improvement (QI) initiatives,[2] and decrease the time for finalizing radiology reports.[3] Considerations for using such incentives include incentive size, maintaining clinicians' intrinsic motivation, and considering a reward versus penalty system.[4] We report participation and some results of 15 years of incentives in an anesthesia department as part of a hospital-wide quality incentive program.

Methods: The design of the Massachusetts General Physicians Organization (MGPO) quality incentive program has been described previously.[5] The incentive system was designed around the framework of prospect theory,[6] starting with a guaranteed reward to all eligible clinicians in the first year before making the reward contingent on meeting specific metrics. Incentives were set at no more than 2% of annual salary. Metrics are selected semiannually and divided into system-wide and department-specific metrics.

Departmental metrics were selected by QI leadership based on organizational quality and safety goals. Some chosen metrics are shown in Figure 1. Metrics were sometimes used to encourage continued improvement over several measurement periods. For example, the target for difficult airway documentation was initially set at 50%, then at 80%, and finally at 90%. Targets were set based on baseline data whenever possible and to be attainable as stretch goals with clinician behavior change.

Results: Participation amongst anesthesia clinicians from the start of the program to now has remained high. Recent individual metrics (e.g., training in time-outs or disclosure of medical errors) reached 96% completion, suggesting high levels of engagement. Metrics repeated to promote continued improvements were successful in doing so; difficult airway documentation improved from 82% to 100% over 3 measurement periods. Intraoperative glucose monitoring showed improvement from 57% to 73% of appropriate cases over 2 periods. Other results are in Figure 1.

Conclusion: A quality incentive program is a sustainable way to increase engagement with Q&S goals. By setting small incentives on easily measured and applicable metrics, behavior can be changed. These financial incentives supplement educational efforts, workflow changes, and system changes to create safer practices. The attainable goals and meaningful financial incentives have maintained a high level of clinician engagement. The flexibility of designing new metrics semiannually allows the program to remain relevant. QI metrics have brought awareness to clinical practice changes and provided an avenue for educational initiatives, improving our healthcare system.

References: [1] Using incentives to improve resource utilization: a quasi-experimental evaluation of an ICU quality improvement program. Crit Care Med 2016. 44(1): 162-170. [2] Financial incentives for residents and fellows A disruptive innovation to drive quality improvement. Academic Medicine 2011. 86(11): 1338. [3] Radiologist report turnaround time: Impact of pay-for-performance measures. American Journal of Radiology 2010. 195: 707-711. [4] Quality-based financial incentives in health care: Can we improve quality by paying for it? Annu Rev Public Health 2009. 30: 357-71. [5] Massachusetts general physicians organization's quality incentive program produces encouraging results. Health Affairs 2013. 32 (10): 1748-1756. [6] A prospect theory: an analysis of decision under risk. Econometrica 1979. 47(2): 263-92.

Figure 1: Select metrics and results

Individual Metrics			
Year	**Metric**	**Eligible Clinicians (#)**	**Engagement (%)**
2010	Glucose Monitoring Training	123	100%
2015	Emergency Manual Training	164	79.1%
2017	Defibrillator Training	154	95%
2018	EEG Monitor Training	154	100%
2021	Emergency Manual Training	167	96%
2021	OR Timeout Audit	167	96%
2021	Apology and Disclosure Training	167	96%
Departmental Metrics			
Year	**Metric**	**Target (%)**	**% Cases Meeting Metric**
2011	Intraoperative Glucose Monitoring	57% (baseline)	73.1%
2011	Airway Documentation for General Anesthesia Cases	75%	84%
2012	Repeat Airway Documentation for General Anesthesia Cases	90%	90%
2011	Difficult Intubation Documentation	50%	82.5%
2012	Repeat Difficult Intubation Documentation	80%	97%
2013	Anesthesia Procedure Time Out	75%	88.7%
2014	Intraoperative Handoff Checklist Documentation	70%	74.7%
2015	Blood Transfusion Documentation	85%	94.4%
2017	Median Tidal Volume <10mL/kg ideal body weight	75%	96%
2018	Post-Operative Nausea/Vomiting Prophylaxis	70%	84%
2018	Hyperglycemia Treatment and Re-Check	80%	93%
2018	Multimodal Analgesia in ERAS Patients	70%	85%
2019	Intraoperative Handoff Documentation	40%	46%
2019	Hemoglobin Monitoring in Blood Transfusion Patients	60%	80%

Patient Safety - 6 The Impact Of A Wellness Intervention On The Burnout Potential Of Urm and Female Anesthesiology Residents

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Introduction: It has been well established through many studies that burnout remains a national issue among U.S physicians with anesthesiologists among those specialities reporting higher than average rates (1). Furthermore, many studies have established a link between burnout and how targeted wellness interventions can help mitigate feelings of burnout (2). However, while women and underrepresented minorities (URM) physicians face unique challenges, there has been a paucity of research evaluating burnout rates and mitigating wellness interventions amongst these populations especially in the field of anesthesiology (3). Thus our objective seeks to investigate whether burnout rates are higher in women and URM anesthesiologists at an academic anesthesiology residency program. We aim to investigate whether an organization-led intervention such as extending morning break time would have any impact on feelings of burnout and/or wellness on residents, as well as the impact that the intervention had on the attendings.

Methods: After obtaining IRB approval, we implemented phase 1 of our uncontrolled experimental study which involved administering a modified and validated 37 item pre-intervention survey addressing burnout and wellness to anesthesiology residents (n= 49) over a period of 2 months. After this period, a department-wide policy of extending morning breaks from 15 to 25 mins for residents went into effect for six months at the Montefiore Anesthesia Department. Residents were subsequently administered a 47 item post-intervention survey to determine whether feelings associated with burnout and wellness improved. Additionally, we administered a 15 item survey to Montefiore Anesthesiology attendings to assess their feelings on burnout as well as their adjustment to the intervention.

Results: Subjects included in this study were CA-1 (class of 2023) , CA-2 (class of 2022), and CA-3 residents (class of 2021); CA-0 (class of 2024) were excluded since they had not began their clinical anesthesia rotations yet. Results: Baseline n= 49 (98%); F - 33%; M - 67%; URM - 14% | Post intervention n = 41 (82%); F - 37%; M - 63%; URM - 17.5% | Attendings n = 41 (50%); F - 56% M - 44% Pre-intervention, all residents reported higher rates of burnout (55%), job frustration (61%), and job emotional drain (59%). Female residents reported higher levels of burnout (69%) compared to URM students (42.9%). Post-intervention, work burnout decreased in female residents (69% vs 60%); job satisfaction increased in all residents (80% vs 88%) including URM residents (57% vs 86%). Lastly, inadequate break reports decreased (73% vs 63%), and 88% of residents favored the 25 minute morning break extension compared to 36% of the attendings. Nevertheless, both residents (90%) and attendings (66%) reported.

Conclusion: Burnout is an important issue that plagues many physicians including Anesthesiologists. Our study showed that, pre-intervention all residents reported higher than average rates of burnout with female anesthesiology residents reporting the highest rates even when compared to URM students. Post-intervention, burnout associated with work decreased in female residents, and ratings of job satisfaction improved among URM residents. Overall, Anesthesiology attendings were less supportive of the concept of extended breaks compared to residents, but did report that a 20 minute break would be acceptable. We hope that this study may shed some light on how specific targeted institutional interventions may mitigate some aspects of burnout and improve wellness. Ultimately, by promoting a culture and environment of compassion and support that can help reduce the negative consequences associated with burnout for physicians, we can advance quality patient care to new levels.

References: 1. Changes in Burnout and Satisfaction With Work-Life Balance in Physicians and the General US Working Population Between 2011 and

2014. Mayo Clin. Proc. 2015; 90:1600-1613. 2. Controlled interventions to reduce burnout in physicians: a systematic review and meta-analysis. JAMA Internal Medicine. 2017;177(2):195-205. 3. Incidence and Factors Associated with Burnout in Anesthesiology: A Systematic Review. Biomed Res Int, vol. 2017; ID:8648925, 10 pages

THE IMPACT OF A WELLNESS INTERVENTION ON THE BURNOUT POTENTIAL OF URM AND FEMALE ANESTHESIOLOGY RESIDENTS

Pre - intervention	All n= 49 (98%)	F n= 16 (33%)	URM n= 7 (14%)	Post - intervention	All n= 41 (82%)	F n= 15 (37%)	URM n= 7 (17.5%)	Att n= 41 (50%)
Job frustration	61%	75%	42.8%	Job frustration	71%	80%	86%	N/A
Job emotional drain	59%	69%	57.1%	Job emotional drain	59%	67%	57%	N/A
Job burnout	55%	69%	42.9%	Job burnout	59%	60%	43%	41%
Job satisfaction/ fulfillment	80%	87.5%	57.1%	Job satisfaction/ fulfillment	88%	80%	86%	N/A
Healthy coping mechanism	84%	87.5%	87.5%	Healthy coping mechanism	90%	93%	100%	N/A
Healthy work balance	85%	100%	100%	Healthy work balance	85%	80%	86%	N/A
Satisfaction with current wellness initiatives	47%	25%	29%	Satisfaction with current wellness initiatives	32%	40%	29%	24%
Break inadequacy	73%	75%	57.1%	Break inadequacy	63%	53%	71%	N/A
				Favor AM break extension	88%	80%	86%	36%
				AM break extension adjustment	90%	85%	81%	66%
				Preferred break time 20/25/30min	20% 42.5% 37.5%	27% 33% 40%	29% 29% 43%	61% 28% 11%
				Best type of wellness intervention	17% 27% 49% 7%	20% 27% 53% 0%	29% 14% 43% 14%	23% 21% 39% 18%

Pediatric Anesthesiology

Pediatric Anesthesiology - 1 Incidence and Risk Factors of Perioperative Respiratory Adverse Events in Children Undergoing Elective Surgery Employing Logistic Regression and Machine Learning Cluster Analysis

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[1]Royal Manchester Children's Hospital, Manchester, England, [2]The University of Manchester, Manchester, United Kingdom, [3]The Royal Macnehster Children's Hospital, Manchester, United Kingdom

Introduction: Perioperative Respiratory Adverse Events (PRAE) are a common causes of paediatric morbidity and mortality during the perioperative epoch, accounting for over three-quarters of adverse incidents. Complications of PRAE include laryngospasm, bronchospasm, hypoxia, airway obstruction, stridulous breathing, persistent coughing and atelectasis. There currently remains a paucity of the use of advanced data-analytical techniques within the PRAE literature, such as multivariate logistic regression and machine learning (ML). Aims and objective: We aimed to ascertain which risk factors are predictive of PRAE in children undergoing anaesthesia with a laryngeal-mask-airway (LMA), comparing and contrasting whether a data-driven epistemological approach using ML yields analogous findings to classical hypothesis-driven research employing logistic regression.

Methods: Data was sourced from existing datasets previously collected (2015/2019) for quality improvement exercises. Our strategy for data-analysis and wrangling to ascertain and rank predictors, included pre-processing, data visualisation, dimensionality reduction (to reduce input variables), exploring the underlying mechanism-of-missingness, univariate analysis, multivariate clinical risk prediction modelling (CRPM) using logistic regression and unsupervised ML cluster-analysis (K-medoids)

Results: The overall frequency of complications of PRAE was 12% . The predictors of PRAE (in order of significance) included fever, younger age, coughing (during LMA insertion), the presence of a productive cough, secretions and the absence of oropharyngeal suctioning prior to LMA removal, rhinorrhoea, a history of respiratory co-morbidities (i.e. asthma), otolaryngology dental surgery and the removal of the LMA asleep (Table. 1). Missing data were handled with multivariate imputation by chained equations (MICE). The missingness was diagnosed by creating dummy variables and testing whether the missingness was related to any of the candidate variables collected (using t-tests and chi-squared as appropriate) as well as using logistic regression where missingness was the outcome measure. These tests found that the mechanism underlying the missingness in the datasets was MAR and not MCAR. This was further supported by Little's test for MCAR which was significant ($p=0.00182$). From multivariate logistic regression stepwise (AIC) selection, our final model performed strongly having an AUCROC be 0.892 ($p<0.001$) and an accuracy of 0.9375 (95% CI: 0.8689, 0.9767) (Table 2). Results from ML cluster analysis was consistent with that of logistic regression (Table 3 and Figure. 2). the silhouette, elbow and gap statistic method for determining the optimal number of clusters (k) was found to be k=6.

Conclusion: The importance of identifying risk factor for developing PRAE can allow anaesthesiologists to risk assess children during the preoperative assessment, to delineate fitness for anaesthesia, as well as tailoring the anaesthetic technique to help ameliorate the risk of developing PRAE, as an application of precision medicine. Moreover, we introduced a new dimension to analysing data from retrospective, quality improvement datasets, by meticulously addressing data quality and completeness. This underscored how a data-driven epistemological approach can work synergistically with classical a priori, hypothesis-driven research.

References: 1. Anesthesiology. 2001;95(2):299-306 2. Anesth Analg. 2016;122(5):1578-85 3. The Lancet. 2010; 376(9743):773-83 4. Anaesthesia. 2015;70(4):440-4 5. European Heart Journal. 2014;35(29):1925-31

Table 1 - Adjusted Odds Ratio and Outcome from Multivariate Logistic Regression

Variable	Coefficient	p-value (Significance)	OR (95% CI)
Age	-0.249	0.000263 ***	0.76 (0.510, 0.920)
Weight	-0.341	0.021598 *	0.776 (0.626, 0.964)
Cough: Dry	0.311	0.017630 *	1.364 (1.190, 1.565)
Productive	1.143	0.002350 **	3.135 (2.757, 3.565)
Rhinorrhoea: Present	0.449	0.006509 **	1.567 (1.156, 1.700)
Fever: Present	-0.225	0.000263 ***	3.215 (2.668, 3.875)
Asthma: Present	0.196	0.0471 *	*1.216 (1.006, 1.472)*
OSA: Present	-0.076	0.263876	0.927 (0.811, 1.059)
Other past medical history			
Respiratory	0.116	0.012133 *	1.123 (1.051, 1.204)
Cardiac	0.073	0.082861	1.013 (0.872, 1.177)
Gastro	0.071	0.166331	1.073 (0.869, 1.245)
Neuro / other	0.095	0.362143	1.250 (0.868, 1.801)
Anticholinergics:	-0.189	0.009419 **	0.828 (0.678, 0.918)
Atropine	0.090	0.4768	1.094 (0.864, 1.387)
Glycopyrrolate			
No. of attempts:	0.275	0.0002	1.316
Other Issues:	0.300	6.63e-06 ***	1.762 (1.397, 2.222)
Coughing	-0.075	0.4284	0.927 (0.556, 1.547)
Laryngospasm	-0.006	0.9731	0.994 (0.693, 1.425)
Obstruction	0.242	0.0984	1.274 (0.146, 1.658)
Reposition			
Removal of LMA:	0.009	0.791180	1.009 (0.944, 1.079)
Deep	2.605	0.04891 *	13.532 (1.070, 26.162)
Awake			
Suctioning prior to LMA removal:	0.479	0.003589 **	1.614 (1.552, 1.701)
No	-0.163	0.000354 ***	0.850 (0.802, 0.899)
Yes			
Other Problems: Secretions	0.7524	0.000721 ***	2.1221 (1.1626, 3.9192)
Bleeding	0.4208	0.0026273 **	1.5231 1.0266, 1.8691
Other	0.4212	0.990509	1.5238 (0.2769, 8.9155)

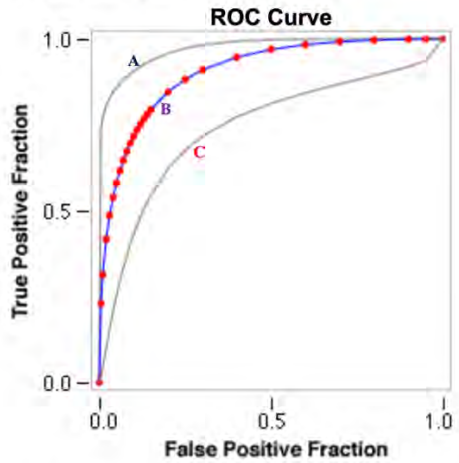
Legend. Note: Pr(>|t|) –p-value, Wald test; significant codes: '***' 0.001, '**' 0.01, '*' 0.05, '-'not significant

Table 1 - Confusion Matrix for Model Appraisal

Test	*Full Model*	*Reduced Model*	*Null Model*
Sensitivity	0.9882	0.7143	0.5000
Specificity	0.8182	0.9663	0.9894
PPV	0.9767	0.6250	0.5000
NPV	0.9000	0.9773	0.9894
Prevalence	0.8854	0.0729	0.0208
Detection Rate	0.8750	0.0521	0.0104
Detection Prevalence	0.8958	0.0833	0.0208
Balanced Accuracy	0.9032	0.8403	0.7447

Note: PPV - positive predative value; NPV - negative predative value. Overall statistics: found an accuracy of 0.9375 (95% CI: 0.8689, 0.9767), no information rate : 0.8854; Kappa : 0.688; Mcnemar's test p-value: 0.0000189. ANOVA (between full and reduced model) was 0.2163 – i.e. non-significant.

Figure 2 - ROC Curve for Model Performance



Note: Curve A represents the full model, curve B represents the reduced model and curve C represents the null model. Fitted ROC_B Area: 0.905; Empiric ROC_B Area: 0.892.

Table 2 - Summary of Characteristics for ML k -Medoids Cluster Analysis

Characteristic	Cluster					
	1	2	3	4	5	6
Sex	M	F	M	M	M	M
Age (years)	6	7	10	1.9	7	8
Duration (mins)	25	28	19	15	20	22
Weight (Kgs)	20.0	31.0	53.0	14.5	22.0	35.4
Procedure	Dental	Orthopaedics	Urology	ENT	Urology	Other
Cough	0	0	0	Productive	0	0
Runny Nose	0	0	0	Yes	0	0
Fever	0	0	0	0	0	0
Asthma	0	0	0	0	0	0
OSA	0	0	0	Yes	v	No
Other PMHx	No	No	No	Respiratory	No	No
Anaesthesia	Sevoflurane	Sevoflurane	Sevoflurane	Sevoflurane	Sevoflurane	Sevoflurane
Anticholinergics	0	0	0	Atropine	0	0
Pre-medication	0	0	0	Midazolam	0	0
Size	2.5	2.5	3.0	2.0	2.5	3.0
Type	fLMA	uLMA	uLMA	fLMA	uLMA	uLMA
No. of attempts	2	1	1	2	1	1
Change size	0	0	0	Size-up	0	0
Leaks	0	0	0	Leak	0	0
Other issues	0	0	0	Nil	0	0
Time LMA in recovery	11	10	9	18	17	15
Position pre	Lateral	Lateral	Supine HU	Lateral	Lateral	Supine
Position during	Lateral	Lateral	Supine HU	Lateral	Lateral	Supine
Position after	Lateral HU	Lateral	Supine HU	Supine HU	Lateral HU	Supine
LMA removal	Awake	Awake	Awake	Deep	Awake	Awake
Suction prior	0	0	0	No	0	Yes
Biting	0	0	0	Nil	0	0
Other problems	0	0	0	Yes *A	0	0
De-saturation	0	0	0	Yes *B	0	0
Coughing	0	0	0	Yes	0	0
Laryngospasm	0	0	0	Yes	0	0
Bronchospasm	0	0	0	Nil	0	0
Number of complications	0	0	0	2	0	0

*Note: *A coughing and reposition; *B Desaturation requiring airway intervention such as head-tilt, chin-lift or jaw thrust; HU – head-up.*

Figure 1 - Correlation Matrix for Univariate Analysis

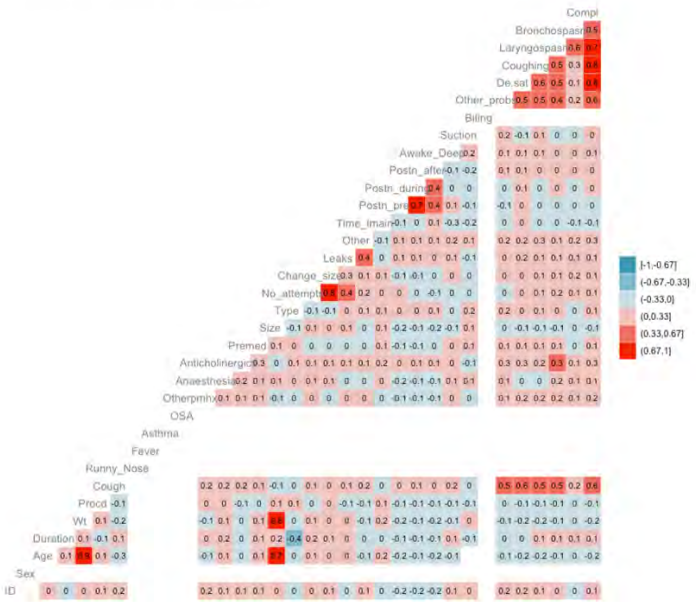


Figure 1 exhibits a correlation matrix disapplying the relationship between the predictors and the outcome measure (complications). this was an important endeavour to undertake since in multivariate regression analysis, multicollinearity (i.e. lack of) is an important assumption made. From critically scrutinizing the matrix, one can observe that the child's age and weight were strongly correlated (r=0.9), as well as age and weight with the size of LMA. These factors would be in keeping with what is expected as an older child would weigh more and require a larger sized LMA. Additionally, the number of attempts and changing the size of the LMA would also be related (r=0.8) since if on the first attempt the LMA was deemed to be of the incorrect size, a larger (and far less commonly a smaller) LMA is then sited. Finally, bronchospasm, laryngospasm, coughing, oxygen desaturation were all examples of complications (PRAE) and as such for multivariate analysis, these were collapsed into a single binary variable of having complications or not.

Pediatric Anesthesiology - 2 Morphine Induced Myoclonus with Sleep Disturbance in Young Children: An Under-Recognised and Distressing Side Effect

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Introduction: Myoclonus is an uncommon side effect of morphine1. With a paucity of clear delineation of frequency, incidence and prevalence rates in children having not been established. Morphine induced myoclonus is an under-recognised side effect in children that is frequently associated with sleep disturbance - especially in younger children. This is commonly misinterpreted as pain which leads to further increases in morphine administration, further aggravating this side effect. A review of morphine induced myoclonus in children has not been published in the literature. We have evaluated the incidence and recognition of morphine induced myoclonus with or without sleep disturbance in young children in our institution.

Methods: A prospective cohort review was undertaken as part of a service evaluation in 200 children under the age of 8 years (median age 2 years) in whom morphine infusion was used to treat their acute pain. Parents were asked to report any 'jumpiness' or 'sleep disturbance' which they considered to be abnormal behaviour for their child. If their child experienced any abnormal behaviour, they were then asked to quantify the frequency as either once, two or three times per hour or every 5 minutes. The incidence of morphine induced sleep disturbance myoclonus (SDM) was also recorded following any reduction or cessation of the morphine infusion. Demographic data, morphine dosage, pain scores and heart rate changes were recorded. Statistical analysis: All tests undertaken were two-sided, and a p value <0.05 was considered as statistically significant, with (bootstrapped) 95% confidence intervals (CI) calculated. For univariable and multivariable logistic regression modelling was undertaken with logit function, along with a robust error variance and age and sex adjustment were fitted to identify the potential risk factors associated with the endpoint. Multivariable analyses were carried out via generalised linear models, with stepwise AIC (Akaike information criterion) in the backwards direction to ground the final model. Clinically relevant continuous variables were included in the multivariable model. Adjusted relative risks (RRadj) with bootstrapped 95% CIs were calculated and reported for the logistic regression model.

Results: 53 children experienced myoclonus: morphine induced SDM was reported in 33 out of 200 children (16.5%) and a further 20 children (10%) experience morphine induced myoclonus without sleep disturbance (Figures 1&2; Table 1); 25/33 children (76%) with morphine induced SDM were under two years of age with a mean maximum infusion rate of morphine was 15.4 mcg/kg/h. The other eight children with morphine induced SDM were aged between two-six years with a morphine infusion rate between 5 to 35mcg/kg/h. From multivariate analysis, age under two years of age significantly increased the risk of developing myoclonus (RR 2.21 95%CI 1.32, 3.71; p<0.001) (Figure 3). The mean morphine infusion rate (in mcg/kg/h) was higher in children with morphine induced SDM (15.09 [95%CI 13.05,17.13; SD 7.33) than in children who did not experience myoclonus (15.15 [95%CI 14.06,16.24; SD 7.33) and was found to be statistically non-significant (two-tailed t-test p=0.95; 95%CI -2.12, 2.24). Myoclonus was recognised as a side effect of morphine in 19/53 children by parents or nurses and by the pain nurse specialist in the remaining 34 children. Morphine induced myoclonus was not recognised as a side effect of morphine in 63% of children by the nursing or medical staff. Morphine infusion rate was reduced or stopped in 12 out of 19 children recognised to have myoclonus and unchanged or increased in the other seven. In the 34 children not initially identified to have myoclonus, the morphine infusion rate was increased in 7 and 2 were given either chloral hydrate or diazepam to treat their myoclonus. Myoclonus stopped completely in 13 children following reduction of the morphine infusion, and a further 11 children had a noticeable improvement. Two children had no improvement following a reduction in morphine. Pain scores

remained unchanged despite a reduction in the morphine infusion rate (ANOVA: p=0.313, adjusted R2 0.0209)

Conclusion: Morphine induced sleep disturbance myoclonus is common in young children, 76% occurring in those under 2 years of age and appears to be more common in female and is dose dependant. This side effect of morphine from our assessment appears to be under recognised and misinterpreted as pain by health professions.

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Pediatric Anesthesiology - 3 Intra-Operative Hyperglycemia in Pediatric Liver Transplantation Associated with Prolonged Hospitalization, Increased Infection Rates and Graft Dysfunction

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Introduction: Alterations in glucose metabolism are frequently seen in patients undergoing surgery and are associated with increased morbidity and mortality (1). End-stage liver disease itself is associated with altered glucose homeostasis, and patients undergoing liver transplantation experience large fluctuations in blood glucose (2). Hyperglycemia is frequently seen following reperfusion in liver transplantation. In adult liver transplantation, hyperglycemia in the early post-transplant period has been associated with liver allograft rejection, surgical site infection and death. A retrospective study revealed improved outcomes in adult orthotopic liver transplant patients when the mean intraoperative blood glucose was kept below 150mg/dL (3). In the pediatric intensive care unit, elevated blood glucose has been found to be associated with increased morbidity and mortality (4). However, there is limited data on the effect of hyperglycemia on post-operative outcomes in pediatric liver transplantation. In this retrospective study, we aim to evaluate the effect of perioperative hyperglycemia on the post-operative outcomes in pediatric liver transplant patients. We hypothesize that perioperative hyperglycemia during pediatric liver transplantation has similarly deleterious consequences as seen in adults including prolonged hospitalization, increased infection rate and increased incidence of graft failure.

Methods: Following IRB approval, we evaluated the records of all patients who underwent a liver transplantation at our institution from January 2014 to June 2021. Hyperglycemia was defined as an intra-operative glucose value greater than or equal to 200mg/dL. Hospital length of stay (LOS) was measured as time from anesthesia end to transfer out of the intensive care unit (ICU) and to discharge from the hospital. Graft issue was defined as the need for a re-transplantation or patient death within 2 weeks of the transplant and/or need for re-exploration due to arterial/venous thrombosis, decreased arterial/venous flow, or increased liver indices. Post-operative infection was defined as infection requiring additional antibiotic coverage and/or fever of unknown origin.

Results: 173 patients were included in our analysis with a median age of 3 years (range:15 days-21 years) and weight 14.4kg (range: 3.5-102.2kg). Mean ICU and hospital LOS was 5.45 and 13.76 days in the normoglycemia group vs 7.74 and 17.78 days in the hyperglycemia group. Incidence of infection was 7.89% in the normoglycemia group vs 20.62% in the hyperglycemia group. Incidence of graft dysfunction was 15.79% in the normoglycemia group vs 19.59% in the hyperglycemia group.

Conclusion: Pediatric liver transplant patients experience large fluctuations in blood glucose levels, with hyperglycemia frequently seen after reperfusion. Often, these episodes of intra-operative hyperglycemia are not treated aggressively. This study demonstrates that the presence of intra-operative hyperglycemia is associated with poor outcomes. A single intra-operative glucose value greater than or equal to 200mg/dL is associated with increased hospital length of stay and increased infection rate. Interestingly, this study also finds a correlation between intra-operative hyperglycemia and graft dysfunction. Further studies looking at tight glucose control are needed to better determine an appropriate intra-operative glucose target in pediatric liver transplant patients.

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Pediatric Anesthesiology - 4 Pediatric Anesthesia Simulation Innovation: High Frequency Oscillatory Ventilation in Micropremies: A Case of NEC in the NICU

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Introduction: Pediatric Anesthesia Bootcamps were started in Philadelphia in fall of 2012. (1) Since then, both fall and spring (advanced) simulation bootcamps have been held across the US. (2) The hallmark of these bootcamps are well-designed simulations that provide hands on training in realistic conditions and a psychologically safe learning environment. Study Aims: To examine a new high-fidelity simulation added to the Midwest Pediatric Anesthesia Fellow Bootcamp (PAFB) that included a novel way to simulate High Frequency Oscillatory Ventilation (HFOV). Fellows learn how to perform a micropreemie case in the NICU setting on an oscillator.

Methods: Eleven pediatric anesthesia fellows from three institutions participated in the fall 2021 Midwest PAFB; less than prior years due to the Covid-19 pandemic. Pre- and Post-simulation surveys were solicited, asking a series of qualitative and quantitative questions regarding the participant's confidence level with the clinical scenario (micropreemine with Necrotizing Enterocolitis (NEC) in the NICU on HFOV) and confidence in their skill level for managing the case. The simulation operation and technical set up included a real oscillator, respiratory therapist, low-fidelity mannequin, and approximately ten faculty members as observers and debriefers.

Results: Pre-simulation survey results showed only one out of eleven participants had experience managing oscillator settings before. Six out of eleven participants had no prior experience managing anesthetic for an extremely premature baby (defined as birth during 26-28 weeks' gestation or birthweight < 700-800 grams). Eight out of eleven participants reported no prior experience with managing anesthetic for a baby with Necrotizing Enterocolitis (NEC). Eight out of eleven participants reported less than ten pediatric anesthetic cases performed outside of the OR. Participant responses regarding confidence levels pre- and post-simulation are shown in Table 1.

Conclusion: This simulation was designed to expose pediatric anesthesia fellows to a NICU case involving a micropreemie with NEC on HFOV for pediatric anesthesia fellows early in training that will increase their preparedness and confidence. The pre-simulation survey showed our simulation participants had very little experience with oscillators, and management of anesthetic for micropreemies and patients with NEC. Post-simulation survey results show a marked increase in confidence, knowledge, and practical skills among the participants. The collective growth in ability and knowledge reported after undergoing the simulation indicates that our simulation was well-timed in their fellowship year, needed, and successful. Conclusion: HFOV can be successfully simulated with a micropreemie mannikin and can improve confidence and knowledge of fall pediatric anesthesia fellows participating in the Midwest PAFB.

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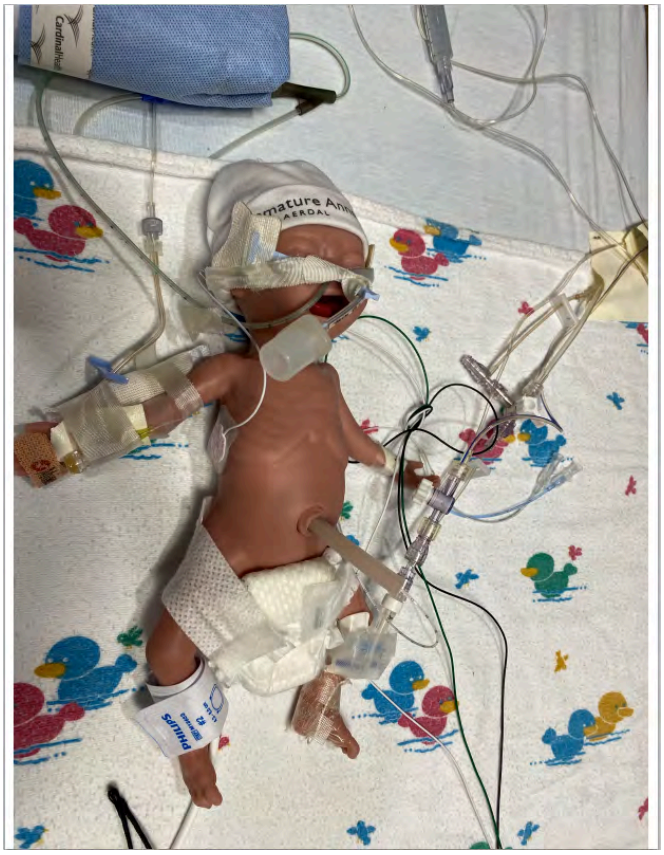
Question	Pre-simulation		Post simulation	
	yes	no	yes	no
Are you confident in your knowledge of oscillator settings and physiology?	1	10	9	2
Are you confident in your ability to manage an oscillator during and anesthetic	3	8	8	3
Are you confident in your knowledge of what drugs and equipment to bring to an out of OR case in NICU	7	4	10	1
Are you confident in your ability to keep a micropreemie warm during a NICU anesthetic	6	5	9	2



Pediatric Anesthesiology - 5 Intrathecal clonidine is associated with intraoperative BP, HR, and respiratory changes without affecting postoperative course in infants receiving spinal anesthesia for urologic day surgery

Andrew L Chen[1], Jacquelin Peck[1], Laura A Santa Cruz Mercado[1], Jack S Elder[1], Diana Liu[1], Christine Mai[1], David August[1], Paul G Firth[1], Michael R Leeman[1], Chang Amber Liu[1]

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Introduction: Spinal anesthesia (SA) for infants undergoing infraumbilical surgeries avoids systemic sedatives, airway instrumentation, reduces the risk of early postoperative apnea [1], and improves hemodynamic stability compared to general anesthesia [2]. A caveat of SA is its limited surgical duration. Clonidine is an adjunct that prolongs SA in infants [3], allowing for more complex procedures to performed; however, the safety and efficiency of intrathecal clonidine in infants undergoing day surgery is not well studied. In this study, we compared bupivacaine only SA (bSA) to SA with adjunctive clonidine (cSA) for infants undergoing urologic day surgery. We examined the intra- and postoperative courses of bSA vs. cSA patients.

Methods: Sixty-two infants undergoing urologic day surgery under SA using a previously described protocol [4] were studied. Clonidine was used as an adjunct on a need-to-treat basis as decided by the surgeon and anesthesiologist during the preoperative huddle. Demographic, intraoperative, and postoperative data were collected from electronic medical records (Table 1). We compared vital signs, airway events, need for additional intraoperative sedation, and PACU length of stay between bSA and cSA groups. Continuous data were analyzed using t-tests or Mann-Whitney U tests based on data normality, whereas Z-tests or Fisher's exact tests were used for categorical data. Analysis was conducted in R.

Results: Twenty-four bSA and 38 cSA patients were studied. Intraoperatively, average mean arterial pressure (MAP) was 59 mmHg in the bSA group and 53 mmHg in the cSA group (t=-2.84, df=46.7, p=0.003, Figure 1a). Mean heart rate (HR) was 135 bpm in the bSA group and 124 bpm in the cSA group (t=-2.69, df=41, p=0.005, Figure 1b). No differences were seen for oxygen saturation (SpO2) between groups (U=467, p=0.88, Figure 1c). In regards to intraoperative airway events, patients in the cSA group had significantly more hiccup-like short shallow inspirations (n=10, p=0.005, Fisher's exact test) and mild airway obstruction relieved by chin-lift (n=8, p=0.02, Fisher's exact test) compared to bSA patients. Additional sedatives were used in 29.2% and 10.5% of bSA and cSA cases, respectively, though this did not reach significance (p=0.09). Mean surgical duration was significantly longer in the cSA (59 min) than the bSA group (52 min, U =574.5, p=0.04). Interestingly, there was no significant difference in the mean length of PACU stay between cSA (69 min) and bSA groups (65 min). No patients required additional medications or interventions in the PACU.

Conclusion: Our study shows that while clonidine is associated with reduced intraoperative MAP and HR, and transient and observable airway changes requiring minimal or no interventions to resolve, PACU course was not affected in infants undergoing urologic day surgery. Additionally, clonidine can prolong surgery length, allowing for more complex procedures to take place.

References: 1. Anesthesiology. 2015 Jul; 123(1): p 38-54. 2. Anesthesia and Analgesia. 2017 Sep;125(3):p 837-845. 3. Journal of Anesthesia Volume 32, p 637-640 (2018) 4. Pediatric Anesthesia 2019 Aug; 29(8):p 881-882.

		bSA (n=24)	cSA (n=38)	p-value
Demographic	Chronological age (days)[a]	144 (range 55-339)	149 (range 37-250)	0.18
	Sex			
	Male (n, %)	23 (96%)	37 (97.4%)	--
	Female (n, %)	1 (4%)	1 (2.6%)	--
	Prematurity (gestational age<37 weeks, %)	3 (12.5%)	4 (10.5%)	1
	Weight (kg)[a]	7 (range 3.2-9.8)	7.4 (range 4.6-9.8)	0.36
	ASA status (I, II)	I (19), II (5)	I (31), II (7)	1
Intraoperative	Length of surgery (min)[b]	50 (IQR 41-64)	57 (IQR 53-65)	0.04*
	Surgery type (n, % of cases)			
	Inguinal hernia repair	8 (33.3%)	6 (15.8%)	--
	Chordee correction/repair	4 (16.7%)	7 (18.4%)	--
	Correction of webbed penis/hidden penis/scrotoplasty	8 (33.3%)	15 (39.5%)	--
	Orchiopexy	1 (4.2%)	5 (13.2%)	--
	Hypospadias repair	2 (8.3%)	3 (7.9%)	--
	Hydrocelectomy	0	1 (2.6%)	--
	Circumcision	1 (4.2%)	1 (2.6%)	--
	Vitals			
	Mean MAP (mmHg)[a]	59 (range 38-73)	53 (range 36-71)	0.003**
	Mean SpO2 (%)[a]	99 (range 96-100)	99 (range 96-100)	0.88
	Mean HR (bpm)[a]	135 (range 98-164)	124 (range 96-148)	0.005**
	Transient airway changes			
	Hiccup-like short shallow inspirations (n, %)	0 (0%)	10 (26.3%)	0.005**
	Mild airway obstruction relieved by chin lift (n, %)	0 (0%)	8 (30.7%)	0.02*
	Use of additional systemic sedatives (n, %)	7 (29.2%)	4 (10.5%)	0.09
Postoperative	Length of PACU stay (min)[a]	65 (range 31-109)	69 (range 33-175)	0.74

Table 1. Demographic and intraoperative data for bSA and cSA patients. [a]=mean, range, [b]=median, interquartile range (IQR). *=p<0.05, **=p<0.01. T-tests or Mann-Whitney U tests were used to compare continuous data depending on normality as determined by the Shapiro-Wilk test, whereas Z-tests and Fisher exact tests were used to compare categorical data (Fisher test used when x^2 expected frequencies in any cell was <5).

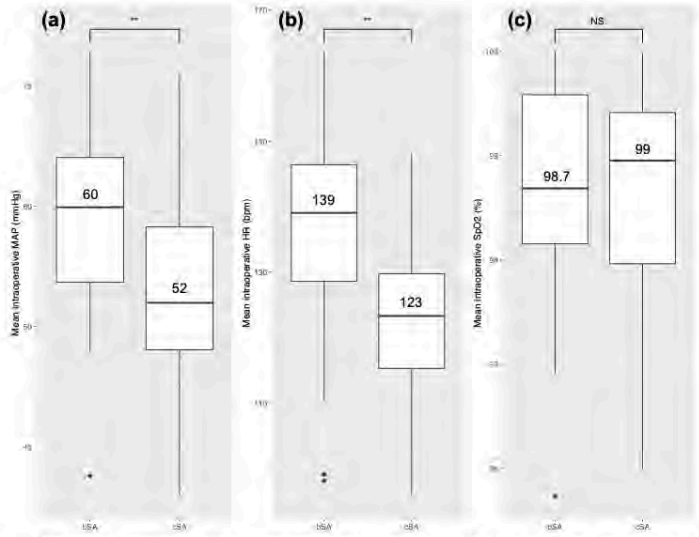

Figure 1. Comparison of intraoperative MAP (a), HR (b), and SpO2 (c) between patients who received bupivacaine only spinal anesthesia (bSA) and spinal anesthesia with adjunctive clonidine (cSA). MAP and HR were compared using one-sided t-tests, whereas SpO2 was compared using a Mann-Whitney U test as the data were not normally distributed. **=p<0.01, NS denotes non-significant differences.

Pediatric Anesthesiology - 6 Age-Dependent EEG Signatures in Infants Receiving Spinal Anesthesia

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Introduction: Infants under spinal anesthesia appear to be sedated despite the absence of systemic sedative medications. In this study, we investigated the electroencephalogram (EEG) of infants under spinal anesthesia and hypothesized that we would observe EEG features similar to those seen during physiologic sleep.

Methods: Continuous 4-channel frontal EEG data were recorded using the SedLine monitor after the administration of spinal anesthesia in infants undergoing infraumbilical surgeries (n = 34). We computed the power spectra and spectrogram for each subject using multitaper spectral estimation methods, and visually scored the data for episodes of EEG discontinuity or spindle oscillations. We characterized the relationship between EEG discontinuity or spindle activity and gestational age (GA), postmenstrual age (PMA), or chronological age using logistic regression analyses.

Results: The predominant EEG patterns observed in infants under spinal anesthesia were slow oscillations, spindles, and EEG discontinuities (Figure 1). We observed spindles in infants under spinal anesthesia starting at about 8 weeks chronological age. The presence of spindle activity was best described by PMA ($p<0.05$), with spindles being more likely in infants with higher PMA (Figure 2). We also observed EEG discontinuities in infants under spinal anesthesia (Figure 3), the presence of which was best described by GA ($p<0.05$), with EEG discontinuities being more likely in infants with lower GA (Figure 4). These age-related changes in the presence of spindle activity and EEG discontinuities in infants under spinal anesthesia appeared to generally correspond to developmental changes in the sleep EEG in infants.

Conclusion: This work illustrates two key age-dependent transitions in EEG dynamics during spinal anesthesia in infants that may reflect the maturation of underlying brain circuits. Despite similarities between the EEG during spinal anesthesia and sleep in infants, the sedative state under spinal anesthesia is distinct in that this sedative state remains largely sustained throughout the duration of the neuraxial anesthetic. This tendency for infants to remain sedated under spinal anesthesia could reflect a shift in the balance between sleep and wakefulness that favors sleep.

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Table 1. Patient Characteristics (n = 34)

Chronological Age (weeks)	11.5 (9,17)
Postmenstrual Age (weeks)	49 (43, 56)
Gestational Age (weeks)	38 (35.2, 39)
Term	24 (71%)
Pre-term	10 (29%)
Gender	
Male	30 (88%)
Female	4 (12%)
ASA	
I	18 (53%)
II	13 (38%)
III	3 (9%)
Weight (kg)	5.3 (1.7)
Type of Procedures	
Inguinal Hernia Repair (Bilateral)	18 (53%)
Circumcision	9 (26%)
Inguinal Hernia Repair (Unilateral)	5 (15%)
Other procedures	2 (6%)

*Variables were reported as mean and standard deviation, median and interquartile range, or count and percentage.
*Spinal anesthesia was performed in the sitting position with maximal hip flexion, midline approach at L4–L5 interspace using a 25-gauge pediatric, Quincke type spinal needle. When free flow of CSF was identified, a mixture of 1 mg/kg of bupivacaine 0.5% (PF) alone or in combination with 1 mcg/kg of clonidine was administered

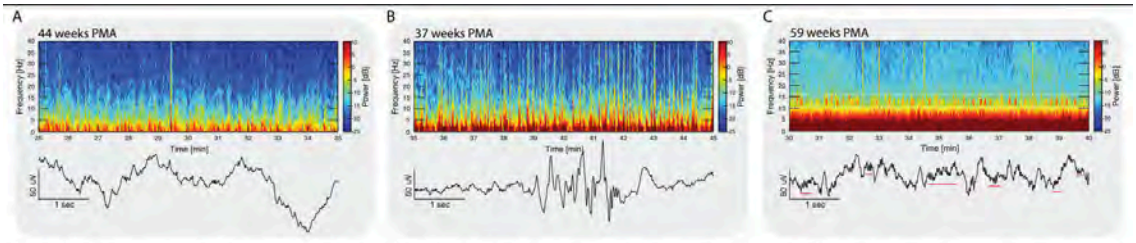

Figure 1. Illustrative spectrograms and time domain waveforms of infants under spinal anesthesia. A. The spectrogram and time domain waveform of a 11-week-old premature infant (33 weeks GA, 44 weeks PMA) under spinal anesthesia for bilateral inguinal hernia repair. The spectrogram shows a dominant low-frequency (slow/delta – 0.1 – 4 Hz) activity. A corresponding ten-second electroencephalogram trace recorded at minute 26 featuring slow-delta oscillations is shown. **B.** The spectrogram and time domain waveform of a 11-week-old premature infant (26 weeks GA, 37 weeks PMA) under spinal anesthesia for bilateral inguinal hernia repair and circumcision. The spectrogram shows an alternating pattern of burst events lasting a few seconds followed by periods of discontinuity of variable duration and amplitude. A corresponding ten-second electroencephalogram trace recorded at minute 44 shows alternating discontinuity events and high frequency bursts. **C.** The spectrogram and time domain waveform of a 20-week-old infant (38 weeks GA, 59 weeks PMA) under spinal anesthesia for chordee repair and circumcision. The spectrogram shows spindles (~10 to 16 Hz oscillations) and slow-delta oscillations (0.1 – 4 Hz). A corresponding ten-second electroencephalogram trace recorded at minute 32 from the spectrogram shows slow waves and spindles (red underlines).

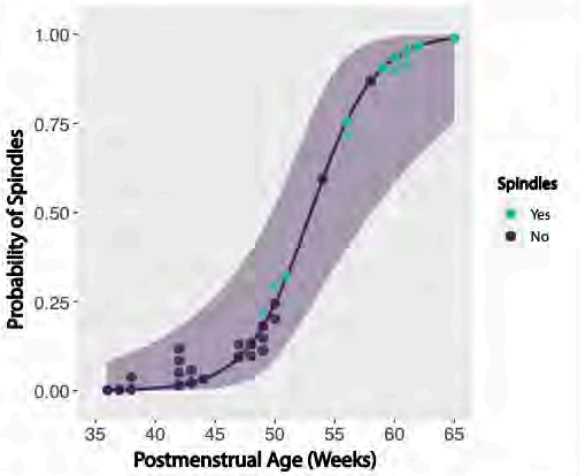

Figure 2. Logistic regression analysis of spindle probability as a function of postmenstrual age (PMA). The central bolded line represents the estimated probability of observing spindle activity as a function of PMA. The shaded bounds represent the 95% confidence interval for this regression model. The individual circles along the central line represent individual subjects, which were filled in green if spindles were observed or purple if spindles were not observed under spinal anesthesia. Model 1 shows that the probability of spindles under spinal anesthesia increases with increasing PMA, especially after approximately 50 weeks PMA.

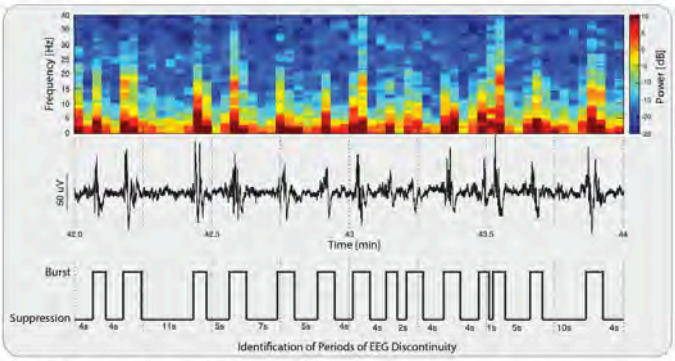

Figure 3. Example of EEG discontinuity in an infant. A two-minute EEG spectrogram and time domain waveform from a 9-week-old premature infant (29 weeks GA, 38 weeks PMA) under spinal anaesthesia for inguinal herniorrhaphy. The spectrogram and time domain waveform above show discontinuous activity characterised by an alternating pattern of burst events lasting a few seconds followed by periods of suppression of variable duration and amplitude. The bottom panel shows the discontinuities identified by visual scoring.

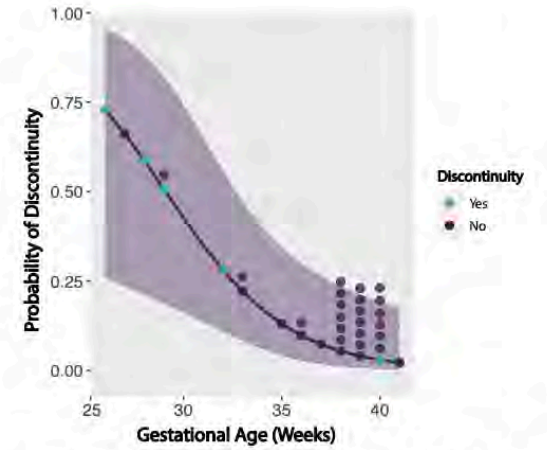

Figure 4. Logistic regression analysis of EEG discontinuity probability as a function of gestational age (GA). The central bolded line represents the estimated probability of observing EEG discontinuity as a function of GA. The shaded bounds represent the 95% confidence interval for this regression model. The individual circles along the central line represent individual subjects, which were filled in green if EEG discontinuities were observed or purple if EEG discontinuities were not observed under spinal anesthesia. This model shows that the probability of EEG discontinuity events under spinal anesthesia increases with decreasing GA, with an increased likelihood of observing EEG discontinuity in infants who were pre-term.

Pediatric Anesthesiology - 7 Low-dose intraoperative opioids and its association with PACU outcomes: a retrospective equivalence study

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Introduction: Opioids are a mainstay of intraoperative and postoperative analgesia in pediatric surgical patients, but also have significant dose-dependent side-effects. Significant variation in intraoperative dose administered occurs, but the relationship between intraoperative opioid administration and postoperative outcomes is unclear. We examined the relationship between intraoperative opioid dose among children and PACU outcomes; we hypothesized that pediatric patients receiving the lowest amounts of opioids intraoperatively would have higher pain scores, more opioid administrations, and less antiemetic administrations than those receiving the highest amounts.

Methods: We performed a retrospective cohort study of eleven select procedures at a single pediatric quaternary care institution. Patients <19 years of age, American Society of Anesthesiologists physical status classification I-III, who underwent one of 11 procedures under general anesthesia, without regional anesthesia, and were admitted to the post-anesthesia care unit (PACU) afterwards at Stanford University Children's Hospital between May 4th, 2014 and August 31st, 2019 were eligible for inclusion. The exposure of interest was total intraoperative opioid dose. It was analyzed as quartiles, comparing each higher quartile to the lowest quartile. The primary outcome of interest was the first conscious pain score in the PACU. Secondary outcomes of interest included mean PACU pain score; PACU opioid use; and PACU antiemetic use. Linear regression models were fitted for continuous outcomes and logistic regression models were fitted for binary outcomes, controlling for confounders. To further explore the effects of opioid-free anesthetics, an exploratory analysis was also performed, categorizing intraoperative opioid dose as none (0 MEU/kg) or any (>0 MEU/kg), and analyzing the same outcomes for procedures where >=5% of cases received no intraoperative opioids.

Results: 2583 patients were included, with mean (standard deviation [SD]) age of 8.10 (5.06) years, 1587 (61.4%) of whom were male. After adjusting for confounders, none of the higher opioid-dose quartiles had CIs for the difference in first conscious pain score or mean PACU pain score that crossed the specified boundaries of -1 or +1. After adjusting for confounders, the ORs (95% CI) for receiving opioids in the PACU were 1.24 (0.96 - 1.59), 1.09 (0.8 - 1.44) and 1.11(0.80 - 1.55) for the second, third and fourth (highest) quartiles respectively. After adjusting for confounders, the OR for antiemetic use in the second quartile compared to the lowest quartile was 1.73 (95% CI: 1.01 - 2.98); for the third quartile compared to the lowest was 2.11 (95% CI: 1.05 - 4.25), and for the highest quartile compared to the lowest it was 1.90 (95% CI: 0.89 - 4.06). Under a post hoc superiority analysis, the second and third quartiles were associated with significantly higher odds of receiving antiemetics than the lowest. The adjusted OR (95% CI) associated with receiving intraoperative opioids was 1.21 (0.86 - 1.70). After adjustment, the estimated mean (95% CI) increase in total PACU opioid dose for patients who received intraoperative opioids was 0.021 (-0.005 - 0.048) MEU/kg.

Conclusion: In this retrospective analysis of the association between total intraoperative opioid dose and PACU outcomes in children who underwent general anesthesia for one of 11 surgeries at a single center, the lowest quartile was not associated with worse PACU pain outcomes. However, higher intraoperative opioid administration was associated with increased odds of receiving antiemetics in the PACU. These results suggest that reducing intraoperative opioid dose may not be detrimental to pediatric patient outcomes. While optimal dosing and combinations of opioid and non-opioid analgesics are not apparent for many surgeries, future investigations may focus on opioid dosing threshold effects on patient outcomes.

Pediatric Anesthesiology - 8 Racial/Ethnic Variability in Use of General Anesthesia for Pediatric Magnetic Resonance Imaging

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Introduction: Children increasingly undergo diagnostic imaging procedures, sometimes with general anesthesia (GA). It is unknown whether or not the use of GA differs by race/ethnicity among children undergoing magnetic resonance imaging (MRI) scans.

Methods: This is a retrospective cohort study of GA use for pediatric patients from 0 to 21 years of age who underwent MRIs from January 1, 2004 to May 31, 2019. The study sample was stratified into five age groups: 0 to 1, 2 to 5, 6 to 11, 12 to 18, and 19 to 21. Analysis was performed separately for each age group and the entire sample.

Results: Among the 525,986 MRI encounters by 457,948 pediatric patients, 33,001 encounters had GA (6.3%). In the all-age sample, after adjusting for confounders and repeated observations, Asian (adjusted odds ratio [aOR], 1.14, 95% confidence interval [CI], 1.05-1.23; P = 0.001), Black (aOR, 1.16, 95% CI, 1.09-1.24; P < .001), and Hispanic (aOR, 1.08, 95% CI, 1.03-1.14; P = 0.004) patients were more likely to receive GA for MRIs than White patients. This finding remained in age-stratified analysis for Black patients 2 to 18 years old, Asian patients 0 to 5 years old, and Hispanic patients aged 0 to 1.

Conclusion: Children of color were more likely to receive GA during MRI scans than White children. Future research is warranted to delineate whether this phenomenon signifies disparate care for children based on their race/ethnicity.

Pediatric Anesthesiology - 9 Early Extubation in Pediatric Liver Transplantation Associated with Improved Post-Operative Outcomes

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Introduction: Early extubation after liver transplantation has been utilized in adult anesthesia since the late 1990s. Initial studies showed that by extubating patients in the early post-operative period, patients required shorter Intensive Care Unit (ICU) stays, decreased hospital length of stay and reduced costs with no increase in respiratory failure and reintubation rates (1,2). Although this method of 'fast-track' liver transplantation has gained popularity, it is still not standard of practice at many pediatric institutions and anesthesiologists facilitating pediatric liver transplantation have only recently begun to adopt early extubation. There are many reasons why pediatric anesthesiologists are concerned about immediate post-operative extubation: graft function, vessel patency, graft-recipient mismatch, pre-existing malnutrition, depressive effects of analgesics and emotional difficulties among children. To date there have been a few manuscripts describing single-center experience in pediatric hospitals with immediate post-operative extubation, but there is scarce data on the post-operative impact this technique confers (3,4). Over the last 6 years, we have actively attempted immediate extubation after pediatric liver transplantation in the majority of our patients and tracked the post-operative course to evaluate if this technique offers similar benefits to that in adult transplantation.

Methods: After IRB approval, we performed a retrospective analysis of all pediatric liver transplantation cases performed at our hospital from January 2014 to June 2021. We collected baseline demographic data and information on the intra-operative management including intravenous fluid, blood product and medication administration. We then collected data on any events that may be related to extubation including need for re-intubation, high flow nasal cannula requirements, issues with graft function (including arterial thrombus, venous thrombus, need for re-exploration, graft failure requiring re-transplantation), PICU length of stay (LOS) and hospital LOS.

Results: 173 patients were included in our analysis with a median age of 3 years (range:15 days-21 years) and weight 14.4kg (range: 3.5-102.2kg). 69.9% (121 patients) were extubated in the OR post-transplant. Average ICU stay in the early extubation group was 4.7 days vs 11.4 days in the delayed extubation group. Average hospital length of stay was 13.1 days in the early extubation group vs 22.8 days in the delayed extubation group. The percentage of patients requiring high flow nasal cannula was 10.7% for the early extubation group and 23.1% for the delayed extubation group. Graft function issues such as arterial or venous thrombus, decreased arterial or venous flow requiring re-exploration and graft failure necessitating re-transplantation occurred in 15.7% of patients in the early extubation group vs 21.2% of patients in the delayed extubation group.

Conclusion: This data shows that our institution's experience with immediate post-operative extubation following liver transplantation has not only been successful, but it has led to improved outcomes in the form of shorter ICU and hospital LOS, decreased high flow requirements and decreased incidence of graft malfunction. This is important because while there have been reports of the ability to successfully extubate pediatric patients post liver transplant, there has been minimal data on if this practice actually improves outcomes. Future research looking at pain scores, analgesic requirements and time to first bowel movement between the two groups may further delineate the improved outcomes seen from early extubation.

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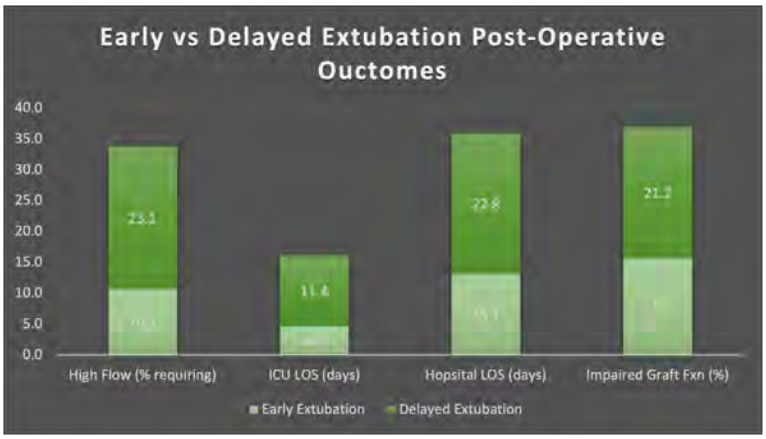
Anesth Analg 1997;84:249-253. 2.Neelakanta G, Sopher M, Chan S, Pregler J, Steadman R, Braunfeld M, Csete M. Early tracheal extubation after liver transplantation. J Cardiothorac Vasc Anesth 1997; 11:1 65-167. 3.Fullington NM, Cauley RP, Potanos KM, et al. Immediate extubation after pediatric liver transplantation: a single-center experience. Liver Transpl. 2015; 21: 57-62. 4.Gurnaney HG, Cook-Sather SD, Shaked A, Olthoff KM, Rand EB, Lingappan AM, Rehman MA. Extubation in the operating room after pediatric liver transplant: A retrospective cohort study. Paediatr Anaesth. 2018; 28(2):174-178.



Pediatric Anesthesiology - 10 Spinal anesthesia as an alternative to general anesthesia in infants undergoing urologic day surgery

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Introduction: The use of spinal anesthesia (SA) in infants avoids endotracheal intubation and use of systemic sedatives [1]. Additionally, SA can reduce the risk of early postoperative apnea [2] and improve hemodynamic stability in infants [3]. Besides being a safe alternative to GA, SA can expedite the operative workflow [4]. We hypothesized that in the urologic day surgery setting, SA is an alternative to GA that avoids intubation and intraoperative opioids and reduces OR and PACU time.

Methods: Eighty-three patients underwent SA at our hospital for urologic day surgery following a previously published infant protocol [4] (2019P002042), 10 of whom were planned inpatients and thus excluded from analysis. Patients <10 months and <10 kg were candidates for SA. Demographic and intraoperative variables were recorded from the electronic medical record (Table 1). As a pilot study, a subset of our SA database (n=19) was matched to GA patients by age, weight, ASA status, and procedure length. Primary outcomes were overall OR time as defined by in-room to room exit, and PACU recovery time between groups. The secondary outcome was use of intraoperative opioids. Matched comparisons were performed in R using one-sided Wilcoxon signed rank tests. Here, we report overall database statistics as well as preliminary results from the matched cohort analysis.

Results: Demographics of 73 patients are outlined in Table 1. Two cases started under SA were converted to GA due to intolerance of laparoscopic insufflation and continued leg movement following spinal placement, respectively. Intrathecal clonidine (ITC) was administered in 44 cases (60.2%), and a novel combined spinal/caudal catheter anesthesia technique [5] was used in 9 (11.8%). Intraoperative airway changes occurred in 7 patients (5 received ITC, 2 did not), with 4 patients requiring chin lift and 3 resolving spontaneously. All patients were brought awake and ready to feed to the PACU without need for additional interventions, and were discharged after feeding. In our pilot study, 19 GA-SA pairs (38 patients) were closely matched (Table 1). Overall OR time was significantly shorter in the SA group ($Z=1.89$, $p=0.03$, effect size $r=0.43$, Figure 1a), despite no significant differences in operative time ($Z=1.59$, $p=0.06$). PACU recovery time was also significantly shorter in the SA cohort ($Z=2.13$, $p=0.016$, effect size $r=0.49$, Figure 1b). SA patients received no opioids whereas 63.1% of GA patients did (n=12, Figure 2).

Conclusion: In this study, we show that SA reduces total OR and PACU time compared to GA while avoiding intraoperative opioids. Our experience demonstrates that SA is a viable alternative to GA in infants undergoing urologic day surgery.

References: 1. Journal of Pediatric Urology. 2017 Aug;13(4):396-400. Epub 2017 Jul 14. 2. Anesthesiology. 2015 Jul; 123(1): p 38,Äì54. 3. Anesthesia and Analgesia. 2017 Sep;125(3):p 837-845. 4. Pediatric Anesthesia 2019 Aug; 29(8):p 881-882. 5. Journal of Pediatric Urology 2019 Oct;15(5):442-447. Epub 2019 Apr 11.

Overall database (n=73)	**Chronological age (months)[a]**			5 (IQR 3.7-6.1)
	Sex			
	Male (n, %)			71 (97%)
	Female (n, %)			2 (3%)
	Born at term (%)			65 (93%)
	Weight (kg)[a]			7.3 (IQR 6.5-8.6)
	ASA status (I, II)			I (60), II (13)
	Length of surgery (min)[a]			75 (IQR 66-90)
	<=60 min			15 (21%)
	61-90 min			41 (56%)
	>90 min			17 (23%)
	Conversion to GA (%)			2 (2.7%)
	Use of adjunctive intravenous sedation (%)			16 (22%)
	Time required for placement of spinal (min)[a]			9 (IQR 7-13)
	Surgery type (n, % of cases)			
	Inguinal hernia repair			15 (21%)
	Hypospadias repair			14 (19%)
	Correction of webbed penis/hidden penis/scrotoplasty			24 (33%)
	Chordee correction			11 (15%)
	Orchiopexy			6 (8%)
	Hydrocelectomy			1 (1 %)
	Circumcision			2 (3%)
Matched analysis (n=38)		**GA (n=19)**	**SA (n=19)**	**Mean pairwise difference**
	Weight (kg)	7.7 (IQR 7-8.7)	7.7 (IQR 7-8.4)	0.38 kg
	Age (days)[a]	184 (IQR 156-227)	198 (IQR 165-229)	5 days
	ASA status (I, II)	I (16), II (3)	I (16), II (3)	N/A
	Surgery length (min)[a]	57 (IQR 44-85)	72 (IQR 61-94)	14.5 min

Table 1. Demographic data for patients in overall database (n=73) and matched cohort analysis. [a]=median, interquartile range (IQR)

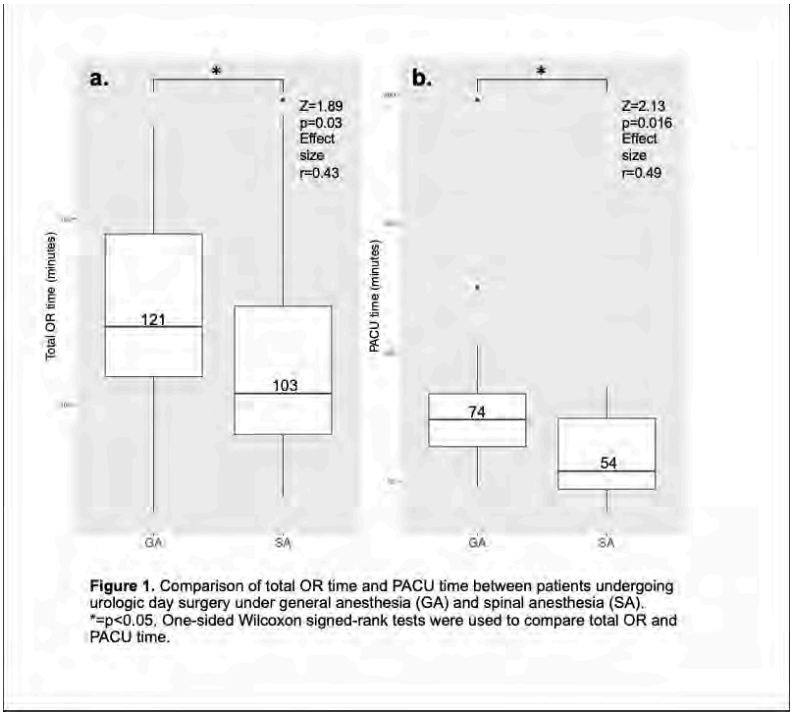

Figure 1. Comparison of total OR time and PACU time between patients undergoing urologic day surgery under general anesthesia (GA) and spinal anesthesia (SA). *=p<0.05, One-sided Wilcoxon signed-rank tests were used to compare total OR and PACU time.

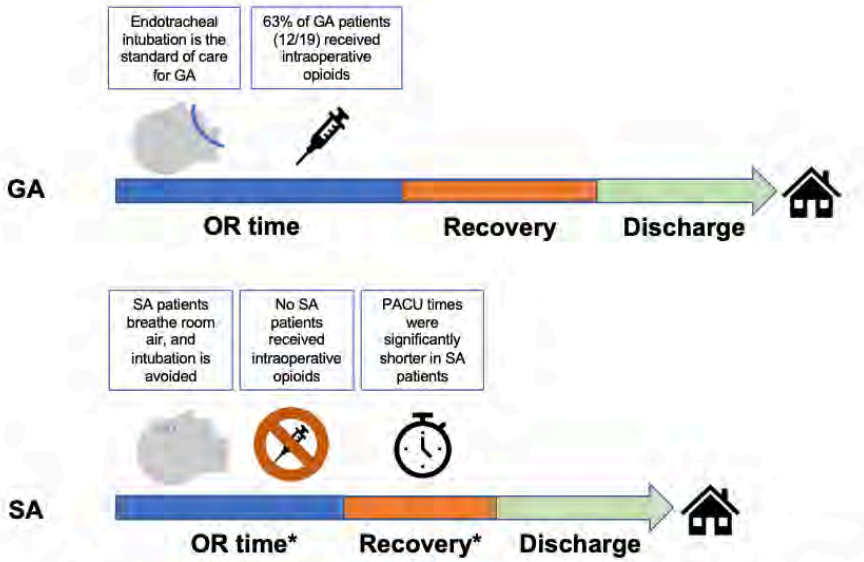

Figure 2. Our pilot study of 19 matched GA-SA pairs shows that SA allows for shorter OR time and faster PACU recovery time in patients undergoing urologic day surgery while avoiding intubation and intraoperative opioid medications. *=statistically significant differences as found by Wilcoxon signed-rank tests ($p<0.05$)

Pediatric Anesthesiology - 11 Anapod™ Humi-Therm Heated Humidification System Breathing Circuit vs Bair Hugger™ Warming Blanket for Intraoperative Maintenance of Body Temperature in Pediatric Patients Undergoing Dental Surgery

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Introduction: Perioperative maintenance of body temperature falls under the purview of the anesthesiologist. Perioperative hypothermia is associated with adverse patient outcomes including morbid cardiac events, hypertension, increased blood loss, increased allogenic transfusion requirements, coagulopathy, reduced immune response and surgical wound infections. Multiple warming methods are in clinical use, with forced-air warming blankets being the most common. However, heating of anesthetic gases via the breathing circuit is another option to influence patient body temperature perioperatively. This modality not only helps with temperature maintenance, it also adds humidity to the breathing gases which might have beneficial effects on the respiratory tract. The Anapod,Ñ¢ Humi-Therm Heated Humidification System Breathing Circuit has successfully been used in adult patients.(1,2) Its safety in pediatric patients has also been confirmed, but so far, no studies have evaluated its efficacy in this patient population. Our study aimed at evaluating whether the Anapod,Ñ¢ Humi-Therm Heated Humidification System Breathing Circuit is non-inferior compared to the Bair Hugger,Ñ¢ Forced-Air Warming Blanket when used in pediatric patients undergoing dental procedures under general anesthesia.

Methods: The study was approved by the Institutional Review Board (IRB) at the University of Minnesota (IRB ID# STUDY00005616). We included patients aged 18 years and younger who underwent dental exams with restorations under general endotracheal anesthesia. Patients were excluded if parents refused consent, if additional procedures involving parts of the patient's body other than the oral cavity were planned and if the patient had a history of diseases associated with temperature dysregulation such as active hyperthyroidism, dysautonomia, osteogenesis imperfecta and history of malignant hyperthermia. Informed consent was obtained from parents. The patients were randomized at the time of induction to temperature maintenance with either 1) the Bair Hugger,Ñ¢ blanket or 2) the Anapod,Ñ¢ Breathing Circuit (both systems were present for all cases). Anesthetic care was determined by the attending pediatric anesthesiologist. Temperature measurements were obtained from a rectal temperature probe. The primary outcome for this study was the last measured core temperature obtained from the rectal temperature probe at conclusion of the procedure prior to removal of the probe. The secondary outcome included the need for hypothermic or hyperthermic rescue in each group. The study was designed as a non-inferiority study with a predefined non-inferiority boundary of 0.3¬∞C.

Results: Patient characteristics are displayed in table 1 while table 2 shows the primary and secondary outcomes. The final rectal temperature was 0.5°C higher in the Bair Hugger™ group compared to the Anapod™ group (37.2 +/- 0.38°C versus 36.7 +/- 0.47°C). The 95% confidence interval for the difference in the final rectal temperature was (-0.709, -0.371) Celsius and excluded the non-inferiority margin of -0.3. The Bair Hugger™ group required more rescue interventions compared to the Anapod™ group (44.0% versus 22.0%; p=0.033), but those were most commonly due to hyperthermia (21 patients). Only one patient in the Bair Hugger group required a rescue intervention for hypothermia. Conversely, most interventions in the Anapod™ group were for hypothermia (8 patients), while 3 patients required hyperthermic rescue.

Conclusion: Both warming modalities resulted in intraoperative increases in body temperature. Based on the predefined non-inferiority margin, the results showed that the Anapod™ Humi-Therm Heated Humidification System Breathing Circuit was NOT non-inferior to the Bair Hugger™ Forced-Air Warming

Blanket. A superiority analysis based on the pre-defined O'Brien-Fleming stopping boundaries confirmed that the Bair Hugger™ Forced-Air Warming Blanket was superior in warming pediatric patients during dental procedures under general anesthesia, although this statistical difference was largely because the Bair Hugger™ system frequently "overheated" patients. When examining the individual patient temperature curves in figures 1 and 2, it becomes apparent that both devices are successful in warming patients after the initial drop in temperature due to induction of general anesthesia resulting in vasodilation and redistribution, although the Bair Hugger™ system achieves a quicker and steeper temperature rise as compared to the Anapod™ system.

References: 1. Anesth Pain Med; 11: 211-216 (2016) 2. Masui. The Japanese journal of anesthesiology; 50(1):76-9 (2001)

Table 1: Patient Characteristics

	Bairhugger (N=50)	Anapod (N=50)
Age (years)	5.1 (4.2 – 6)	5.3 (4.1 – 6.3)
Sex (male/female)	30/20	28/22
Height (m)	1.13 (0.27)	1.1 (0.12)
Weight (kg)	19.96 (4.93)	21.6 (8.99)
ASA I	27	22
ASA II	19	21
ASA III	4	7
Total anesthesia time (min)	172.5 (29.69)	173.68 (30.85)

Values are mean (SD), median (interquartile range [range]), or number (proportion) as appropriate

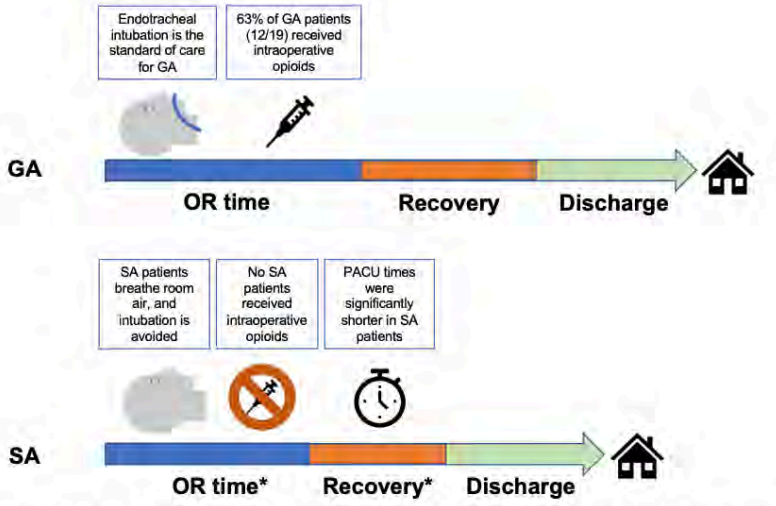


Figure 2. Our pilot study of 19 matched GA-SA pairs shows that SA allows for shorter OR time and faster PACU recovery time in patients undergoing urologic day surgery while avoiding intubation and intraoperative opioid medications. *=statistically significant differences as found by Wilcoxon signed-rank tests ($p<0.05$)

Figure 1: Anapod Rectal Temperature Curve

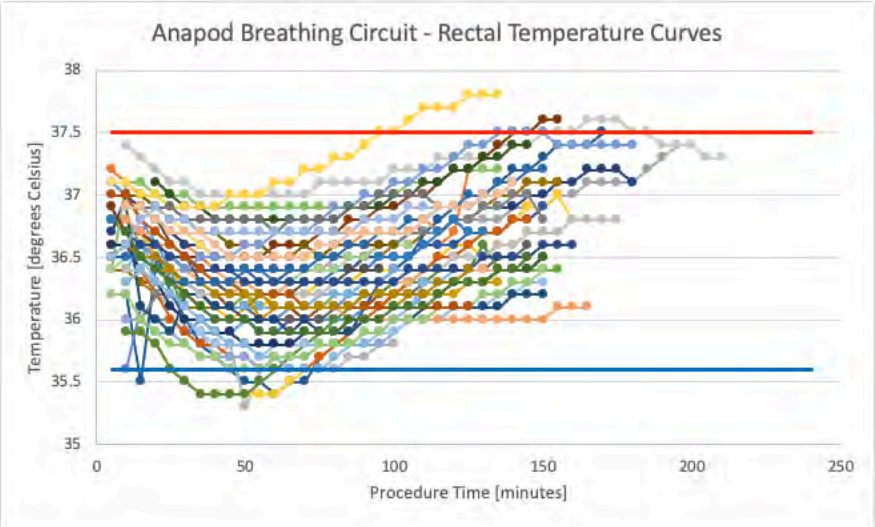
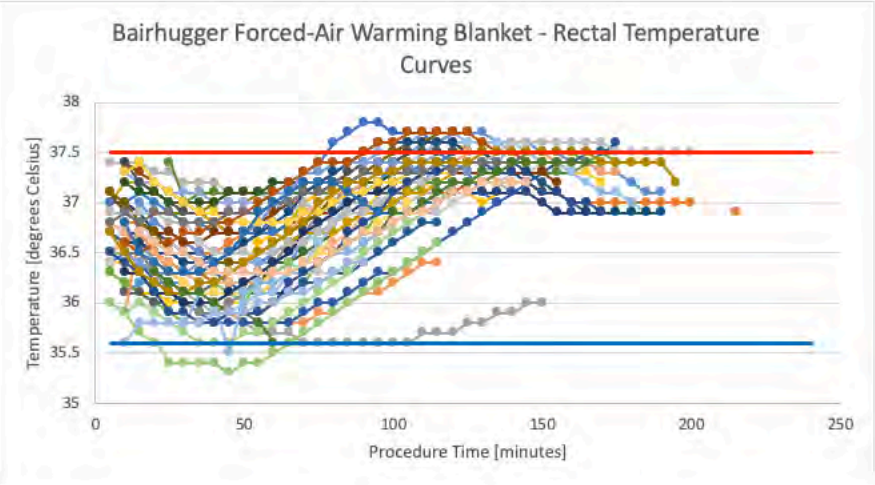


Figure 2: Bairhugger Rectal Temperature Curve



Pediatric Anesthesiology - 12 Combined Spinal Caudal Anesthesia is a Safe and Effective Technique for Longer-Duration Urological Day Surgery

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Introduction: Spinal anesthesia (SA) is a safe and effective technique for infants undergoing infraumbilical surgery. It avoids endotracheal intubation and systemic sedation while maintaining hemodynamic stability[1]. It is shown to improve operating room (OR) and post-anesthesia recovery unit (PACU) utilization[2] and reduce postoperative pain scores[3]. Applications of SA in infants are limited however by its fixed time duration. To overcome this, we piloted a case series to study the novel technique of Combined SA and Caudal catheter (CSC) to assess its feasibility, safety, and effectiveness for infants undergoing urological day surgery over 90 minutes.

Methods: Eight infants underwent CSC for hypospadias repair. SA was performed using a previously described protocol[2]. Following SA onset, the infant was positioned laterally and a 20-gauge angiocatheter was inserted into the caudal space under ultrasound guidance and confirmation. Sixty minutes following SA onset, the caudal catheter was activated with chloroprocaine 2% with epinephrine at a dose of 1 ml/kg over 10 minutes, followed by an infusion of 1ml/kg/hr4. The infusion was stopped 15 minutes before procedure end to allow for chloroprocaine metabolism. Ropivacaine 0.2% 1ml/kg was given for postoperative analgesia before catheter removal.

To compare CSC to the standard of care general anesthesia (GA), we retrospectively matched 8 patients who had GA to the 8 who had CSC by age, weight, ASA status, and surgical procedure (Table 1). The GA cohort underwent inhalational induction with sevoflurane, intravenous insertion, endotracheal intubation, and a caudal single shot block with ropivacaine 0.2% 1ml/kg with epinephrine for postoperative analgesia. Opioids were administered at the discretion of the anesthesiologist. We compared the length of induction time, procedure end to OR exit time, and PACU recovery time between the cohorts using paired t-tests.

Results: The mean age of CSC patients was 6.8 months. All 8 CSC patients remained under regional anesthesia for the entire duration of surgery. Four CSC patients received intravenous dexmedetomidine, all at a dose ≤1 mcg/kg. Mean surgery length under CSC was 110 minutes, with the longest length of 138 minutes (Table 1). None of the CSC patients received opioids, while 4 of the 8 GA patients (50%) received intraoperative opioids. Induction lengths and PACU times were not significantly different (p=0.15 and p=0.52 respectively, Figure 1). Procedure end to OR exit times were significantly shorter in CSC patients (one-tailed paired t-test, p=0.04).

Conclusion: Our case series demonstrated the feasibility, safety, and effectiveness of the novel CSC technique for urologic day surgery in infants. CSC allowed for surgeries as long as 138 minutes. Patients in the CSC group were spared intubation and systemic opioids, adding to the safety of the technique. Furthermore, all were able to be discharged on the day of surgery with shorter emergence periods and without incurring longer PACU recovery times.

References: 1. (2017) Differences in Blood Pressure in Infants After General Anesthesia Compared to Awake Regional Anesthesia (GAS Study-A Prospective Randomized Trial). Anesthesia and Analgesia, 125(3), 837-845. 2. (2019) Application of an Infant Spinal Anesthesia Protocol in Infants Presenting for Inguinal Herniorrhaphy Improves Operating Room and Postanesthesia Recovery Unit Utilization. Pediatric Anesthesia, 29(8), 881-882. 3. (2020) Infant Spinal Anesthesia Reduces Postoperative Pain Scores and Pain Medication Consumption in Infants undergoing Inguinal Herniorrhaphy. Journal of Pediatric Surgery, 55(12), 2840-2843. 4. (2016) Continuous Chloroprocaine Infusion for Thoracic and Caudal Epidurals as a Postoperative Analgesia Modality in Neonates, Infants, and Children. Pediatric Anesthesia, 26(1):84-91.

	CSC (n=8)	GA (n=8)	p-value
Chronological age (months)[a]	6.8 (range 3.3-9.6)	6.8 (range 3.6-9)	0.64[1]
Weight (kg)[a]	8.5 (range 6.8-10.3)	8.2 (range 6.9-9.5)	0.46[1]
ASA status (I, II)	I (7), II (1)	I (7), II (1)	--
Length of induction (min)[b]	28.5 (IQR 25-32)	26 (IQR 13-27)	0.15[1]
Length of surgery (min)[b]	109 (IQR 97-126)	127 (IQR 115-141)	0.08[1]
End of procedure to room exit (min)[b]	9 (IQR 8-10)	14 (IQR 9-15)	0.04[1]*
Length of PACU stay (min)[b]	51 (IQR 40-72)	69 (IQR 55-77)	0.68[1]
Use of intraoperative dexmedetomidine ≤1 mcg/kg (n, %)	4 (50%)	N/A	--
Use of intraoperative opioids (n, %)	0 (0%)	4 (50%)	0.08[2]

Table 1. Demographic and intraoperative data for CSC and GA patients. [a]=mean, range, [b]=median, interquartile range (IQR). *=p<0.05, **=p<0.01. [1]=paired t-test, [2]=Fisher's exact test.

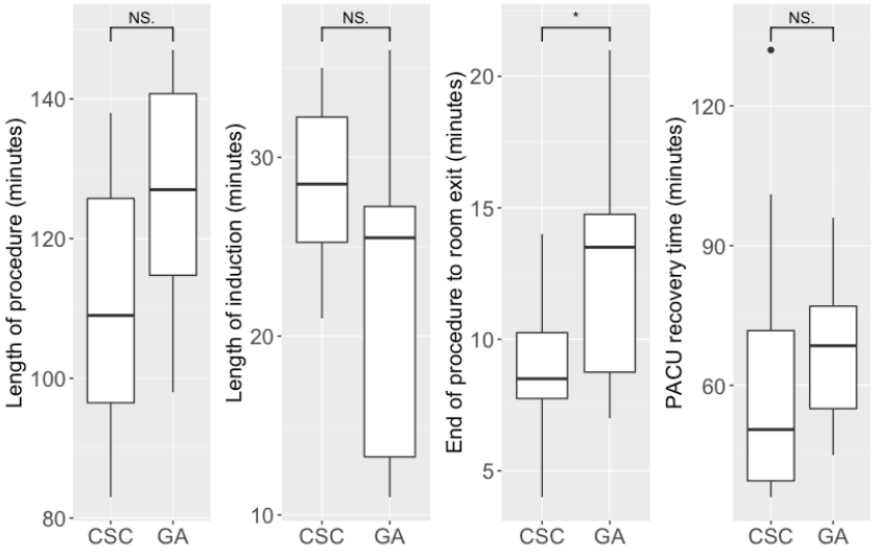

Figure 1. Differences between CSC and GA cases in perioperative efficiency. The end of procedure to room exit time was found to be significantly shorter in CSC cases (p=0.04), while other comparisons remained insignificant.

Pediatric Anesthesiology - 13 Natural airway as a safe alternative to intubation for pediatric endoscopic foreign body removal

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Introduction: Pediatric foreign body (FB) ingestions occur frequently, with an annual estimated 116 000 patients presenting to emergency departments1. However, there are no clearly defined guidelines for airway management during anesthesia for endoscopic FB removal procedures. Specifically, it is unclear as to when intubation is indicated over noninvasive airway management. The primary aim of this study was to evaluate pre-, intra-, and post-operative factors associated with planned intubation during FB removal among pediatric patients. We hypothesized that pre-, intra- and post-operative outcomes including duration and type of retained FB, total operating time, and hospital admission rates were significantly different among intubated patients in comparison to non-intubated patients.

Methods: This retrospective cohort study included pediatric patients ages 0-18 years presenting to Johns Hopkins All Children's Hospital from July 2013 to September 2020 who were assigned an ICD-9 or ICD-10 code indicating esophageal FB and underwent endoscopic removal. Patients with foreign bodies in the airway, those that underwent surgical removal, or in whom the FB moved to the stomach prior to intervention were excluded. Descriptive statistics summarized patient, object, and provider variables by intubation status while Chi-square and Fisher's exact tests determined unadjusted associations.

Results: The sample included 281 patients, 53 (18.9%) who were initially managed for their endoscopy with intubation and 228 (81.1%) initially managed with natural airway and nasal cannulae for oxygen supplementation. Eleven non-intubated natural airway patients (3.9%) required intra-procedural 'rescue' intubation. Nearly half (45.3%, n=24) of intubated patients had a history of foreign-body-related drooling, compared to under a third (31.1%, n=71) of non-intubated patients. Among intubated patients, 11.3% (n=6) had fasted for <6 hours compared to 1.8% (n=4) of non-intubated patients (p =0.004). The median duration of retained foreign body was also lower in intubated patients (13.3 hours) vs. non-intubated (16.0, p=0.02). There was a higher proportion of food bolus ingestions among intubated patients (15.1%, n=8) than non-intubated patients (1.8%, n=4; p<0.001). The proportion of patients admitted to the hospital (intubated 20.8%, n=11; non-intubated: 4.8%, n=11; p<0.001) and median total operating time (intubated: 26.0 minutes; non-intubated: 11.0 minutes; p<0.001) were also increased for intubated patients.

Conclusion: This study is one of the first to compare airway management techniques for foreign body ingestion procedures. Patients' airways for endoscopic removal of esophageal foreign body were managed without intubation in 81% of this cohort. Only 3.9% of patients managed without intubation were subsequently intubated during the procedure. Intubation was associated with history of drooling and a food bolus FB; intubated patients were less likely to have met pre-operative fasting requirements and had a shorter duration of FB retention. Intubated patients were more likely to require postoperative hospital admission. This study shows that anesthetic management of selected patients undergoing endoscopic removal of esophageal foreign body is safe and possible without the need for intubation. Further confirmatory studies are necessary. However, the median total operating time for patients managed with natural airway was only 11 minutes, which may limit generalizability of these findings at institutions with slower perioperative times.

References: 1. Kramer RE, Lerner DG, Lin T, Manfredi M, Shah M, Stephen TC, Gibbons TE, Pall H, Sahn B, McOmber M, Zacur G, Friedlander J, Quiros AJ, Fishman DS, Mamula P; North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Endoscopy Committee. Management of ingested foreign bodies in children: a clinical report of the NASPGHAN Endoscopy Committee. J Pediatr Gastroenterol Nutr. 2015 Apr;60(4):562-74. doi: 10.1097/MPG.0000000000000729. PMID: 25611037.

Pediatric Anesthesiology - 14 A Systematic Review of Epileptiform Changes During Sevoflurane Anesthesia in Infants and Children

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Introduction: Sevoflurane is the most commonly used potent volatile agent for inhalation induction of general anesthesia in pediatric patients. Early clinical case reports have described involuntary movements, seizure-like behaviors, and incidental findings of epileptiform changes during brain monitoring. Subsequent studies recording the electroencephalogram (EEG) have demonstrated epileptiform activity, defined as abnormal patterns reflecting underlying neurophysiologic dysfunction. The objective of this study was to perform a systematic review of the literature describing epileptiform activity during pediatric anesthesia using sevoflurane. A secondary aim was to begin to classify the heterogeneous reporting of EEG changes in the literature to determine the feasibility of a meta-analysis.

Methods: A targeted clinical question was crafted using the PICO framework and registered a priori on PROSPERO on 3/19/21 (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=237719). Under the guidance of a librarian from the Gottesman Library at Albert Einstein College of Medicine, a boolean search string was generated to search for articles and gray literature focusing primarily on 'pediatric', 'sevoflurane' and 'electroencephalogram' in PubMed, OVID, the Cochrane Library, Google Scholar, etc. We utilized the COVIDENCE software platform (Cochrane Collaborative Group, UK) to manage our literature review. We selected English language articles only. 495 references were imported for initial screening. After title and abstract screening, 56 full-text studies were included for further assessment. The final systematic review included 13 references. A PRISMA flow chart of the data extraction is shown in Figure 1. A preliminary screening of the extracted literature was conducted by three researchers (JC, MT, AF) with the addition of two research members (DI, LG) for data extraction and bias assessment. An assessment for risk of bias was made using the Newcastle-Ottawa Quality Assessment Scale. Data extraction and assessment of bias were discussed as a group during weekly meetings. The characteristics of the studies and their primary outcomes were collected (Table 1) and strategies for data synthesis were discussed with the larger team.

Results: A total of 13 studies were included. The incidence of epileptiform changes reported in individual studies ranged from 0 - 95%. There were a total of 649 subjects ranging in age from neonate to 18 years of age with EEG abnormalities reported in 204 (31.4%). EEG data were acquired using a variety of recording systems with variable number of leads and heterogeneous outcomes reported. The majority of studies utilized less than 16 channels of EEG (10/13, 76.9%) with five utilizing processed monitors or 2 channels or less. Three studies (23.1%) utilized 16 or more channels of unprocessed EEG taking into account activity over the entire head. There was variability in sevoflurane dosing as well as premedication practices with midazolam or hydroxyzine. The periods of anesthesia monitoring were also heterogeneous. Characteristics of the studies are presented in Table 1.

Conclusion: There was heterogeneity in the reported incidences of epileptiform changes during pediatric anesthesia using sevoflurane. Clinical studies varied in the age range assessed, study design, phases of anesthesia under investigation, number of EEG leads recorded, and adjuvant anesthetics administered. Methods of ventilation also varied. Next steps would be the development of a process to classify study outcomes based on the quality and comprehensiveness of EEG data with the eventual goal of performing a meta-analysis.

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	Reference Age (Sample Size)	Phase of anesthesia Sevoflurane Dose	EEG - Number of Channels	Abnormal EEG Outcomes
1	Chao. et al 2020 0-3 yrs (n= 54)	Induction Up to 8% sevoflurane	26 channels	5/54 patients
2	Giberb. et al 2012 3-11 yrs (n=76)	Maintenance 6% sevoflurane in 50% N_2O	1 channel	12/76 patients
3	Vakkuri et al 2000 6±2 yrs (n=32)	Induction 8% sevoflurane	4-channel	27/32 patients
4	Bigouzzo et al 2018 5- 18 yrs (n=36)	Maintenance Randomized between 1%, 2%, 3%, 4%, 5% sevoflurane	1-channel BIS monitor	17/52 trials
5	Nieminen et al 2002 3-8 yrs (n=30)	Maintenance 2% sevoflurane in air/oxygen	5 channel EEG	—
6	Kreuzer et al 2014 4.6 ± 3.0 yrs (n=100)	Induction sevoflurane 8% or 6%	2-channel Narcotrend EEG	64/100
7	Constant et al 1999 2-12 yrs (n=32)	Induction 7% sevoflurane OR incremental 2%, 4%, 6%, 7% sevoflurane in 100% oxygen OR 7% sevo in oxygen and nitrous oxide 50:50	16 channels	—
8	Koch et al 2018 0.5-8 yrs (n=18)	Induction Average induction dose: 6.2%	4 channels	12/18
9	Schultz et al 2012 7 months- 8 yrs (n=70)	Induction 8% induction, 4% maintenance	3 channel narcotrend	14/70
10	Sonkajärvi et al 2009 4-10 yrs (n=20)	Induction 8% sevoflurane in 50|50 oxygen:nitrous oxide	21 leads according to the international 10–20 system	19/20
11	Stolwijk et al 2017 Neonatal period- average agee 38.28 weeks (n=111)	Induction Absolute dose: 1.26% (0.04-3.5)	2 channels	11/111
12	Moran et al 2011 36 to 54 weeks post-conceptual age (n=23)	Induction Sevoflurane concentrations from 0.16 to 9.25	8-channel referential EEG montage	6/23
13	Vakkuri et al 2001 2 to 12 years old (n=31)	Induction Sevoflurane (8% in N_2O/O_2 2:1)	bipolar 8-channel EEG	17/31

Perioperative Anesthesia

Perioperative Anesthesia – 1

Perioperative Point-of-Care Ultrasound Use by Anesthesiologists

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Introduction: Point-of-Care ultrasound (POCUS) is the bedside utilization of ultrasound, in real-time, to aid in the diagnosis and treatment of patients. Image acquisition from POCUS utilization by anesthesiologists involves the assessment of multiple organs in different perioperative situations. POCUS can be utilized to enhance clinical decision-making in a variety of perioperative situations due to its ability to assess endotracheal tube placement, cardiac function, pulmonary function, aspiration risk, hemodynamics, vascular access, and nerve visualization for regional procedures. The mounting clinical evidence for the value of POCUS in perioperative settings, its growing affordability, and its low associated risks are responsible for the nationwide movement across many anesthesiology residency programs to increase the focus on perioperative ultrasound training. The purpose of this review is to present to current anesthesiologists and anesthesiology trainees, a broad discussion regarding the diverse utility and importance of POCUS in perioperative settings.

Methods: We reviewed point-of-care ultrasound studies by conducting a keyword search on the PubMed database. The search keywords included: 'ultrasound', 'POCUS' combined with 'anesthesiologist', 'anesthesia', or 'perioperative'. Publications were screened by title and abstract.

Results: POCUS is a valuable bedside tool that is increasingly utilized in perioperative settings due to its reliability, accuracy, speed, and ease of use. POCUS can be utilized to confirm correct endotracheal tube placement and be utilized in complex airway situations. Cardiac POCUS provides invaluable information that aids in assessing challenging hemodynamically unstable situations. Pulmonary POCUS can identify numerous pulmonary conditions including pneumothorax, pulmonary edema, pleural effusion, and lung consolidation. POCUS is also utilized for the assessment of aspiration risk, vascular access, and ultrasound-guided nerve blocks.

Conclusion: The diverse utility of POCUS by anesthesiologists enriches the quality of healthcare patients receive in perioperative settings. Thus, the current and growing clinical evidence supporting the value of POCUS will continue to increase its utility in perioperative settings and its significance in aiding in perioperative clinical decision-making.

References: 1. Ramsingh D, Frank E, Haughton R, Schilling J, Gimenez KM, Banh E, Rinehart J, Cannesson M. Auscultation versus Point-of-care Ultrasound to Determine Endotracheal versus Bronchial Intubation: A Diagnostic Accuracy Study. Anesthesiology 2016;124:1012-20. 2. Muscholl MW, Oswald M, Mayer C, von Scheidt W. Prognostic value of 2D echocardiography in patients presenting with acute chest pain and non-diagnostic ECG for ST-elevation myocardial infarction. Int J Cardiol 2002;84:217-25. 3. Kendall JL, Hoffenberg SR, Smith RS. History of emergency and critical care ultrasound: the evolution of a new imaging paradigm. Crit Care Med.2007;35(suppl 5):S126-S130. doi:10.1097/01.CCM.0000260623.38982.83

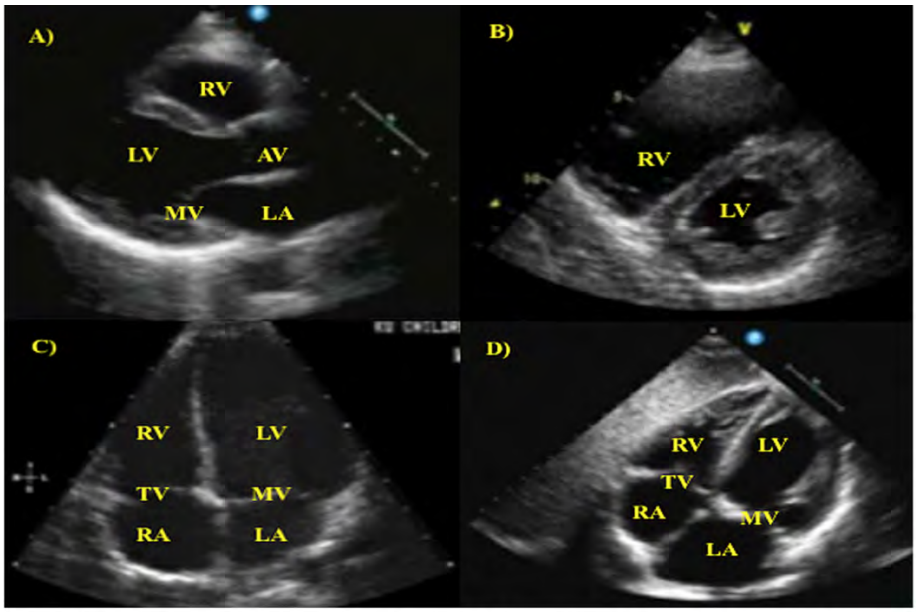

Figure 1: Transthoracic echocardiogram images from four cardiac views. A) parasternal long-axis view. B) parasternal short-axis view. C) apical four chamber view. D) subcostal four chamber view.

VIEW	PROBE POSITION	ASSESSMENT
Parasternal long-axis	Probe at 3rd- 4th intercostal space with indicator directed to 10 o'clock position	Assesses EF, ventricular size, mitral valve, aortic stenosis or regurgitation, hypertrophic obstructive cardiomyopathy, and congestive heart failure
Parasternal short-axis	Probe at 3rd- 4th intercostal space with indicator directed to 2 o'clock position	Assesses volume status, RV volume overload, coronary ischemia
Apical four chamber	Probe at 6th midclavicular line intercostal space with indicator directed to 3 o'clock position	Assesses valvular function, atrial sizes, ventricular sizes, systolic function
Subcostal four chamber	Probe at subxiphoid space with indicator directed to 3 o'clock position	Assesses pericardial effusions, RV, tricuspid valve

Table 1: Transthoracic cardiac POCUS views, probe position, and assessment.

Perioperative Anesthesia - 2

Preoperative oral carbohydrate and post-operative hyperglycemia in patients undergoing hip fracture surgery under combined spinal epidural anesthesia: Preliminary results

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Introduction: Preoperative fasting leads to a catabolic state further aggravated by surgical stress.1 Preoperative oral carbohydrate (POC) administration mitigates the development of postoperative hyperglycemia, insulin resistance and may improve patient outcome.2,3 This study explores the effect of POC administration on postoperative hyperglycemia in patients undergoing hip fracture surgery under combined spinal epidural anaesthesia (CSEA).

Methods: This prospective, randomized study was done on 60 consenting adult ASA I/II patients between 18-65 years of age scheduled for hip fracture fixation under CSEA after obtaining institutional ethical committee clearance. Patients with diabetes mellitus, pheochromocytoma, carcinoid tumor, pancreatitis, alcoholism, jaundice or liver disorders, obesity, gastro-esophageal reflux, gastric outlet/ intestinal obstruction, pregnancy, contraindications to CSEA, on continuous steroid therapy for >5 days in the last one year were excluded. As per a computer generated random number table, patients were randomized to either group F (n=30, nil per orally for both solids and liquids for at least 6 h before surgery) or group C (n=30, nil per orally for solids for at least 6 h and received 200 ml oral carbohydrate solution 2 h before surgery). An independent anesthesiologist, not involved with the further conduct of the study, administered the carbohydrate drink. Under all aseptic precautions CSEA was given at L2-L3/L3-L4 intervertebral space. After adequate subarachnoid block level, the surgery was allowed to proceed. Blood samples were drawn at baseline (T0: before CSE), immediately after surgery (T1) and 24hrs after surgery (T2). Primary outcome measure was blood glucose and secondary outcomes included serum insulin, blood urea, anxiety, hunger, thirst, postoperative complications, length of hospital stay, 30-day readmission and 3-month mortality. Descriptive statistics were reported as mean ¬± S.D. or median [IQR]. Repeated measure ANOVA followed by Dunnett's test was used for repeatedly measured variables. Qualitative parameters were compared using Chi-square/Fisher's test. Statistical analysis was carried in SPSS v.20.0 and STATA v.15.0. Relative risk was calculated using the MedCalc from www.medcalc.org. A p-value<0.05 was taken as significant.

Results: A total of 49 patients have been assessed for eligibility so far (study ongoing). Five of these did not meet the inclusion criteria and another four did not give consent to participate. Results of the first 40 patients is being presented. The two groups were demographically comparable. Blood glucose values increased from T0 to T2 in both groups and the rise was significantly more in group F than in group C (group F: 112.80 ¬± 21.04 mg/dl vs 143.20 ¬± 33.90 mg/dl, p=0.007; group C: 109.70 ¬± 24.88 mg/dl vs 136.05 ¬± 23.58 mg/dl, p=0.002). In group F, insulin was significantly higher than T2 compared to T0 (p=0.012) and T1 (p=0.001). In group C, insulin was comparable at T0 and T1 (p= 0.149) and T0 and T2 (p=0.178), but T2 value was significantly higher than T1 (p=0.017). Blood urea was comparable between groups. Hunger scores were comparable in the preoperative (p=0.379) and postoperative (p=0.769) time point. Preoperative thirst score (4.30 ¬± 2.87 vs 6.50 ¬± 3.66, p=0.041) and anxiety was lower in group C than group F (p=0.035). The chance of having postoperative hyperglycemia and anxiety at T2 was 1/4th in group C compared to group F. (RR: 0.025, 95% CI: 0.030 to 2.045; p=0.196). There was a significantly lower risk of having pre-operative anxiety in group C compared to group F (RR: 0.222, 95% CI: 0.054 to 0.902, p=0.035). Incidence of postoperative complications and the length of hospital stay (p=0.206) was comparable.

Conclusion: Administration of POC reduces the chances of developing postoperative hyperglycemia by 1/4th when compared to fasting from midnight. The consumption of POC increases patient comfort by considerably decreasing the preoperative thirst and anxiety level.

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Perioperative Anesthesia – 3 The effect of tidal volume on postoperative respiratory complications is dependent on patients' respiratory system elastance: A multicenter hospital registry study

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Introduction: Trials investigating the effects of intraoperative low-tidal volume ventilation have been equivocal, with some studies [1,2] reporting lowered postoperative respiratory complications (PRC), while others found no effects [3]. A retrospective study even indicated harmful effects of using very low tidal volumes [4]. In patients with Acute Respiratory Distress Syndrome (ARDS), the mortality benefit of using lower tidal volumes varied with the patients' respiratory system elastance [5]. However, the clinical significance of this interaction in surgical patients is unclear. We hypothesized that the association between tidal volume during mechanical ventilation and PRC is modified by the patient's respiratory system elastance.

Methods: In this multicenter retrospective hospital study, we analyzed adult patients with American Society of Anesthesiologists (ASA) class < V undergoing non-cardiothoracic surgery under general anesthesia between January 2006 and December 2018 at two competing healthcare networks in Boston, MA. We excluded emergency surgeries, laparoscopic surgeries and microlaryngoscopies. The primary exposure was an interaction term between tidal volume per kilogram ideal body weight (IBW) and standardized respiratory system elastance (SEl) (expressed in cmH2O/[ml/kg]). Patients were categorized into two groups according to the tidal volume: >8 ml/kg IBW (high tidal volume group) and ,â§8 ml/kg IBW (low tidal volume group). The primary outcome was PRC, defined as the need for mechanical ventilation within seven days after surgery or post-extubation desaturation (SpO2) <90% within the first 10 minutes [6-9]. In the primary analysis, we tested whether the association between tidal volume and PRC was modified by the patient's SEl using multivariable logistic regression with interaction term analysis, adjusted for patient demographics, comorbidities and markers of procedural severity. In the secondary analyses, we examined the association between driving pressure (DP) and PRC, and investigated whether the association between tidal volumes and PRC was mediated by the resulting DP.

Results: 197,474 cases were included (Figure 1). 10,821 patients suffered PRC (5.5%). Baseline characteristics and distribution of variables are shown in Table 1. The median (IQR) SEl was 1.77 (1.46-2.18) cmH2O/(ml/kg). The intraoperative tidal volume was associated with PRC, and was modified by a patient's SEl (p-for-interaction<0.001, Figure 2A): In patients with a high SEl (>1.65 cmH2O/[ml/kg], poor compliance), the risk of PRC was higher if patients received high (>8 ml/kg) tidal volumes. Risk differences between high and low tidal volumes in this group ranged from 0.3% ([0.0-0.5], p=0.030) in patients with a SEl of 1.7 cmH2O/[ml/kg] to 5.8% ([3.8-7.8], p<0.001) in patients with an SEl of 5.0 cmH2O/[ml/kg] (red part, Figure 2B). By contrast, patients with a very low SEl (<0.8 cmH2O/[ml/kg], good compliance) showed a decreased risk of PRC by as much as -0.6% ([-1.03 to -0.24], p<0.001) when high compared to low tidal volumes were applied (green part, Figure 2B). There was no effect of high versus low tidal volumes in patients with a moderate SEl (blue part, Figure 2B). The median (IQR) DP in our study population was 15 (12-19) cmH2O. Higher DPs were associated with an

increased risk of PRC ('adjusted odds ratio' aOR 1.04 [1.03-1.04], p<0.001 per 1 cmH2O increase). Mediation analysis revealed that increased DP completely mediated adverse effects of high tidal volumes on PRC in patients with SEI >1.65 cmH2O/[ml/kg] (indirect effect: 100%, p<0.001 (Figure 3)). The DP that was associated with the average risk in the study population ('adjusted relative risk' RRadj=1) was 14.1 cmH2O. DPs exceeding this threshold increased the predicted risk of PRC (Figure 4A). 2nd-order fractional polynoms supported the linear model with slightly corrected estimations of predicted PRC at extreme values of DP (Figure 4B).

Conclusion: The effects of intraoperative tidal volume on PRC depend on patients' respiratory system elastance. Physicians should consider assessing the individual patients' lung mechanics and apply low tidal volumes in patients with high elastance (i.e. poor compliances), with the goal to limit the application of high driving pressures.

References: [[1] N Engl J Med; 2013; 369: 428-37. [2] Anesthesiology; 2013; 118: 1307-21. [3] JAMA; 2020; 324: 848-58. [4] Br J Anaesth; 2014; 113: 97-108. [5] Am J Respir Crit Care Med; 2021; 203: 1378-85. [6] Br J Anaesth; 2020; 125: e130-9. [7] J Clin Anesth; 2021; 73: 110376. [8] Anaesthesia; 2021; 76: 36-44. [9] Br J Anaesth; 2020; 125: 629-36.

Table 1. Patient characteristics and distribution of variables.

Characteristics	No PRC (n= 186,653)	PRC (n= 10,821)
Centre		
BIDMC	94,745 (50.8%)	5,772 (53.3%)
MGH	91,908 (49.2%)	5,049 (46.7%)
Age, years	54.6 ± 16.1	56.5 ± 16.1
Gender		
Male	82,138 (44.0%)	5,140 (47.5%)
Female	104,515 (56.0%)	5,681 (52.5%)
Body mass index	28.3 ± 6.6	30.1 ± 7.8
ASA class		
1	21,133 (11.3%)	764 (7.1%)
2	105,387 (56.5%)	4,824 (44.6%)
3	56,841 (30.5%)	4,713 (43.6%)
4	3,292 (1.8%)	520 (4.8%)
Type of surgery		
Acute care surgery	4,270 (2.3%)	374 (3.5%)
Burn	1,510 (0.8%)	141 (1.3%)

Colorectal	1,490 (0.8%)	96 (0.9%)
Eye	336 (0.2%)	26 (0.2%)
General surgery	26,499 (14.2%)	1,198 (11.1%)
Gastrointestinal	44 (0.0%)	1 (0.0%)
Gynaecology	19,504 (10.4%)	902 (8.3%)
Neurosurgery	14,856 (8.0%)	960 (8.9%)
Oral/maxillofacial surgery	2,595 (1.4%)	144 (1.3%)
Orthopaedic surgery	45,053 (24.1%)	3,081 (28.5%)
Other	5,996 (3.2%)	276 (2.6%)
Otolaryngology	5,331 (2.9%)	288 (2.7%)
Paediatric surgery	332 (0.2%)	11 (0.1%)
Plastic surgery	14,860 (8.0%)	685 (6.3%)
Podiatry	623 (0.3%)	23 (0.2%)
Radiology	1,129 (0.6%)	93 (0.9%)
Surgical oncology	10,712 (5.7%)	440 (4.1%)
Transplant	3,891 (2.1%)	318 (2.9%)
Urology	19,137 (10.3%)	940 (8.7%)
Vascular surgery	8,485 (4.5%)	824 (7.6%)
Comorbidities		

CCI	1.0 (0.0 - 2.0)	1.0 (0.0 - 3.0)
History of COPD	7,884 (4.2%)	787 (7.3%)
History of CHF	10,540 (5.6%)	1,250 (11.6%)
History of smoking	21,167 (11.3%)	1,432 (13.2%)
SPORC score ≥7	3,616 (1.9%)	495 (4.6%)
Surgical factors		
Duration of surgery, min	138.0 (89.0 - 213.0)	152.0 (100.0 - 237.0)
Work RVU	14.0 (7.4 - 20.0)	15.6 (7.9 - 22.6)
Mean arterial pressure < 55 mmHg, min	0.0 (0.0 - 3.0)	0.0 (0.0 - 4.0)
Total vasopressor dose (Norepinephrine equivalents), mg	0.0 (0.0 - 0.1)	0.0 (0.0 - 0.3)
Packed red blood cells, units		
0	181,893 (97.4%)	10,077 (93.1%)
1	2,260 (1.2%)	312 (2.9%)
2	1,749 (0.9%)	269 (2.5%)
≥3	751 (0.4%)	163 (1.5%)
Crystalloids and colloids, ml	1008.0 (800.0 - 1950.0)	1200.0 (800.0 - 2130.0)

Total short-acting opioid dose (oral morphine equivalents), mg	37.5 (25.0 - 62.5)	50.0 (25.0 - 62.5)
Total long-acting opioid dose (oral morphine equivalents), mg	6.8 (0.0 - 20.0)	8.5 (0.0 - 23.8)
NMBA ED_{95} dose[b], mg	1.9 (0.0 - 3.1)	2.0 (0.2 - 3.3)
Neostigmine dose, mg	1.0 (0.0 - 3.0)	2.0 (0.0 - 3.0)
Age-adjusted minimum alveolar concentration of volatile anaesthetics & nitrous oxide	1.0 (0.8 - 1.1)	0.9 (0.8 - 1.1)
Respiratory parameters		
Respiratory rate	12.0 (10.0 - 12.5)	12.0 (10.0 - 13.0)
Tidal volume per kg IBW	8.4 ± 2.0	8.6 ± 2.0
Driving pressure, cmH_2O	15.5 ± 5.6	17.2 ± 5.9
PIP, cmH_2O	19.9 ± 6.0	22.0 ± 6.2
PEEP, cmH_2O	4.1 (2.0 - 5.0)	5.0 (2.0 - 5.0)
FiO_2	53.6 ± 16.0	56.0 ± 17.2
Airway device		
Endotracheal tube	127,104 (83.6%)	7,993 (91.2%)
Laryngeal mask airway	24,472 (16.1%)	735 (8.4%)
Combined	400 (0.3%)	40 (0.5%)

Standardised compliance, (ml/kg)/cmH_2O	0.6 (0.5 - 0.7)	0.5 (0.4 - 0.6)
Standardised elastance, cmH_2O/(ml/kg)	1.8 (1.5 - 2.2)	1.9 (1.6 - 2.3)

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range [25th-75th percentile]).

PRC: postoperative respiratory complications; BIDMC: Beth Israel Deaconess Medical Centre; MGH: Massachusetts General Hospital, ASA: American Society of Anaesthesiologists; CCI: Charlson Comorbidity Index; COPD: chronic obstructive pulmonary disease; CHF: congestive heart failure; RVU: relative value units; IBW: ideal body weight; NMBA: neuromuscular blocking agents; PIP: peak inspiratory pressure; PEEP: positive end-expiratory pressure; FiO_2: fraction of inspired oxygen.

a: Score for Prediction of Postoperative Respiratory Complications.

b: ED95 dose of neuromuscular blocking agents (NMBA): median effective dose required to achieve a 95% reduction in maximal twitch response from baseline.

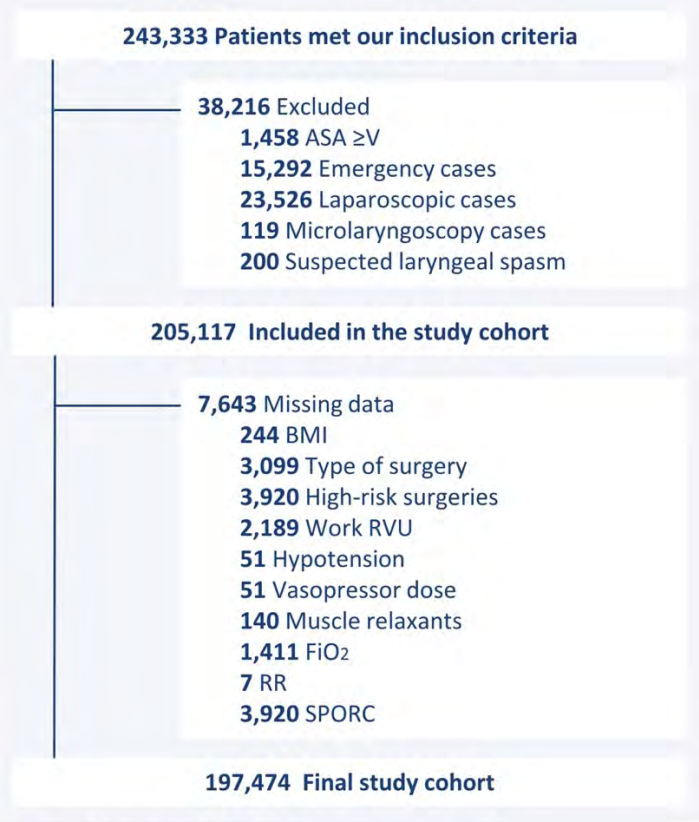

Figure 1. Study flow diagram.
ASA: American Society of Anaesthesiologists; BMI: body mass index; RVU: relative value units; FiO2: fraction of inspired oxygen; RR: respiratory rate; SPORC: Score for Prediction of Postoperative Respiratory Complications. Multiple exclusion criteria may apply.

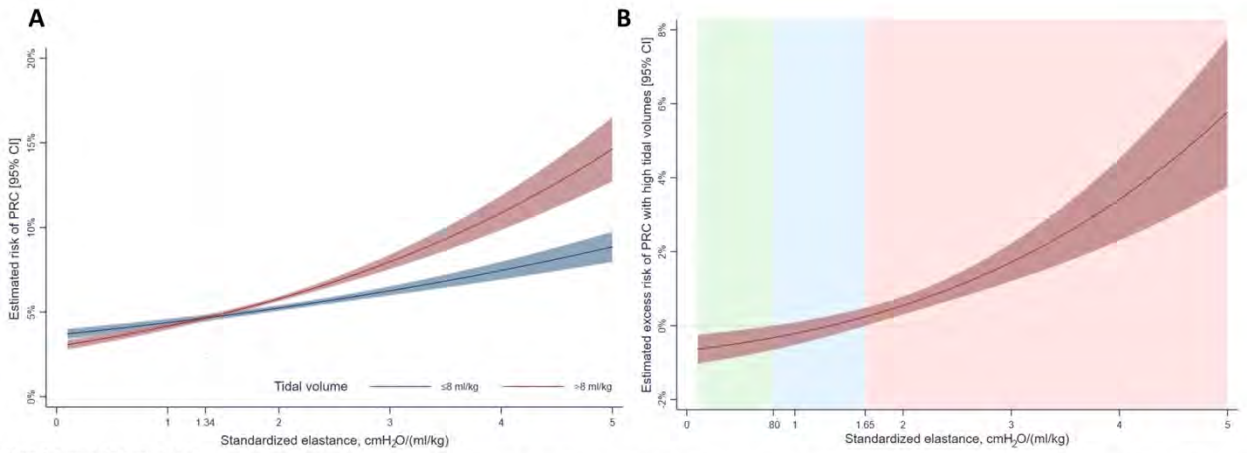

Figure 2. Results of primary analysis
2A. Estimated risk of postoperative respiratory complications (PRC) in patients who received high (>8ml/kg predicted body weight, maroon) and low (≤8ml/kg predicted body weight, navy) tidal volumes, stratified by the patient's standardized respiratory system elastance (cmH2O/[mL/kg]). Contingent on the interaction (p<0.001) between tidal volume and standardized respiratory system elastance, the adjusted risk estimates with corresponding 95% confidence intervals (CI) for PRCs are presented. The two curves cross at a lung elastance of 1.34 cmH2O/(ml/kg).
2B. Estimated excess risk (95% Confidence Interval) of postoperative respiratory complications in patients who received high (>8ml/kg predicted body weight) compared to low (≤8ml/kg predicted body weight) tidal volumes stratified by the patient's standardized respiratory system elastance (cmH2O/[mL/kg]). In patients with a standardized respiratory system elastance of >1.65 cmH2O/(ml/kg) (red), the estimated risk was higher (up to 5.8%; 95% CI 3.8 to 7.8%; p<0.001) if patients received a high tidal volume compared to a low tidal volume. No significant association was found between high tidal volumes and PRCs in patients with a lung elastance between 0.8 and 1.65 cmH2O/(ml/kg) (blue). Patients with a standardized respiratory system elastance of <0.8 cmH2O/(ml/kg) (green) had a significantly decreased estimated risk of PRCs by as much as -0.6% (95% CI -1.0 to -0.2%; p<0.001), when using high tidal volumes compared to low tidal volumes.

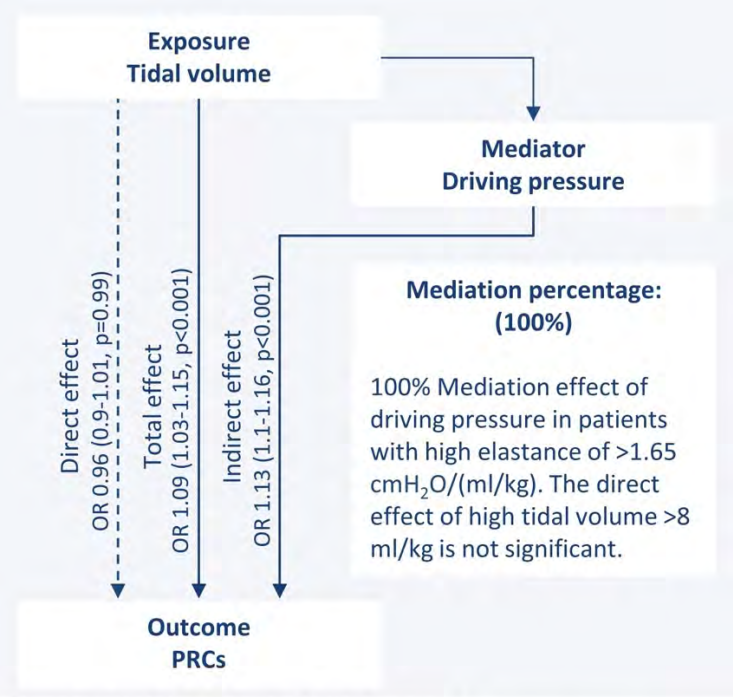

Figure 3. Mediating effect of driving pressure
Driving pressure (DP) completely mediated the effect of high tidal volumes on postoperative respiratory complications (PRC) in patients with a standardized elastance >1.65 cmH2O/[ml/kg] (indirect effect: 100%; p<0.001). The direct effect of high tidal volumes on PRC was not significant when adjusted for DP (p=0.99).

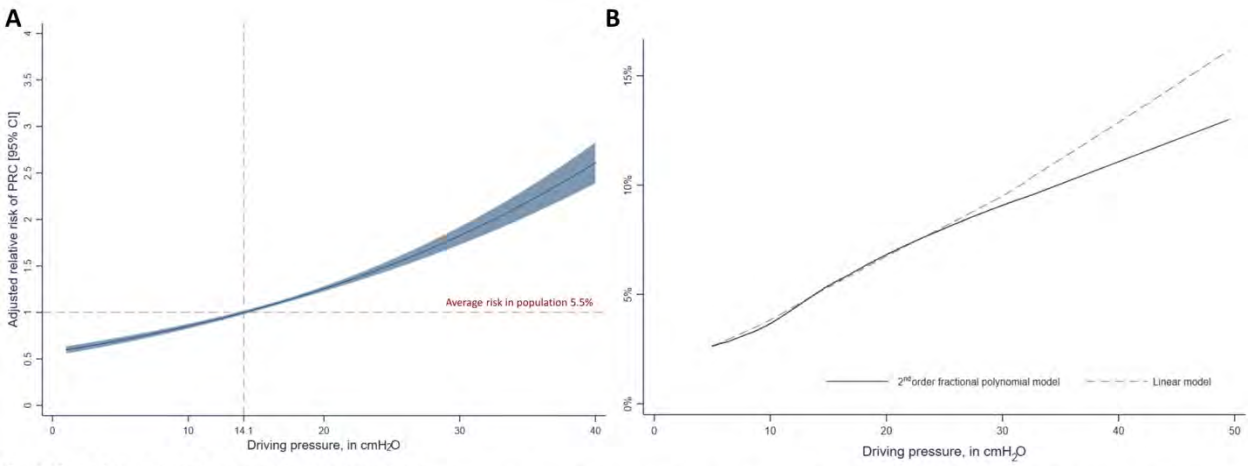

Figure 4. Effects of driving pressure on postoperative respiratory complications.
4A. Association of driving pressure (DP) with postoperative respiratory complications (PRC) after confounder adjustment. In the general study population, the overall risk of PRC was 5.5%, which was the estimated risk when a DP of 14.1 cmH2O was applied. DP values exceeding 14.1 cmH2O were associated with higher relative risks compared to the general study population.
4B. 2nd order fractional polynomial association compared to linear model in predicting the adjusted probability of PRC at different driving pressure levels using Lowess smoothing. The fractional polynomial line deviates from the linear model at extreme values of driving pressure, indicating that the fractional polynomial model minimally improved the estimation of PRC for extreme values of DP.

Perioperative Anesthesia - 4 Oxygen Administration during Surgery and Postoperative Organ Injury

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Introduction: Patients undergoing surgery frequently receive a greater amount of supplemental oxygen than required to maintain normal oxygen levels in the blood.(1) Whether the administration of excess supplemental oxygen is associated with organ injury is uncertain. We examined whether excess oxygen administration during surgery is associated with postoperative kidney, heart, and lung injury.

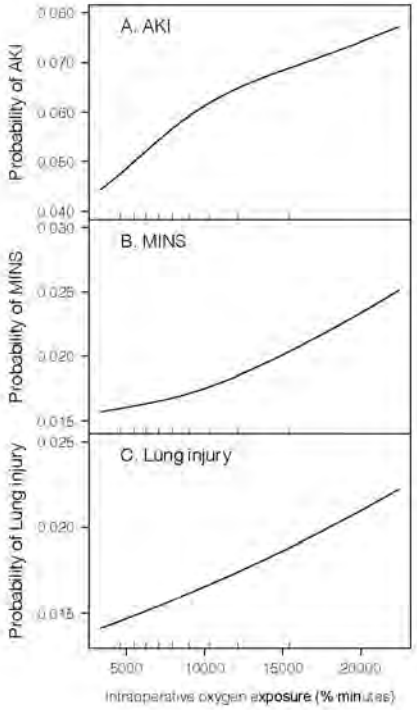
Methods: We conducted an observational cohort study of patients drawn from 42 medical centers across the United States participating in the Multicenter Perioperative Outcomes Group data registry. Eligible patients included adults undergoing surgery of 120 minutes or longer, with general anesthesia and endotracheal intubation, and who were admitted to the hospital after surgery between January 2016 and November 2018. Minute-to-minute data for the fraction of inspired oxygen (FIO2) and non-invasively measured hemoglobin oxygen saturation (SpO2) data were used to calculate excess oxygen administration, defined as the area under the curve of the FIO2 above air (21%) during minutes when the SpO2 was greater than 92% (AUC FIO2). Co-primary endpoints were acute kidney injury, myocardial injury following noncardiac surgery, and lung injury. The association between excess oxygen administration (AUC FIO2) and each of the co-primary endpoints was evaluated using multivariable logistic regression, adjusting for pre-specified baseline covariates and other potential confounding variables. A detailed pre-specified sensitivity analysis was undertaken, redefining the exposure variable (AUCFIO2), restricting the cohort, and conducting an instrumental variable analysis.

Results: The cohort comprised 350,647 cases (median [interquartile range] age, 59 [46-69] years; 51.5% women; duration of surgery, 205 [158-279] minutes). Acute kidney injury was diagnosed in 19,256 cases (5.8%), myocardial injury in 10,323 (2.9%), and lung injury in 14,430 (4.1%). The median FIO2 was 54.0 (47.5-60.0) %, and the area under the curve of the fraction of inspired oxygen was 7,951 (5,870-11,107) %,Ä¢minutes. After accounting for baseline covariates and other potential confounding variables, greater excess oxygen administration was independently associated with a higher risk of acute kidney injury, myocardial injury, and lung injury: compared to patients at the 25th percentile for the area under the curve of the fraction of inspired oxygen patients at the 75th percentile had 26% greater odds of acute kidney injury (95% CI: 21-30%), 11% greater odds of myocardial injury (95% CI: 6-16%), and 13% greater odds of lung injury (95% CI: 12-16%) [Figure 1]. Our findings were generally robust to a detailed, pre-specified sensitivity analysis.

Conclusion: Greater excess oxygen administration during surgery was independently associated with a higher incidence of renal, cardiac, and pulmonary injury. A large clinical trial to detect small but clinically significant effects on organ injury and patient-centred outcomes is needed to guide oxygen administration during surgery.

References: 1. Anesthesiology. 129:67-76; 2018

Figure 1. Independent association between intraoperative oxygen exposure and **A**. acute kidney injury (AKI), **B**. myocardial injury following non-cardiac surgery (MINS), and **C**. lung injury. Tick marks on the x-axis identify each decile of cases.



Perioperative Anesthesia - 5 Association of Post-operative ICU Delirium and Intraoperative Triple Low State

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Introduction: Post-operative delirium (POD) is a common complication, occurring in up to 52% of non-cardiac surgical patients, and is a significant cause of increased mortality and morbidity (1,2). While general risk factors for POD have been identified, such as age, surgical duration, and pre-operative cognitive function, potential modifiable risk factors are less established (3). The triple low state (TLS) is a period of concurrent low bispectral index (BIS), minimum alveolar concentration (MAC), and mean arterial pressure (MAP) values, associated with increased postoperative mortality and a hypothesized indicator of poor physiologic reserve (4). This preliminary study aimed to determine whether intraoperative TLS is associated with POD.

Methods: This retrospective study included non-cardiac and non-liver transplant surgical patients within a multi-hospital health system from 2016 ‚Äì 2018 who had Intensive Care Delirium Screening Checklist (ICDS) scores documented during a post-operative ICU stay (ICDS >3 was considered positive for delirium). Patients were excluded if there was evidence of pre-operative delirium or did not have intraoperative values for BIS, MAC and MAP. TLS was defined as simultaneous BIS < 45, MAP < 75 mmHg and MAC < 0.7. Logistic regression was performed to determine the association between TLS events and the development of POD. Covariates included age, gender, ASA physical status, emergency surgery, surgical specialty, hospital site, and the presence of a TLS during the procedure. Multiple comparisons were accounted for using Benjamani-Hochberg correction to calculate the False-Discovery Rate (FDR).

Results: Of the 259 patients that met inclusion criteria, 95 patients had TLS events and 164 did not. Demographic and clinical variables are in Fig. 1. Average cumulative TLS duration within the TLS cohort was 30.7 min [6 min (Q1), 38.75 min (Q3)]. POD occurred more often in the TLS subgroup (28.4%) compared to patients without TLS events (11.6%). Logistic regression analysis demonstrated a trend towards TLS being associated with POD, OR 3.0 (1.35 - 6.69), FDR-adj p=0.06 (Figure 2).

Conclusion: In a multihospital surgical population with post-operative ICU care, TLS was common and prolonged. TLS may be associated with post-operative ICU delirium, however, the sample size limited our analysis including the ability to account for all confounders (e.g. with propensity matching). This study demonstrates how intraoperative data may be used to identify patients at elevated risk for postoperative delirium, and should motivate larger studies evaluating the relationship between TLS and POD.

References: 1) Moskoqitz, E.E, et al. Post-operative delirium is associate with increased 5-year mortality. Am J Surg (2017) 214:1036-1038 2) Iamaroon, A., et al. Incidence of and risk factors for postoperative delirium in older adult patients undergoing noncardiac surgery: a prospective study. BMC Geriatrics (2020) 20:40 3) Kang, T., et al. Incidence and risk factors of postoperative delirium after spinal surgery in older patients. Sci Rep (2020) 10:9232 4) Sessler, D.I. et al. Hospital stay and mortality are increased in patients having a 'triple low' of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. Anesthesiology (2012) 6:1195-1203

Characteristics	Delirium	No Delirium	p value
Total Patients	46	213	
Patients with TLS	27 (58.7 %)	63 (29.6 %)	< 0.001
Surgical_Site:			< 0.001
MUH	7 (15.2 %)	12 (5.6%)	
PUH	39 (84.8 %)	201 (94.4%%)	
Year:			< 0.001
2016	21 (45.7 %)	67 (31.5%)	
2017	15 (32.6 %)	112 (16.0%)	
2018	10 (21.7 %)	34 (16.0%)	
Age	71.2 +/- 15.8	62.4 +/- 15.3	< 0.001
Gender:			< 0.001
Female	26 (56.5 %)	91 (42.7%)	
Male	20 (43.5 %)	122 (57.3%)	
ASA:			< 0.001
5	3 (6.5 %)	1 (0.5%)	
4	19 (41.3 %)	59 (27.7 %)	
3	21 (45.7 %)	132 (60.2%)	
2	3 (6.5 %)	20 (9.4%)	
1	0 (0.0 %)	1 (0.5%)	
Emergency	19 (41%)	53 (25%)	
Procedure_Length	211.6 +/- 150.6	239 +/- 159.4	0.273
Surgical_Specialty:			< 0.001
General	16 (34.8 %)	70 (32.9%)	
Vascular	8 (17.4 %)	21 (9.9 %)	
Thoracic	7 (15.2 %)	80 (37.6%)	
Orthopaedic	9 (19.6 %)	30 (14.1%)	
Other	6 (13%)	12 (5.6 %)	

Characteristic	Odds Ratio (95% CI)	p value	FDR
Surgical Site	3.31 (0.90 – 12.2)	0.071	0.142
Emergency	2.37 (0.99 – 5.69)	0.053	0.13
ASA Physical Status	1.35 (0.75 – 2.41)	0.316	0.379
TLS	2.74 (1.26 – 5.96)	0.011	0.066
Year	1.08 (0.64 – 1.85)	0.771	0.771
Age	1.03 (1.00 – 1.06)	0.024	0.096
Procedure Length	1.00 (0.99 – 1.00)	0.254	0.38
Gender	0.7 (0.36 – 1.57)	0.440	0.48
Surgical Specialty:			
General	0.27 (0.07 – 1.02)	0.054	0.13
Vascular	0.34 (0.07 – 1.57)	0.167	0.286
Thoracic	0.12 (0.02 – 0.59)	0.010	0.066
Orthopaedic	0.45 (0.1 – 1.96)	0.290	0.38

Perioperative Anesthesia - 6

Intraprocedural hypoxemia, delirium and effect modification by obstructive sleep apnea: A hospital registry study.

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Introduction: Postoperative delirium (POD) increases hospitalization and is associated with a 1.5-fold higher one-year-mortality (1). Previous studies reported an association between the occurrence of perioperative hypoxemia and postoperative cognitive dysfunction (2). Further, perioperative hypoxemia is a common complication in patients suffering from obstructive sleep apnea (OSA) (3). At the same time, chronic, recurrent episodes of hypoxemia, which occur frequently in patients with OSA, might have protective effects on POD through hypoxic preconditioning (4). We hypothesized that intraprocedural desaturation is associated with POD. Contingent on this association, we hypothesized that this association is modified by a diagnosis or high susceptibility for OSA.

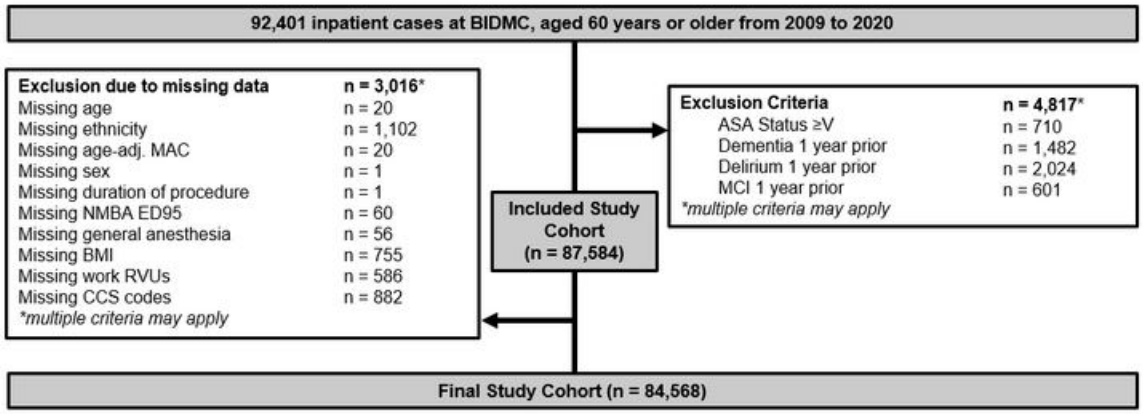
Methods: Inpatients aged 60 years or older who underwent general anesthesia or monitored anesthesia care (MAC) for surgery and interventional procedures between 2009 and 2020 at a tertiary academic healthcare network in Boston, Massachusetts, United States of America, were included in this retrospective cohort study. Patients with an American Society of Anesthesiologists physical status classification ≥V or with a pre-existing diagnosis of dementia, delirium or cognitive impairment were excluded (Figure 1). The primary exposure was the occurrence of intraprocedural hypoxemia, defined as a recording of an intraprocedural peripheral oxygen saturation of less than 90% for an episode of more than two consecutive minutes. The co-primary exposure was a diagnosis of OSA based on International Classification of Diseases (9th/10th Revision, Clinical Modification [ICD-9/10-CM]) codes, pulmonary and anesthesia alert notes and standardized nurse assessment notes prior to the procedure, or high susceptibility for OSA according to the BOSTN-score (5). The primary outcome was the occurrence of POD within 30 days, identified based on ICD-9/10-CM codes (6) and available Confusion Assessment Method (7) assessments in the intensive care unit. We applied multivariable logistic regression analysis adjusted for a priori defined factors including patient demographics, comorbidities, procedural severity and anesthesia-related factors. Linear combinations of the main effect and interaction terms were performed to assess effect modification of the association between intraoperative hypoxemia and POD by a diagnosis or high susceptibility for OSA. Adjusted odds ratios with 95% confidence intervals with alpha set to 0.05 are reported.

Results: The study cohort consisted of 84,568 patients (Figure 1), among which 4,900 (5.8%) experienced intraoperative hypoxemia. 27,175 (32.1%) patients had a diagnosis or high susceptibility for OSA. 2,835 patients (3.4%) developed POD, 354 (7.2%) of patients with and 2,481 (3.1%) of patients without intraoperative hypoxemia. Patient characteristics are provided in Table 1. In adjusted analysis, the occurrence of intraprocedural hypoxemia was associated with an increased risk of POD (aOR 1.34 [95% CI 1.17-1.53]; p<0.001). This association was characterized by a dose response (Figure 2) and was modified by a diagnosis or high susceptibility for OSA: A diagnosis or high susceptibility for OSA magnified the risk of POD associated with desaturation (aOR 1.68 [95% CI 1.35-2.09]; p<0.001 in patients with OSA, compared to aOR 1.20 [95% CI 1.02-1.41]; p=0.024 in patients without OSA, p-for-interaction=0.011) (Table 2). Episodes of desaturation in patients with a diagnosis or high susceptibility for OSA were comparable to patients without OSA with regard to their duration (mean 24.1 ± 36.8 min, median 11 [IQR 5.5-22.5] min versus 26.6 ± 41.2 min, median 10.5 [IQR 5-26.3] min, p=0.97). The association between intraprocedural hypoxemia

and POD was not modified by MAC versus general anesthesia (p-for-interaction=0.61).

Conclusion: Patients who experience intraprocedural hypoxemia are at higher risk of POD. Our results do not support the hypothesis that patients with OSA are less vulnerable to hypoxemia-associated delirium. Rather, physicians should aim to avoid oxygen desaturation particularly in patients with OSA.

References: (1) Psychiatr Clin North Am. 41(1): 1-17, 2017. (2) Ann Thorac Surg. 87(1): 36-45, 2009. (3) Dtsch Arztebl Int. 113(27-28): 463-469, 2016. (4) Curr Opin Pulm Med. 20(6): 565-571, 2014. (5) Anesth Analg. 130(5): 1415-1424, 2020. (6) Anesth Analg. doi: 10.1213/ANE.0000000000005739, 2021. (7) Crit Care Med. 29(7): 1370-1379, 200



ASA: American Society of Anesthesiologists; BIDMC: Beth Israel Deaconess Medical Center; BMI: Body Mass Index; ED95: median effective dose required to achieve a 95% reduction in maximal twitch response from baseline; NMBA: neuromuscular blocking agents; work RVUs: work Relative Value Units; CCS: Clinical Classifications Software; MCI: mild cognitive impairment; age-adj. MAC: age-adjusted mean alveolar concentration of inhalational anesthetics.

Figure 1. Study flow diagram.

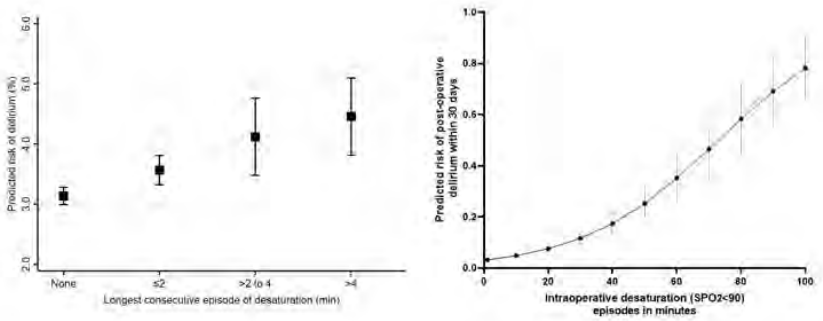


Figure 2. Adjusted, estimated risk of postoperative delirium (%) by duration of desaturation, defined as peripheral oxygen saturation <90%.

	No intraprocedural desaturation	Intraprocedural desaturation	Standardized difference
	N=79,668	N=4,900	
Demographics			
Age, years	70.0 (65.0 - 78.0)	70.0 (65.0 - 77.0)	0.041
BMI, kg/m²	27.3 (23.8 - 31.4)	28.6 (25.1 - 33.3)	-0.226
Sex			0.213
Male	40,175 (50.4%)	2,987 (61.0%)	
Female	39,493 (49.6%)	1,913 (39.0%)	
Ethnicity			-0.111
Asian	2,165 (2.7%)	89 (1.8%)	
Black	6,092 (7.6%)	275 (5.6%)	
Hispanic	2,363 (3.0%)	130 (2.7%)	
Other	199 (0.2%)	10 (0.2%)	
Two or more	32 (0.0%)	1 (0.0%)	
White	58,236 (73.1%)	3,664 (74.8%)	
Unspecified	10,581 (13.3%)	731 (14.9%)	
Comorbidities			
Smoking	15,082 (18.9%)	1,210 (24.7%)	-0.140
Alcohol abuse	2,611 (3.3%)	154 (3.1%)	0.007
Drug abuse	1,103 (1.4%)	56 (1.1%)	0.022
Anemia	24,125 (30.3%)	1,826 (37.3%)	-0.148
Schizoaffective disorders	8,330 (10.5%)	380 (7.8%)	0.094
BOSTN-score	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	-0.165
High susceptibility for OSA	11,754 (14.8%)	966 (19.7%)	-0.132
Diagnosis of OSA	16,243 (20.4%)	1,145 (23.4%)	-0.072
Procedural characteristics			
Duration of surgery, min	139.0 (78.0 - 217.0)	243.0 (125.0 - 318.0)	-0.621
Emergency surgery	10,674 (13.4%)	661 (13.5%)	-0.003
Work relative value units	15.4 (7.2 - 23.5)	27.3 (12.1 - 44.8)	-0.765
Crystalloid and colloid infusion, ml	1000.0 (500.0 - 1740.5)	2000.0 (900.0 - 3000.0)	-0.568
Units of packed red blood cells	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	-0.293
Age-adjusted mean alveolar concentration of inhalational anesthetics	0.9 (0.0 - 1.1)	0.8 (0.6 - 1.0)	-0.032
Short acting opioid dose, mg OME	25.0 (0.0 - 50.0)	100.0 (25.0 - 250.0)	-0.624
Long acting opioid dose, mg OME	0.0 (0.0 - 13.6)	0.0 (0.0 - 0.0)	0.266
Non-depolarizing NMBA, ED95	1.7 (0.0 - 3.1)	3.4 (1.1 - 5.5)	0.622
Neostigmine dose, mcg/kg	0.0 (0.0 - 3.0)	0.0 (0.0 - 2.0)	0.153
Vasopressor dose, mg norepinephrine	0.0 (0.0 - 0.3)	0.4 (0.0 - 0.9)	-0.117
Mean arterial pressure below 55 mmHg, min	1.0 (0.0 - 3.0)	8.0 (0.0 - 36.0)	-0.786

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range [25th-75th percentile]).

OSA: obstructive sleep apnea; BMI: body mass index; ED95: median effective dose required to achieve a 95% reduction in maximal twitch response from baseline; NMBA: neuromuscular blocking agents; OME: oral morphine equivalents.

Table 2. Estimated risk of delirium in %.

	Obstructive sleep apnea	No obstructive sleep apnea	p-value
Desaturation	4.64 (3.82-5.46)	4.00 (3.47-4.54)	<0.001
No desaturation	2.93 (2.69-3.16)	3.40 (3.24-3.55)	<0.001

Table 2. Adjusted, estimated risk of postoperative delirium (%) for patients experiencing intraprocedural hypoxemia (peripheral oxygen saturation of less than 90% for an episode of more than two consecutive minutes) with and without a diagnosis or high risk of obstructive sleep apnea.

Perioperative Anesthesia - 7

Intraoperative Spinal Cord Stimulation Mitigates Pain after Spine Surgery in Mice

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Introduction: Managing postoperative pain after spine surgery is challenging; up to 40% of patients develop failed back surgery syndrome resulting in intractable back and/or leg pain. While spinal cord stimulation (SCS) has been shown to effectively alleviate such chronic pain, it is unknown if SCS during spine surgery can mitigate the development of intense postoperative pain after spine surgery. In this study, we modeled spine surgery-induced pain hypersensitivity in mice and then examined if intraoperative SCS inhibits the development of such hypersensitivity.

Methods: Unilateral T13 laminectomy was performed in mice to expose the dorsal part of L4-5 spinal segments that receive sensory inputs from the hind limb. After the laminectomy, a group of mice received intraoperative SCS (0.2 ms biphasic pulse at 50 Hz frequency and 50% motor threshold intensity) epidurally applied to the exposed side of dorsal column for an hour under anesthesia before closing the surgical wounds. Mechanical pain sensitivity in hind paws was measured using von Frey assay one day before and at predetermined times after surgery.

Results: Mice that underwent unilateral T13 laminectomy developed mechanical hypersensitivity in both hind paws, which gradually resolved in 1-2 weeks. The extent of the hypersensitivity was less in the contralateral hind paw (relative to the laminectomy) than in the ipsilateral hind paw. Intraoperative SCS applied to the exposed side of dorsal column significantly inhibited the development of hind paw mechanical hypersensitivity only in the SCS-applied side. This inhibition of hypersensitivity was more pronounced in males than in females on the first 2 days post-laminectomy.

Conclusion: These results demonstrate that spine surgery for unilateral laminectomy induces central sensitization that results in bilateral postoperative pain hypersensitivity. Intraoperative SCS after laminectomy can mitigate the development of this hypersensitivity in the SCS-applied side and the effects are more profound in males than in females.

References: 1. Chan C, Peng P: Failed Back Surgery Syndrome. Pain Med 2011; 12:577-606 2. Gray DT, Deyo RA, Kreuter W, Mirza SK, Heagerty PJ, Comstock BA, Chan L: Population-based trends in volumes and rates of ambulatory lumbar spine surgery. Spine 2006; 31:1957-63; discussion 1964 3. Wilkinson HA: The Failed Back Syndrome: Etiology and Therapy. Springer Science & Business Media, 2012 4. Lehmann TR, LaRocca HS: Repeat lumbar surgery. A review of patients with failure from previous lumbar surgery treated by spinal canal exploration and lumbar spinal fusion. Spine 1981; 6:615-9 5. Law JD, Lehman RA, Kirsch WM: Reoperation after lumbar intervertebral disc surgery. J Neurosurg 1978; 48:259-63 6. Thomson S: Failed back surgery syndrome - definition, epidemiology and demographics. Br J Pain 2013; 7:56-9 7. Sinatra R: Causes and consequences of inadequate management of acute

Figure 1

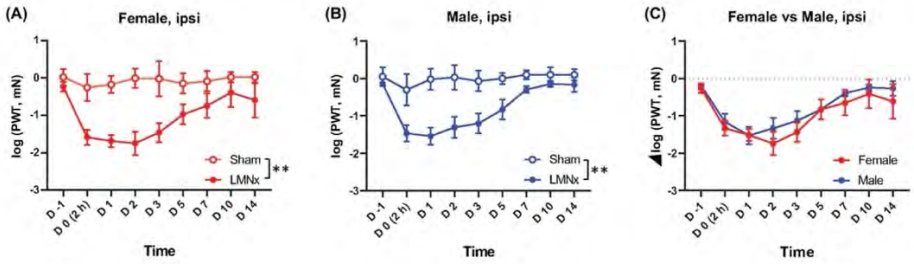


Figure 2

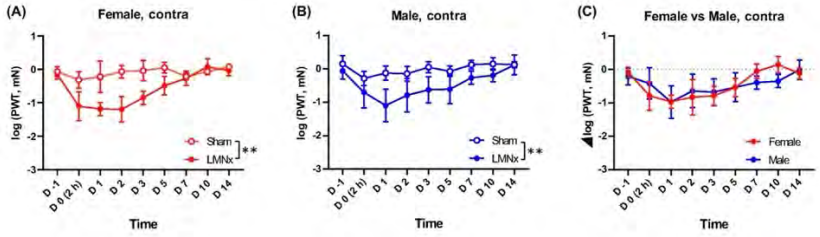
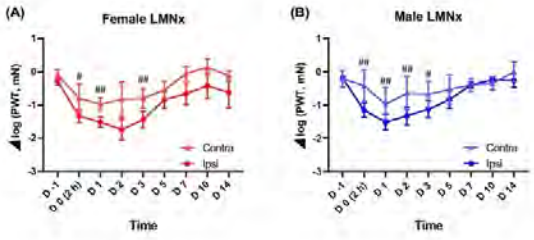


Figure 3



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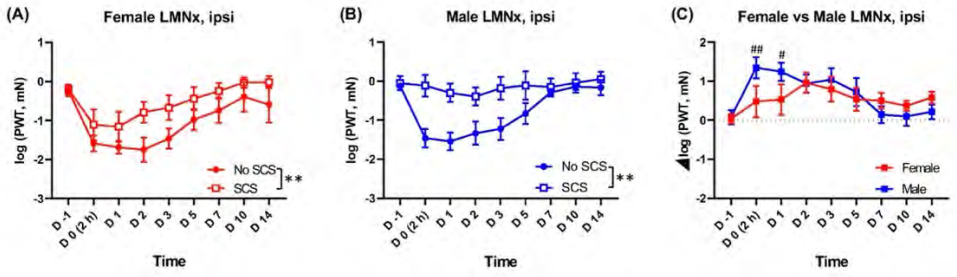

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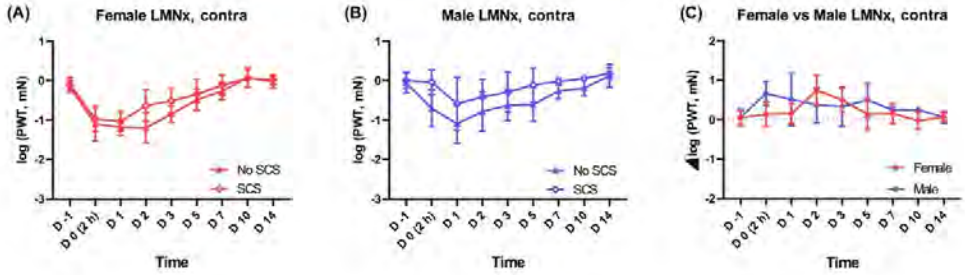

Perioperative Anesthesia - 8 Metabolic flexibility in patients undergoing Radical Cystectomy

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[1]University College London, London, United Kingdom, [2]University College London Hospital, London, United Kingdom, [3]Duke University Medical School, Durham, NC, [4]Duke University Medical Center, Durham, NC

Introduction: Aerobic fitness predicts the development of postoperative complications [1]. Preoperative cardiopulmonary exercise testing (CPET) is used to stratify patients' ability to handle the physiological demands of surgery and post-operative recovery. A preoperative ventilatory anaerobic threshold (AT) of <11 mL/min/Kg in patients listed for radical cystectomy predicts an increased length of stay and the development of postoperative morbidity [2] [3]. The underlying mechanisms linking reduced aerobic fitness to the development of postoperative morbidity are not well described. Aerobic exercise capacity hinges on mitochondrial function, and efficiency of substrate usage. Lipid oxidation during exercise is a surrogate of mitochondrial function and is increasingly being proposed as a marker of metabolic and cellular health [4] [5]. Whole body fat oxidation during exercise has been associated with insulin sensitivity, metabolic flexibility, and reductions in factors associated with metabolic risk [6]. The relationship between established metabolic inflexibility and the metabolic response to surgery is unknown. The primary objective of this pilot study was to describe the relationship between lipid and carbohydrate oxidation derived from metabolic cart data during CPET and aerobic fitness in patients with bladder cancers listed to undergo radical cystectomy. The secondary objective was to establish if any relationship exists between preoperative and postoperative lipid and carbohydrate oxidation in higher and low fitness individuals

Methods: In this prospective observational study 18 patients underwent fasted CPET on a bicycle ergometer preoperatively and within 12 weeks after radical cystectomy at Duke University Medical Centre, Durham, NC. CPET consisted of a 5-minute warmup followed by a 5,10, 15 or 25 watt/minute ramp protocol dependent on gender, age and activity level to peak oxygen consumption (VO2 peak). Oxygen consumption and CO2 production were measured by metabolic cart (COSMED Quark). Fat and glucose oxidation (FATox, CHOox) were calculated using stoichiometric equations up to ventilatory anaerobic threshold (VAT) [7]. Cohorts were separated according to perioperative risk by ventilatory anaerobic threshold (< 12 mls/O2/kg and ,â• 12 mls/O2/kg) [3]. Comparison between before and after surgery and between AT groups was carried out using Student's t-test and one-way ANOVA/MANOVA as appropriate. Significance was set at $P < 0.05$.

Results: 10 patients had an VAT of ≥ 12 mls/O2/kg (higher fitness) and 8 had an VAT of < 12 mls/O2/kg (lower fitness). Demographic data is presented in Table 1. Peak VO2 did not change in either group from pre to post surgery, higher fitness group (1290 mL/min vs 1219 mL/min p =0.4502) and lower fitness group (842mL/min vs 975 mL/min p=0.0860). Longitudinal FATox and CHOox were different between higher and lower fitness groups both pre and postoperatively (p=<0.05) Figure Maximal fat ox in the higher fitness group increased from pre to post operatively (0.264 ± 0.013 gram/min vs. 0.272 ± 0.017 gram/min, p=<0.0001). This was also the case in the lower fitness group (0.112 ± 0.01 gram/min vs 0.128 ± 0.009 gram/min, p=<0.0001).

Conclusion: While overall fuel utilization as determined by stoichiometric equations did not differ significantly pre to one month post operatively in either the low or higher fitness cohorts, significant differences in terms of FATox were observable at both time points between cohorts. Importantly, the lower fitness group appeared to demonstrate metabolic inflexibility, with both an abnormal pattern of fat oxidation with increasing metabolic demand & reduced maximal fat oxidation. This has important potential implications for this population's ability to respond to conditional changes in metabolic demand, such as those expected in the perioperative period and raises a novel paradigm to be investigated in terms of unpicking the relationship between fitness and surgical outcome. The improvement in MFO postoperatively in both cohorts may reflect systemic metabolic changes consequent to removal of the tumor [8] and may also have important

implications for tumor free survival. Importantly, targeted nutritional and exercise interventions have, in other contexts, been demonstrated to ameliorate metabolic inflexibility and improve outcomes and may therefore be applicable to the perioperative space.

References Curr Anesthesiol Rep, vol. 10, pp. 1-11, 2020 BJU Int., vol. 115, no. 4, pp. 554-561, 2015 Liver Transpl, vol. 18, no. 2, pp. 152-159, 2012 Sport Med, vol. 2, no. 48, p. 467-479, 2018 Cell Metab., vol. 5, no. 25, pp. 1027-1036, 2017 Med. Sci. Sports Exerc, vol. 40, no. 3, p. 495-502, 2008 Journal of applied physiology: respiratory, environmental and exercise physiology, vol. 55, no. 2, pp. 628-634, 1983 Mol Metab., vol. 33, p. 83-101, 2020

	Ventilatory Anaerobic threshold >12 group	Ventilatory Anaerobic threshold <12 group
Age, Median (IQR)	67 (63 - 73)	75 (68 - 82)
Sex		
Male	10	7
Female	0	1
BMI, Median (IQR)	27.7 (26.4 – 33.2)	30.2 (23.6 – 38.1)

Table 1. Demographic data of higher fitness group <12 mls/O_2/kg and lower fitness group VAT >12 mls/O_2/kg

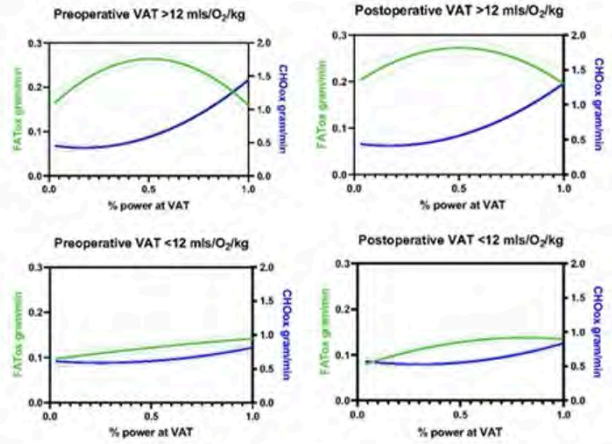

Figure 1. Relationships between fat oxidation (FATox) and Carbohydrate oxidation (CHOox) as a function of power output during ramped cardiopulmonary exercise testing in surgical patients around radical cystectomy. Longitudinal data for FATox & CHOox are presented as fitted regression curves (locally weighted scatter plot smoothing, with a 10-point smoothing window, mean,sd). AT = Ventilatory anaerobic threshold

Perioperative Anesthesia - 9 Association between cannabinoid use and stroke after surgery: A retrospective cohort study.

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Introduction: An increasing number of patients who present for surgery reports use of cannabinoids for recreational or medical purposes, which was accelerated by its legalization in various states throughout the United States (1). Retrospective studies in non-surgical patients who consume cannabinoids for recreational purposes suggested neurotoxic effect of cannabis on the adolescent brain (2) and an increased risk of acute ischemic stroke requiring hospitalization (3). It is unclear whether patients with cannabinoid use are also at higher risk of stroke after surgery. Previous studies were limited to patients with cannabinoid abuse identified by International Classification of Disease Ninth and Tenth revision (ICD-9/10) diagnostic codes, as well as in their ability to control for important demographic and socioeconomic confounding variables (4). In this study, we evaluated whether cannabinoid use for medical or recreational purposes is associated with postoperative ischemic stroke within 1 year after surgery using data from a large hospital network in New England.

Methods: Adult patients undergoing non-cardiac surgery at a tertiary academic healthcare network in Boston (MA, USA) between 2006 and 2020 with available pre-admission or pre-procedural notes were included in this hospital registry study. Recreational use of cannabinoids was identified based on physician and nursing notes from structured patient interviews during pre-admission or pre-procedural testing, ICD-9/10 diagnostic codes of cannabinoid abuse, or prescriptions of medical cannabinoids. The primary outcome was a diagnosis of ischemic stroke within 1 year after surgery. Multivariable logistic regression analysis adjusted for a priori defined factors including patient demographics, socioeconomic factors, concomitant substance abuse, markers of procedural severity and comorbidities including patient's baseline risk of stroke based on the STRoke After Surgery (STRAS) prediction score (5) was applied. In secondary analyses, we differentiated the risk of postoperative ischemic stroke by types of cannabinoid use (recreational use, medical use, and abuse of cannabinoids) and investigated whether a high baseline stroke risk based on the STRAS prediction model modified the association between cannabinoid use and postoperative ischemic stroke. Exact matching for age (± 2 years) and sex at a 1:3 ratio was performed in sensitivity analyses. Standardized differences and odds ratios with 95% confidence intervals are reported. A P-value <0.05 was considered as statistically significant. All analyses were performed in Stata (Version 16, StataCorp, TX, USA).

Results: Among 308,077 included patients (Figure 1), 25,264 (8.9%) used cannabinoids for recreational or medical purposes. 2,651 (0.8%) patients had a diagnosis of stroke within one year after surgery, of which 197 (0.8%) used cannabinoids and 2,454 (0.9%) did not. The incidence of postoperative stroke increased with patient age (Table 1, Figure 2). After adjusting for confounding factors, cannabinoid use was not significantly associated with postoperative ischemic stroke (adjusted OR [ORadj] 0.91; 95% CI 0.77–1.06; p=0.25; Table 2), independent of as to whether the patients used the drug recreationally or based on a medical indication (Table 3). This finding was not modified by the predicted risk of postoperative stroke (P-for-interaction=0.31). Sensitivity analyses conducted in a sub-cohort matched for sex and age (± 2 years) confirmed the primary findings (ORadj 0.96; 95% CI 0.79–1.16; p=0.69).

Conclusion: Cannabinoid use is not associated with an increased risk of ischemic stroke within one year after surgery.

References: 1 U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration; 2020 2 Proc Nat Acad Sci U S A. 2012 Oct 2; 109(40): E2657-64. 3 J Neurol Sci. 2016 May 15;364:191-6. 4 Anesthesiology. 2020 Apr; 132(4):625-635. 5 Br J Anaesth. 2021 Nov

Figure 1. Study cohort.

ASA, American Society of Anesthesiologists. STRAS, STRoke After Surgery.

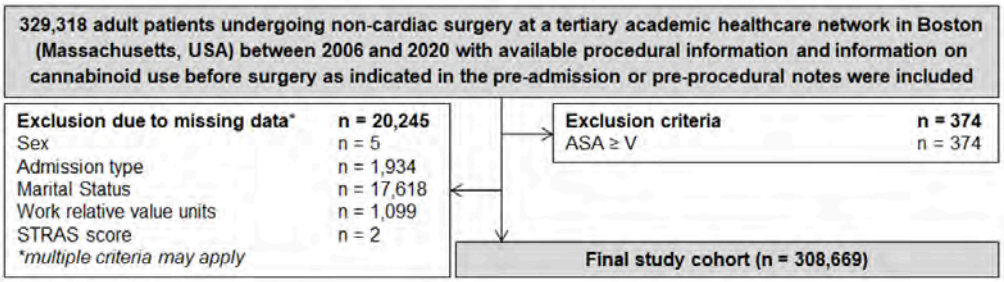


Table 1. Baseline characteristics.

ASA, American Society of anesthesiologists; USD, United States Dollar; ENT, Ear, Nose, and Throat.

Characteristics	No Stroke (n = 306,681)	Stroke within 1 year (n= 25,264)	Standardized difference
Demographics			
Age, years	55.24 ± 16.42	66.52 ± 12.84	-0.765
Sex, female	176,817 (57.8%)	1,227 (46.3%)	0.232
Body mass index (BMI), kg/m²	28.34 ± 6.83	27.99 ± 6.03	0.055
ASA physical status			-1.014
I	37,974 (12.4%)	10 (0.4%)	
II	148,509 (48.6%)	449 (16.9%)	
III	107,465 (35.2%)	1,794 (67.7%)	
IV	11,733 (3.8%)	398 (15.0%)	
Ethnicity and race			0.053
Asian	11,933 (4.5%)	85 (3.6%)	
Black	29,546 (11.2%)	341 (14.5%)	
Hispanic	15,856 (6.0%)	162 (6.9%)	
Other	11,245 (4.2%)	69 (2.9%)	
Two or more	412 (0.2%)	0 (0.0%)	
White	195,664 (73.9%)	1,691 (72.0%)	
Socioeconomic factors			
Estimated household income, USD	68,413 ± 39,074	64,043 ± 39,977	0.110
Federal Insurance	98,345 (32.2%)	1,470 (55.5%)	-0.482
Education Level			0.157
No education	241 (0.4%)	12 (1.2%)	
Attended high school	4,493 (6.9%)	87 (8.4%)	
Graduated high school	21,121 (32.6%)	386 (37.2%)	
Attended college	12,965 (20.0%)	202 (19.5%)	
Graduated college	26,000 (40.1%)	350 (33.8%)	
Marital Status			-0.001
Divorced	20,727 (6.8%)	252 (9.5%)	
Life Partner	382 (0.1%)	2 (0.1%)	
Married	162,612 (53.2%)	1,337 (50.4%)	
Separated	4,009 (1.3%)	48 (1.8%)	
Single	98,336 (32.2%)	687 (25.9%)	
Widowed	19,615 (6.4%)	325 (12.3%)	
Preoperative factors			
Admission type			-0.557
Ambulatory	179,225 (58.6%)	911 (34.4%)	
Same-day admission	90,274 (29.5%)	964 (36.4%)	
Inpatient	36,182 (11.8%)	776 (29.3%)	
Emergency surgery	18,586 (6.1%)	278 (10.5%)	-0.160
Intraoperative factors			
Duration of surgery, min	118.85 (98.24)	127.77 (98.96)	-0.090
Work relative value units	11.23 (8.88)	13.78 (11.19)	-0.251

Surgical service			-0.325
Colorectal	8,122 (2.7%)	46 (1.7%)	
Dent/Oral/ENT	9,706 (3.2%)	70 (2.6%)	
Ophthalmology	16,017 (5.2%)	207 (7.8%)	
General Surgery	40,016 (13.1%)	197 (7.4%)	
Gastroenterology	11,791 (3.9%)	130 (4.9%)	
Gynecology	47,875 (15.7%)	154 (5.8%)	
Neurology	11,115 (3.6%)	359 (13.5%)	
Orthopedic	66,126 (21.6%)	353 (13.3%)	
Plastic	18,752 (6.1%)	54 (2.0%)	
Podiatry	7,600 (2.5%)	68 (2.6%)	
Surgical Oncology	11,196 (3.7%)	47 (1.8%)	
Thoracic	14,742 (4.8%)	193 (7.3%)	
Transplant	7,359 (2.4%)	135 (5.1%)	
Trauma/Surgical Critical Care	6,606 (2.2%)	112 (4.2%)	
Urology	19,568 (6.4%)	163 (6.1%)	
Vascular	9,090 (3.0%)	363 (13.7%)	
STRAS prediction score	6.0 (3.0-10.0)	18.0 (12.0-24.0)	-1.701
Comorbidities			
Myocardial Infarction	9,841 (3.2%)	337 (12.7%)	-0.356
Chronic heart failure	16,385 (5.4%)	557 (21.0%)	-0.475
Cardio vascular disease	11,197 (3.7%)	1,318 (49.7%)	-1.219
Diabetes mellitus	18,770 (6.1%)	547 (20.6%)	-0.435
Chronic kidney disease	21,226 (6.9%)	626 (23.6%)	-0.476
Cancer	17,274 (5.7%)	715 (27.0%)	-0.187
Chronic liver disease	3,978 (1.3%)	49 (1.8%)	-0.043
Hypertension	122,220 (40.0%)	1,938 (73.1%)	-0.708
Hyperlipidemia	109,570 (35.8%)	1,774 (66.9%)	-0.654
History of stroke	6,209 (2.0%)	1,113 (42.0%)	-1.100
Psychiatric comorbidities			
Anxiety	35,800 (11.7%)	446 (16.8%)	-0.146
Depression	49,567 (16.2%)	746 (28.1%)	-0.290
Schizoaffective Disorder	889 (0.3%)	10 (0.4%)	-0.014
Schizophrenia	1,104 (0.4%)	22 (0.8%)	-0.060
Psychosis	3,006 (1.0%)	59 (2.2%)	-0.098
Substance abuse			
Alcohol abuse	4,971 (1.8%)	1,404 (5.6%)	-0.204
Cocaine abuse	275 (0.1%)	8 (0.3%)	-0.047
Intravenous drug abuse	5,030 (1.6%)	82 (3.1%)	-0.095
Medication abuse	1,570 (0.5%)	29 (1.1%)	-0.065
Psychedelic drug abuse	72 (0.0%)	3 (0.1%)	-0.034

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range (25th-75th percentile), values separated by comma).
** Descriptive data is provided in a subgroup of non-missing data.*

Table 2. Results of the primary analysis.

	No Cannabinoid use (n = 280,113)	Cannabinoid use (n = 25,219)	Unadjusted Analysis		Adjusted Analysis	
			OR 95% CI	P-value	OR 95% CI	P-value
Stroke within 1 year	2,245 (0.9%)	197 (0.8%)	0.90 0.78–1.04	0.158	0.91 0.78–1.07	0.25

Data are expressed as frequency (prevalence in %). Statistical analyses were performed using multivariable logistic regression. Odds ratios (OR) are reported for multivariable logistic regression analyses.

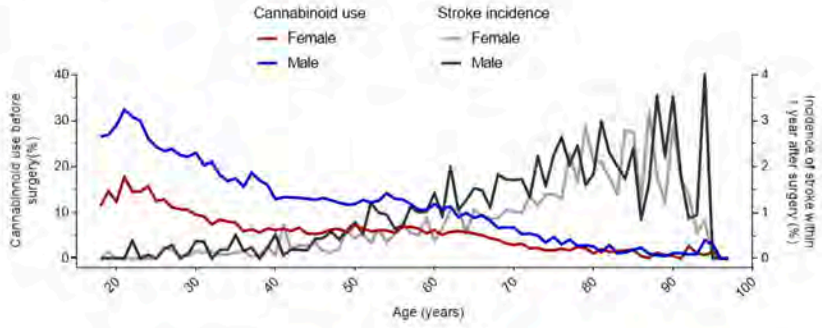
Table 3. Results of multivariable logistic regression with categorized exposure.

Cannabinoid use	No stroke (n = 305,681)	Stroke within 1 year (n = 2,651)	Unadjusted Analysis		Adjusted Analysis	
			OR 95% CI	P-value	aOR 95% CI	P-value
No use	280,659 (99.1%)	2,454 (0.9%)	Reference		Reference	
Recreational use	18,160 (99.4%)	116 (0.6%)	0.73 0.61–0.88	0.001	0.91 0.74–1.11	0.35
Abuse	2,795 (99.2%)	23 (0.8%)	0.94 0.62–1.42	0.77	0.73 0.47–1.14	0.16
Medical use	4,067 (98.6%)	58 (1.4%)	1.63 1.25–2.12	<0.001	1.20 0.90–1.58	0.22

Data are expressed as frequency (incidence in %). Statistical analyses were performed using multivariable logistic regression. Unadjusted odds ratios (OR) and adjusted odds ratios (aOR) are reported from multivariable logistic regression analyses.

Figure 2. Cannabinoid use and stroke by age and sex.

Prevalence of cannabinoid use (left y-axis) and stroke within 1 year after surgery (right y-axis) by patient age and sex.



Perioperative Anesthesia - 10

Socioeconomic factors, psychiatric disorders and substance abuse associated with cannabinoid use in surgical patients

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Introduction: Recreational and medical use of cannabinoids has steadily increased over the past decade and was accelerated by the legalization of medical cannabinoids in 2012 and for recreational purposes in 2016 in Massachusetts (1). Previous studies in non-surgical populations suggested that the use of cannabinoids is associated with an increased incidence of psychiatric disease, neuropsychological decline, and a higher risk of adverse cardiovascular and cerebrovascular events (2-4). There is little information about relevant other factors including socioeconomic variables associated with cannabinoid use in patients undergoing surgery. We tested the hypothesis that use of cannabinoids in surgical patients is associated with household income, psychiatric disease, and concomitant substance abuse. We further investigated whether the prevalence of cannabinoid use in surgical patients increased in the period after legislative changes in Massachusetts in 2012 and again after 2016.

Methods: Adult patients undergoing anesthesia care at a tertiary academic healthcare network in Boston (Massachusetts, USA) between 2006 and 2020 with available procedural data and pre-admission or pre-procedural notes were included in this study. Cannabinoid use before surgery was defined as recreational use of marijuana and other cannabinoids identified based on physician and nursing notes from structured patient interviews during pre-admission or pre-procedural testing, abuse was identified through International Classification of Disease Ninth and Tenth revision diagnostic codes, or prescription of medical cannabinoids. In the primary analysis, we compared estimated household income (5), disorders of the schizoaffective spectrum based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) classification and concomitant substance abuse of alcohol, medications, as well as intravenous and other drugs between patients with and without cannabinoid use (6). We then investigated whether the prevalence of cannabinoid use increased in the period between 2012 and 2016, and 2017 to 2020 as compared to before 2012 in a multivariable logistic regression model encompassing the aforementioned variables as well as patient demographics, other socioeconomic factors and comorbidities. Standardized differences and odds ratios with 95% confidence intervals are reported with alpha set to 0.05. A standardized difference ,â•0.1 was considered as clinically relevant threshold. All analyses were performed in Stata (Version 16, StataCorp, TX, USA).

Results: Among 338,839 patients undergoing surgery included in this study, 27,462 (8.1%) patients were identified who consumed cannabinoids. Most of these patients used non-medical cannabinoids (Figure 1). Patients with reported cannabinoid abuse had a 15.5% lower estimated household income (p<0.001), a higher prevalence of psychiatric disorders (30.21% versus 19.6%; p<0.001) and a higher incidence of concomitant substance abuse (9.7 % versus 3.0%; p<0.001, Table 1). Compared to recreational cannabinoid users, patients with medical cannabinoid prescriptions were on average older, more often female with a higher comorbidity load, including higher rates of cancer and psychiatric disorders (Table 2). The preoperative use of cannabinoids increased steadily throughout the study period (Figure 2). In the period of 2006 to 2011, 6.0% of patients consumed cannabinoids, as opposed to 7.7% in the period after legislation of medical cannabinoids between 2012 and 2016, and 11.7% between 2017 and 2020 after legislation of recreational cannabinoids. The increase of cannabinoid use between 2017 and 2020 remained robust in adjusted analyses in a subgroup of patients with available data for all variables (n = 62,864, ORadj 1.65; 95% CI 1.48-1.83; p<0.001 for the period after 2017-2020; (ORadj 1.31; 95% CI 1.20-1.43; p<0.001 for 2012-2016, both compared to before 2012).

Conclusion: Based on our data, patients presenting for surgery and anesthesia who use cannabinoids have a higher prevalence low household income and more often present with concomitant substance abuse and schizoaffective spectrum disorders comorbidities including depression and anxiety. Studies investigating the implications of cannabinoid use on postoperative outcomes should consider these factors to substantiate potential effects of cannabinoids.

References: 1. U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration; 2020 2. N Engl J med. 2014 Jun 5; 370(23):2219-27 3. Proc Nat Acad Sci U S A. 2012 Oct 2; 109(40): E2657-64. 4. Schizophr Bull. 2016 Sep;42(5):1262-9. 5. BMC Public Health 2020 Jan 14;20(1):60. 6. Diagnostic and Statistical Manual of Mental Disorders, 5th, ed. 2013.

Figures

Figure 1. Study Cohort.

ASA, American Society of Anesthesiologists.

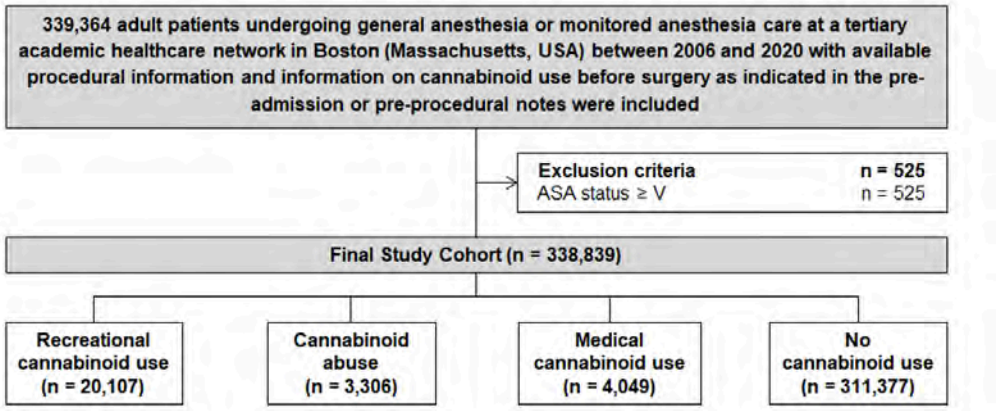

Figure 2. Cannabinoid use over time.

Cannabinoid use over time. Vertical line depicts legalization of medical and recreational cannabinoids in the state of Massachusetts.

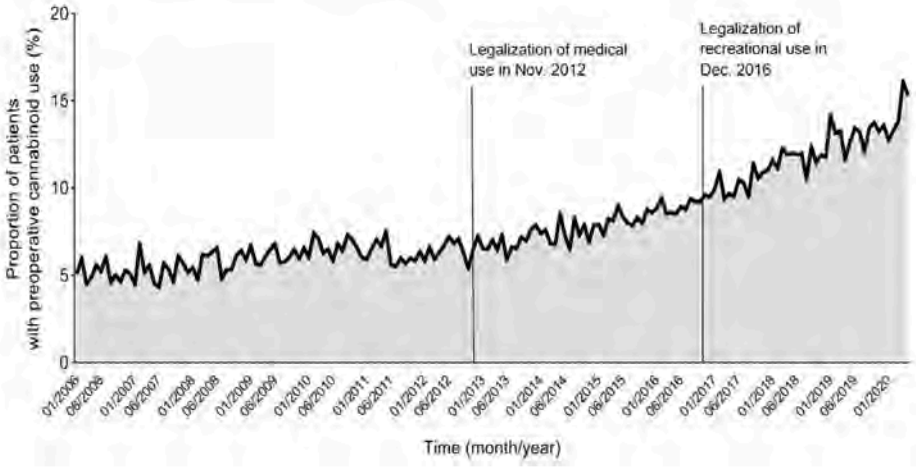

Table 1. Cohort Characteristics compared between patients who used and did not use cannabinoids.

ASA, American Society of Anesthesiologists; USD, United States Dollar; ENT, Ear, Nose, and Throat.

Characteristics	No cannabinoid use (n = 311,377)	Cannabinoid use (n = 27,462)	Standardized difference
Demographics			
Age	56.0 ± 16.5	47.6 ± 15.9	0.519
Sex, female	181,390 (58.3%)	11,318 (41.2%)	0.346
Body mass index, kg/m²	28.4 ± 6.78	27.9 ± 6.74	0.073
ASA physical status			-0.015
I	39,139 (12.6%)	3,385 (12.3%)	
II	146,415 (47.0%)	12,553 (45.7%)	
III	107,567 (34.5%)	10,093 (36.8%)	
IV	18,256 (5.9%)	1,431 (5.2%)	
Ethnicity and Race*			-0.048
Asian	12,252 (4.7%)	211 (1.0%)	
Black	27,775 (10.7%)	3,115 (14.3%)	
Hispanic	15,595 (6.0%)	1,115 (5.1%)	
Other	11,117 (4.3%)	904 (4.1%)	
Two or more	380 (0.1%)	45 (0.2%)	
White	191,737 (74.1%)	16,451 (75.3%)	
Socioeconomic factors			
Estimated household income*, USD	68,932 (39,051)	58,274 (38,883)	0.273
Federal Insurance	101,271 (32.7%)	8,362 (30.6%)	0.044
Education Level*			0.084
No education	271 (0.4%)	6 (0.1%)	
Attended high school	4,660 (7.0%)	420 (5.9%)	
Graduated high school	21,458 (32.4%)	2,656 (37.1%)	
Attended college	12,919 (19.5%)	1,661 (23.2%)	
Graduated college	26,924 (40.7%)	2,414 (33.7%)	
Marital Status*			-0.252
Divorced	19,930 (6.8%)	1,928 (7.4%)	
Life Partner	346 (0.1%)	64 (0.2%)	
Married	162,118 (55.0%)	9,164 (35.1%)	
Separated	3,817 (1.3%)	387 (1.5%)	
Single	88,105 (29.9%)	13,864 (53.1%)	
Widowed	20,459 (6.9%)	686 (2.6%)	
Preoperative Factors			
Admission type*			-0.063
Ambulatory	177,169 (57.5%)	14,862 (69.0%)	
Same-day admission	91,797 (16.7%)	8,243 (18.7%)	
Inpatient	38,404 (1.0%)	3,995 (1.3%)	
Emergency surgery	19,165 (6.2%)	2,060 (7.5%)	-0.053

Intraoperative factors			
Duration of surgery, min	122.24 (100.49)	127.71 (105.02)	-0.053
Work relative value units*	11.95 (9.90)	11.91 (10.54)	0.004
Surgical Service			-0.054
Cardiology	9,330 (3.0%)	565 (2.1%)	
Colorectal	7,533 (2.4%)	1,025 (3.7%)	
Dent/Oral/ENT	9,421 (3.0%)	994 (3.6%)	
Ophthalmology	17,296 (5.6%)	542 (2.0%)	
General Surgery	38,891 (12.5%)	3,201 (11.7%)	
Gastroenterology	11,107 (3.6%)	1,446 (5.3%)	
Gynecology	48,878 (15.7%)	3,392 (12.4%)	
Neurology	10,577 (3.4%)	1,324 (4.8%)	
Orthopedic	65,205 (20.9%)	6,386 (23.3%)	
Plastic	18,459 (5.9%)	1,853 (6.7%)	
Podiatry	7,481 (2.4%)	536 (2.0%)	
Surgical Oncology	10,823 (3.5%)	730 (2.7%)	
Thoracic	14,238 (4.6%)	1,378 (5.0%)	
Transplant	7,127 (2.3%)	923 (3.4%)	
Trauma/Surgical Critical Care	6,457 (2.1%)	770 (2.8%)	
Urology	19,344 (6.2%)	1,747 (6.4%)	
Vascular	9,210 (3.0%)	650 (2.4%)	
Comorbidities			
Myocardial Infarction	12,113 (3.9%)	896 (3.3%)	0.034
Chronic heart failure	19,749 (6.3%)	1,395 (5.1%)	0.054
Cardiovascular disease	13,639 (4.4%)	1,008 (3.7%)	0.036
Diabetes mellitus	19,717 (6.3%)	1,559 (5.7%)	0.027
Chronic kidney disease	22,753 (7.3%)	1,966 (7.2%)	0.005
Cancer	56,107 (18.0%)	5,429 (19.8%)	-0.044
Chronic liver disease	3,595 (1.2%)	724 (2.6%)	-0.108
Hypertension	124,684 (40.0%)	9,719 (35.4%)	0.097
Hyperlipidemia	112,439 (36.1%)	8,376 (30.5%)	0.119
Psychiatric diseases			
Anxiety	33,337 (10.7%)	5,070 (18.5%)	-0.221
Depression	46,479 (14.9%)	6,543 (23.8%)	-0.226
Schizoaffective disorder	795 (0.3%)	152 (0.6%)	-0.047
Schizophrenia	1,027 (0.3%)	152 (0.6%)	-0.033
Psychosis	2,763 (0.9%)	452 (1.6%)	-0.067
Psychiatric disorders**	61,005 (19.6%)	8,296 (30.2%)	-0.278
Substance Abuse			
Cocaine abuse	192 (0.1%)	124 (0.5%)	-0.077
Intravenous drug abuse	4,261 (1.4%)	1,245 (4.5%)	-0.187
Medication abuse	1,208 (0.4%)	472 (1.7%)	-0.130
Psychedelic drug abuse	49 (0.0%)	37 (0.1%)	-0.043
Alcohol abuse	5,520 (1.8%)	1,547 (5.6%)	-0.205
Substance abuse***	9,286 (3.0%)	2,657 (9.7%)	-0.247

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range (25th-75th percentile), values separated by comma).

** Descriptive data is provided in a subgroup of non-missing data.*

*** Psychiatric disorders defined as a composite consisting of anxiety, depression, schizoaffective disorders and psychosis.*
**** Substance abuse defined as a composite consisting of cocaine abuse, intravenous drug abuse, medication abuse, psychedelics, and alcohol abuse.*

Table 2. Cohort characteristics compared between medical versus non-medical cannabinoid use.

ASA, American Society of Anesthesiologists; USD, United States Dollar; ENT, Ear, Nose, and Throat.

Characteristics	Medical cannabinoid use (n = 4,308)	Non-medical cannabinoid use (n = 23,154)	Standardized difference
Demographics			
Age	57.7 ± 14.3	45.7 ± 15.5	0.800
Sex, female	2,392 (55.5%)	8,926 (38.6%)	0.345
Body mass index, kg/m²	26.6 ± 6.4	28.1 ± 6.8	-0.221
ASA physical status			0.674
I	75 (1.7%)	3,310 (14.3%)	
II	1,356 (31.5%)	11,197 (48.4%)	
III	2,453 (56.9%)	7,640 (33.0%)	
IV	424 (9.8%)	1,007 (4.3%)	
Ethnicity and Race*			0.107
Asian	81 (2.1%)	130 (0.7%)	
Black	432 (11.4%)	2,683 (14.9%)	
Hispanic	117 (3.1%)	998 (5.5%)	
Other	117 (3.1%)	787 (4.4%)	
Two or more	4 (0.1%)	41 (0.2%)	
White	3,023 (80.1%)	13,428 (74.3%)	
Socioeconomic factors			
Estimated household income*, USD	66,044 (40,317.6)	56,838 (38,441.8)	0.233
Federal Insurance	1,787 (41.7%)	6,575 (28.6%)	0.277
Education Level*			0.225
No education	1 (0.1%)	5 (0.1%)	
Attended high school	64 (4.9%)	356 (6.1%)	
Graduated high school	423 (32.2%)	2,233 (38.2%)	
Attended college	238 (18.1%)	1,423 (24.3%)	
Graduated college	586 (44.7%)	1,828 (31.3%)	
Marital Status*			
Divorced	323 (7.6%)	1,605 (7.3%)	-0.228
Life Partner	8 (0.2%)	56 (0.3%)	
Married	2,084 (49.2%)	7,080 (32.4%)	
Separated	56 (1.3%)	331 (1.5%)	
Single	1,482 (35.0%)	12,382 (56.6%)	
Widowed	280 (6.6%)	406 (1.9%)	
Preoperative Factors			
Admission type*			0.239
Ambulatory	2,007 (47.1%)	12,855 (56.3%)	
Same-day admission	1,308 (30.7%)	6,935 (30.4%)	
Inpatient	948 (22.2%)	3,047 (13.3%)	
Emergency surgery	343 (8.0%)	1,717 (7.4%)	0.020

Intraoperative factors			
Duration of surgery, min	130.98 (118.96)	127.1 (102.21)	0.035
Work relative value units*	12.4 (12.16)	11.8 (10.21)	0.056
Surgical Service			0.122
Cardio	59 (1.4%)	506 (2.2%)	
Colorectal	155 (3.6%)	870 (3.8%)	
Dent/Oral/ENT	110 (2.6%)	884 (3.8%)	
Ophthalmology	112 (2.6%)	430 (1.9%)	
General Surgery	596 (13.8%)	2,605 (11.3%)	
Gastroenterology	245 (5.7%)	1,201 (5.2%)	
Gynecology	583 (13.5%)	2,809 (12.1%)	
Neurology	212 (4.9%)	1,112 (4.8%)	
Orthopedic	563 (13.1%)	5,823 (25.1%)	
Plastic	193 (4.5%)	1,660 (7.2%)	
Podiatry	52 (1.2%)	484 (2.1%)	
Surgical Oncology	206 (4.8%)	524 (2.3%)	
Thoracic	405 (9.4%)	973 (4.2%)	
Transplant	205 (4.8%)	718 (3.1%)	
Trauma/Surgical Critical Care	212 (4.9%)	558 (2.4%)	
Urology	278 (6.5%)	1,469 (6.3%)	
Vascular	122 (2.8%)	528 (2.3%)	
Comorbidities			
Myocardial Infarction	230 (5.3%)	666 (2.9%)	0.124
Chronic heart failure	411 (9.5%)	984 (4.2%)	0.209
Cardiovascular disease	218 (5.1%)	790 (3.4%)	0.081
Diabetes mellitus	409 (9.5%)	1,150 (5.0%)	0.175
Chronic kidney disease	523 (12.1%)	1,443 (6.2%)	0.205
Cancer	2,001 (46.4%)	3,428 (14.8%)	0.730
Chronic liver disease	200 (4.6%)	524 (2.3%)	0.130
Hypertension	2,241 (52.0%)	7,478 (32.3%)	0.407
Hyperlipidemia	2,097 (48.7%)	6,279 (27.1%)	0.455
Psychiatric diseases			
Anxiety	2,097 (48.7%)	3,944 (17.0%)	0.222
Depression	1,531 (35.5%)	5,012 (21.6%)	0.311
Schizoaffective disorder	10 (0.2%)	142 (0.6%)	-0.057
Schizophrenia	4 (0.1%)	148 (0.6%)	-0.090
Psychosis	104 (2.4%)	348 (1.5%)	0.065
Psychiatric disorders**	1,898 (44.1%)	6,398 (27.6%)	
Drug Abuse			
Cocaine abuse	10 (0.2%)	114 (0.5%)	-0.043
Intravenous drug abuse	170 (3.9%)	1,075 (4.6%)	-0.034
Medication abuse	63 (1.5%)	409 (1.8%)	-0.024
Psychedelic drug abuse	1 (0.0%)	36 (0.2%)	-0.044
Alcohol abuse	1.69 (3.9%)	1,379 (6.0%)	-0.095
Substance abuse	329 (7.6%)	2,328 (10.1%)	-0.085

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range (25th-75th percentile), values separated by comma).
** Descriptive data is provided in a subgroup of non-missing data.*
*** Psychiatric disorders defined as a composite consisting of anxiety, depression, schizoaffective disorders and psychosis.*
**** Substance abuse defined as a composite consisting of cocaine abuse, intravenous drug abuse, medication abuse, psychedelic drug abuse, and alcohol abuse.*

Perioperative Anesthesia - 11 Use of a novel Relative Index to estimate changes in volume status after non-cardiac surgery

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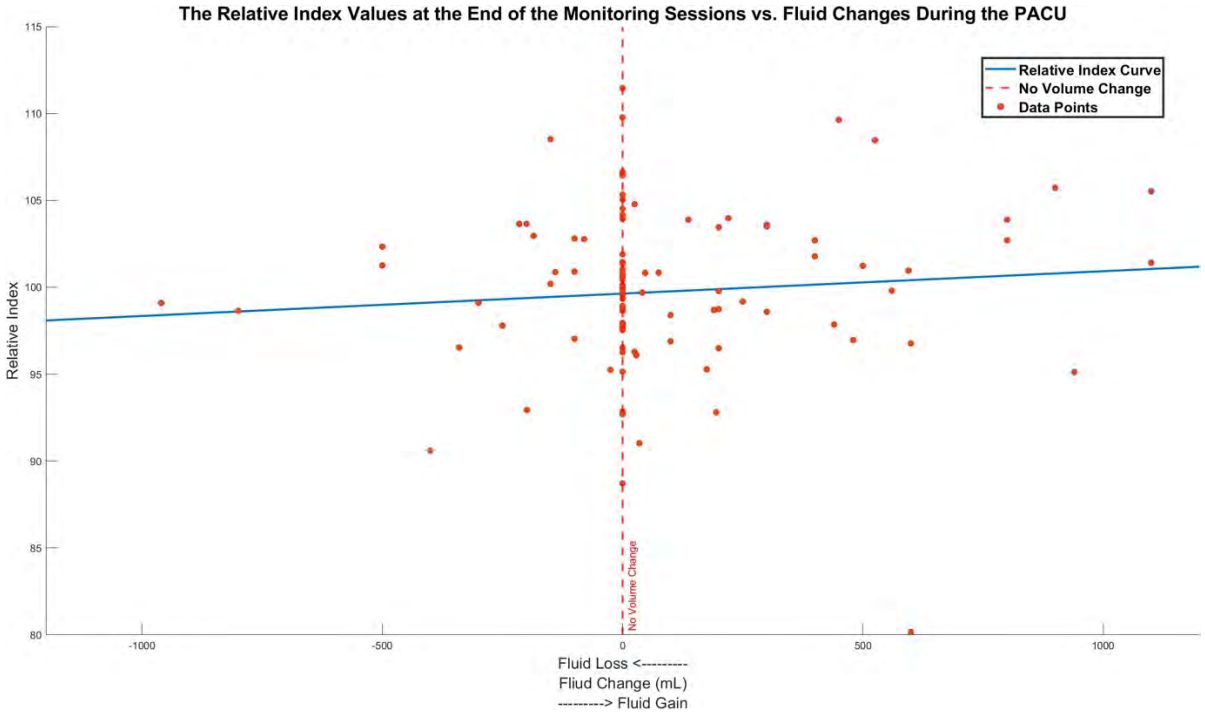
Introduction: Accurate perioperative fluid assessment remains a challenge.1 We present the first clinical use of a non-invasive patient fluid monitor being investigated to improve perioperative assessment of patient fluid status. This technology simplifies patient fluid monitoring by continuously monitoring five parameters and outputting a single value, the Relative Index (RI). The RI is a unitless parameter calculated with a proprietary algorithm from changes in the measured parameters (bioelectrical impedance, heart rate, ECG amplitude, PPG amplitude, and skin temperature), reflecting respective fluid volume change. An RI of 100 represents the patient's baseline volemic state, and deviations indicate relative fluid changes. This descriptive analysis utilized the RI to monitor relative fluid status of patients after major non-cardiac surgery.

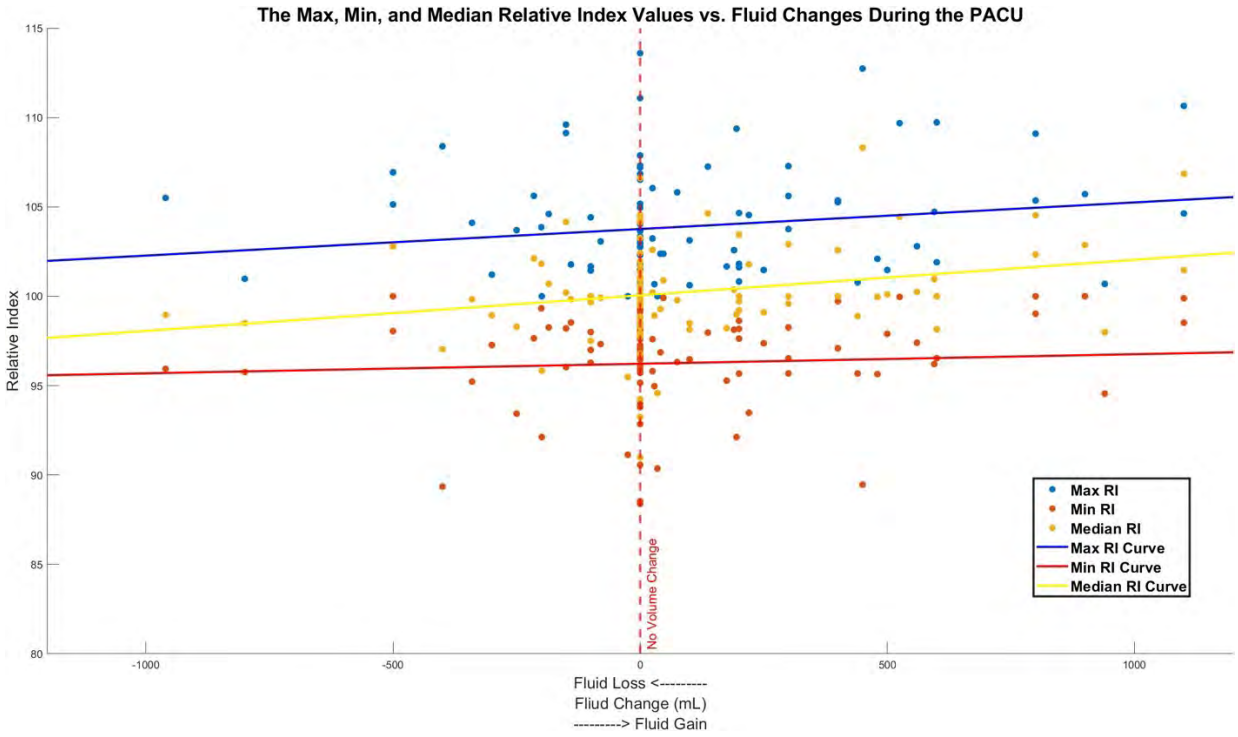
Methods: Adult patients undergoing laparoscopic or open abdominal surgery were consecutively enrolled in this prospective observational study. Patients were connected to the fluid monitor upon entering the PACU, and user-blinded monitoring continued until patients left the PACU. Perioperative fluid balances were recorded. Subjects with a RI change of ± 5 from baseline were examined further for adverse events. Data was evaluated using descriptive statistics. From 160 monitored subjects, those with one or more irregular parameters during monitoring and those with a monitoring session < 1hr were excluded from the final analysis, leaving 98 evaluable subjects. Final RI values and minimum (min), median (med), and maximum (max) RI values were correlated with total fluid changes during subjects' time in the PACU and OR/PACU combined.

Results: Mean patient age (years) was 61.2 ± 13.7 for open abdominal surgery subjects and 54.8 ± 12.8 for laparoscopic. The mean BMI for open surgery was 28.6 ± 7.4 kg/m2 and 33.8 ± 7.6 kg/m2 for laparoscopic. The min and max RI values for subjects with a net fluid change <200mL trended between 95 and 109, with a med RI of 99 ± 2.3. For net fluid changes >200mL, the lowest min RI value observed was 80, and the highest max RI value observed was 113. The med RI values continued to trend at 100 ± 2.4. Of the patients analyzed, no post-operative adverse events were observed, which correlates with the med RI for all patients remaining close to 100.

Conclusion: This novel, non-invasive method of monitoring utilizes an algorithm which simplifies patient fluid monitoring through the Relative Index (RI). Additional studies are necessary to further validate the significance of this device on improving clinical outcomes.

References: Goal-directed fluid therapy in the perioperative setting. J Anaesthesiol Clin Pharmacol. 2019 Apr;35(Suppl 1)


The Relative Index Values at the End of the Monitoring Sessions vs. Fluid Changes During the PACU
Relative Index Curve
No Volume Change
Data Points
Relative Index
115
110
105
100
95
90
85
80
-1000
-500
0
500
1000
No Volume Change
Fluid Loss <---------
Fliud Change (mL)
---------> Fluid Gain


The Max, Min, and Median Relative Index Values vs. Fluid Changes During the PACU
Max RI
Min RI
Median RI
Max RI Curve
Min RI Curve
Median RI Curve
Relative Index
115
110
105
100
95
90
85
80
-1000
-500
0
500
1000
No Volume Change
Fluid Loss <---------
Fliud Change (mL)
---------> Fluid Gain

Perioperative Anesthesia - 12 Variation in anesthesiology provider-volume for complex gastrointestinal cancer surgery: a population-based study.

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Introduction: While the association between higher hospital and surgeon procedure-volume and better patient outcomes is well defined, anesthesiologists' contribution to volume-outcome is understudied. We previously showed that anesthesiologists with higher provider-volume (PV) of complex gastrointestinal (GI) cancer surgery have better patient outcomes. However, the factors linking anesthesiology practice, processes of care, and team organization to volume-outcome are unknown. We examined the extent and importance of between-hospital and between-anesthesiologist variation in anesthesiology provider-volume (PV) and delivery of HV anesthesiology care.

Methods: We identified patients who underwent elective complex GI cancer surgery (esophagectomy, hepatectomy, pancreatectomy) using linked administrative health datasets (2007-2018). Anesthesiology PV was the annual number of complex GI cancer surgery done by the primary anesthesiologist in the 2 years before the index surgery. HV anesthesiology care was care by an anesthesiologist with PV >6 procedures/year (defined using restricted cubic splines in previous work). We used funnel plots to describe variation in anesthesiology PV and delivery of HV care adjusted for patient case-mix. Hierarchical regression models quantified between-anesthesiologist and between-hospital variation in delivery of HV care use with variance partition coefficients (VPC) and median odds ratios (MOR), adjusted for patient case-mix.

Results: Of 7,893 patients cared for by 737 unique anesthesiologists and 163 unique surgeons at 17 hospitals, 53.3% received HV anesthesiology care. Funnel plots showed variation in anesthesiology PV (median ranging from 1.5, IQR 1-2 to 11.5, IQR 8-16) and delivery of HV care (ranging from 0 to 87%) across hospitals. This variation persisted over time. After adjusting for patient characteristics, 32% (VPC 0.32) and 16% (VPC 0.16) were due to systematic between-anesthesiologist and between-hospital differences, respectively. This translated to an anesthesiologist-level median OR of 3.04 (95%CI 2.14-.77) and hospital-level median OR of 4.81 (95%CI 3.27-10.30).

Conclusion: Substantial variation in anesthesiology PV and delivery of HV anesthesiology care existed for complex GI cancer surgery across hospitals, within a regionalized cancer surgery system. The primary anesthesiologist and the hospital were key determinants of the variation in HV anesthesiology care delivery. After accounting for patient case-mix, similar patients had a 3-fold and 4.8-fold increase in the odds of receiving HV anesthesiology care depending on who is their anesthesiologist or which hospital they are operated at, respectively. This suggests that interventions targeted at anesthesiology structures of care and team organization could reduce variation, with a view to improve patient outcomes.

Perioperative Anesthesia - 13 Total Intravenous Anesthesia (TIVA) vs. Inhalational Anesthesia for Cancer Resection: The Anesthesiologist's Perspective

Anoushka Afonso[1], Ricardo Lopez-Betancourt[1], Janice Zhang[1], Sabrina Lin[1], Mithat Gonen[1], Vijaya Gottumukkala[2], Gregory W Fischer[3]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, [2]The University of Texas MD Anderson Cancer Center, Houston, TX, [3]Memorial Sloan Kettering Cancer, New York, NY

Introduction: TIVA and volatile anesthetics are two common techniques used for induction and maintenance of general anesthesia. Strong evidence has shown that TIVA, compared to inhalational anesthesia, offers a more favorable side effect profile in adult patients, including a lower risk of postoperative nausea and vomiting (PONV) by as much as 38% (1), as well as a rapid recovery profile (2). Some in vitro studies have revealed anti-metastatic effects of the intravenous anesthetic propofol (3); however conflicting results have been found in clinical studies (4-7). TIVA is more burdensome to setup and manage by the anesthesiologist, especially in the US where automated TIVA pumps/targeted controlled infusion (TCI) systems have not been approved for perioperative use (8). Inhalational anesthesia is much more commonly used because of greater familiarity and its ease of setup and monitoring (9). Inhalational anesthesia, compared to TIVA, has also been shown to offer improved cardiac, pulmonary, and cerebral protection (2,10). As more evidence begins to emerge on TIVA's indications for use within oncologic surgery, it is crucial to understand anesthesiologists' current landscape of use of TIVA compared to inhalational anesthetics. Information on the factors influencing TIVA's use remains limited. A study conducted by Lim et al. of 275 anesthesiologists conducted in Australia assessed practice patterns and perspectives comparing TIVA and inhalational anesthetics (11). Another international study of 763 anesthesiologists in Australia, Asia, and Europe assessed factors influencing use of TIVA (9), but no such studies to date have been conducted in the US. There is little insight on the frequency of use of TIVA among anesthesiologists in the US and specifically within oncologic surgery. Our study aims to address this gap in knowledge and investigate TIVA - its practices, perceived benefits, and barriers - compared to inhalation anesthetics among anesthesiologists in designated cancer centers in the US. Ultimately, identifying anesthesiologists' understanding, indications for use and barriers for TIVA will help inform future guidelines and increase TIVA uptake in the profession.

Methods: Data for this study was collected from a survey conducted between September 2019 and February 2020 and between May 2021 and August 2021. The survey consisted of 21 questions based on the 18-question survey by Lim et al. that was used in a study previously conducted among Australian anesthesiologists. [2] This survey assessed the practice patterns and perspectives of inhalational anesthesia versus TIVA among US anesthesiologists at 10 institutions within the Alliance of Dedicated Cancer Centers. Statistical analyses were performed with R (version 4.1.0, R Foundation).

Results: 281 anesthesiologists were contacted by email. 78 completed the entire survey and were included in the analysis, yielding an overall 27.8% response rate. Physician characteristics are shown in Table 1. Respondents were from the following US regions: New England, Middle Atlantic, East North Central, South Atlantic, West south Central, and Pacific. 1 respondent does not primarily practice in the US. 87.2% of participants practice at a designated cancer center, and 12.8% practice at a university hospital. 84% of respondents practice in an impatient setting, and 16% practice in an outpatient setting. Only 16% of respondents use TIVA for >50% of the cases.

Conclusion: Given that evidence remains uncertain if TIVA is the anesthetic of choice for oncologic surgery, anesthesiologists among cancer centers in the US are generally slow to uptake TIVA. The results from this survey also show that patterns of practice among anesthesiologists in the US are like those previously explored among anesthesiologists around the world, but familiarity levels with TIVA may be lower in the US. Given the results of this study, we infer that the usage

of TIVA among all US hospitals, considering all surgical cases beyond cancer resections, is even lower than what we have found. Therefore, broadly increasing TIVA uptake poses an even greater challenge and requires more evidence-driven understanding of the benefits of TIVA versus inhalational anesthetics and addressing TIVA's barriers to use. As variations in practice and perspectives remain, prospective randomized control trials would provide stronger evidence to inform a preferred anesthetic method for oncologic surgery and provide improved treatment for cancer patients worldwide.

References: 1. Anaesthesia. 2020/01/01 2020;75(S1):e90-e100. 2. Anaesth Intensive Care. Sep 2018;46(5):480-487. 3. Digestive Medicine Research. 2020;3 4. Anesthesiology. 2019;130(1):31-40. 5. Oncotarget. 2017;8(52):90477-90487. 6. Cancer Control. Jan-Mar 2018;25(1):1073274818775360. 7. Br J Anaesth. May 2021;126(5):921-930. 8. Anesthesia & Analgesia. 2016;122(1):70-78. 9. Anaesthesia and Intensive Care. 2018;46(3):332-338. 10. BMJ Open. Oct 11 2017;7(10):e014629. 11. Anaesthesia and Intensive Care. 2018/09/01 2018;46(5):480-487.

Figure 1. Percentage of Cancer Resection Cases using TIVA

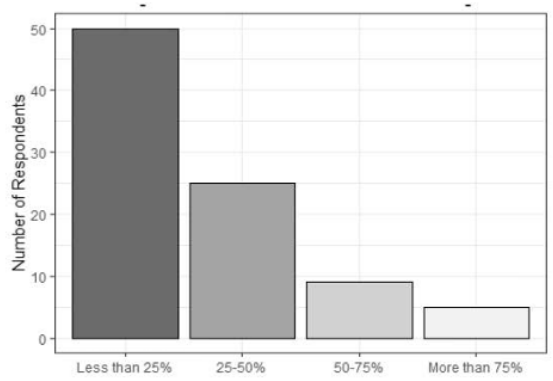


Figure 2. Technical Aspects of TIVA vs Inhalational Anesthetics

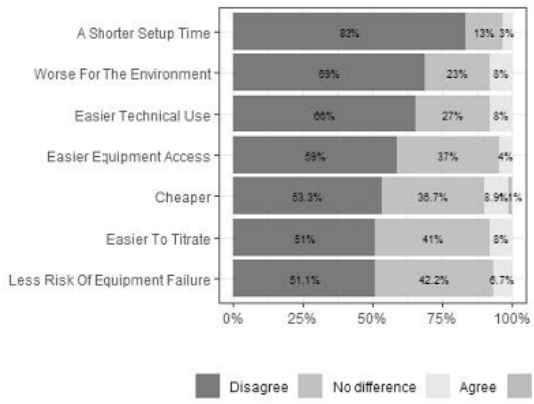


Figure 3. Barriers to TIVA use

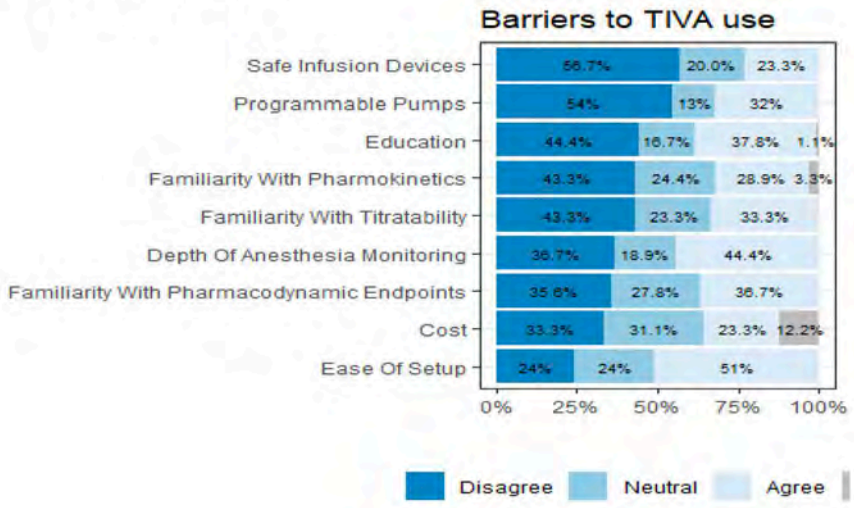


Figure 4. TIVA Usage in Clinical Settings

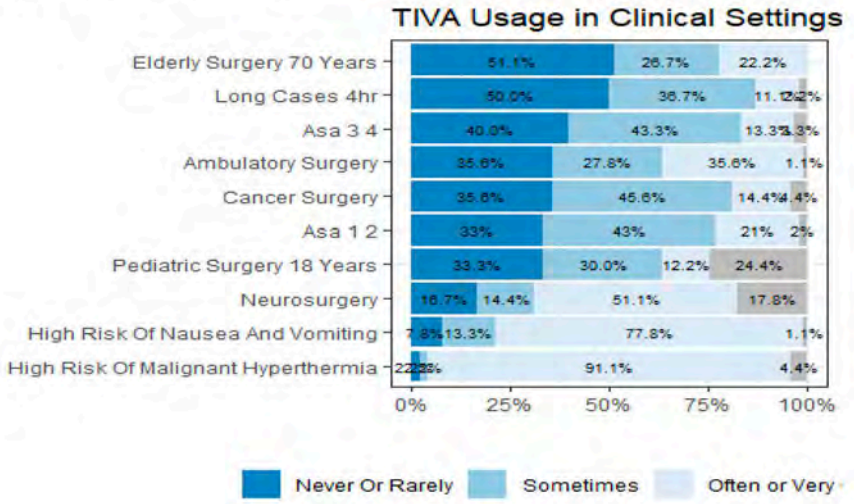


Figure 6. Clinical Impact of TIVA vs. Inhalational Anesthetics

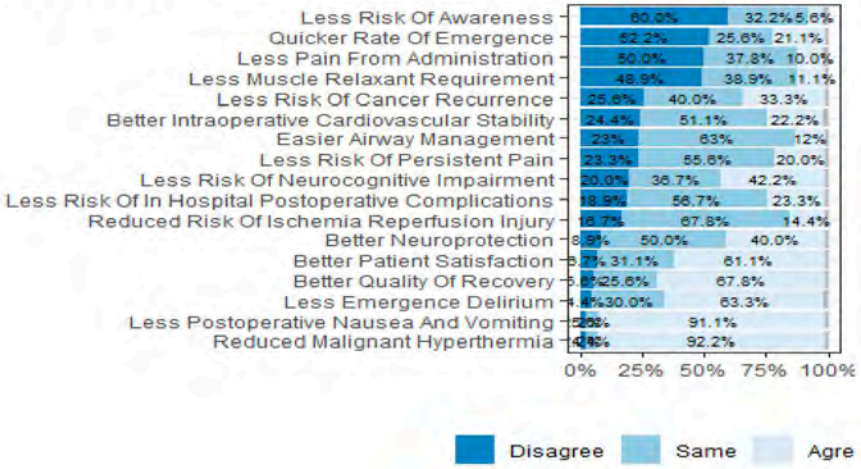


Figure 6. TIVA Perspectives

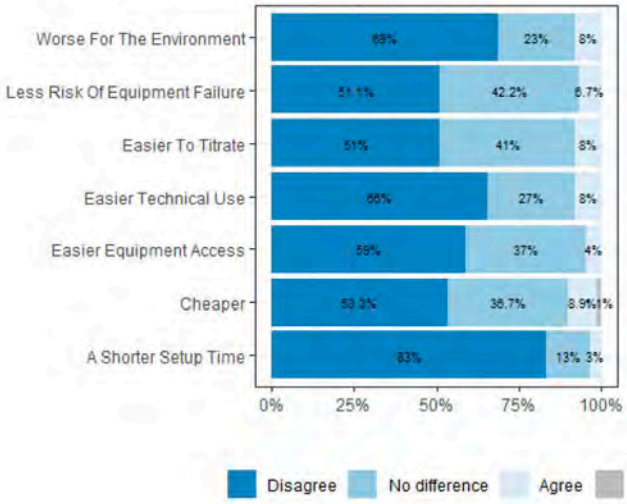


Table 1. Demographic Characteristics of Respondents

Characteristic	N = 90
Location of Practice (Within United States)	
New England (Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut)	2 (2.5%)
Middle Atlantic (New York, New Jersey, Pennsylvania)	30 (38%)
East North Central (Ohio, Indiana, Illinois, Michigan, Wisconsin)	10 (13%)
West North Central (Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas)	0 (0%)
South Atlantic (Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida)	8 (10%)
West South Central (Arkansas, Louisiana, Oklahoma, Texas)	23 (29%)
Mountain (Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada)	0 (0%)
Pacific (Washington, Oregon, California, Alaska, Hawaii)	5 (6.3%)
N/A (I do not work in the US)	1 (1.3%)
Unknown	11
Gender	
Female	26 (32%)
Male	51 (64%)
Other (please specify)	3 (3.8%)
Unknown	10
Percentage of Cancer Resection Cases	
Less than 25%	3 (3.8%)
25-50%	11 (14%)
50-75%	6 (7.5%)

More than 75%	60 (75%)
Unknown	10
Institution Type	
Cancer Center	70 (88%)
University Hospital	10 (12%)
Unknown	10
Workplace Setting	
Inpatient	68 (85%)
Outpatient	12 (15%)
Unknown	10
Year of Anesthesia Training Completion	
Prior to 1980	2 (2.5%)
1980-1984	4 (5.0%)
1985-1989	3 (3.8%)
1990-1994	10 (12%)
1995-1999	8 (10%)
2000-2004	10 (12%)
2005-2009	13 (16%)
2010-2014	21 (26%)
2015 or later	9 (11%)
Unknown	10

Perioperative Anesthesia - 14 Cognitive and cerebrospinal fluid Alzheimer's Disease biomarker changes over time in older surgical patients and matched nonsurgical controls

Megan Wong[1], Melody Reese[2], Mary Cooter[2], Jeffrey N Browndyke[2], Joseph P Mathew[3], Harvey J Cohen[2], Heather E Whitson[2], Miles Berger[2]

[1]Duke University School of Medicine, Durham, NC, [2]Duke University Medical Center, Durham, NC, [3]Duke University, Durham, NC

Introduction: Some older patients have lasting cognitiv impairment after anesthesia/surgery,[1,2] though it remains unclear if this cognitive decline is caused by anesthesia/surgery versus whether it simply reflects the natural cognitive trajectory due to other patient risk factors.[2,5,6] Some human studies have found that older adults have altered postoperative CSF levels of AD-related biomarkers, such as tau and p-tau, raising the possibility that perioperative care could contribute to long term cognitive decline by accelerating AD pathogenesis.[6-8] Yet, to our knowledge, no prior study has compared CSF AD-related biomarker and cognitive trajectories over time in surgical patients and matched non-surgical controls.

Methods: We prospectively enrolled 140 patients age ≥60 years old undergoing major non-cardiac, non-neurologic surgery under general anesthesia for >2 hours, and 51 non-surgical controls who were matched to the surgical cohort based on age, sex, and education via strata-based matching. CSF samples were obtained by lumbar puncture at baseline, 24 hrs, 6 weeks after surgery in surgical patients and at the same time intervals in controls. CSF levels of Aβ42, tau, and phosphorylated tau (p-tau) were measured at according to established methods.[9,10] Cognitive testing was administered at baseline and 6 weeks postoperatively and the cognate time intervals in the control group. Cognitive performance was measured by the continuous cognitive index (CCI),[3] a weighted average of multiple individual tests in our test battery. AD biomarker and CCI trajectories and were compared overall via Friedman's test, and at each time point by Wilcoxon Rank Sum tests.

Results: The surgical and non-surgical groups were well-matched on age, gender, and years of education, yet a higher percentage of the non-surgical controls had baseline CSF biomarker evidence of AD pathology (p=0.002) even though there was no difference in baseline MMSE scores between groups (p=0.577) (Table 1). There was no significant difference between the surgical and control groups in median CSF Aβ42, tau, p-tau, tau/Aβ42, or p-tau/Aβ42 change from baseline to 24 hours, 6 weeks (p>0.05 for all). There was also no difference in CCI change from baseline to 6 weeks later (p>0.05) between the surgical and matched non-surgical control groups (Figure 1). In a multivariate analysis for predictors of CCI change at 6 weeks, there was a significant effect of baseline CCI (p=0.009) but no effect of group (surgical vs non-surgical p=0.159).

Conclusion: These findings suggest that non-cardiac, non-neurological surgery does not cause acceleration of AD pathology or cognitive decline. However, accurate comparison of cognitive decline or CSF biomarker changes between surgical and non-surgical patients selected based on demographic matching (i.e. rather than randomization) remains challenging given our finding that groups with matching demographic information may nonetheless have significant differences in preclinical AD pathology.

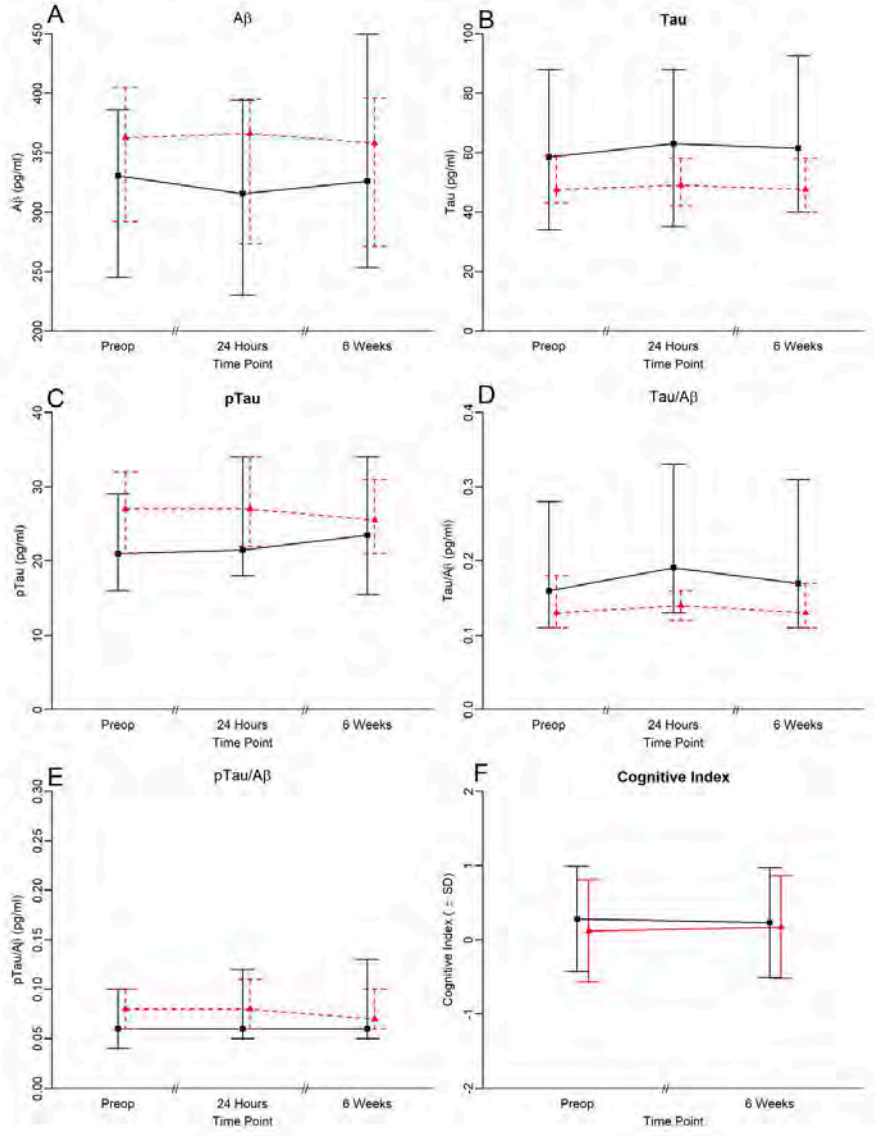
References: 1. Lancet. 1955; 269: 259-63 2. J Anaesthesiol Clin Pharmacol. 2015; 31: 30-6 3. Anesthesiology. 2010; 112: 852-9 4. Anesthesiology. 2008; 108: 18-30 5. J Alzheimers Dis. 2011; 24: 201-16 6. BMC Anesthesiol. 2019; 19: 241 7. Anesthesiology. 2016; 124: 353-61 8. Anesthesiology. 2011; 115: 727-32 9. Acta Neuropathol. 2011; 121: 597-609 10. Alzheimers Dement. 2010; 6: 230-8

Table 1. Patient Summary

	Surgical (N=107)	Control (N=46)	p value
Patient Demographics			
Age	68 [64, 73]	68 [64, 73]	0.921[1]
White/Caucasian Race	96 (89.7%)	36 (78.3%)	0.059[2]
Male Sex	67 (62.6%)	28 (60.9%)	0.838[2]
Years of Education	16 [13, 18]	16 [14, 18]	0.214[1]
Baseline Cognitive Performance			
BL MMSE	29 [28, 29]	29 [28, 30]	0.577[1]
BL MMSE <25	5 (4.7%)	1 (2.2%)	0.669[4]
Baseline Cognitive Index	0.12 (0.69)	0.28 (0.71)	0.205[3]
Baseline Biomarkers			
APOE4 Positive*	34 (32.1%)	12 (27.9%)	0.618[2]
BL Tau**	47.5 [43.0, 59.0]	58.5 [34.0, 88.0]	0.239[1]
BL p-Tau**	27 [21, 32]	21 [16, 29]	0.006[1]
BL AB**	362.5 [292.0, 405.0]	330.5 [245.0, 386.0]	0.166[1]
BL Tau/AB**	0.13 [0.11, 0.18]	0.16 [0.11, 0.28]	0.306[1]
BL p-Tau/AB**	0.08 [0.06, 0.10]	0.06 [0.04, 0.10]	0.052[1]
Shaw Group**			0.002[4]
A+ | T+	2 (2.0%)	3 (6.5%)	
A+ | T-	15 (15.3%)	10 (21.7%)	
A- | T+	1 (1.0%)	6 (13.0%)	
A- | T-	80 (81.6%)	27 (58.7%)	

[1]Wilcoxon [2]Chi-Square [3]Chi-Square [4]Fisher Exact
*Missing for1 Surgical patient, 3 Control patients
**Missing for 9 Surgical patients

Figure 1. Trends in CSF AD biomarkers and cognitive function



Perioperative Anesthesia - 15 How do you take your coffee before anesthesia? A randomized controlled crossover study comparing gastric emptying with black coffee vs coffee with half and half vs coffee with non-dairy creamer.

Jessica Yeh[1], Nadir Sharawi[1], Mohamed Abdeldayem[1], Nicholas Kaukis[1]

[1]University of Arkansas for Medical Sciences, Little Rock, United States of America

Introduction: An important component in the pre-operative patient evaluation is to determine fasting status to reduce the risk of pulmonary aspiration.[1] The American Society of Anesthesiologists guidelines recommend a minimum fasting period of 6 hours for nonhuman milk and 2 hours for clear liquids including black coffee. The European Society of Anaesthesiology states tea or coffee with some milk could be considered clear fluid but there is not a consensus.[2] About 68% of adults in the United States consume coffee with add-ins such as cream or sugar.[3] This study aims to assess the effects that dairy or sugar additives to coffee will have on gastric emptying via serial ultrasound of the gastric antrum in healthy adults.

Methods: This randomized controlled crossover study with 3 arms received institutional review board approval and was registered at ClinicalTrials.gov (NCT04786691). One arm was the consumption of 355 ml black coffee. The second was 355 ml coffee with 30 ml of half and half and the third arm was 355 ml coffee with 30 ml of liquid non-dairy coffee creamer. Study volunteers participated in all 3 arms of the study, the order of which was randomized, with a minimum 2-day washout period between each arm (Fig. 1). A total of 24 volunteers were screened between the ages of 18 and 65. Study participants were excluded if they had a history of diabetes, delayed gastric emptying, previous gastric surgery, lactose intolerance, or current pregnancy (Table 1). After informed consent, participants were instructed to consume nothing by mouth for 6 hours. The cross-sectional area (CSA) of the gastric antrum was measured using ultrasound with the participant in the right lateral decubitus position which served as the baseline measurement. The participant then consumed one of the 3 coffee options according to the randomization sequence and returned in 2 hours to repeat the gastric antrum ultrasound measurement. The primary outcome was the difference between gastric volume post coffee consumption compared to the baseline gastric volume which was calculated using the participant's age and CSA (Fig. 2).[4] Descriptive statistics were used for data analysis.

Results: 18 participants completed the study. The mean gastric volume difference was 13 ml (95% CI, -0.6 to 26.6) after black coffee alone, 5 ml (95% CI, -8.6 to 18.6) with half and half, and -1.5 ml (95 CI%, -15 to 12.1) with non-dairy creamer (Table 2, Fig. 3).

Conclusion: This pilot study demonstrated no significant difference in gastric volume 2 hours after consumption of black coffee, coffee with half and half, and coffee with non-dairy creamer. These results are consistent with other studies performed in Europe demonstrating no difference in gastric volume with the addition of milk to coffee or tea.[5,6] We used half and half and non-dairy creamer as additives in our study as this is more representative of an American demographic. Further studies with larger sample sizes would be beneficial to determine its applicability to the general population.

References: 1. Anesthesiology. 2017;126:376,Äì393. 2. Eur J Anaesthesiol. 2011;28(8):556-569. 3. Public Health. 2017;146:1-3. 4. Anesth Analg. 2013;116(2):357-363. 5. Eur J Anaesthesiol. 2016;33(6):457-462. 6. Br J Anaesth. 2014;112(1):66-71.

Figure 1. Consort Diagram

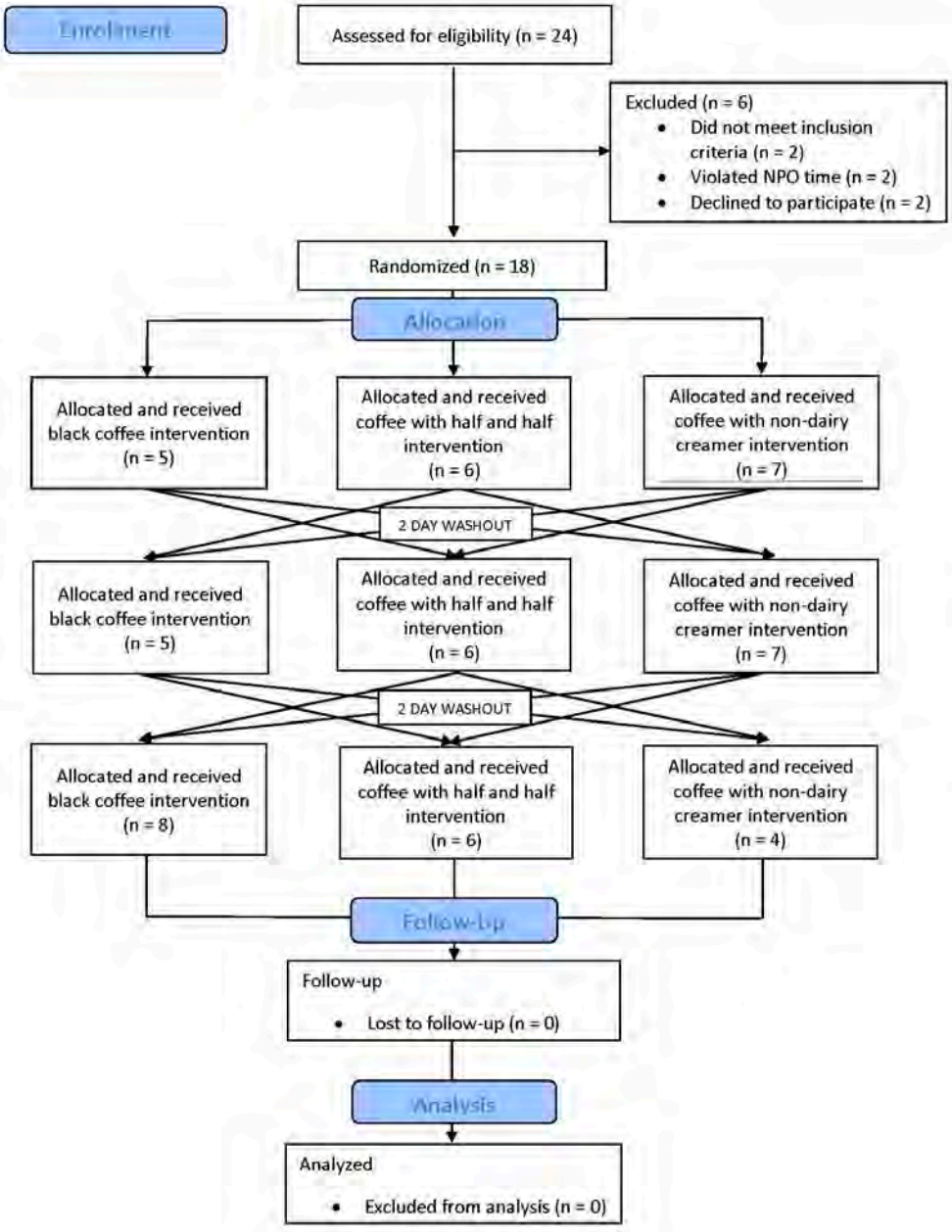


Table 1. Characteristics of Participants

	Total Number	Median	Minimum	Maximum	Interquartile Range
Gender (male/female)	7 / 11				
Age (years)	18	34	28	55	30 - 42
Height (cm)	18	166	150	191	165 - 182
Weight (kg)	18	72	50	100	62 - 81
BMI (kg / m^2)	18	24	20	34	23 - 26

Figure 2. Predictive model equation used to estimate gastric volume

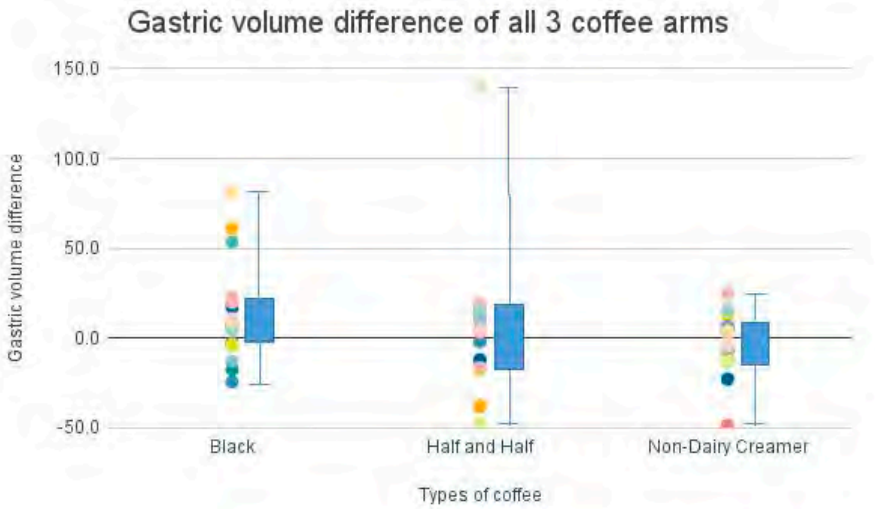
Predictive model used to assess gastric volume using cross-sectional area (CSA) of gastric antrum in the right lateral decubitus position and age. Applicable to non-pregnant adults for gastric volumes up to 500 ml.[4]

$$\text{GASTRIC VOLUME (ML)} = (27.0 + 14.6 * \text{CSA}) - (1.28 * \text{AGE})$$

Table 2. Difference in gastric volume between all 3 coffee arms

	Mean Difference Gastric Volume (95% CI)	Standard Deviation	Minimum	Maximum
Black coffee	13 (-0.6 to 26.6)	27.4	-24.4	80.9
Half and half	5 (-8.6 to 18.6)	39.6	-46.8	139.8
Non-dairy creamer	-1.5 (-15.1 to 12.1)	16.7	-48.5	24.8

Figure 3


Gastric volume difference of all 3 coffee arms
150.0
100.0
50.0
0.0
-50.0
Gastric volume difference
Black
Half and Half
Non-Dairy Creamer
Types of coffee

Perioperative Anesthesia -16

Telemedicine improves Anesthesia Pre-operative Evaluation Appointment Adherence: A Retrospective Analysis

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[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, [2]Ronald Reagan UCLA Medical Center, Los Angeles, CA, [3]Hospital for Special Surgery, New York, NY, [4]UCLA Health, Los Angeles, CA

Introduction: Amidst the COVID-19 pandemic, the sudden demand for virtual medical visits drove the drastic expansion of telemedicine across all medical specialties [1]. Current literature demonstrates limited knowledge on the impact of telehealth on appointment adherence particularly in preoperative anesthesia evaluations [2-4]. We hypothesized that there would be increased completion of preoperative anesthesia appointments in patients who received telemedicine visits.

Methods: We performed a retrospective cohort study of adult patients at UCLA who received preoperative anesthesia evaluations by telemedicine or in-person within the Department of Anesthesiology and Perioperative Medicine from January to September 2021 and assessed appointment adherence. The primary outcome was incidence of appointment completion. The secondary outcomes included appointment no show and cancellations. Patient demographic characteristics including sex, age, ASA physical status class, race, ethnicity, primary language, interpreter service requested, patient travel distance to clinic, and insurance payor were also evaluated. Patient reported reasons for cancellations were also reviewed and categorized into thematic groups by two physicians. Statistical comparison was performed using independent samples t test, Pearson's chi-square, and Fischer's exact test.

Results: Of 1332 patients included in this study, 956 patients received telehealth visits while 376 patients received in-person preoperative anesthesia evaluations. Compared to the in-person group, the telemedicine group had more appointment completions (81.38% vs 76.60%, p = 0.0493). There were fewer cancellations (12.55% vs 19.41%, p = 0.0029) and no statistical difference in appointment no-shows (6.07% vs 3.99%, p = 0.1337) in the telemedicine group (Table 1, Figure 1). Compared to the in-person group, patients who received telemedicine evaluations were younger (55.81 ¬± 18.38 vs 65.97 ¬± 15.19, p < 0.001), less likely Native American and Alaska Native (0.31% vs 1.60%, p = 0.0102), more likely of LatinX ethnicity (16.63% vs 12.23%, p = 0.0453), required less interpreter services (4.18% vs 9.31%, p = 0.0003), had more private insurance coverage (53.45% vs 37.50%, p < 0.0001) and less Medicare coverage (37.03% vs 50.53%, p < 0.0001) (Table 2). Main reasons for cancellation included patient request, surgery rescheduled/cancelled/already completed, and change in method of appointment (Table 3).

Conclusion: In 2021, preoperative anesthesia evaluation completion was greater in patients who received telemedicine appointments compared to those who received in-person evaluations at UCLA. We also demonstrate potential shortcomings of telemedicine in serving patients who are older, require interpreter services, or are non-privately insured. Knowledge of these factors can provide feedback to improve access and equity to telehealth for patients from all backgrounds, particularly during the COVID pandemic as virtual evaluations increase.

References: [1] The Impact of Telehealth Implementation on Underserved Populations and No-Show Rates by Medical Specialty During the COVID-19 Pandemic, 27, 874-880, 2021. [2] Does the Choice Between a Telehealth and an In-Person Appointment Change Patient Attendance?, 27, 733-738, 2021. [3] Adherence and acceptability of telehealth appointments for high-risk obstetrical patients during the coronavirus disease 2019 pandemic, 2, 1-9, 2020. [4] Socioeconomic Disparities in Patient Use of Telehealth during the Coronavirus Disease 2019 Surge,147, 287-295, 2021.

	Telemedicine	In-Person Clinic	P-Value
Total Patients	956	376	0.0029**
Cancelled	120 (12.55%)	73 (19.41%)	0.0014**
No-Show	58 (6.07%)	15 (3.99%)	0.1337
Completed	778 (81.38%)	288 (76.60%)	0.0493**

Table 1. Comparison of cancellation, no-show, and completion of appointments between patients who received telemedicine or in-person preoperative evaluation appointments. Data presented as n (%). **P values < 0.05 were considered significant.

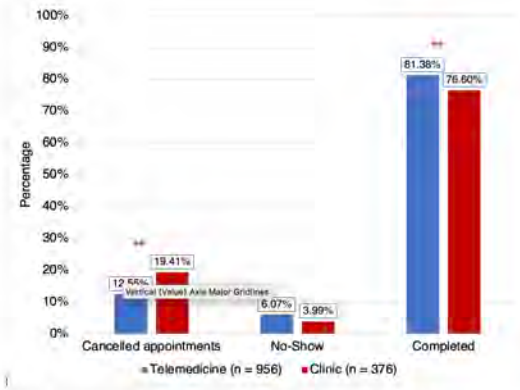

Figure 1. Comparison of cancellation, no-show, and completion of appointments between patients who received telemedicine or in-person preoperative evaluation appointments. **P values < 0.05 were considered significant.

	Telemedicine	In-Person Clinic	P-Value
Sex			0.0435**
Male	309 (32.32%)	148 (39.36%)	
Female	646 (67.57%)	228 (60.64%)	
Age	55.81 (18.38)	65.97 (15.19)	<0.001**
ASA			0.3804
I	12 (1.26%)	3 (0.80%)	
II	302 (31.59%)	110 (29.26%)	
III	598 (62.55%)	238 (63.30%)	
IV	44 (4.60%)	25 (6.65%)	
Race			
Native American and Alaska Native	3 (0.31%)	6 (1.60%)	0.0102**
Asian	72 (7.53%)	30 (7.98%)	0.7823
Black or African American	84 (8.79%)	31 (8.24%)	0.7513
Declined	29 (3.03%)	9 (2.39%)	0.5278
Other	172 (17.99%)	58 (15.43%)	0.2647
White	588 (61.51%)	236 (62.77%)	0.6701
Native Hawaiian and other Pacific Islander	1 (0.10%)	2 (0.53%)	0.1387
Unknown	7 (0.73%)	4 (1.06%)	0.5472
Ethnicity			
LatinX	159 (16.63)	46 (12.23%)	0.0453**
Not LatinX	742 (77.62%)	309 (82.18%)	0.066
Declined	9 (2.39%)	25 (2.62%)	0.8176
Unknown	30 (3.14%)	12 (3.19%)	0.9600
English as Primary Language	903 (94.46%)	324 (86.17%)	<0.001**
Interpreter Required	40 (4.18%)	35 (9.31%)	0.0003**
Distance to Clinic	99.84 (343.09)	91.55 (503.21)	0.7693
Insurance Coverage			
Medicaid	57 (5.96%)	30 (7.98%)	0.18
Medicare	354 (37.03%)	190 (50.53%)	<0.0001**
Private	511 (53.45%)	141 (37.50%)	<0.0001**
Self-Pay	1 (0.10%)	0 (0%)	0.5304
Other	8 (0.84%)	6 (1.60%)	0.2215
Unknown	25 (2.62%)	9 (2.39%)	0.8176

Table 2. Demographic Characteristics between patients who received telemedicine and in-person Clinic Preoperative Evaluations. Data presented as n (%) or mean (SD). **P values < 0.05 were considered significant.

Reasons for Cancellation	Percentage
Patient request/reason	45 (32.61%)
Surgery rescheduled/cancelled/already completed	23 (16.67%)
Change of method of appointment	17 (12.32%)
Time conflict with another medical appointment	10 (7.25%)
Other	8 (5.8%)
System error	8 (5.8%)
Team request	8 (5.8%)
Appointment no longer needed	7 (5.07%)
Patient no show/late	6 (4.35%)
Appointment Rescheduled	3 (2.17%)
Technology Issue	3 (2.17%)

Table 3. Patient reported reasons for cancellations. Data presented as n (%).

Perioperative Anesthesia - 17 A 5-year, 830,528 Patient, Multi-Center Study of Inpatient Post-Surgical Morbidity (Pre and Post COVID-19)

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Introduction: Annually, 234 million major operations are performed worldwide,[1] 48 million of which are performed in the United States. Of these, between 5% and 45% will suffer post-surgical complications [2,3,4,5] that increase physical and psychosocial suffering [6], hospital length of stay [7], increased level of care at discharge,[7,8] cost, [9,10] and decreased long term survival.[11, 12] It is also known that variation in post-surgical complication rates exist between surgical service lines and between specific procedures within a service line. [13] Furthermore, older patients following non-cardiac surgery have been shown to experience higher postoperative complication rates.[14, 15] The primary purpose of this large, 830,528 patient, multi-center, 5-year, retrospective database study was to validate the findings of several smaller trials showing that major inpatient surgery is associated with high post-surgical complication rates. Secondary findings include type of complication, day on which the complication occurs, and associations with both age and gender. Pre and post COVID-19 pandemic post-surgical complications rates are described. This study offers a more accurate picture of perioperative morbidity than is provided by self-reported event data, and, thus, better informs perioperative shared-decision making and the development of best-evidence pathways and protocols to mitigate these complications.

Methods: This is a retrospective, 35-center, administrative database study including patients who were selected based on inpatient surgical status between October 1, 2017 and November 10, 2021 who were cared for by Envision Medical Group's anesthesiology and hospital medicine service lines. Current Procedural Terminology (CPT) codes for specific surgical procedures were bucketed into surgical service lines, such as cardiac surgery, thoracic surgery, general surgery, neurosurgery, urology, gynecology, orthopedics, etc. Post-surgical morbidities were defined and bucketed into categories, such as pulmonary, cardiac, renal, neurologic, hemorrhagic, and septic complications using International Classification of Diseases, Tenth Revision (ICD-10) codes. Age, gender, and postoperative day that a complication was reported were abstracted from the database. The proportion of post-surgical complications was defined as the total number of complications divided by the total surgical inpatient population, which was further stratified by service line, procedure type, and the post-operative day on which the complication was noted. (Figure 1)

Results: Study Dates: 10/1/2017 - 11/10/2021 Surgical Inpatients: n= 830,528, Total Complications: n= 71,513, Proportion of Complications: Average 8.61% Range [0.45% - 26.55%] Proportion of Complications for Specific Surgical Service lines: Cardiac Surgery: 26.55%, Neurosurgery: 24.13%, Thoracic Surgery: 20.1%, Vascular Surgery: 13.78%, General Surgery: 11.61%, Orthopedic Surgery: 10%, Urology: 8.45%, Gynecology: 2.4%, Ophthalmology: 0.45% Most Frequent Major Complications within 7 days of surgery per 1000 patients (Figure 2): Acute Kidney Injury: 6 Post-operative pulmonary complications: 6.7 Post surgical sepsis: 5.1 Acute Coronary Syndrome: 1.07 Stroke and new neurologic deficit: 0.8 Cardiac Arrest: 0.63 Complications occurred more often in males than in females (10% vs 7.31% respectively), and increased with age (Figure 3): Age Group : Proportion of Complications 0-10 0.67% 11-20 2.75% 21-30 4.06% 31-40 5.75% 41-50 8.52% 51-60 9.93% 61-70 9.67% 71-80 9.84% 81-90 13.36% 91-100 16.98% Influence of COVID-19 on Post-Surgical Complication Rates: Pre-COVID-19 (10/1/2017 - 3/31/2020) overall complication rate: 8.27% [n= 549,192] Post-COVID-19 (4/1/2020- 6/1/2020) overall complication rate: 10.44% [n=24,701] (Period of emergency cases only) Post-COVID-19 (6/2/2020 -

11/10/2021) over all complication rate: 8.96% [n= 262,570]

Conclusion: Our study confirms prior findings that complications following major inpatient surgery occur in up to 1:4 patients. Pulmonary, renal, and post-surgical sepsis occur more frequently than cardiac or neurologic events, and increase with age and male gender. Post-pandemic surgical complication rates remain higher than pre-pandemic.

References: 1. Lancet 372:139 - 144 2008 2. N Engl J Med 361:1368-1375 2009 3. Br J Surg. 101:1499-1508 2014 4. The Journal of surgical research 181(1), 106-113 2013 5. Crit Care 17, 226 2013 6. BMJ open 6(2) e007224 2014 7. Ann Surg 240(2):205-13 2004 8. J Surg Res 181(1):106-13 2013 9. World J Gastroenterol. 7;26(21):2682-2690 2020 10. Health Aff (Millwood) 31:2571-2578 2012 11. Ann Surg 242:326 - 341 2005 12. Br J Anaesth. 113(6):977-84 2014 13. J Surg Res. 229:134-144 2018 14. Ann Intern Med. 17;134(8):637-43 2001 15. Anesthesiology clinics, 29(1) 83-97 2010

Figure 1. Data Curation Along the Continuum of Care.

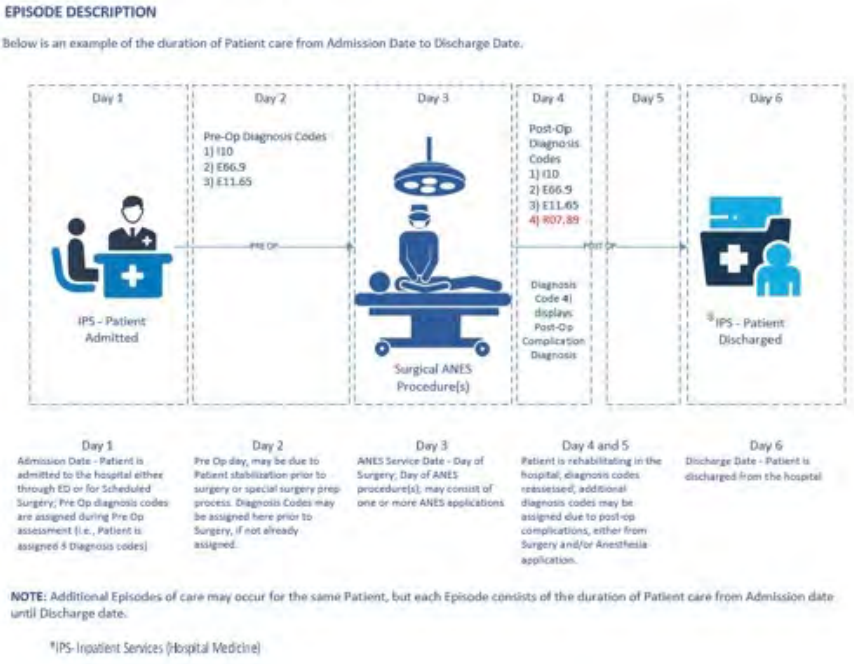


Figure 2. Post-Surgical Complication Type by Day per 1000 Patients.

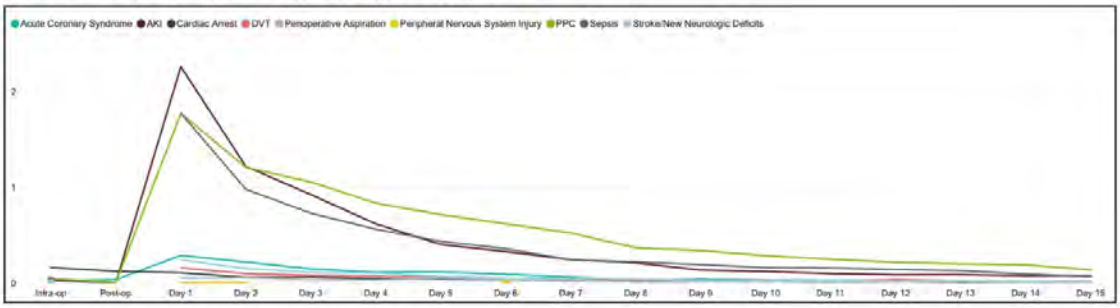
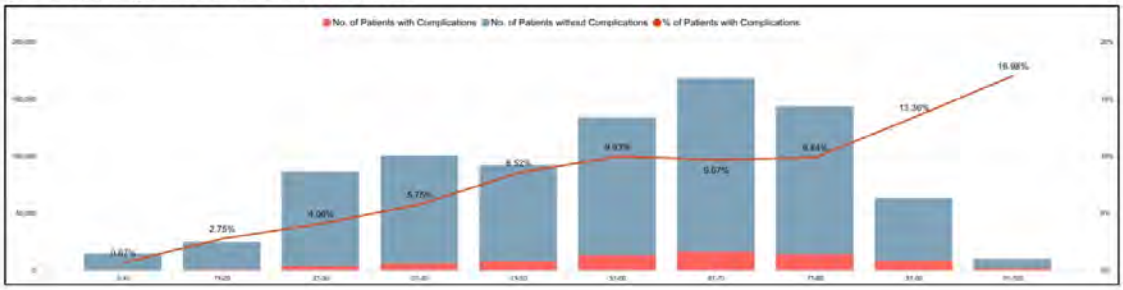


Figure 3. Post-Surgical Complications by Age-Group.



Perioperative Anesthesia - 18 Association of Preoperative Cannabinoid Use with Postoperative Cardiac Complications: A Retrospective Cohort Study

Denys Shay[1], Laetitia S Chiarella[1], Tim M Tartler[1], Jo Ann Jordan[2], Annika S Witt[3], Bijan Teja[4], Felix C Linhardt[1], Maximilian S Schaefer[1]

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Introduction: An increasing number of patients present for surgery who use cannabinoids for recreational or medical purposes, which has been augmented by legislature changes in various states of the United States between 2012 and 2016. (1) Previous retrospective studies have raised concerns about an increased risk of cardiovascular events including myocardial infarction (2, 3) in patients who abuse cannabis. However, there is little data on whether surgical patients who consume cannabinoids are at higher risk of postoperative cardiac events. We investigated the association of recreational and medical cannabinoid use with adverse cardiac outcomes in a large hospital network in New England.

Methods: Adult patients undergoing non-cardiac surgery under general anesthesia at a tertiary academic healthcare network in Boston, MA, USA, between 2006 and 2020 with available pre-admission or pre-procedural notes were included in this hospital registry study. Recreational use of cannabinoids was identified based on physician and nursing notes from structured patient interviews during pre-admission or pre-procedural testing, prescriptions of medical cannabinoids, or ICD-9/10 diagnostic codes of cannabinoid abuse. The primary outcome was major adverse cardiac events (MACE) (4), which included myocardial infarction, cardiac arrest, acute heart failure or revascularization procedures within 30 days after surgery. Multivariable logistic regression analyses adjusted for a priori defined factors including patient baseline characteristics, socioeconomic factors, concomitant substance abuse, markers of procedural severity and comorbidities including the Revised Cardiac Risk Index (RCRI) (5) were fitted. In secondary analyses, we differentiated the risk of postoperative MACE by types of cannabinoid use (recreational use, medical use, and abuse of cannabinoids) and investigated whether a high perioperative cardiovascular risk based on the RCRI modified the association between cannabinoid use and postoperative MACE. Exact matching for age (± 2 years) and sex at a 1:3 ratio was performed in sensitivity analyses. Standardized differences and odds ratios with 95% confidence intervals are reported. A p-value <0.05 was considered as statistically significant. All analyses were performed in Stata (Versions 15 and 16, StataCorp, TX, USA).

Results: In the primary cohort of 308,330 patients, 25,219 (8.2%) reportedly used cannabinoids before surgery for recreational or medical purposes (Figure 1). 8,583 (2.8%) patients experienced MACE within 30 days after surgery. 516 (2.1%) of those who reportedly used cannabinoids experienced MACE, whereas 8,067 (2.8%) of those who did not reportedly use cannabinoids experienced MACE (odds ratio [OR], 0.71 [95% confidence interval [CI], 0.65-0.79]; p<0.001). The incidence of postoperative MACE increased with patient age (Table 1, Figure 2). After confounder adjustment, preoperative cannabinoid use was not significantly associated with MACE (adjusted OR [aOR], 1.02 [95% CI, 0.92-1.13]; p=0.77). These findings were independent from recreational, medical, or abuse of cannabinoids (Table 2). A high perioperative cardiovascular risk profile defined as an RCRI class of 3 or more did not significantly modify these findings (p-for-interaction=0.07). There was no significant association between cannabinoid use and postoperative myocardial infarction within 30 days alone (aOR, 1.11; 95% CI 0.90-1.39; p=0.33). Sensitivity analyses after exact matching for sex and age (± 2 years) confirmed the results (aOR, 1.04; 95% CI 0.92–1.17; p=0.57 and p-for-interaction = 0.49).

Conclusion: Cannabinoid use for recreational or medical purposes was not associated with an increased risk of postoperative cardiac complications within 30 days after non-cardiac surgery.

References: 1) U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration (US); 2020 2) Am J Cardiol. 2014;113(1):187-190. 3) Cureus. 2017;9(11):e1816. 4) Ann Surg. 2021, Advance online publication 5) Circulation. 1999;100(10):1043-1049.

Table 1. Patient Baseline Characteristics and Covariates by MACE

MACE, major adverse cardiac events; SD, standard deviation; ASA, American Society of Anesthesiologists; IQR, interquartile range; USD, United States Dollar; ENT, ear, nose, and throat; RCRI, Revised Cardiac Risk Index

Characteristics	No MACE within 30 postoperative days n=299,747	MACE within 30 postoperative days n=8,583	Standardized difference
Demographics			
Mean age ± SD, y	54.9 ± 16.3	69.6 ± 12.4	-1.013
Sex (female), n (%)	174,066 (58.1)	3,978 (46.3)	0.236
Median body mass index (IQR), kg/m2	27.1 (23.6 – 31.5)	28.8 (24.7 – 34.4)	-0.259
ASA classification, n (%)			-1.336
I	37,971 (12.7)	13 (0.2)	
II	148,350 (49.5)	608 (7.1)	
III	103,000 (34.4)	6,257 (72.9)	
IV	10,426 (3.5)	1,705 (19.9)	
Race/ ethnicity, n (%)[a]			-0.021
White	191,577 (73.9)	5,778 (75.1)	
Black	28,770 (11.1)	1,117 (14.5)	
Hispanic	15,623 (6.0)	395 (5.1)	
Asian	11,847 (4.6)	171 (2.2)	
Other	11,084 (4.3)	230 (3.0)	
Two or more	409 (0.2)	3 (0.0)	
Socioeconomic factors			
Estimated median household income (IQR), USD[b]	70163 (43919 – 91597)	67028 (43532 – 89451)	0.066
Federal insurance, n (%)	94,317 (31.5)	5,496 (64.0)	-0.690
Education level n (%)[c]			0.210
No education	246 (0.4)		
Attended high school	4,352 (6.9)		
Graduated high school	20,497 (32.3)		
Attended college	12,737 (20.1)		
Graduated college	25,559 (40.3)		
Marital status, n (%)			-0.090
Divorced	20,240 (6.8)	739 (8.6)	
Life partner	372 (0.1)	12 (0.1)	
Married	159,780 (53.3)	4,167 (48.5)	
Separated	3,889 (1.3)	168 (2.0)	
Single	96,998 (32.4)	2,025 (23.6)	
Widowed	18,468 (6.2)	1,472 (17.2)	
Preoperative factors			
Admission type, n (%)			-0.290
Ambulatory	176,479 (58.9)	3,657 (42.6)	
Same-day admission	87,698 (29.3)	3,538 (41.2)	
Inpatient	35,570 (11.9)	1,388 (16.2)	
Emergency surgery, n (%)	17,999 (6.0)	865 (10.1)	-0.150
Intraoperative factors			
Median duration of surgery (IQR), min	92 (52 – 153)	91 (51 – 152)	0.007
Median work relative value units (IQR)	8.5 (5.0 – 15.6)	8.5 (5.0 – 15.9)	-0.063
Surgical service, n (%)			-0.308
Colorectal	8,023 (2.7)	145 (1.7)	

Dent/oral/ENT	9,582 (3.2)	194 (2.3)	
Ophthalmology	15,428 (5.1)	796 (9.3)	
General surgery	39,481 (13.2)	732 (8.5)	
Gastroenterology	11,363 (3.8)	558 (6.5)	
Gynecology	47,288 (15.8)	741 (8.6)	
Neurology	11,234 (3.7)	240 (2.8)	
Orthopedic	65,229 (21.8)	1,250 (14.6)	
Plastic	18,613 (6.2)	193 (2.2)	
Podiatry	7,389 (2.5)	279 (3.3)	
Surgical oncology	11,078 (3.7)	165 (1.9)	
Thoracic	14,162 (4.7)	773 (9.0)	
Transplant	6,634 (2.2)	860 (10.0)	
Trauma/surgical critical care	6,512 (2.2)	206 (2.4)	
Urology	19,143 (6.4)	588 (6.9)	
Vascular	8,588 (2.9)	863 (10.1)	
Comorbidities/ history, n (%)			
Myocardial infarction	8,391 (2.8)	1,787 (20.8)	-0.581
Cardiovascular disease	11,462 (3.8)	1,053 (12.3)	-0.314
Chronic kidney disease	18,770 (6.3)	3,082 (35.9)	-0.780
Chronic liver disease	3,824 (1.3)	203 (2.4)	-0.082
Hypertension	117,595 (39.2)	6,562 (76.5)	-0.814
Cancer	57,184 (19.1)	2,000 (23.3)	-0.104
Heart failure	12,049 (4.0)	4,893 (57.0)	-1.407
Ischemic stroke	6,609 (2.2)	713 (8.3)	-0.276
Dyslipidemia	105,447 (35.2)	5,896 (68.7)	-0.712
Diabetes mellitus	17,018 (5.7)	2,299 (26.8)	-0.597
RCRI class			-1.443
I	199,313 (66.5)	1,274 (14.8)	
II	73,960 (24.7)	2,227 (25.9)	
III	17,640 (5.9)	2,263 (26.4)	
IV	8,834 (2.9)	2,819 (32.8)	
Psychiatric comorbidities, n (%)			
Anxiety	34,780 (11.6)	1,466 (17.1)	-0.157
Depression	47,985 (16.0)	2,328 (27.1)	-0.273
Schizoaffective disorder	860 (0.3)	39 (0.5)	-0.028
Schizophrenia	1,077 (0.4)	49 (0.6)	-0.031
Psychosis	2,877 (1.0)	188 (2.2)	-0.099
Substance abuse, n (%)			
Alcohol abuse	6,104 (2.0)	271 (3.2)	-0.071
Cocaine abuse	268 (0.1)	15 (0.2)	-0.024
Intravenous drug abuse	4,839 (1.6)	272 (3.2)	-0.102
Medication abuse	1,509 (0.5)	90 (1.0)	-0.062
Psychedelic drug abuse	72 (0.0)	3 (0.0)	-0.006

[a] Cohort size due to missing data: n = 267,004
[b] Cohort size due to missing data: n = 278,266
[c] Cohort size due to missing data: n = 65,856

Table 2. Results of multivariable logistic regression with categorized exposure

MACE, major adverse cardiac events; OR, odds ratio; aOR, adjusted odds ratio.

Cannabinoid use	No MACE within 30 postoperative days (n = 299,747)	MACE within 30 postoperative days (n = 8,583)	Unadjusted Analysis		Adjusted Analysis	
			OR 95% CI	P-value	aOR 95% CI	P-value
No use	275,044 (97.15%)	8,067 (2.85%)	Reference		Reference	
Recreational use	17,985 (98.41%)	291 (1.59%)	0.55 0.49–0.62	<0.001	1.02 0.89–1.16	0.82
Abuse	2,728 (96.81%)	90 (3.19%)	1.12 0.91–1.39	0.28	1.20 0.94–1.53	0.15
Medical use	3,990 (96.73%)	135 (3.27%)	1.15 0.97–1.37	0.11	0.93 0.76–1.12	0.44

Data are expressed as frequency (incidence in %). Statistical analyses were conducted using multivariable logistic regression. Unadjusted odds ratios (OR) and adjusted odds ratios (aOR) are reported from multivariable logistic regression analyses.

Figure 1. Study flow

ASA, American Society of Anesthesiologists; RCRI, Revised Cardiac Risk Index.

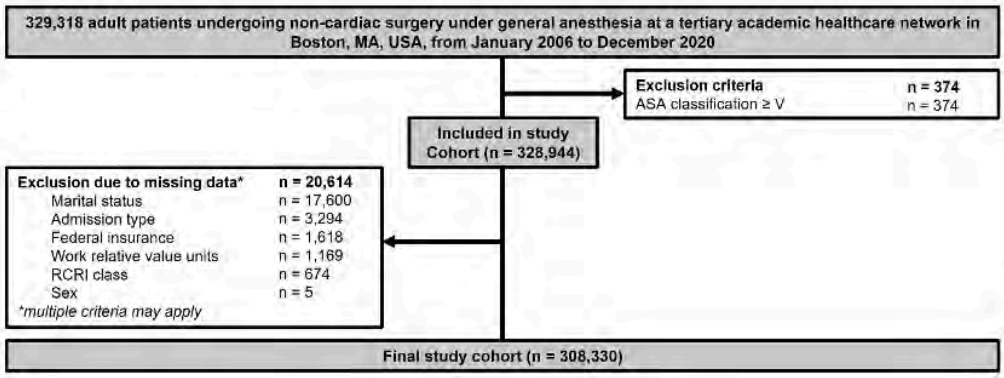
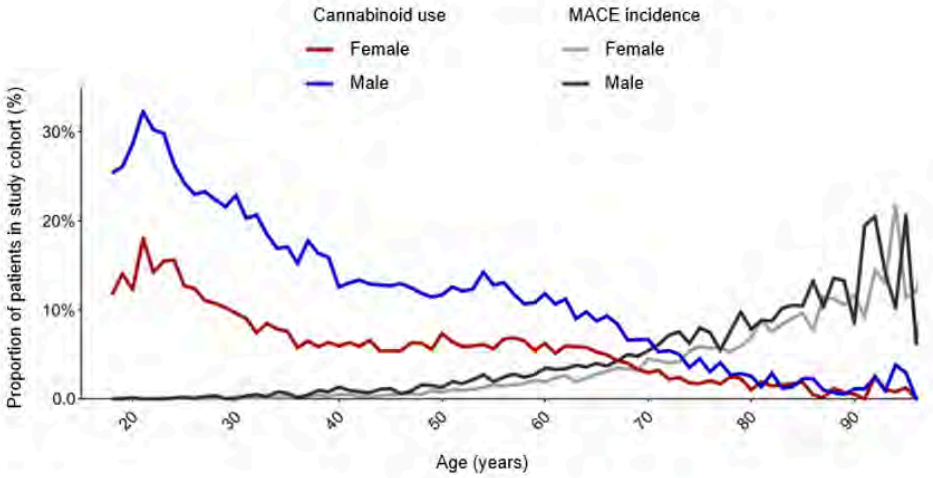


Figure 2. Cannabinoid use and MACE by age and sex

Prevalence of cannabinoid use before surgery and incidence of MACE within 30 days after surgery by patient age and sex.

MACE, major adverse cardiac events.



Perioperative Anesthesia - 19

Retrospective Analysis Investigating Intraoperative Opioid Administration and Anesthetic Recovery with a Focus on Identifying Risk and Protective Factors

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Introduction: Increased use of intraoperative opioids can lead to delayed arousal, respiratory depression, acute opioid tolerance, and increased postoperative pain [1,2]. These undesirable effects can lead to increased length of stay in the postoperative care unit (PACU) and increased costs [3]. This study aims to identify both risk and protective factors that affect intraoperative opioid administration and PACU length of stay (LOS). Our goal is to improve patient outcomes, efficiency, and reduce costs.¬†

Methods: Subjects: Patients over age 18 who have undergone surgical procedures under general anesthesia at Emory University Hospital and Emory University Hospital Midtown from 1/1/2014 through 12/31/2018. Exclusion Criteria: ICU patients, patients that did not have a documented PACU stay duration, surgical procedures completed under sedation, and PACU durations deemed to be out of range. Total of 103,778 patients were included. Analysis: Charts were reviewed, and data was collected on patient demographics, type of surgery, intraoperative opioids administered, PACU length of stay, use of opioid sparing medications and regional/neuraxial anesthesia. Log-transformed PACU minutes data were analyzed with the General Linear Model. Intraoperative MME data were analyzed with Multinomial Logistic Regression.

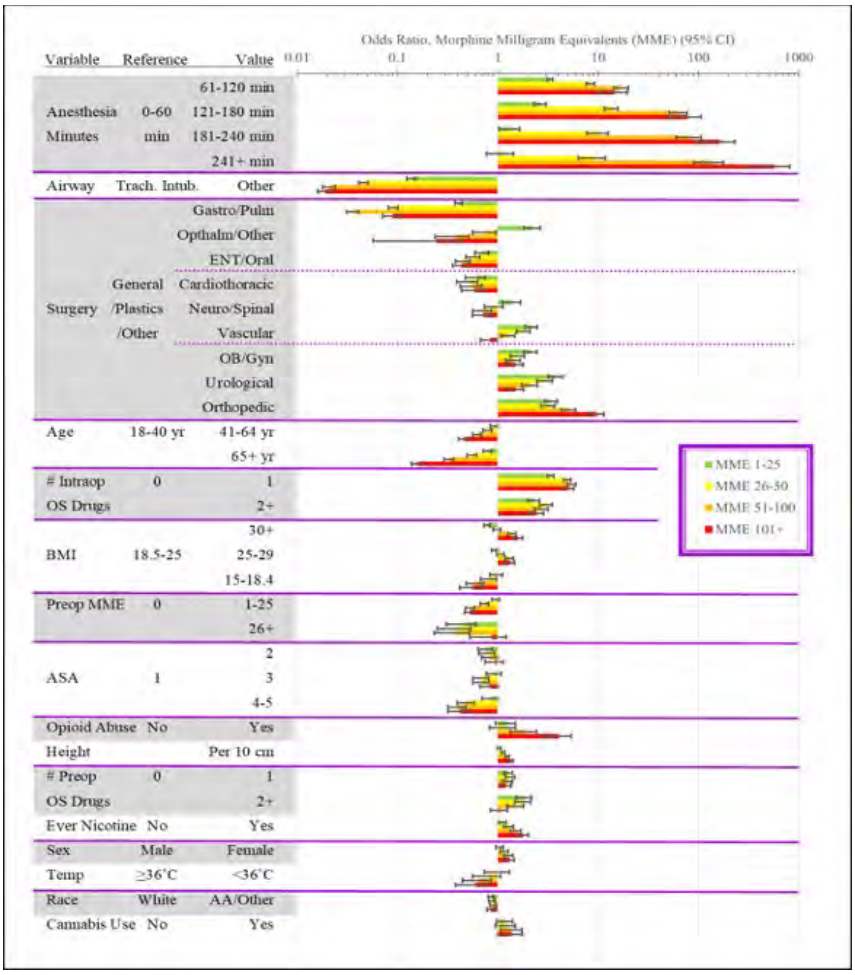
Results: We found that female sex increased the odds of receiving more opioids when compared to males on average by 1.25x (CI 1.19-1.47; p <0.0001) ; Temp < 36 C decreased the odds of receiving more opioids by 1.5x (CI 0.44-0.86; p <0.0001); White patients were 1.2x more likely to receive more opioids than AA patients (CI 0.78-0.96; p<0.001). Patients who received one opioid sparing agent intraoperatively had 4.7x increased odds of receiving more intraoperative opioids than those who received none and patients who received two or more opioid sparing agents intraoperatively had a 2.6x increased odds of receiving more intraoperative opioids (p<0.0001). We also found that giving up to 25 MME intraoperatively increased PACU LOS by 2 mins (CI 1.3-2.7; p <0.0001), giving up to 50 MME increased PACU LOS by 4.5 mins (CI 3.6-5.4; p<0.0001), and giving up to 100 MME increased PACU LOS by 6 mins (CI 5.1-7.1; p<0.0001). Females have 3 min longer PACU LOS than males (CI 2.5-3.3; p<0.0001). AAs had longer PACU LOS by 2.5 mins than Whites (CI 2-2.9; p<0.0001). Temperature: being <36 C increased PACU LOS by about 5.5 mins (CI 4.0-6.9; p<0.0001). The utilization of intraoperative opioid sparing drugs increased PACU LOS (1 min for 1 drug (CI 0.4-1.5; p<0.0001), 2 min for 2 drugs (CI 1.4-2.8; p<0.0001). For all results, we controlled for 16 different variables including American Society of Anesthesiologists (ASA) physical classification, length of time under anesthesia, type of surgery, gender, race, age, and chronic opioid use.

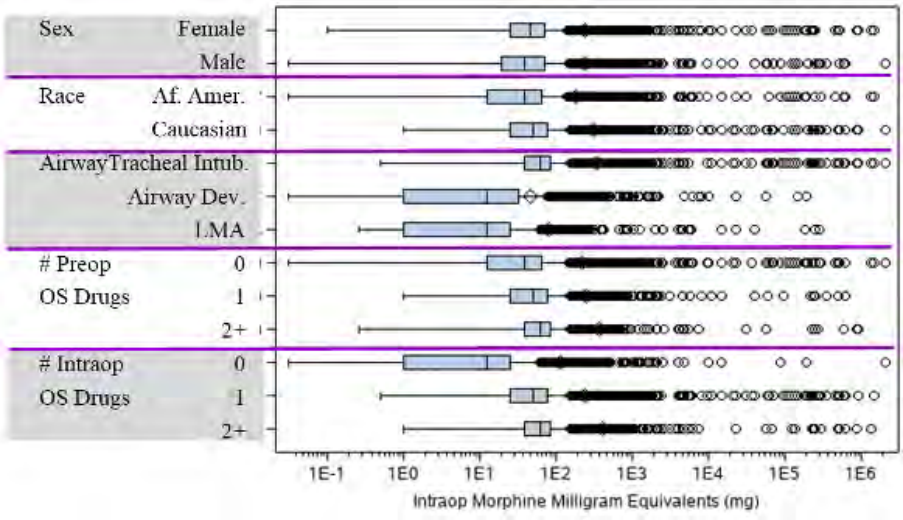
Conclusion: This study has identified both risk and protective factors that affect intraoperative opioid administration and PACU LOS. We discovered an unanticipated significant effect of sex and race/ethnicity on opioid administration in the peri-operative period, with African Americans receiving significantly less intraoperative opioids (37.5 MME) on average than other races/ethnicities including Asians (47.5 MME), non-Hispanic Whites (50 MME), and 'other' (47.2 MME) p<0.0001. We also found that females received significantly more intraoperative opioids on average (45 MME) than males (37.5 MME) p<0.0001. These results warrant further investigation into the reasons behind these variations, and whether they have a biologic basis or are related to provider biases. Intra-operative and pre-operative utilization of opioid sparing adjuncts may not be as impactful as we had hoped, as we did not find reduction in PACU LOS nor intraoperative opioid administration related to these techniques.

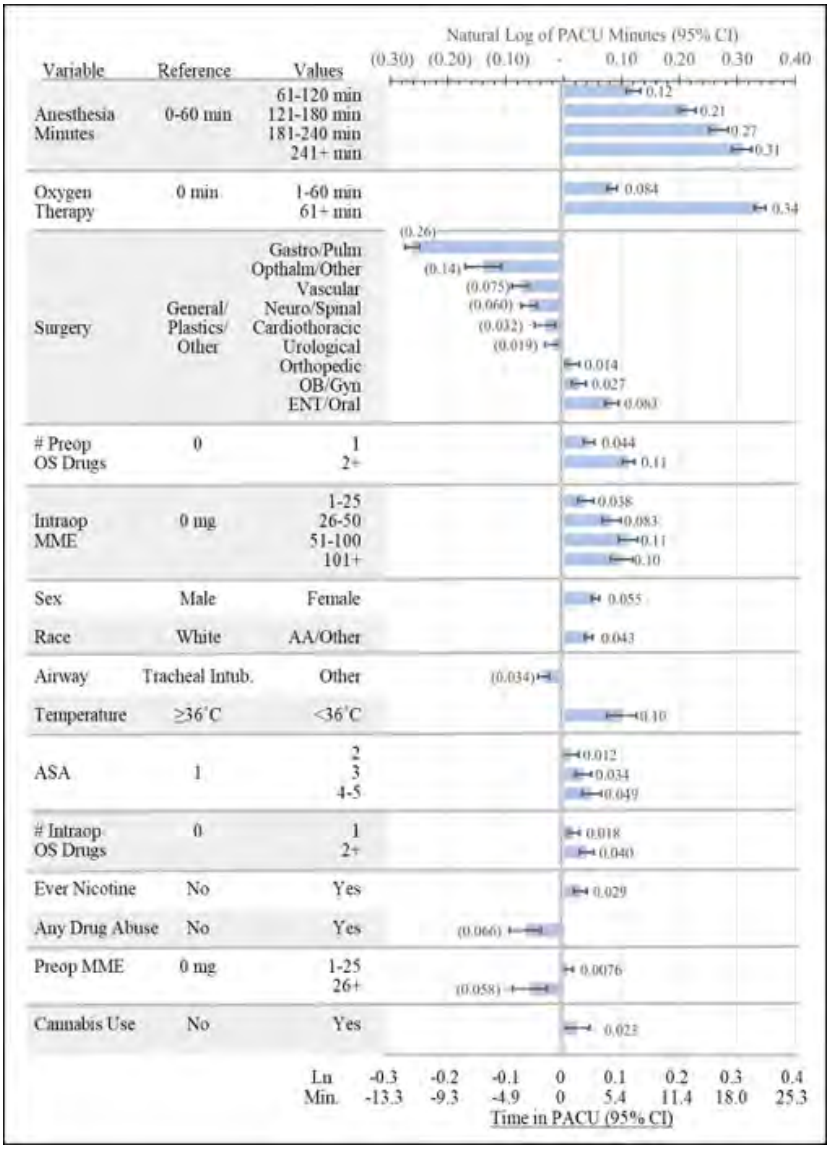
References: 1. Opioids, respiratory depression, and sleep-disordered breathing. Vol 31. Pages 469-485. 2017. 2. Higher Doses of Intra-op Opioids Cause Greater Post-op Pain. May 2020. 3. Postanesthesia Care Unit Length of Stay Quantifying and Assessing Dependent Factors. Vol 87. Pages 628-633. 1998.

Variable	Values	N (%)	Grouping	N (%)
Sex	Male	42,577 (59.0%)	NA	NA
	Female	61,201 (41.1%)		
Race	White	47,610 (45.9%)	White	47,610 (45.9%)
	Af. Amer.	50,421 (48.6%)	Af. Amer.	50,421 (48.6%)
	Asian	1,679 (1.6%)	Other	5,747 (5.5%)
	Multiple	1103 (1.1%)		
	Am.	1269 (1.2%)		
	Indian	114 (0.1%)		
	Hawaiian	1582 (1.5%)		
	Unknown			
Ethnicity	Hispanic	2,500 (2.6%)	NA	NA
	Other	92,433 (97.4%)		
ASA Class	1	6,320 (6.1%)	1	6,320 (6.1%)
	2	29,833 (28.8%)	2	29,833 (28.8%)
	3	52,449 (50.5%)	3	52,449 (50.5%)
	4	15,155 (14.6%)	4-5	15,176 (14.6%)
	5	21 (0.02%)		

Abbreviations: IQR: Interquartile Range; AA: African American; ASA: Amer. Society of Anesthesiologists Physical Status Classification


Odds Ratio, Morphine Milligram Equivalents (MME) (95% CI)
0.01
0.1
1
10
100
1000
Variable
Reference
Value
Anesthesia Minutes
0-60 min
61-120 min
121-180 min
181-240 min
241+ min
Airway
Trach. Intub.
Other
Surgery
General /Plastics /Other
Gastro/Pulm
Opthalm/Other
ENT/Oral
Cardiothoracic
Neuro/Spinal
Vascular
OB/Gyn
Urological
Orthopedic
Age
18-40 yr
41-64 yr
65+ yr
Intraop OS Drugs
0
1
2+
BMI
18.5-25
30+
25-29
15-18.4
Preop MME
0
1-25
26+
ASA
1
2
3
4-5
Opioid Abuse
No
Yes
Height
Per 10 cm
Preop OS Drugs
0
1
2+
Ever Nicotine
No
Yes
Sex
Male
Female
Temp
≥36°C
<36°C
Race
White
AA/Other
Cannabis Use
No
Yes
MME 1-25
MME 26-50
MME 51-100
MME 101+


Sex
Female
Male
Race
Af. Amer.
Caucasian
AirwayTracheal Intub.
Airway Dev.
LMA
Preop OS Drugs
0
1
2+
Intraop OS Drugs
0
1
2+
1E-1
1E0
1E1
1E2
1E3
1E4
1E5
1E6
Intraop Morphine Milligram Equivalents (mg)


Natural Log of PACU Minutes (95% CI)
(0.30) (0.20) (0.10) - 0.10 0.20 0.30 0.40
Variable
Reference
Values
Anesthesia Minutes
0-60 min
61-120 min
121-180 min
181-240 min
241+ min
0.12
0.21
0.27
0.31
Oxygen Therapy
0 min
1-60 min
61+ min
0.084
0.34
Surgery
General/ Plastics/ Other
Gastro/Pulm
Opthalm/Other
Vascular
Neuro/Spinal
Cardiothoracic
Urological
Orthopedic
OB/Gyn
ENT/Oral
(0.26)
(0.14)
(0.075)
(0.060)
(0.032)
(0.019)
0.014
0.027
0.063
Preop OS Drugs
0
1
2+
0.044
0.11
Intraop MME
0 mg
1-25
26-50
51-100
101+
0.038
0.083
0.11
0.10
Sex
Male
Female
0.055
Race
White
AA/Other
0.043
Airway
Tracheal Intub.
Other
(0.034)
Temperature
≥36˚C
<36˚C
0.10
ASA
1
2
3
4-5
0.012
0.034
0.049
Intraop OS Drugs
0
1
2+
0.018
0.040
Ever Nicotine
No
Yes
0.029
Any Drug Abuse
No
Yes
(0.066)
Preop MME
0 mg
1-25
26+
0.0076
(0.058)
Cannabis Use
No
Yes
0.023
Ln -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4
Min. -13.3 -9.3 -4.9 0 5.4 11.4 18.0 25.3
Time in PACU (95% CI)

Perioperative Anesthesia - 20

Perioperative hypothermia in the presence of poor glycemic control nearly triples the risk of surgical site infection

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Introduction: Surgical site infection (SSI) is the leading cause of nosocomial infections among surgical patients in the U.S [1]. Currently, there is compelling evidence suggesting temperature regulation in surgical patients may be a risk factor for the development of SSI [2-7]. We believe that if an association between perioperative hypothermia (PH) and SSI exists, it would be more apparent, and potentially compounding in a population already at increased risk such as patients with diabetes mellitus (DM).

Methods: This retrospective chart review was conducted of patients with a history of DM undergoing elective orthopedic surgery at our teaching institution between May 1, 2018, and June 9, 2021. Surgeries were performed within a single hospital. Included patients were over the age of 15 with a history of DM or a recent HbA1c level ≥6.5% and receipt of general anesthesia for an elective orthopedic operation at least 60 minutes in duration. Poor glucose control was defined as a HbA1c level ≥6.5% or a serum glucose >200 at the time of surgery. T-tests, Chi-squared analysis, and univariate logistic regression were used to compare demographic data and outcomes between the normothermic and hypothermic cohorts and infection and non-infection cohorts.

Results: One hundred and eighty-nine patients were included in the final analysis. Seventy-one (38%) patients became intraoperatively hypothermic. The overall incidence of SSI was 6.87%. Among the seventy-one patients who experienced PH, poor glycemic control was associated with nearly a two-fold increased risk of SSI (OR = 2.7, 95% CI = 1.09-6.69, p-value = 0.032).

Conclusion: Poor glycemic control in the presence of perioperative hypothermia increased the risk of surgical site infection nearly two-fold. These results suggest that in patients at increased risk of SSI, the presence of PH may confer a substantial additive risk. Fortunately, there exist effective interventions for reducing the incidence of PH.

References: [1] American Journal of Infection Control. 1996 24:380-8. [2] Advances in Surgery. 2011;45:249-63. [3] Current Opinion in Infectious Diseases. 2015;28(2):158-63. [4] New England Journal of Medicine. 1996;334(19):1209-15. [5] Lancet. 2016;387(10038):2655-2664. [6] Handbook of Clinical Neurology. 2018;157:687-697. [7] Surgical Infections. 2006;7 Suppl 1:S7-11.

Risk of Surgical Site Infection Among PH Cohort

Factor	OR (95% CI)	p-value
Poor glycemic control (HbA1c ≥6.5%; serum glucose >200)	2.697 (1.087-6.688)	0.0322

Perioperative Anesthesia - 21 Association of Perioperative Beta-Blocker Therapy and Major Adverse Cardiovascular and Cerebrovascular Events in Patients undergoing Major Abdominal Surgery: A Retrospective Cohort Study

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Introduction: Major adverse cardiac and cerebrovascular events (MACCE) are a significant complication following major non-cardiac surgery, with a frequency between 1.4% and 3.9% [1,2]. Initial RCTs demonstrated that beta blockade reduced myocardial infarctions and in-hospital mortality, while the POISE trial found an association between perioperative beta blockade and increased stroke risk [2,3,4]. However, the association between starting a beta blocker prior to the day of surgery or the association of chronic beta-blockader use on the risk of stroke is still unknown. We investigated the association between perioperative beta-blocker therapy started within 60 days of surgery or existing beta blockade (> 60 days) and the risk of stroke in patients undergoing major abdominal surgery.

Methods: This study was a retrospective population-based cohort study of patients undergoing elective major abdominal surgery. This study identified all major abdominal surgeries in patients 18 or older and identified all major adverse cardiovascular and cerebrovascular events. We used inverse propensity weighted scores and the average treatment effect on the treated to determine the association between perioperative beta-blocker therapy and cerebrovascular events, myocardial infarction, and cardiac arrest the average.

Results: There were 230,535 patients with our inclusion criteria who underwent a major abdominal surgery from 2005 to 2017. Perioperative beta-blocker therapy within 60 days of surgery was initiated for 4,416 patients (1.9%), 51,060 patients (22.2%) were on an existing beta-blocker and 175,059 patients (75.9%) were not on a beta-blocker. The unadjusted frequency of stroke for patients on perioperative beta-blocker therapy (0.38%, 17/4,416) was greater than for patients not on beta-blocker therapy (0.15%, 263/175,059) (P <0.001). The adjusted odds ratio for perioperative beta blockade or existing beta blockade therapy demonstrated no change in stroke risk (OR: 0.999, 95% CI: 0.997, 1.001; P = 0.55) and (OR: 1.001, 95% CI: 0.999-1.003; P = 0.44) respectively. Perioperative beta-blocker therapy was associated with a lower risk for myocardial infarction (OR: 0.996, 95% CI: 0.992 – 0.999; P = 0.002).

Conclusion: No association between clinically prescribed perioperative or existing beta-blocker therapy and stroke was identified in patients undergoing major abdominal surgery when controlling for confounders. We identified a modest decrease in perioperative myocardial infarction or cardiac arrest, which suggests that a clinically relevant dose of perioperative beta blockade may not mitigate the risk of MACCE in high-risk patients.

References: References: 1. CMAJ. 2005;173(6):627-34 2. J Am Coll Cardiol. 2015;66(19):2140-2148 3. Anesthesiology. 1998;88(1):7-17 4. Lancet. 2008; 371(9627):1839-47

Table 1. Primary Outcomes for Patients undergoing Major Abdominal Surgery separated by: No Beta-blocker prescription, Existing Beta-blocker prescription (more than 60 days before surgery), and Perioperative Beta-blocker prescription (60 days before surgery)

Primary outcomes	Entire Cohort (n = 230,535)	No Beta Blocker Prescription (n = 175,059)	Existing Beta Blocker Prescription (n = 51,060)	Perioperative Beta Blocker Prescription (n = 4,416)	*P* value
All Major Adverse Cardiac and Cerebrovascular Events	2,038 (0.88)	1,009 (0.58)	943 (1.85)	86 (1.95)	<0.0001
Myocardial Infarction	1,283 (0.56)	599 (0.34)	636 (1.25)	59 (1.34)	<0.0001
Cerebrovascular Event	478 (0.21)	263 (0.15)	198 (0.39)	17 (0.38)	<0.0001
Cardiac Arrest	338 (0.15)	183 (0.10)	144 (0.28)	11 (0.25)	<0.0001

Frequencies and precents are reported for categorical variables. Chi-square analysis was used to determine significant differences among the two groups. A *P* value ≤ 0.016 was considered significant.

Table 2. Average Effect of Treatment on the Treated (ATT) Odds Ratio Estimate of Perioperative Beta-Blocker therapy (60 days before surgery) on Myocardial Infarction, Cerebrovascular Events, and Cardiac Arrest in patients undergoing major abdominal surgery from the MarketScan® Inpatient Database from 2005-2017

Primary outcomes	Cohort (n = 179,475) Effect Estimate OR (95% CI)	*P* value	RCRI Score of 0 or 1 (n = 175,335) OR (95% CI)	*P* value	RCRI Score of 2 or more (n= 4,140) OR (95% CI)	*P* value
All Major Adverse Cardiac and Cerebrovascular Events	0.9941 (0.9894 - 0.9989)	0.0148	0.9928 (0.9885 – 0.9970)	0.0008	1.0017 (0.9782 - 1.0256)	0.8916
Myocardial Infarction	0.9943 (0.9908 - 0.9979)	0.0019	0.9939 (0.9904 – 0.9974)	0.0006	0.9970 (0.9803 - 1.0139)	0.7251
Cerebrovascular Event	0.9994 (0.9973 - 1.0014)	0.5466	0.9984 (0.9964 - 1.0005)	0.1274	1.0072 (0.9990 - 1.0155)	0.0854
Cardiac Arrest	1.0007 (0.9983 - 1.0031)	0.5873	1.0005 (0.9991 - 1.0020)	0.4865	0.9990 (0.9847 - 1.0136)	0.8966

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treatment estimates. A *P* value ≤ 0.05 was considered significant.

Perioperative Anesthesia - 22

Personalized Scrub Caps for Improved Communication and Professional Wellness

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[1]Stanford Health Care, Palo Alto, CA, [2]Stanford University School of Medicine, Stanford, CA

Introduction: Effective communication in perioperative settings at an academic institution can be challenging. Team members change frequently and each residency matriculation cycle brings new resident members to the operating room. While standard name badges are mandatory, they are likely printed in small font, may flip backwards, and may be covered by PPE. Communication problems were identified as the root cause of approximately 70% of adverse events reported to the Joint Commission and it has been shown that communication failures in the OR occur in approximately 31% of team exchanges [1]. Personalized scrub caps with visible name and role have been proposed as a potential method of improvement [2]. In 2021 at Stanford Healthcare a three-stage project was completed with an attempt to demonstrate whether the introduction of personalized scrub caps can improve perioperative communication among OR team members and decrease depersonalization among anesthesiology residents, fellows, and attendings.

Methods: The research design of the Personalized Scrub Caps quality improvement project was a three-part design. All information gathered was subjective, anonymous, and collected via online surveys. The Stanford IRB considered this project to be part of quality improvement and non-human subject research with no written consent required, though all participation was voluntary. 1) Small Group Resident Pilot Project; six representative resident volunteers over 14 day work period. 2) Departmental Implementation; eight week trial period utilizing personalized embroidered scrub caps within Stanford general OR locations. 3) Follow-up and Feedback Collection; survey from those electively wearing personalized embroidered scrub caps. Small Group Resident Pilot Project Goal: Assess effectiveness of a simple, visible name sticker (Image 1) on increasing appropriate use of anesthesia resident names and the impact on resident wellness, specifically feelings of depersonalization in perioperative settings. First week: resident volunteers completed a pre-survey, no cap name stickers worn. Second week: cap name stickers worn, completed post-survey. Survey responses indicated that appropriate name use during perioperative communication was an area that necessitated significant improvement. The responses also demonstrated a positive response to name visibility on scrub caps. Departmental Implementation Personalized embroidered scrub caps were provided at no cost to all residents, fellows, and attendings within the general OR pool. Name and role, cap color (solid), embroidery color (contrasting color), and cap style were included as customizable options (Image 2). Four caps were provided at no cost to each individual. Total of 80 anesthesia professionals requested caps. Follow-Up and Feedback Collection After eight weeks of voluntary personalized scrub cap use, survey data was collected with a total of 17 anonymous responses collected including attendings, fellows, and residents.

Results: Small Group Resident Pilot Project (Survey results displayed in Image 3) Given the positive response from the representative resident cohort, survey data was presented to department leaders who proceeded with the approval process for funding of personalized embroidered scrub caps. Post-Implementation Follow-Up and Feedback (Survey results displayed in Image 4 and Image 5). Overwhelmingly positive feedback from voluntary users of the personalized scrub caps. Improvements of 52% to 88% were seen across nine separate areas of perioperative/intraoperative communication and workplace-related wellness. Voluntary follow-up survey response rate of 22% may decrease the representative accuracy of survey findings.

Conclusion: The simple implementation of name and role displayed on surgical scrub caps can improve multiple areas of perioperative communication and professional wellness for anesthesia attendings and trainees. Further areas of data collection could potentially include feedback collection from patients,

study of the effect on communication and efficiency in simulated critical OR crises scenarios, and mixed-methods studies including interprofessional colleagues i.e. surgeons, OR nursing, technicians, and other staff.

References: [1] Lingard L, Espin S, Whyte S, Regehr G, Baker GR, Reznick R, et al. Communication failures in the operating room: an observational classification of recurrent types and effects. BMJ Qual Saf. 2004 Oct 1;13(5):330-4. [2] Brodzinsky L, Crowe S, Lee HC, Goldhaber-Fiebert SN, Sie L, Padua KL, Daniels K. What's in a Name? Enhancing Communication in the Operating Room with the Use of Names and Roles on Surgical Caps. The Joint Commission Journal on Quality and Patient Safety. 2021 Apr 1;47(4):258-64.

Small Group Resident Pilot Project Results

During the surgical timeout I feel that other OR team members are attentive to my introduction.

Always	0%
Usually	17%
Sometimes	17%
Rarely	67%
Never	0%

I feel that other members of the OR team take a personal interest in me.

A great deal	0%
A lot	0%
A moderate amount	17%
A little	67%
None at all	17%

I prefer to be called by my name rather than "anesthesia", etc.

Yes I prefer my name	84%
Slight preference for my name	16%
No preference	0%
I prefer that other team members do not know my name	0%

In general, do you feel more comfortable speaking to other OR team members if you know their name?

Yes, I am more likely to speak to members if I know their name	100%
No, it doesn't make a difference	0%

In the main OR I feel included as a valuable member of the OR team.

Pre		Post	
Always	0%	Always	0%
Usually	33%	Usually	75%
Sometimes	50%	Sometimes	25%
Rarely	17%	Rarely	0%
Never	0%	Never	0%

I feel that I am treated respectfully by non-anesthesia team members in the OR.

Pre		Post	
Strongly agree	0%	Strongly agree	25%
Agree	67%	Agree	50%
Neither agree nor disagree	17%	Neither agree nor disagree	25%
Disagree	17%	Disagree	0%
Strongly disagree	0%	Strongly disagree	0%

How often do (non-anesthesia) OR team members refer to you by name?

Pre		Post	
Always	0%	Always	0%
Usually	0%	Usually	25%
Sometimes	33%	Sometimes	50%
Rarely	67%	Rarely	25%
Never	0%	Never	0%

How often do pre-op and post-op RNs refer to you by name?

Pre		Post	
Always	0%	Always	0%
Usually	0%	Usually	50%
Sometimes	33%	Sometimes	0%
Rarely	50%	Rarely	50%
Never	17%	Never	0%

In the event of an OR emergency (i.e. code situation, unstable patient, large-scale resuscitation) do you feel that knowing the name and role of other OR team members is beneficial to communication?

Yes, the information is beneficial	100%
It likely does not make a difference	0%
No, there is no benefit in this information	0%

I noticed an increased use in my name when it was visible on my scrub cap.

Yes, some increased use	100%
No change	0%

When my name was used I felt more included as a part of the care team.

Yes	100%
No difference	0%

If made available to me, I would choose to wear a scrub cap with my name visible more frequently.

Yes	100%
No	0%

Do you feel that wearing personalized scrub caps has the potential to increase anesthesia resident inclusion and improve work-related wellness?

Yes	100%
No	0%

Comments volunteered by participating residents:

"When I started this study, I had no idea how much I'd like having my name on my scrub cap! During the week when I had my name sticker on my cap, I found that a greater number of team members called me by name, including surgical attendings and residents. Before using the name tag, I might have days where my name was used a lot, but it was generally because one circulator or resident knew me and reliably called me by name. This may have skewed the results somewhat if looking at only numbers. What matters to me is that MORE members of the team use my name in the OR when I have my name visible. Furthermore, there were several instances when members of the OR team specifically commented on how great it was to have my name visible, and several circulators/scrub nurses mentioned that more people should do this. I believe that caps with names would be well received, and having my name displayed made me feel more like an actual member of the team."

"I wish everyone in the OR had a personalized scrub cap! Would be so easy to identify people's roles and call them by their name instead of sneakily using the log navigator."

"Overall helped with name use a bit but it seems very dependent on the culture of the room."

"I LOVE this idea. I've noticed your name on scrub cap and have copied it occasion when I have a case I really want the team to communicate with me during (liver transplant etc)."

"Many people commented on how having my name visible was a clever idea. I've started wearing a name sticker on my cap more frequently after receiving such positive feedback."

Interdepartmental Personalized Scrub Caps Follow-Up and Feedback

Survey data (subjective, anonymous) collected 8 weeks after caps distributed.
Respondents: 17 Total (8 attendings, 2 fellows, 7 residents)
Representative selected responses below.

Q1: What was your motivation for utilizing personalized scrub caps?
15 Total responses

"So that everyone involved during the pre-, intra- and post-op process will know what role I play."
"Wanting to identify as an MD to patients and provide an alternative to being called 'anesthesia' in the OR."
"Making myself less anonymous in a big OR suite where one can be assigned to work with a team they don't know on any given day."
"Free scrub cap and ease of communication."
"Helping create a more friendly environment in the OR"

Q2: Have you noticed improvements in intra/perioperative communication aided by personalized scrub caps?
(16/16 respondents said YES)

"Yes - people have used my name far more often than they had in the past. Several people have told me that it is easier to communicate when seeing my name on the cap."
"Yes! The other day I took over a case in a location I rarely work. The surgeons wanted the table moved and politely called me by my name to move the table. It was so civilized and made me feel appreciated, part of the team, and respected."
"Yes, people know my name more when they see my cap. It's easier to identify others as well, particularly when wearing lead."
"Yes. I can call the nurses by name and we notice each other more when we see someone who is wearing the scrub caps."

Q3: Will you continue electively wearing personalized scrub caps in the OR?
(16/16 respondents said YES)

"Definitely and beyond residency."
"Yes! And I want more colors!"
"Definitely - I enjoy wearing them and I think that have been a great addition to the interventional platform setting."
"Yes on/off. I do like my scrub caps with other designs as well. Would be open to having them embroidered if covered by the department."

Have you noticed improvements in any of the specific areas listed below?

ANSWER CHOICES	RESPONSES	
None of the above	11.76%	2
Communication with pre-op nursing staff	64.71%	11
Communication with patient	52.94%	9
Recognition of role (ie resident, attending, physician, anesthesia member)	76.47%	13
Communication with intra-operative nursing staff	76.47%	13
Intraoperative communication with residents and surgeons	70.59%	12
Increase in use of name	88.24%	15
Improved communication during emergent or critical scenario	47.06%	8
Improved wellness in the workplace	70.59%	12
More team-centered OR	52.94%	9
Total Respondents: 17		

Perioperative Anesthesia - 23

Postoperative Hyponatremia in Oncologic Orthopedic Patients: Incidence, Risk Factors, and Outcomes

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Introduction: Hyponatremia is the most common electrolyte abnormality encountered in the hospital associated with poorer outcomes and increased economic burden. The purpose of this study is to determine the incidence of hyponatremia among cancer patients undergoing orthopedic procedures, to characterize associated risk factors and outcomes, and determine which outcomes are associated with hyponatremia.

Methods: This retrospective cohort analysis included all adult patients who underwent surgery with a minimum of two hours of anesthesia time and with post-surgical sodium labs within 30 days at an academic cancer center in 2019 (N = 24,137). Of these, 1445 patients underwent orthopedic surgery. We assessed incidence of post-operative hyponatremia (serum [Na+] < 133 mEq/L) with age, sex, race, BMI, admission service, ASA physical status, Elixhauser comorbidity index, drug intake, GFR, glucose concentration, length of surgery, and post-operative complications. Univariable and multivariable logistic regression models were used to assess associations between hyponatremia and secondary outcomes: 30-day all-cause mortality and length of stay (LOS). A subgroup analysis of hip vs. knee procedures within orthopedic surgery was also conducted.

Results: Post-operative hyponatremia was noted in 217 out of 1445 orthopedic patients (15%) and 3061 out of 22692 other surgical service patients (13.5%). Post-operative hyponatremia (OR = 2.58 [95% confidence interval (CI), 2.01 - 3.30], p < 0.001) and orthopedic surgery (1.85 ([95% CI, 1.28 - 2.66], p=.001) were independently associated with higher 30-day mortality. Post-operative hyponatremia was also associated with longer hospital LOS [7.0 (4.0 - 13.0) vs. 3.0 (2.0 - 7.0); P < 0.001]. Multivariate analysis showed a 32% increase in LOS for hyponatremia patients (exp(estimate)= 1.32, estimate=0.28, [95% confidence interval (CI), 0.26 - 0.30], p < 0.001) and 20% increase for the orthopedic patients compared to all other services (exp(estimate)= 1.20, estimate=0.18, [95% confidence interval (CI), 0.15 - 0.21], p < 0.001). Subgroup analysis within the orthopedic patient population showed higher prevalence of developing post-operative hyponatremia in hip procedures compared to knee (21.5% vs 11.4%, p = 0.042). Within orthopedic patients, multivariable analysis of LOS showed a 27% increase in hyponatremic patients (exp(estimate)= 1.27, estimate=0.24, [95% confidence interval (CI), 0.11 - 0.36], p < 0.001). However, there was no difference in LOS between knee and hip procedures.

Conclusion: Post-operative hyponatremia, especially in orthopedic cancer patients, is associated with longer hospital stay and higher mortality. There is higher prevalence of developing post-operative hyponatremia in hip procedure compared to knee procedures.

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Perioperative Anesthesia - 24 Leveraging MPOG ASPIRE quality metrics for assessment of disparities in perioperative care and postoperative outcomes: an exploratory quality improvement analysis

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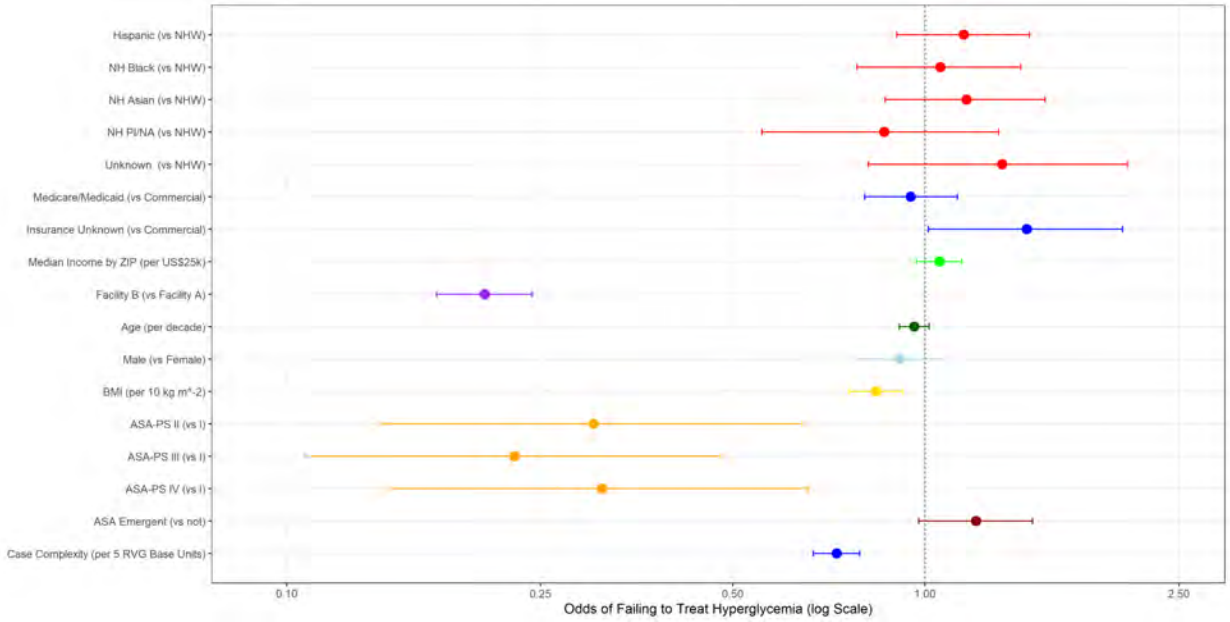
Introduction: Identifying and mitigating racial and ethnic disparities in healthcare are critical to ensuring the provision of equitable care, a core pillar of quality care (O'Kane 2021). A promising approach to identifying these disparities is to stratify existing high-quality metrics of process and outcome measures according to race and ethnicity and other markers of vulnerability such as language of care and rurality, and adjusting for potential confounders and effect modifiers. The Multicenter Perioperative Outcomes ASPIRE team has developed detailed, evidence-based definitions and business logic for a large number of these metrics.

Methods: A local implementation of 5 ASPIRE metrics (intraoperative hypotension avoidance; intraoperative use of lung protective ventilation; intraoperative hyperglycemia treatment; postoperative acute kidney injury; postoperative troponinemia) had previously been deployed using data from the University of Washington Medicine perioperative electronic medical record. Success at the case level was calculated for appropriately included cases performed between January 2017 and March 2021. Patient ZIP codes were used to retrieve and stratify median income and rurality using publicly accessible US Census data. A safe-harbor deidentified dataset was generated including the following data elements: age, sex, body mass index (BMI), race, ethnicity, insurance, rurality, median income by ZIP, ASA relative value guide base units, ASA physical status, emergency case, anonymized facility. Race and ethnicity were combined into a single multilevel categorical variable using previously described logic (Groenewald 2021). Due to differences in underlying inclusion and exclusion criteria, the final case count for each ASPIRE metric varied. Using R v4.1.1 and RStudio v1.4.1717, multiple variable logistic regression models were developed and assessed using c-statistic and Hosmer-Lemeshow tests. Because different subgroups were tested, no adjustment for multiple comparisons was deemed necessary.

Results: The full data set encompassed 125,518 cases, with (as indicated) variable subsets for each metric examined. For ASPIRE process metrics, adjusted analysis revealed substantial disparities in care for use of lung protective ventilation (Fig 1a; N = 81,145 with 33,069 failures) but not for hypotension avoidance (Fig 1b; N = 113,392 with 8,495 failures) or treatment of hyperglycemia (Fig 1c; N = 7,044 with 1,074 failures). For outcome metrics, significant disparities were observed for acute kidney injury (Fig 2a; N = 104,485 with 3,347 events) but not for troponinemia (Fig 2b; N = 116,271 with 246 events).

Conclusion: Our adjusted analysis of a selection of ASPIRE process and outcome metrics suggested significant disparities in care and outcomes. Next steps in this project will be confirmation of these findings through sensitivity analyses, assembly of prediction models, multicenter implementation of this analysis, and identification of modifiable factors that could drive improvements in these disparities.

References: Groenewald CB, Lee HH, Jimenez N, Ehie O, Rabbitts JA. Racial and ethnic differences in pediatric surgery utilization in the United States: A nationally representative cross-sectional analysis. J Pediatr Surg [Internet]. 2021 Oct 22 O,ÄôKane M, National Committee for Quality Assurance, Agrawal S, Binder L, Dzau V, Gandhi TK, et al. An equity agenda for the field of health care quality improvement. NAM perspect [Internet]. 2021 Sep 15;11(9).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Medicare/Medicaid (vs Commercial)
Insurance Unknown (vs Commercial)
Median Income by ZIP (per US$25k)
Facility B (vs Facility A)
Age (per decade)
Male (vs Female)
BMI (per 10 kg m^-2)
ASA-PS II (vs I)
ASA-PS III (vs I)
ASA-PS IV (vs I)
ASA Emergent (vs not)
Case Complexity (per 5 RVG Base Units)
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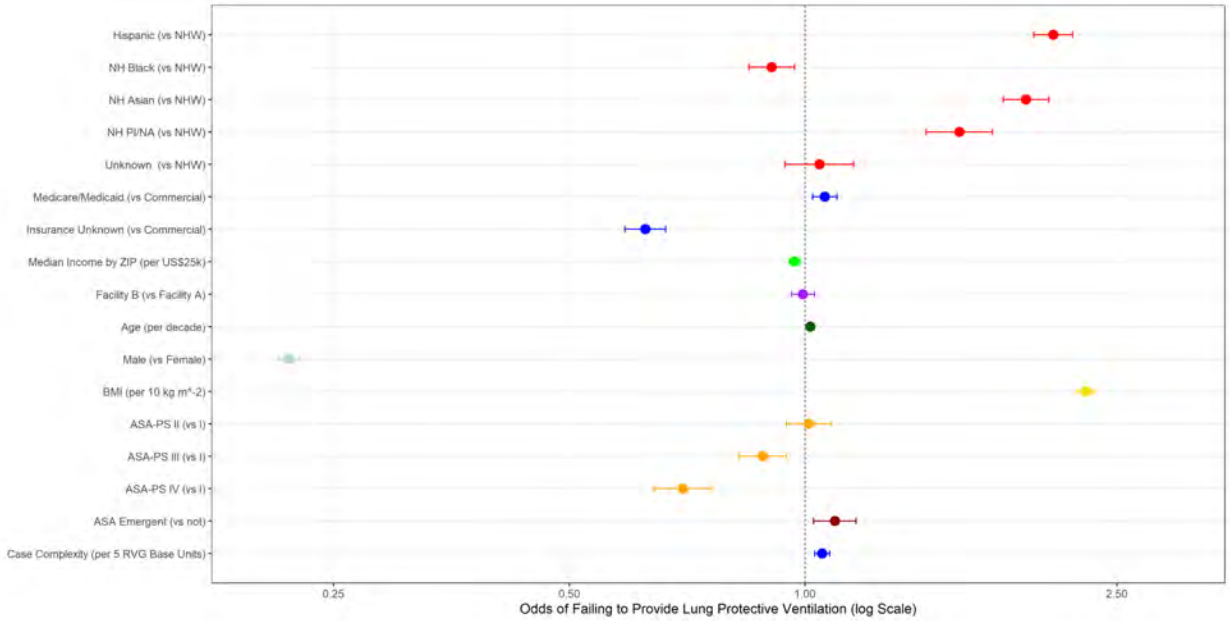
0.25
0.50
1.00
2.50
Odds of Failing to Treat Hyperglycemia (log Scale)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ASA-PS II (vs I)
ASA-PS III (vs I)
ASA-PS IV (vs I)
ASA Emergent (vs not)
Case Complexity (per 5 RVG Base Units)
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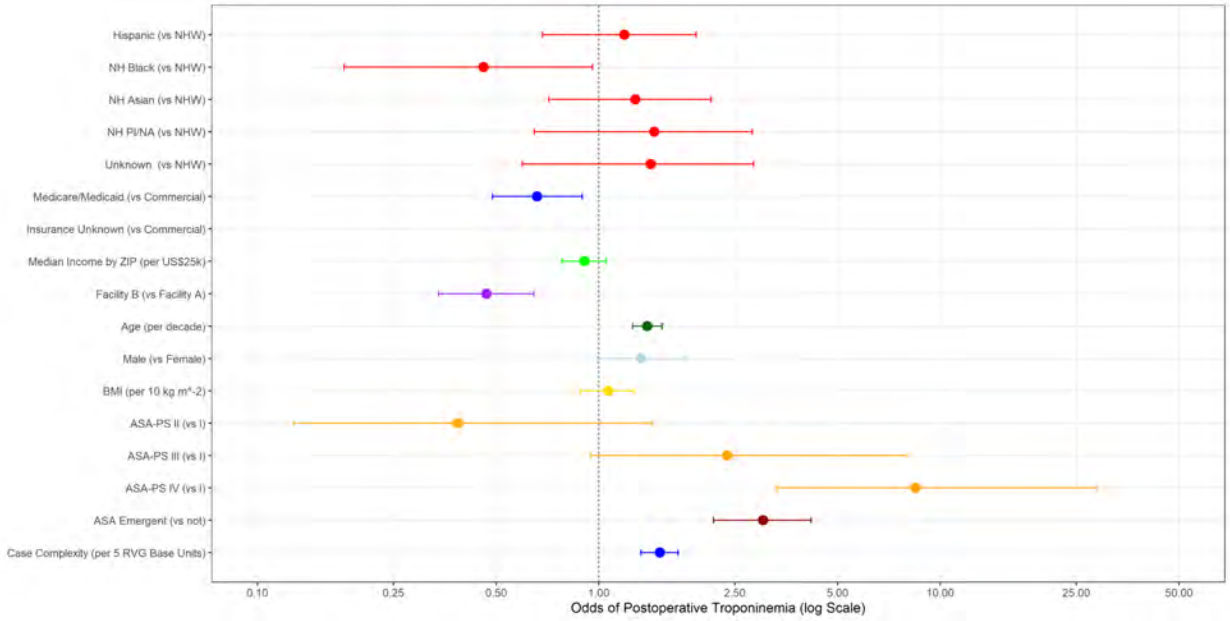
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Median Income by ZIP (per US$25k)
Facility B (vs Facility A)
Age (per decade)
Male (vs Female)
BMI (per 10 kg m^-2)
ASA-PS II (vs I)
ASA-PS III (vs I)
ASA-PS IV (vs I)
ASA Emergent (vs not)
Case Complexity (per 5 RVG Base Units)
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0.50
1.00
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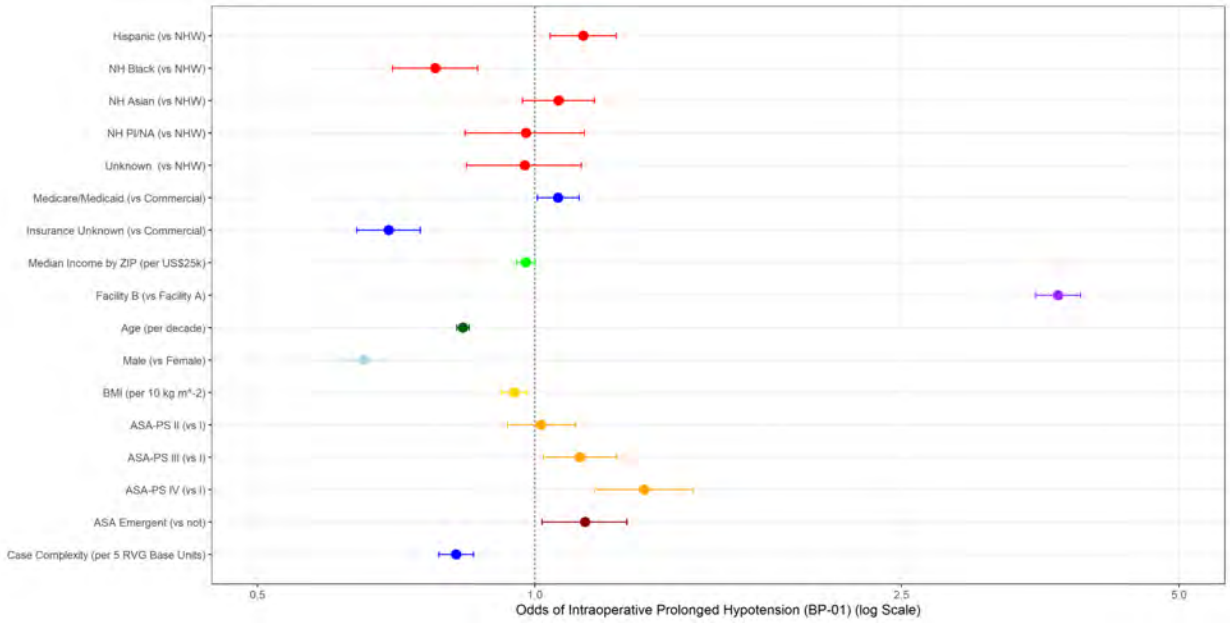
10.00
25.00
50.00
Odds of Postoperative Troponinemia (log Scale)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Medicare/Medicaid (vs Commercial)
Insurance Unknown (vs Commercial)
Median Income by ZIP (per US$25k)
Facility B (vs Facility A)
Age (per decade)
Male (vs Female)
BMI (per 10 kg m^-2)
ASA-PS II (vs I)
ASA-PS III (vs I)
ASA-PS IV (vs I)
ASA Emergent (vs not)
Case Complexity (per 5 RVG Base Units)
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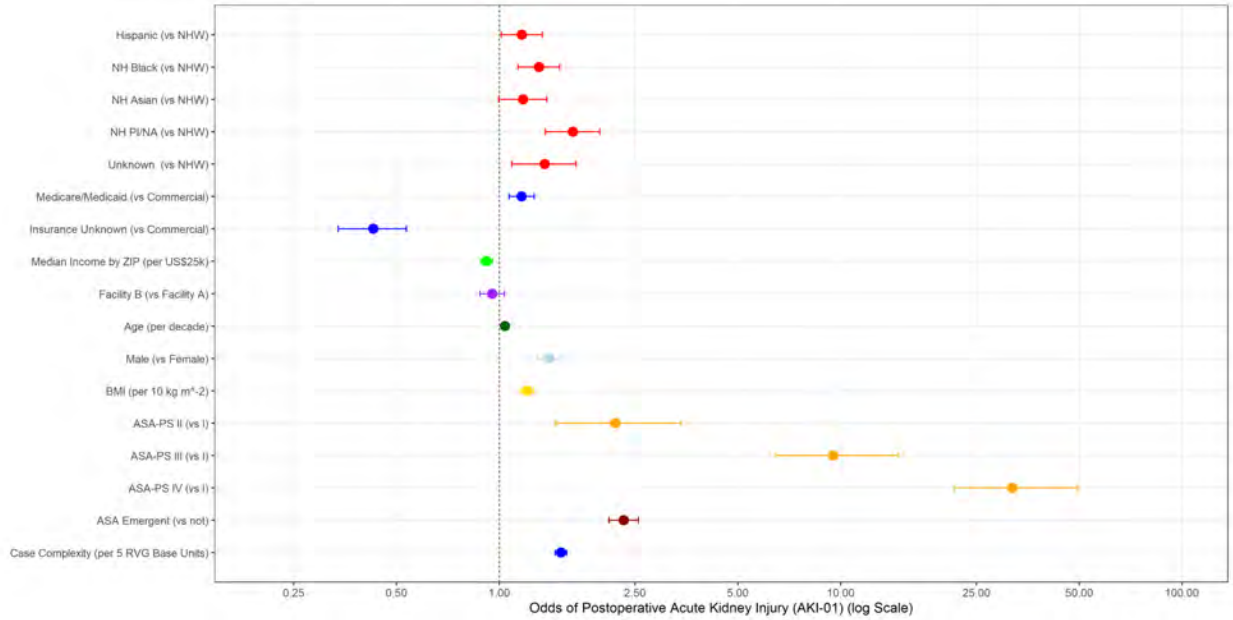
1.0
2.5
5.0
Odds of Intraoperative Prolonged Hypotension (BP-01) (log Scale)


Hispanic (vs NHW)
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NH PI/NA (vs NHW)
Unknown (vs NHW)
Medicare/Medicaid (vs Commercial)
Insurance Unknown (vs Commercial)
Median Income by ZIP (per US$25k)
Facility B (vs Facility A)
Age (per decade)
Male (vs Female)
BMI (per 10 kg m^-2)
ASA-PS II (vs I)
ASA-PS III (vs I)
ASA-PS IV (vs I)
ASA Emergent (vs not)
Case Complexity (per 5 RVG Base Units)
0.25
0.50
1.00
2.50
5.00
10.00
25.00
50.00
100.00
Odds of Postoperative Acute Kidney Injury (AKI-01) (log Scale)

Perioperative Anesthesia – 25

Decreasing Emergence Agitation with Personalized Music (DEAP Music): A Pilot Trial

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Introduction: In the perioperative setting, music has been shown to decrease anxiety and perceived pain, each of which independently increases the risk for emergence agitation (EA).1-8 Personalized music (PM), or selected music that is familiar and meaningful to each patient, has been shown to be a particularly effective adjunct to medical treatment in a variety of settings.9,10 Played intraoperatively, auditory stimulation with maternal voice and standardized music have shown promise in decreasing EA.11,12 There is no research to date studying the perioperative impact of PM. The primary aim of the present study is to assess the effect of PM on EA in pediatric patients recovering from elective procedures under general anesthesia (GA). Secondary aims include assessment of the impact of PM on preoperative anxiety and parental satisfaction with perioperative care. The purpose of this pilot trial was to evaluate implementation feasibility and to test the overall study design before expanding enrollment necessary for adequately powered data analysis..

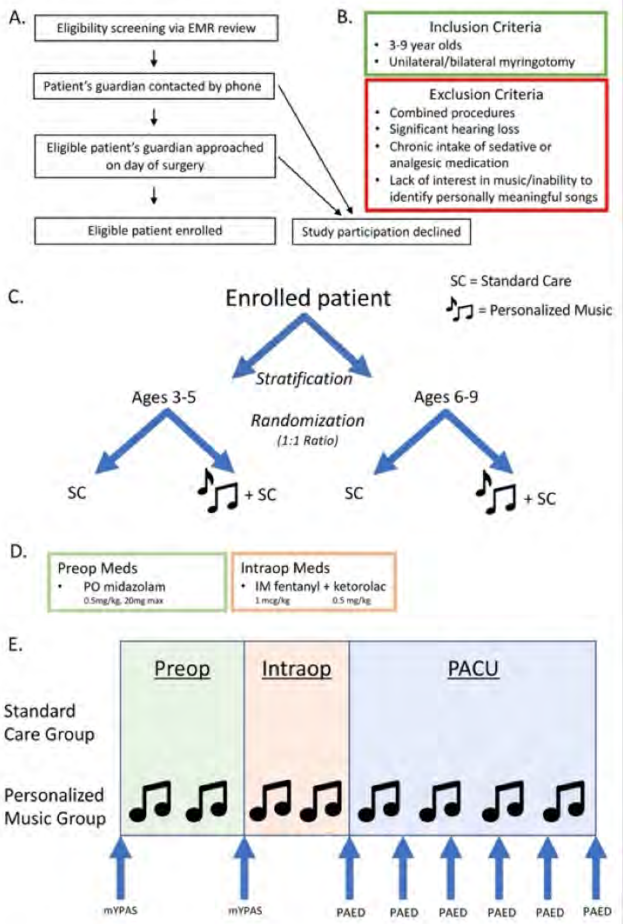
Methods: This was a prospective, 1:1 parallel-group, superiority randomized controlled pilot trial in children 3-9 years of age undergoing myringotomies at a tertiary level care center in the United States. Six patients were enrolled in this pilot study, divided between two groups: a PM group and a standard care (SC) group. Patient eligibility was determined prior to surgery (Fig 1a) based on inclusion and exclusion criteria (Fig 1b). Patients enrolled in this study were randomly assigned to receive SC or SC + PM during the perioperative period (Fig 1c). A standardized anesthetic regimen was utilized for study subjects (Fig 1d), consistent with common practice for simple myringotomies at the University of Vermont Medical Center (UVMMC). The Pediatric Anesthesia Emergence Delirium (PAED) scale was used as the primary outcome measure to assess for EA, collected at 10-minute intervals following discontinuation of the anesthetic (Fig 1e). Secondary measures included the modified Yale Preoperative Anxiety Scale (mYPAS), induction approach (used as a surrogate for mask acceptance), and parent satisfaction surveys. Potential confounders were tracked to assess for an even distribution of patient characteristics in each study group (Table 1). Descriptive statistics were used to analyze our pilot data.

Results: From March through October 2021, seven patients met eligibility criteria for this pilot study, of which six patients were enrolled. No major feasibility issues were encountered in implementing perioperative PM or in the overall study design. Comments recorded by research staff were positive, finding that perioperative teams generally welcomed the integration of PM during their care (Fig 2a). PM intervention was consistent among study patients and never paused, despite reassurance that any staff member was welcome to stop it if it was felt to interfere with patient care. Minor issues were identified during the pilot which prompted adjustments to study processes and slight modifications to the RCT design (Fig 2b). Case volume was also lower than anticipated as projected case numbers were estimated prior to the COVID-19 pandemic; however, enrollment was high (Fig 2c). No patients were withdrawn after enrollment. Patients assigned to receive music did well in all measures of assessment (Fig 3). A PAED score of greater than 12 was considered to be diagnostic of EA, which served as the primary outcome measure.13,14 In this pilot study, no patients in the music group developed EA compared to 66% of patients in the control group (Fig3a). Parent satisfaction was also high in the music group (Fig 4). Study groups were not large enough to evaluate for statistical significance. The methods for data collection and plans for analysis serve as the foundation for beginning the randomized controlled trial.

Conclusion: The results of this pilot show proof-of-concept and proved essential in assessing the feasibility of implementation for a broader randomized controlled trial. Though this initial cohort did not allow in-depth analysis and no conclusions can be drawn at this time, this pilot revealed results that suggest that PM may be a safe and easy non-pharmacologic intervention to decrease EA. The insights gained from the planned multi-center expanded randomized controlled trial present a unique opportunity to improve perioperative care for children, particularly those at high risk for EA.

References: 1. Anesth Analg. 2003;96(6):1625-1630. 2. Anesthesiology. 1961;22:667-673. 3. Anesth Analg. 1998;86(4):781-785. 4. Anesth Analg. 2004;98(1):60-63. 5. Anesth Analg. 2001;92(5):1164-1168. 6. Anesthesiology. 2000;93(6):1378-1383. 7. Br J Anaesth. 2017;118(3):335-343. 8. Paediatr Drugs. 2017;19(1):11-20. 9. Geriatr Nurs. 2018;39(5):560-565. 10. J Am Med Dir Assoc. 2020;21(8):1045-1050.e2. 11. JAMA Otolaryngol Head Neck Surg. 2021;147(7):638-645. 12. Trials. 2017;18(1):430. 13. Paediatr Anaesth. 2018;28(4):332-337. 14. Paediatr Anaesth. 2013;23(12):1131-1137.

Figure 1: Enrollment/Eligibility, Randomization, Meds, and Assessment Timepoints



Legend: After eligibility screening and enrollment (A and B), patients were randomized to receive institutional standard care +/- personalized music in a 1 to 1 ratio, divided between two age groups (C). Once assigned to a study arm, patients were assessed for baseline anxiety and anxiety on parental separation (mYPAS). A standardized anesthetic regimen was planned, consistent with common practice at UVMMC (D). Following the procedure, patients were assessed for emergence delirium (PAED) at 10 minutes intervals (E).

Table 1: Comparison of Study Groups

	Control (n=3)	Music (n=3)
Patient Characteristics		
Age in years, mean (range)	3.5 (3.1-3.8)	6.8 (4.4-9.1)
BMI, mean (range)	18.33 (17.0-20.0)	21.00 (17.0-28.0)
Sex, M:F	2	0.5
PMH related to procedure, % pts	0%	33%[1]
PMH unrelated to procedure, % pts	33%[2]	0%
Anesthetic Factors (% of patients)		
Preop analgesia given	0%	0%
Preop midazolam given	66%	66%
Parental presence	0%	0%
Intraop analgesia (any)	100%[3]	33%
Intraop analgesia per protocol	66%	33%
Perioperative complications (minor)[4]	33%	33%
Perioperative complications (major)[5]	0%	0%
Surgical Factors		
Tympanostomy Tubes Placed, % pts	100%	100%
Ear Drops placed, % pts	100%	33%
Number of tubes places, mean (range)	1.33 (1-2)	2
Number of Ears Receiving Ear Drops, mean (range)	1.33 (1-2)	.33 (0-1)
Surgical Time in minutes, mean (range)	10 (6-15)	8.33 (5-12)
Social Factors		
Parental State Anxiety (STAI-S), mean (range)	43.5 (43-44)	43.67 (40-47)
Parental Trait Anxiety (STAI-T), mean (range)	43.50 (43-44)	44.00 (41-50)

Legend: A difference in mean age and sex is seen in comparing the two study groups. More patients were given intraoperative analgesia and ear drops in the control group compared to the music group. All other patient characteristics and perioperative factors is similar between study groups.

1. Pt w/ Hx of 5 prior myringotomies in music group
2. Pt w/ hx of skull fx in control group, no major sequelae
3. IV fentanyl given to 1 pt in control group instead of IM fentanyl/ketamine per protocol
4. Pt w/ cough in control group, pt with PONV in music group
5. Major complications would include cardiorespiratory compromise requiring intervention (intubation, CPR, overnight admission)

Figure 2: Assessment and Analysis of Feasibility

A.

Comments recorded by research staff related to music intervention:

- *"Surgical resident and med student dancing, smiling, and singing in OR"*
- *"Patient singing in PACU"*
- PACU RN: *"I think he's listening! This is cool."*

B.

Logistical Issue	Pilot Resolution	Plan for RCT
Crowding in preop room during consent	Consent moved to preop holding	Same
Mask acceptance difficult to assess	Used method of induction (gentle vs rapid) as measure of mask acceptance	Add Induction Compliance Checklist (ICC) to assessment measure
Speaker in way during myringotomy	Speaker moved from IV pole to bedrail	Same
Case volume less than anticipated	Extended duration of pilot trial	Expand eligibility criteria to include tonsillectomies (>5x myringotomy case volume) with standardized anesthetic regimen
Uneven distribution of ages seen in study groups	n/a	Decrease size of block randomization to facilitate mid-study analysis

C.

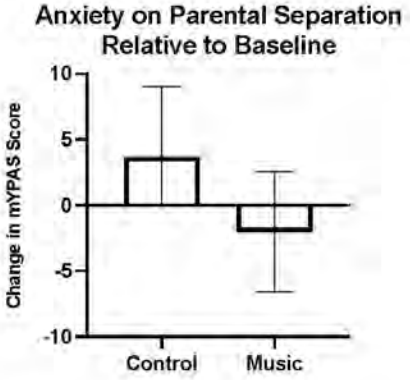
Case Volume fitting Selection Criteria during Enrollment (05-10/2021)	Eligible Case Volume during Enrollment (05-10/2021)	Patients Enrolled	Eligible : Enrolled %	Dropout %
9	7[1]	6[2]	86%	0

Legend: Review of pilot implementation is encouraging for initiating RCT. Perioperative care team comments (A) are positive regarding implementation of PM. Logistical issues (B) encountered allowed for minor revisions to pilot and design modifications for RCT. Low case volume during enrollment was attributed to changes in patient needs following COVID-19 pandemic, which prompted addition of tonsillectomies to inclusion criteria for RCT. Despite low case volume in pilot, enrollment was high relative to eligibility, and dropout was low (C).

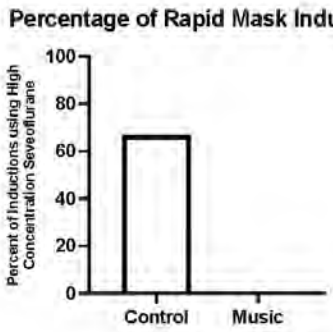
1. Two patients ineligible due to degree of hearing loss/lack of interest in music
2. One patient not enrolled due to research staff availability

Figure 3: Comparison of Perioperative Outcomes

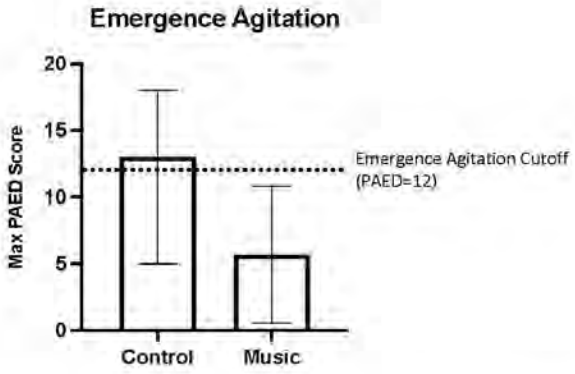
A.



B.

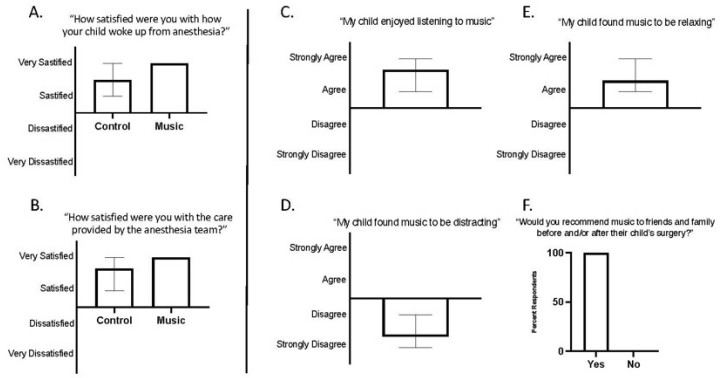


C.



Legend: Pilot data comparing patient anxiety on parental separation (A), percentage of rapid mask inductions (B), and emergence agitation (C), between control and music groups. Data are reported as means with brackets showing range within each set. Percentage of rapid mask indications (B) is reported as a surrogate for mask acceptance, as it indicates the anesthesiologist's decision to slowly vs rapidly titrate inhalational agent on mask induction. Dotted line (C) indicates a PAED score of 12, which is the study's cutoff for emergence agitation.

Figure 4: Parent Satisfaction



Legend: Parental satisfaction in the music group was especially high, with 100% reporting "very high" satisfaction regarding their child's emergence (A) and overall anesthetic care (B). Parents of patients assigned to the music group also reported favorable opinions towards perioperative music (C-E), with 100% of parents stating that they would recommend music for children before/after surgery (F).

Perioperative Anesthesia - 26 Impact of tranexamic acid use on perioperative blood transfusion in pediatric cranioplasty: a retrospective review

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Introduction: Cranioplasty is the surgical reshaping of the skull. It may be required due to several pediatric conditions usually involving the early fusion of one or more suture lines between bony skull plates resulting in asymmetric skull growth and deformity. If left uncorrected, this deformity can result in raised intracranial pressure, cognitive and neurodevelopmental delay, including feeding and speech, as well as psychosocial effects (1). A wide range of surgical procedures can be performed at varying ages involving different surgical complexities. Minimal access techniques are being developed; however, most of the surgery performed at our institution involves open repair. The main intraoperative hazards specific to these procedures are hemorrhage and venous air embolism: blood loss may be massive and sudden, principally from the periosteum and venous sinuses (1). Tranexamic acid (TXA) is an antifibrinolytic drug that has been shown to reduce blood loss in several situations (2). Its use in cranioplasty procedures has been previously described (3). However, evidence of benefit in this group has yet to be established. Our study retrospectively investigated perioperative records for the last six years. We hypothesized that the use of TXA reduced perioperative blood loss and red cell transfusion requirements, while also reducing the length of stay in critical care (LOS). The primary outcome measure looked at the effect of TXA use on the volume of red cells transfused perioperatively. The secondary outcome measures looked at the lowest recorded postoperative hemoglobin, LOS, and the estimated perioperative blood loss (EBL).

Methods: After obtaining IRB approval we performed a retrospective observational investigation on the electronic pediatric patient charts of all those from 0-8 years of age who underwent cranioplasty procedures from 2015 to 2021 at our institution. A data collection form in Excel (Microsoft 365) was designed to collect de-identified patient data. The accessed fields were patient demographics (age, gender, and weight), type of surgery, lowest postoperative hemoglobin, perioperative receipt of TXA, EBL, intraoperative hematocrit, the volume of transfused blood per kilogram of body weight, and LOS. A secondary data sheet was then created to filter and separate those patients that received tranexamic acid (TXA group) from those that did not (non TXA group) to test our study hypothesis. We performed a comparative statistical analysis using the Mann Whitney U test on: the volume of red cells transfused per kilogram body weight; EBL; LOS; and the lowest postoperative hemoglobin. The level of significance used was 0.05.

Results: A total of 71 pediatric patient records were analyzed. Our study included all those aged 0-8 years who underwent cranioplasty procedures between 2015 and 2021. All other patients were excluded. Table 1 lists the median values for the various parameters with the interquartile ranges (IQR) mentioned within brackets. The median age of the TXA group was younger than that of the non TXA group. The median weight of the TXA group was less heavy than that of the non TXA group. The median volume of transfused blood per kg body weight in the TXA group was more than the non TXA group. The median value for the lowest postoperative hemoglobin was similar amongst both groups. The median EBL in the TXA group was less than the non TXA group. The median LOS for the TXA group was less than the non TXA group. The p-value was more than 0.05 for the red cell transfusion volumes, EBL, and lowest postoperative hemoglobin. The p-value was less than 0.01 for the LOS. Figure 1 shows a graphical representation from 2015 to 2021 of the medians and IQRs for the LOS amongst both TXA and non TXA groups.

Conclusion: Our study found no difference in the volume of red cells transfused per kilogram body weight between the two groups. However, there was a significant clinical and statistical difference in the LOS between the TXA and non TXA groups. The reduction

in LOS over time in the TXA group could be a direct effect of the drug; however, other possible confounders were not controlled for in our study. Surprisingly, the TXA group was smaller and younger than their counterparts which might be expected to result in longer critical care stay. We believe our study justifies a prospective controlled investigation of the effect of TXA on LOS and recovery after surgery.

References: (1) Anaesthetic management for craniosynostosis repair in children. 16, 410-416 (2016). (2) Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. 376, 23-32 (2010). (3) The case for the use of tranexamic acid. 23, 281-284 (2013).

Figure 1. Line plot of the TXA vs Non TXA groups. Points are Median (whiskers represent the IQR)

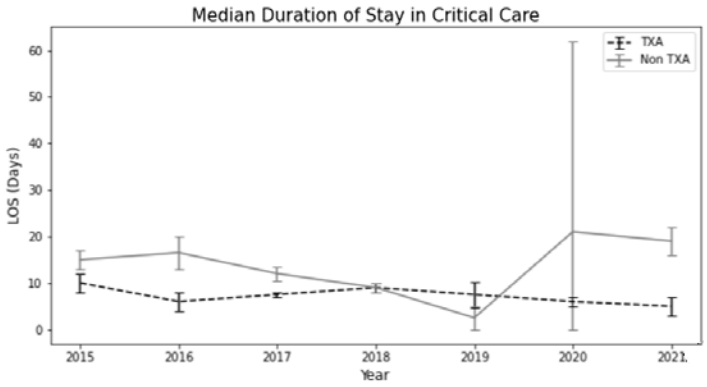

Table 1. Variable parameter values in the TXA vs Non TXA groups. Numbers are Median (IQ range)

	Age (months)	Weight (kg)	Red cell transfusion volumes (ml/kg)	EBL (ml)	Lowest postoperative Hb (g/L)	LOS (days)
TXA	14 (9-21)	10 (8-12)	26 (21-36)	225 (150-300)	96 (86-111)	6 (5-8) *
Non TXA	23 (16-36)	12 (10-14)	23 (9-39)	250 (140-400)	98 (91-114)	12 (9-15) *

*$p < 0.01$

Perioperative Anesthesia - 27 Validation of the modified DASI in the non-cardiac surgical population

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Introduction: The original 12-question Duke Activity Status Index (DASI) has recently been suggested to predict post-operative 30 mortality or adverse myocardial infarction.(1) A further sub-study has suggested that a modified 4 or 5 question DASI (4M-DASI and 5M-DASI, respectively) is equally predictive of peak oxygen uptake (peak VO2) compared to the original DASI.(2) This study also recalibrated the DASI to predict peak VO2, which was shown to predict in-hospital complications in the METS study. We examined a non-cardiac surgery population using these version of DASI to ascertain their ability to predict composite 30-day mortality and post-operative myocardial infarction.

Methods: We conducted a single-center, retrospective study in patients undergoing elective major non-cardiac surgery with hospital stay of greater than 24 hours from January 2018 to August 2021, with a completed DASI within 90-days preoperatively and at least one cardiac risk factor, comprising a prior diagnosis of coronary artery disease, heart failure, cerebral vascular disease, diabetes mellitus, chronic kidney disease, peripheral vascular disease, hypertension, smoking and age greater than 70 years. Our primary outcome was to assess the predictive capacity of the original, recalibrated, the 4M-DASI and 5M-DASI for 30-day mortality and suspected or proven myocardial infarction.

Results: The total patient cohort included 4204 patients, with a median of 66 years [IQR 57-73], 47.5% male, 71.4% Caucasian/white, and 21.4% black or African American. While the predominance of patients were American Society of Anesthesiology (ASA) score 3 or above (73.3%), the predicted peak VO2 (mL/kg) was 22.59 [IQR 17.59-27.96] for the original DASI and 39.61 [IQR 26.63-32.42]. The median 4M-DASI score was 2 [IQR 1-3] and 5M-DASI score was 2 [IQR 1-4]. The proportion of the composite outcome was 2.5% (107 patients) in comparison to the total population. We found the unadjusted versions to the DASI to be weakly predictive of our primary outcome. (Table 1) When adjusting for ASA score 3 or greater and patients with 3 or more risk factors, we found an improvement in the predictive value of all the each of the respective DASI versions (Table 2).

Conclusion: The DASI is weakly predictive of 30-day mortality and confirmed or suspected myocardial infarction in the broader non-cardiac surgery cohort, but its predictive capacity is increased in ASA equal or greater than 3 or for patients with 3 or more cardiac risk factors. The 5M-DASI and 4M-DASI were equally predictive compared to the original 12-question DASI.

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Table 1: Univariate logistic model results describing the predictive impact of each DASI variant on the composite mortality and MI outcome.

Model	OR (95% CI)	p-value	AUC (95% CI)
DASI (per 5 units)	0.85 (0.793, 0.904)	<0.0001	0.63 (0.59, 0.69)
Recalibrated DASI (per 5 units)	0.88 (0.834, 0.933)	<0.0001	0.63 (0.58, 0.68)
M-DASI (Four question)	0.70 (0.603, 0.829)	<0.0001	0.62 (0.57, 0.67)
M-DASI (Five question)	0.74 (0.652, 0.841)	<0.0001	0.63 (0.58, 0.68)

Table 2: Results of multivariable logistic regression models describing the predictive impact of each DASI variant on the composite mortality and MI outcome with covariate adjustments. All models were adjusted by binary covariates describing a patient having an ASA score of 3 or greater, and having 3 or more risk factors.

Model	OR (95% CI)	p-value	AUC (95% CI)
Covariates only	---	---	0.72 (0.68, 0.76)
DASI (5 units) + **Covariates**	0.91 (0.846, 0.970)	0.0048	0.75 (0.70, 0.79)
Recalibrated DASI (5 units) + **Covariates**	0.92 (0.875, 0.974)	0.0036	0.72 (0.68, 0.76)
M-DASI (Four question) + **Covariates**	0.83 (0.700, 0.972)	0.0212	0.74 (0.69, 0.79)
M-DASI (Five question) + **Covariates**	0.84 (0.739, 0.962)	0.0092	0.75 (0.70, 0.79)

Perioperative Anesthesia - 28 Use of intravenous fat emulsion to suppress 18F-fluorodeoxyglucose uptake in non-ischemic myocardium for cardiac positron emission tomography

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Introduction: Determining need for definitive care following post-operative myocardial injury remains challenging.1 We aim to determine whether intravenous fat emulsion suppresses physiological metabolic uptake of 18F-fluorodeoxyglucose (18F-FDG) in non-ischemic myocardium for enhanced cardiac positron emission tomography (PET) imaging. Optimal imaging of ischemic myocardium via 18F-FDG PET imaging requires suppression of background carbohydrate metabolism in normal non-ischemic myocardium. Administration of intravenous lipid emulsion has not previously been used to rapidly prepare unfasted patients, such as during emergent postoperative care.2-4 We assess whether intravenous lipid emulsion as the single preparatory step in unfasted, hyperglycemic patients suppresses non-ischemic myocardial uptake of 18F-FDG.

Methods: We conducted an ethics-approved, single-blind, randomized-crossover trial of 10 healthy volunteers selected via convenience sampling. Participants were unfasted and rendered hyperglycemic before being administered either intravenous lipid emulsion or saline prior to 18F-FDG injection and subsequent cardiac PET/CT imaging, before alternating to the other intervention of either intravenous lipid emulsion or saline. Two blinded nuclear medicine physicians undertook image analysis for maximum standard uptake value (SUVmax), minimum standard uptake value (SUVmin) and qualitative assessment, and groups were compared using univariate analysis. Baseline patient characteristics were summarized using descriptive statistics and were reported for continuous variables as the number of patients, mean, standard deviation, median, inter-quartile range, minimum and maximum, depending on data distribution. Categorical variables were reported as counts and percentages. All patients who completed the 18F-FDG PET study were included in the feasibility analysis. Endpoints of quantitative SUV measurements and the quantitative visual scale for cardiac 18F-FDG PET imaging quality were compared between groups with a Wilcoxon signed rank at $\alpha = 0.05$.

Results: All 10 participants completed the study. The study population age was 44.5 years [IQR 32.5-56.5], with 50% male and a median BMI of 22.75 [IQR 25.0-28.5] kg/m2. The study was feasible and there were no adverse side effects from the interventions. In these participants with normal myocardium, 18F-FDG uptake was significantly reduced by intravenous lipid emulsion as assessed by SUVmax and qualitative assessment ($p = 0.042$, $r = 0.454$ and $p = 0.009$, $r = -0.581$, respectively). There were no significant differences between SUVmin assessments.

Conclusion: We provide proof-of-concept evidence that intravenous lipid emulsion suppresses physiological uptake of 18F-FDG in non-ischemic myocardium of healthy volunteers. Our findings suggest the possibility of future applications for cardiac 18F-FDG PET in acute settings, such as evaluating for myocardial ischemia and establishing the area of myocardium that is at-risk.

References: 1. Devereaux PJ, Sessler DI. Cardiac Complications in Patients Undergoing Major Noncardiac Surgery. New England Journal of Medicine. 2015/12/03 2015;373(23):2258-2269. doi:10.1056/NEJMra1502824 2. Dietz M, Paulmier B, Berthier F, et al. An Intravenous 100-mL Lipid Emulsion Infusion Dramatically Improves Myocardial Glucose Metabolism Extinction in Cardiac FDG PET Clinical Practice. Clin Nucl Med. Jun 1 2021;46(6):e317-e324. doi:10.1097/rlu.0000000000003556 3. Scholtens AM, van den Berk AM, van der Sluis NL, et al. Suppression of myocardial glucose metabolism in FDG PET/CT: impact of dose variation in heparin

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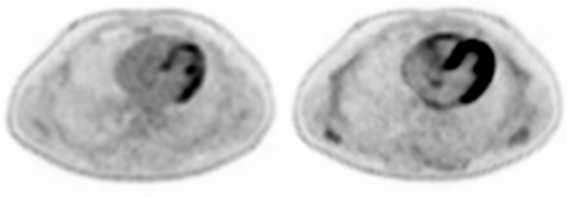

Perioperative Anesthesia - 29 Analysis of Attending Cardiac Anesthesiologists' Physiological Arousal While Taking Over Trainee Tasks in the Operating Room

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Introduction: While academic medicine is essential to provide clinical experience for trainees, intraoperative teaching activities may also introduce unintentional burden on senior team members. Sensor data, including heart rate variability (HRV), affords objective monitoring for physiological arousal analysis, representative of cognitive burden. Previous work has explored the role of cognitive burden according to HRV metrics among perfusionists ,1 surgeons,2 and surgical teams,3-7 but anesthesiologists have received less attention. This preliminary, descriptive study sought to characterize attending anesthesiologists' physiological arousal 1) during trainees' poor performance on discrete tasks and 2) after task takeover.

Methods: The anesthesia induction phase (including induction, intubation and acquisition of lines and invasive access) of non-emergent open cardiac surgery procedures (N=27) was analyzed to identify takeover episodes, marked by times when an individual task transferred from the trainee (resident or SRNA) to the attending anesthesiologist. Using audio-video recordings collected as part of an NIH-funded, IRB-approved research study, episodes were specifically defined as times when the trainee started a task, took their hands off the patient, and the attending took over the task. The subset of cases with takeover episodes (N=6) were further analyzed by calculating HRV values for the attending anesthesiologist over the course of the episodes identified. The low-frequency to high-frequency (LF/HF) ratio HRV component, an indicator of physiological arousal, was calculated for each consecutive minute of the episodes identified. Under resting conditions, reference LF/HF ratio values range from 1.86 to 2.01 units,8 and higher values represent higher levels of physiological arousal.

Results: Seven takeover episodes were identified. Tasks included intubation (N=1), IV placement (N=1), central venous line (CVL) placement (N=2), and arterial line (a-line) placement (N=3). Episodes were categorized into: trainee attempted the task for ‚â§ 5 minutes (N=2) and > 5 minutes (N=5) before the attending took over. For episodes in the latter category, the attending anesthesiologists' physiological arousal was notably higher during periods when observing the trainee's attempt (average LF/HF ratio=7.06 units), and reduced after taking over (average LF/HF ratio=6.28 units). In each episode, the height of physiological arousal was observed preceding the attendings' takeover, evidenced by elevated peaks in LF/HF ratio (Figure 1).

Conclusion: This novel study demonstrated for the first time that objective markers of physiological arousal, including the LF/HF ratio, may be reflective of cognitive burden states during task management with trainees. Accordingly, this study demonstrates that when trainees displayed prolonged difficulty in critical tasks (> 5 minutes), attending anesthesiologists' arousal tended to be higher compared to the time periods corresponding to when they were physically completing the task(s) themselves.

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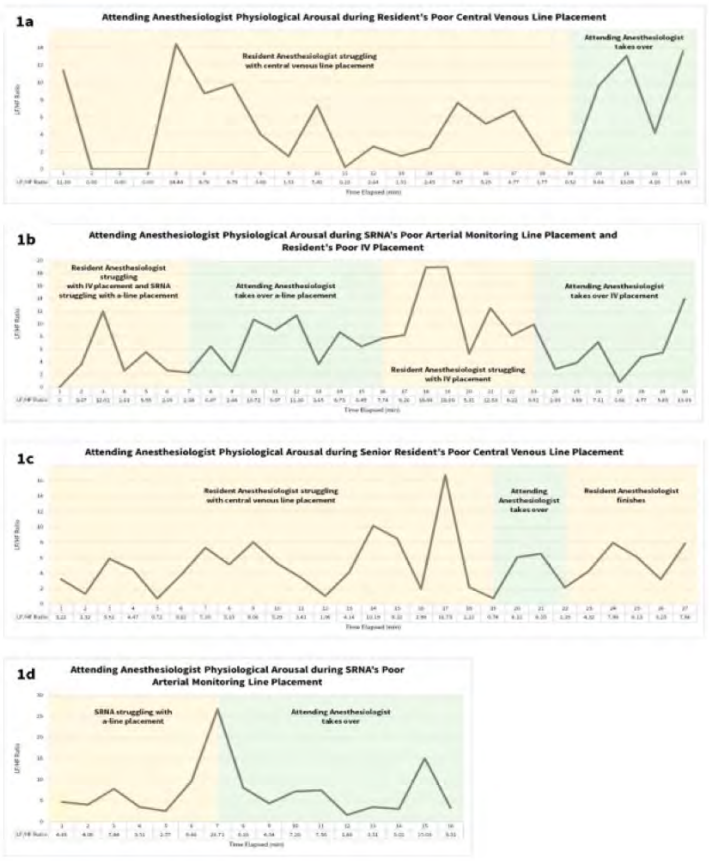

Figure 1. Episodes in which the trainee began a task and persisted for more than 5 minutes (yellow panels), followed by the attending anesthesiologist taking over the task completely (green panels). **1a** demonstrates the attending anesthesiologists' minute-by-minute physiological arousal during a resident's attempted central venous line (CVL) placement; **1b** shows the same data during a resident's attempted IV placement and simultaneously a SRNA's attempted arterial monitoring line (a-line) placement; **1c** represents a resident's attempted CVL placement; and **1d** represents a SRNA's a-line placement.

Perioperative Anesthesia - 30

Preoperative guideline adherent treatment of diabetes and hypertension mitigates the effects of race on adverse discharge

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Introduction: Diabetes mellitus and arterial hypertension are more prevalent among Black compared to White patients in the United States (1-3) and are associated with adverse outcomes after surgery (4-5). The effect of a patient's self-identified race on the postoperative loss of the ability to live independently through adverse discharge to a nursing home after surgery is mediated by severe diabetes mellitus and arterial hypertension (6). In this study, we tested the research hypothesis that adequate preoperative treatment of diabetes mellitus and arterial hypertension adherent to published guidelines mitigates the association between a patient's race and the loss of the ability to live independently after surgery.

Methods: Adult patients of self-identified non-Latinx White and non-Latinx Black race with preoperatively diagnosed severe diabetes mellitus or arterial hypertension who lived at home prior to undergoing surgery at two competing tertiary academic healthcare networks in Boston (Massachusetts, USA) between January 2007 and February 2020 were included in this multicenter hospital registry study. The primary exposure was a patient's self-identified non-Latinx Black compared to non-Latinx White race. The primary outcome was the loss of the ability to live independently after surgery, defined as postoperative adverse discharge to a nursing home or skilled nursing facility (7). To test the primary hypothesis of a modifying effect of adequate guideline adherent treatment on the association between a patient's self-identified race and the primary outcome, we defined guideline adherent treatment of diabetes mellitus and arterial hypertension as prescriptions of medications included in the 2020 American Heart Association and International Society of Hypertension guidelines for these diseases (8-9). We then calculated the proportion of guideline adherent treatment, defined as the number of months with a prescription within 12 months before surgery. This variable was subsequently categorized into no guideline adherent treatment as well as a low (≤ 2 months with prescriptions) and a high (> 2 months with prescriptions) proportion of guideline adherent treatment based on the median number of months with prescriptions in the study cohort. Multivariable logistic regression analysis adjusted for a priori defined patient demographics, comorbidities and intraoperative factors was used to assess the interaction term 'self-identified race*proportion of guideline adherent treatment' on the primary outcome.

Results: Among 129,747 patients who underwent surgery (Figure 1), 17,639 (13.6%) patients identified themselves as non-Latinx Black and 112,108 (86.4%) as non-Latinx White. 13.0% (n=16,852/129,747) of patients lost the ability to live independently after surgery. In adjusted analysis, patients of non-Latinx Black race were at a higher risk of losing the ability to live independently after surgery compared to non-Latinx White patients (adjusted odds ratio [ORadj] 1.27; 95%CI 1.19-1.35; p<0.001). 30.2% of patients received no guideline adherent treatment while 44.3% received a low proportion and 25.5% received a high proportion of guideline adherent treatment. Guideline adherent treatment before surgery modified the association between a patient's race and the loss of the ability to live independently after surgery (p-for-interaction<0.001 for no versus a low proportion of guideline adherent treatment and p-for-interaction<0.001 for no versus a high proportion of guideline adherent treatment) towards a more pronounced effect in patients who did not receive guideline adherent treatment before surgery (ORadj 1.59; 95%CI 1.43-1.78; p<0.001; Figure 2). By

contrast, in patients who received a low proportion of guideline adherent treatment, the effect was mitigated (ORadj 1.20; 95%CI 1.09-1.32; p<0.001; Figure 2) and in patients who received a high proportion of guideline adherent treatment, the effect of self-identified race on the loss of the ability to live independently was insignificant (ORadj 1.07; 95%CI 0.97-1.19; p=0.20; Figure 2).

Conclusion: Adequate preoperative treatment adherent to published guidelines mitigated the effect of a patient's self-identified race on the loss of the ability to live independently after surgery towards a complete effect attenuation. These findings emphasize the value of preoperative treatment in the prevention of racial disparities in perioperative medicine.

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Table 1. Cohort characteristics

ASA, American Society of Anesthesiologists; USD, United States Dollar; ENT, Ear Nose and Throat; MAP, Mean Arterial Pressure; OME, Oral Morphine Equivalent dose.

Characteristic	Non-Latinx White (n = 112,108)	Non-Latinx Black (n = 17,639)
Demographics		
Age, years	64.99 ± 12.71	60.56 ± 13.08
Sex, female	5,3465 (47.7%)	11,057 (62.7%)
Body mass index, kg/m^2	30.79 ± 12.74	31.58 ± 8.10
ASA physical status	3 (2–3)	3 (2–3)
Federal Insurance	58,780 (52.4%)	8,055 (45.7%)
Estimated household income, USD	85,191 (66,556–105,380)	55,333 (49,048–73,034)
Admission Type		
Ambulatory surgery	34,475 (30.8%)	8,193 (46.5%)
Same-day admission	50,456 (45.0%)	5,562 (31.5%)
Inpatient surgery	27,177 (24.2%)	3,884 (22.0%)
Emergency surgery	6,725 (6.0%)	1,143 (6.5%)
Surgical service		
Dent / Oral / ENT	1,993 (1.8%)	271 (1.5%)
Cardiac	4,844 (4.3%)	380 (2.1%)
Gastroenterology	4,442 (4.0%)	1,001 (5.7%)
Interventional Radiology	925 (0.8%)	103 (0.6%)
Ophthalmology	3,974 (3.5%)	1,605 (9.1%)
General Surgery	16,640 (14.8%)	2,152 (12.2%)
Gynecology	7,916 (7.1%)	1,751 (9.9%)
Neurosurgery	6,569 (5.9%)	595 (3.4%)
Orthopedic	22,057 (19.7%)	3,579 (20.3%)
Plastic	3,485 (3.1%)	557 (3.2%)
Podiatry	2,560 (2.3%)	635 (3.6%)
Surgical Oncology	3,760 (3.4%)	664 (3.8%)
Thoracic	7,646 (6.8%)	675 (3.8%)
Transplant	2,992 (2.7%)	980 (5.6%)
Trauma / Surgical Critical Care	5,941 (5.3%)	762 (4.3%)
Urology	9,483 (8.5%)	1,223 (6.9%)
Vascular	6,881 (6.1%)	703 (4.0%)
Comorbidities		
Charlson Comorbidity Index	2 (1–4)	2 (1–5)
Non-severe diabetes mellitus	32,382 (28.9%)	7,650 (43.4%)
Severe diabetes mellitus	15,672 (14.0%)	4,595 (26.1%)
Moderate to severe renal disease	16,608 (14.8%)	4,166 (23.6%)
Arterial hypertension	107,729 (96.1%)	16,701 (94.7%)
Intraoperative factors		
Duration of surgery, min	125 (67–205)	97 (53–162)
Work relative value units	12.71 (6.41–21.79)	9.53 (5.32–17.40)
General anesthesia	89,388 (79.8%)	11,437 (64.9%)
Monitored anesthesia care	21,753 (19.4%)	5,944 (33.7%)
Fluids, ml	1,000 (500–1,800)	700 (400–1250)
MAP < 55 mmHg, min	0 (0–2)	0 (0–1)
Total vasopressor dose, mg	0.02 (0.00–0.21)	0.00 (0.00–0.06)
Total opioid dose (OME), mg	42.00 (17.00–75.00)	25.00 (5.00–59.00)

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range (25th-75th percentile), values separated by comma).

Figure 1. Study flow diagram

ASA, American Society of Anesthesiologists.

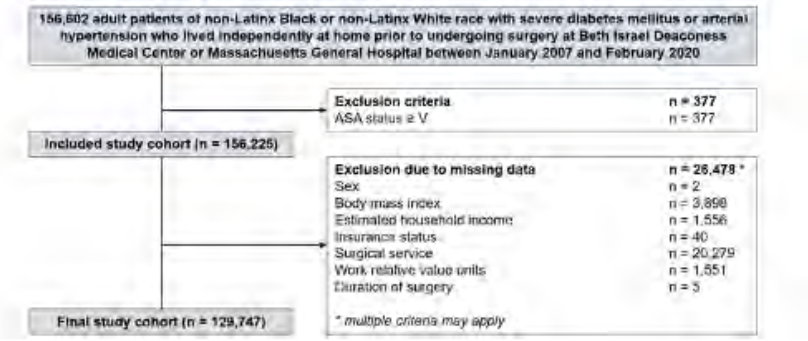
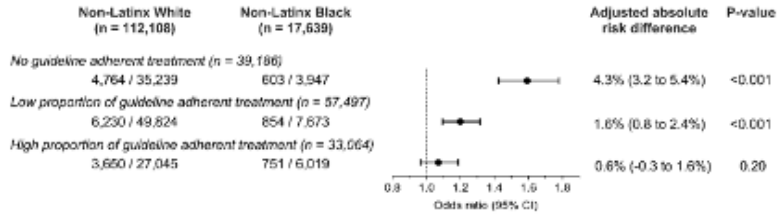


Figure 2. Effect modification by guideline adherent treatment before surgery

The results of the effect modification and subgroup analyses are shown. Preoperative guideline adherent treatment significantly modified the association between a patient's self-identified race and the loss of the ability to live independently after surgery. If patients did not receive guideline adherent treatment before surgery, the adverse effect in non-Latinx Black compared to non-Latinx White patients was magnified. By contrast, in patients who received a low proportion of guideline adherent treatment, the effect was mitigated and in patients who received a high proportion of guideline adherent treatment, the effect of self-identified race on the loss of the ability to live independently was insignificant.



Perioperative Anesthesia - 31 Failure of Sugammadex to Improve Operating Room Discharge Times following Laparoscopic Cholecystectomy

Danielle Esnard[1], Christian Lee[1], David Broussard[2], Stuart Hart[3], Alex Allain[2], Brittany Bond[2], Eric Busch[2], Preya Jhita[2], Melissa Matte[2], Robin Stedman[4], Jacob Lessing[2], Bobby D Nossaman[3]

[1]Ochsner Health, New Orleans, LA, [2]Ochsner Health, New Orleans, United States of America, [3]Ochsner Clinic Foundation, New Orleans, LA, [4]Ochsner Health System, New Orleans, LA

Introduction: Studies examining perioperative time savings with sugammadex have been limited to small group analyses,[1,2] meta-analysis,[3] or in hypothetical time efficiency models.[4-6] The purpose of this study was to determine the clinical effectiveness of sugammadex when compared to neostigmine under real-world, non-Hawthorne effect[7] conditions on operating room discharge times in patients following laparoscopic cholecystectomy.

Methods: Following institutional review board approval, data from 1,614 consecutive surgical records for laparoscopic cholecystectomy were electronically abstracted from May 2020 to May 2021. Patient characteristics, type of primary neuromuscular blocking reversal agent, and operating room (OR) discharge times were the measures of interest. Categorical variables were presented as counts and percentages with 95% confidence intervals (CI) with group differences assessed using chi-square (œá¬≤) tests. Continuous variables with skewed distributions were presented as medians with 25%-75% interquartile range [IQR] with differences between the two groups assessed by the Wilcoxon rank sum test. Geometric means were expressed with associated CI.

Results: Patient demographics are shown in Table 1. There were no statistically significant differences in age, gender, or in the ASA PS scores between the two neuromuscular blocker reversal agents (Table 1). The OR discharge times for the two neuromuscular blocking agents are shown in Figure 1. Box-plots for OR discharge times for sugammadex and for neostigmine are shown in the left panel and when the OR discharge times are expressed as Normal Quantile plots on the right panel (Fig. 1). The median and 25-75% interquartile (IQR) times for sugammadex was 9.0 min IQR 7.0-13 min and neostigmine 8.0 min IQR 6.0-11 min. Geometric mean times for sugammadex were 9.1 min CI 9.1-9.2 min and 8.0 min CI 8.01-8.03 min for neostigmine. A discernable difference in the slopes of the OR discharge times for the two neuromuscular blocking reversal agents begins to declare at the .64 quantile (green line, right panel) with the slope of the OR discharge times progressively increasing more for sugammadex when compared to neostigmine. The OR discharge times slope for neostigmine (blue line) was less acute when compared to the OR discharge times slope for sugammadex (right panel).

Conclusion: These results suggest no benefit of sugammadex when used as a primary neuromuscular blocking reversal agent to improve OR discharge times when compared to neostigmine following laparoscopic cholecystectomy.

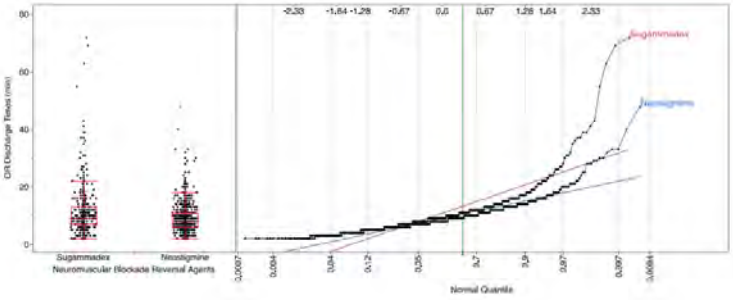
References: 1. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. Anaesthesia. 67(9):991-8. 2012. 2. Impact of Neostigmine and Sugammadex on Time to Leaving the Operating Room in a Community Hospital. Innov Pharm. 11(3). 2020. 3. Role of sugammadex in accelerating postoperative discharge: A meta-analysis. J Clin Anesth. 39:38-44. 2017. 4. A Clinical and Budgetary Impact Analysis of Introducing Sugammadex for Routine Reversal of Neuromuscular Blockade in a Hypothetical Cohort in the US. Adv Ther. 38(5):2689-708. 2021. 5. A discrete event simulation model of clinical and operating room efficiency outcomes of sugammadex versus neostigmine for neuromuscular block reversal in Canada. BMC Anesthesiol. 16(1):114. 2016. 6. Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: a systematic review and economic evaluation. Br J Anaesth. 105(5):558-67. 2020

Table 1: Baseline Characteristics in 1,614 Patients with Sugammadex or Neostigmine as the Primary Neuromuscular Blocking Reversal Agent following Laparoscopic Cholecystectomy

	Sugammadex	Neostigmine	P Value
Age, yrs median [IQR]	49 [35-62]	47 [33-61]	0.2778
Gender, m (%)	151 (26.7)	294 (29.9)	0.1658
ASA PS, counts (%)			
I	28 (4.7)	63 (6.2)	
II	331 (55)	613 (61)	0.0196
III	229 (38)	322 (32)	
IV	14 (2.3)	14 (1.8)	

IQR: 25-75% interquartile range; Gender, m: male; ASA PS: American Society of Anesthesiologists' Physical Status Score; P values <0.005 are statistically significant.

Figure 1



Perioperative Anesthesia - 32 The Preoperative Skin Microbiome is Associated with Causes of Surgical Site Infection in Spinal Fusion Surgery and Varies by Operative Level

Dustin R Long[1], Chloe Bryson-Cahn[2], Jeannie Chan[2], Rajiv Saigal[3], Adam Waalkes[1], John Lynch[4], Stephen J Salipante[1]

[1]University of Washington, Seattle, WA, [2]Harborview Medical Center, Seattle, WA, [3]University of California, San Francisco, San Francisco, CA, [4]Harborview Medical Center, Seattle , WA

Introduction: Surgical site infection (SSI) is a devastating outcome of instrumented spine surgery, occurring in as many as 1 in 30 procedures with adverse impacts on patient satisfaction, pain, functional outcomes, and healthcare costs[1,2]. Quality improvement in this arena is limited by a poor fundamental understanding of the pathogenesis of these infections. We and others have previously described an anatomic gradient in the pathogens causing SSI following spinal fusion, transitioning along the length of the back from gram-positive infection at cervical levels to gram-negative infection at lumbosacral levels [3,4]. These observations suggest that the patient skin microbiome may be a primary source for SSI in modern spine surgery; however, the back is a poorly characterized region of the human skin microbiome. The objective of this study was to determine whether observed anatomic differences in the causes of SSI are associated with differences in the preoperative skin microbiome at various operative levels.

Methods: Adult patients undergoing posterior spinal fusion surgery at a single, high-volume academic medical center between September 2019 and August 2020 were included. Preoperative swabs from skin overlying the intended surgical site were obtained on the day of surgery, immediately prior to surgical skin preparation. Multiple samples spanning 10 positions from C2 to coccyx were also collected prior to the day of surgery among a subset of enrolled patients. Standard processes for DNA extraction, 16S PCR, and amplicon sequencing were followed5. Analysis of sequence data was performed using QIIME 2[6] and R[7].

Results: Among 209 enrolled patients, adequate specimens were obtained from 204 (97%). A subset of 110 samples from cases confined to only cervical (21%) or lumbosacral (79%) operative levels and further stratified by patient sex (to provide balanced representation within each region) were selected for sequencing and analysis. The relative abundance of potentially pathogenic gram-positive flora was greater in cervical skin regions while gram-negative organisms predominated in preoperative lumbosacral skin regions (Fig 1). This anatomic gradient persisted at the individual patient level, with most patients showing a graded transition in skin flora along the length of the back (Fig 2). Marked differences in the anatomic distribution of several specific taxa were observed. Staphylococci demonstrated the greatest enrichment in preoperative skin samples collected at cervical levels whereas Escherichia, Pseudomonas, Enterobacter, and anaerobes were more abundant at lumbosacral levels. (Fig 3).

Conclusion: Anatomic differences in the preoperative skin microbiome are closely correlated with the causative bacteria identified in postoperative wound cultures from cases of spinal fusion SSI. Future infection prevention research in spine surgery should prioritize strategies targeting perioperative control of the patient skin microbiome. The efficacy of alternative or personalized prophylactic antibiotic regimens that account for anatomic and individual differences in preoperative skin colonization should be evaluated.

References: 1. Clinical outcomes after lumbar fusion complicated by deep wound infection: a case-control study. Spine 2012; 37:1370-4 2. Global Treatment Outcome after Surgical Site Infection in Elective Degenerative Lumbar Spinal Operations. Surg Infect 2020 doi:10.1089/sur.2019.344 3. Anatomic Gradients in the Microbiology of Spinal Fusion Surgical Site Infection and Resistance to Surgical Antimicrobial Prophylaxis. Spine (Phila Pa 1976) 2021; 46:143-51 4. Surgical site infections in spine surgery: identification of microbiologic and surgical

characteristics in 239 cases. Spine 2013; 38:E1425 31 5. Optimisation of methods for bacterial skin microbiome investigation: primer selection and comparison of the 454 versus MiSeq platform. Bmc Microbiol 2017; 17:23 6. Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2. Nat Biotechnol 2019; 37:852-7 7. R Foundation for Statistical Computing, Vienna, Austria., 2021 at <https://www.R-project.org/>

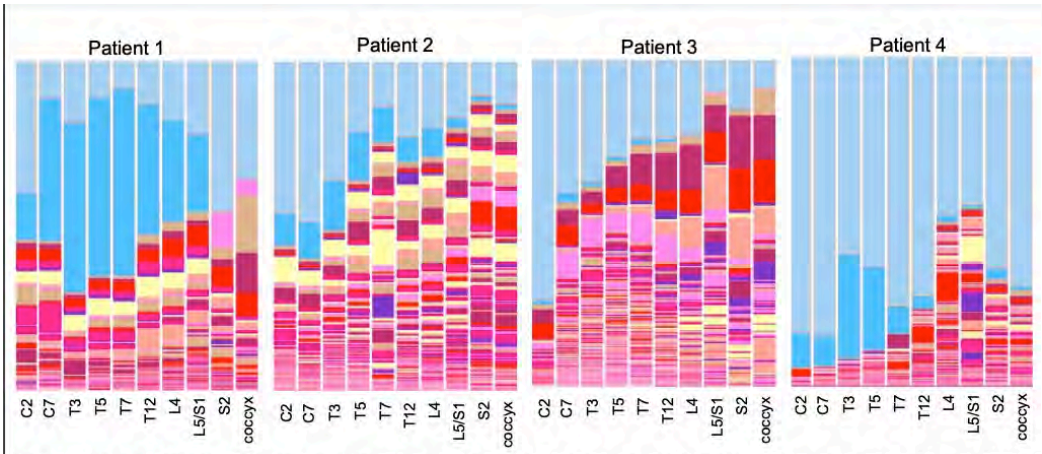


Figure 2. Anatomic gradients in the skin microbiome along the length of the back in individual patients. As in Figure 1, the relative abundance of preoperative skin flora is shown on the vertical axis with bars shaded to discriminate key gram-positive (blue) vs. gram-negative (red/purple) organisms. However, in this analysis, multiple samples from four patients were collected at ten points along the length of the back (stratified along the horizontal axis from C2 to coccyx). These results indicate that the shift from gram-positive (cervical) to gram-negative (lumbosacral) skin colonization represents true gradient across anatomic space, rather than a population-level phenomenon arising from generalized differences in the skin microbiomes of patients undergoing cervical vs. lumbar fusion.

Table 1: Baseline Characteristics in 1,614 Patients with Sugammadex or Neostigmine as the Primary Neuromuscular Blocking Reversal Agent following Laparoscopic Cholecystectomy

	Sugammadex	Neostigmine	P Value
Age, yrs median [IQR]	49 [35-62]	47 [33-61]	0.2778
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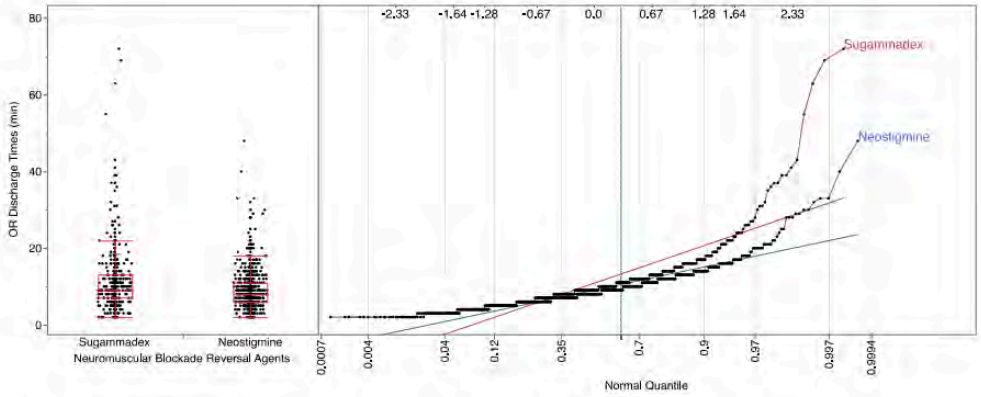
IQR: 25-75% interquartile range; Gender, m: male; ASA PS: American Society of Anesthesiologists' Physical Status Score; P values <0.005 are statistically significant.

Figure 1



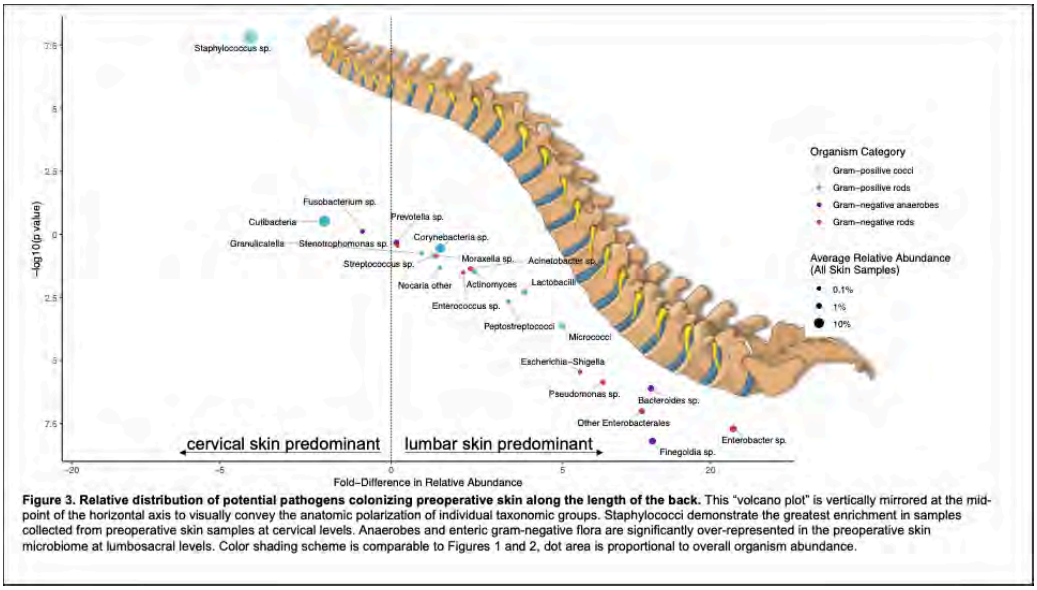


Figure 3. Relative distribution of potential pathogens colonizing preoperative skin along the length of the back. This "volcano plot" is vertically mirrored at the mid-point of the horizontal axis to visually convey the anatomic polarization of individual taxonomic groups. Staphylococci demonstrate the greatest enrichment in samples collected from preoperative skin samples at cervical levels. Anaerobes and enteric gram-negative flora are significantly over-represented in the preoperative skin microbiome at lumbosacral levels. Color shading scheme is comparable to Figures 1 and 2, dot area is proportional to overall organism abundance.

Perioperative Anesthesia - 33

Implementation and Evaluation of Point-of-Care Ultrasound OSCEs Amongst CA3 Residents across Multiple Residency Programs

Timothy T Tran[1], Nibras Bughrara[2], Clinton Kakazu[3], Sara Nikravan[4], Charandip Sandhu[5], Mandeep Singh[6], Christine Vo[7], Ryan Tone[8], Jay Y Shen[9]

[1]University of Colorado, Denver, United States of America, [2]Albany Medical College, Albany, NY, [3]Harbor-UCLA Medical Center, Los Angeles, CA, [4]University of Washington Medical Center, Seattle, WA, [5]University of California Davis, Sacramento, CA, [6]University of Southern California, Keck School of Medicine, Los Angeles, CA, [7]University of Oklahoma, Oklahoma City, OK, [8]Loma Linda University, Loma Linda, CA, [9]UC Irvine Health, Irvine, CA

Introduction: POCUS educational curriculums across anesthesiology residencies are currently variable in structure. To aid curriculum development, we proposed a multi-institutional study during which each participating program performed a standardized POCUS OSCE on their graduating Clinical Anesthesiology-3 residents. Each program followed standardized scripts, POCUS OSCE scenarios, and grading rubrics to evaluate resident POCUS capabilities with a focus on the cardiopulmonary system. Our primary goal of this study was to describe how to implement a POCUS OSCE and evaluate anesthesia residents on their POCUS skills in their last 6 months of training to prepare them for their upcoming OSCE board examinations. Objectives included resident satisfaction surveys and resident OSCE scores.

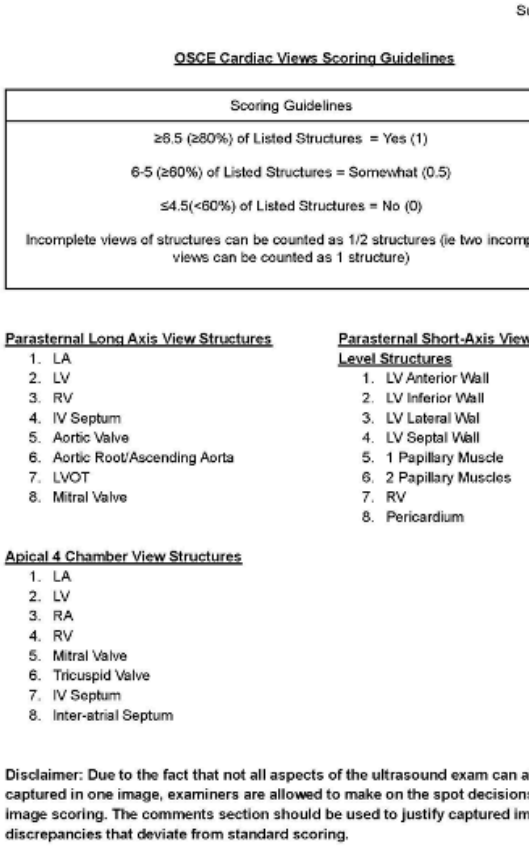
Methods: Nine institutions participated in the study (Albany Medical Center, University of Colorado, UCLA-Harbor, Loma Linda University, University of Oklahoma, University of California-Davis, University of California-Irvine, University of Washington, University of Southern California). Each site obtained individual institutional review board approval and signed a data-sharing agreement with the primary site (UC-Irvine). Examine Site Preparation The primary site distributed testing preparation materials to each site prior to examination to ensure standardized OSCE setup and grading. The test preparation materials included the following: 1. A OSCE demonstration video demonstrating room setup, time structure, and various instructions. 2. An OSCE POCUS views scoring rubric which included examples of views and their corresponding scores. 3. A 7-criteria general competency Likert scoring scale to aide in scoring the general competency question. OSCE Examination Study participants were pre-randomized to receive one of three test forms to ensure normalized distribution. Each test form contained 2 sections; Section 1 focused on cardiac ultrasound and Section 2 focused on pulmonary ultrasound. Emulating the structure of the current ABA Applied Examination, subjects were given an introduction prompt to read prior to entering the testing room for 4 minutes. Subjects then had 8 minutes in the testing room. Each section of the test contained 4 questions with a time limit of three minutes per section. This allowed 1 minute for setup and 1 minute for examiner grading. Thus, each OSCE examination totaled 12 minutes. Each section of the exam had the general format of: 1. Obtain specific ultrasound view 2. Identify relevant structures 3. Identify relevant structures 4. Question on topic Images and answers from the exam were saved and were graded according to the pre-defined scoring rubric with 1=Yes, 0.5=somewhat, 0=None which is structured similarly to the ABA Applied Exam matrix

Results: 36 Subjects took Test Form A, 38 took Test Form B, 36 took Test Form C. Scores for obtaining the A4C view were the lowest (Mean 0.731, SD 0.36), compared to PSAX (Mean 0.833, SD .316) and PLAX (Mean 0.806, SD 0.344). Mean scores for identifying structures were overall high > 0.7 with the notable exception of identifying the left ventricular inferior wall on PSAX (mean 0.611, SD 0.494), and where to measure Fractional Shortening on PLAX (mean 0.472, SD 0.506). In addition, subjects positioned the patients well (mean > 0.9) Scores for the lung portion were more variable. Subjects who took the pneumothorax exam scored well (> 0.8) all questions except how to describe what a pneumothorax would like in M-Mode (Mean 0.609 SD 0.492). The most difficult test for the subjects was the pleural effusion exam; approximately 1/3 of the subjects did not choose the correct probe for the exam, choosing a linear probe over the phased array or curvilinear probe. This likely led to overall low

scores in structure identification and interpretation. The mean total score for this exam was 2.95/5 with a SD 1.5 which was below a passing score.

Conclusion: This is first study to evaluate the impact of a practice POCUS OSCE exam in graduating anesthesiology residents. The pre- and post-examination survey demonstrated positive feedback from graduating residents regrading POCUS OSCEs. The scores on the OSCE examination highlighted areas to improve resident POCUS education in preparation for the ABA Applied Examination. Additional in-depth analysis on program POCUS education and scoring are on-going.

References: 1. Accreditation Council for Graduate Medical Education. ACGME Program Requirements for Graduate Medical Education In Anesthesiology. 25-26. 2.Johnson, DW, Oren-Grinberg, A Perioperative point-of-care ultrasonography: The past and the future are in anesthesiologists,Äô hands.. ANESTHESIOLOGY. (2011). 115 460-2 3. Conlin F, Roy Connelly N, Raghunathan K, et al. Focused transthoracic cardiac ultrasound: a survey of training practices. J Cardiothorac Vasc Anesth. 2016;30(1):102-106. doi: 10.1053/j.jvca.2015.05.111. 4. Ramsingh D, Rinehart J, Kain Z, et al. Impact Assessment of Perioperative Point-of-Care Ultrasound Training on Anesthesiology Residents. Anesthesiology 2015;123(3),670-682. 5. Epstein RM. Assessment in medical education. N Engl J Med. 2007;356:387-396. 6. Sloan D, Donnelly MB, Schwartz R, Strodel W. The objective structured clinical examination - the new gold standard for evaluating postgraduate clinical performance. Ann Surg. 1995;222(6):735-742.



OSCE Cardiac Views Scoring Guidelines

Scoring Guidelines
≥6.5 (≥80%) of Listed Structures = Yes (1)
6-5 (≥60%) of Listed Structures = Somewhat (0.5)
≤4.5(<60%) of Listed Structures = No (0)
Incomplete views of structures can be counted as 1/2 structures (ie two incom views can be counted as 1 structure)

Parasternal Long Axis View Structures
1. LA
2. LV
3. RV
4. IV Septum
5. Aortic Valve
6. Aortic Root/Ascending Aorta
7. LVOT
8. Mitral Valve

Parasternal Short-Axis View Level Structures
1. LV Anterior Wall
2. LV Inferior Wall
3. LV Lateral Wal
4. LV Septal Wall
5. 1 Papillary Muscle
6. 2 Papillary Muscles
7. RV
8. Pericardium

Apical 4 Chamber View Structures
1. LA
2. LV
3. RA
4. RV
5. Mitral Valve
6. Tricuspid Valve
7. IV Septum
8. Inter-atrial Septum

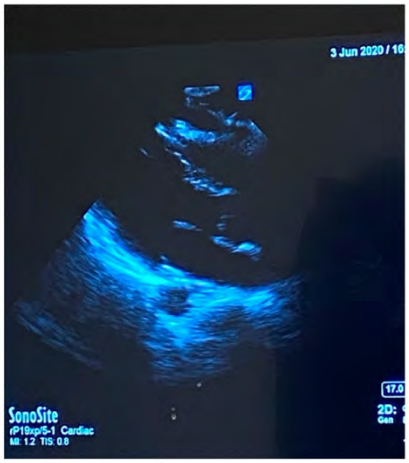
Disclaimer: Due to the fact that not all aspects of the ultrasound exam can a captured in one image, examiners are allowed to make on the spot decision image scoring. The comments section should be used to justify captured im discrepancies that deviate from standard scoring.

Subject ID_____

Cardiac Image Scoring Examples

Parasternal Long Axis Examples

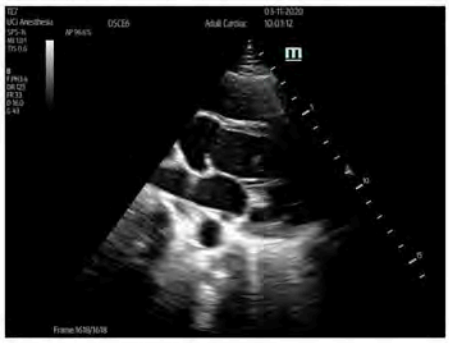
Examples of Yes (1) views:



Comment: Good View

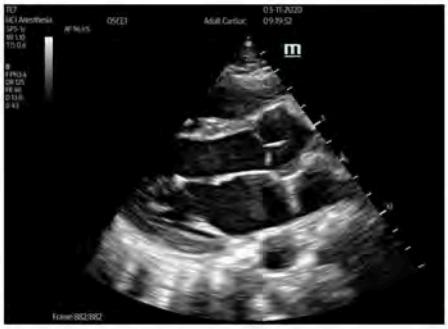
Subject ID_____

Examples of Somewhat (0.5) views:



Comment: Incomplete view of LA, LV, IV Septum, Mitral Valve

Subject ID_____

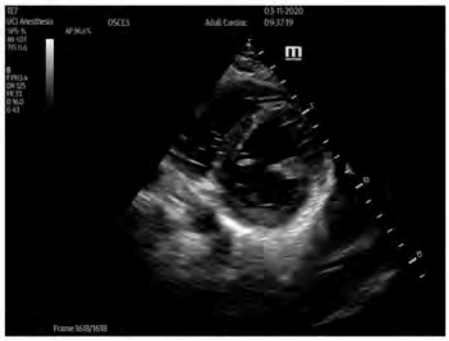


Comment: Incomplete view of LA but still good

Subject ID_____

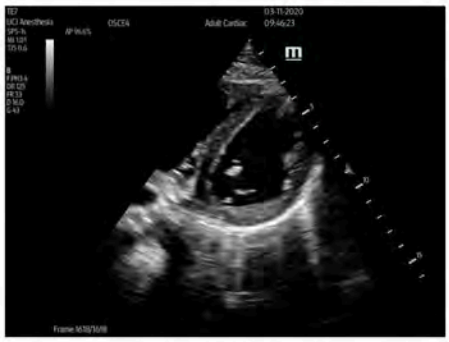
Parasternal Short Axis Examples

Examples of Yes (1) views:



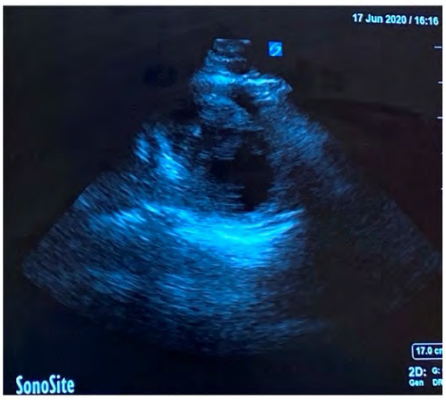
Comment: Good view, both papillary muscles seen in short axis

Subject ID____



Comment: We see One papillary muscle in short axis, but still acceptable

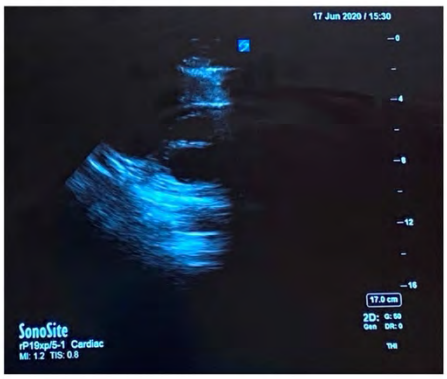
Subject ID____



Comment: Short axis towards apex (no papillary muscles seen)

Subject ID____

Examples of Somewhat (0.5) views:

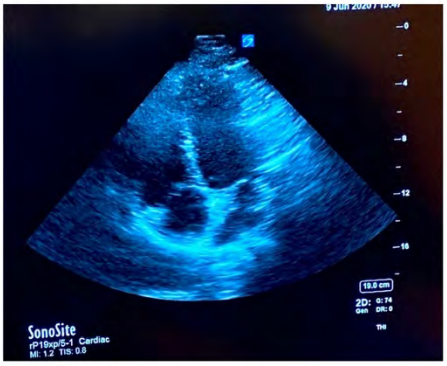


Comment: More of a short axis basal (lvl of mitral valve view)

Subject ID____

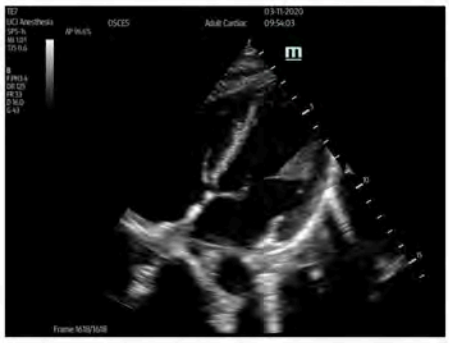
Apical 4 Chamber Examples

Examples of Yes (1) views:



Comment: All 4 chambers visualized although 3 partially incomplete

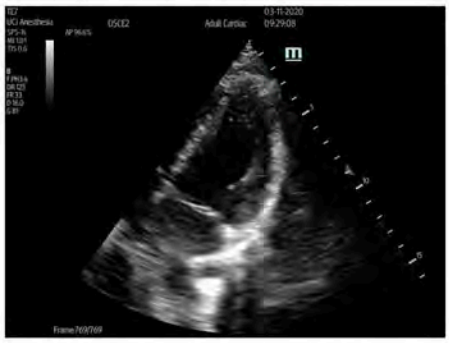
Subject ID_____



Comment: All 4 chambers visualized, but too zoomed in

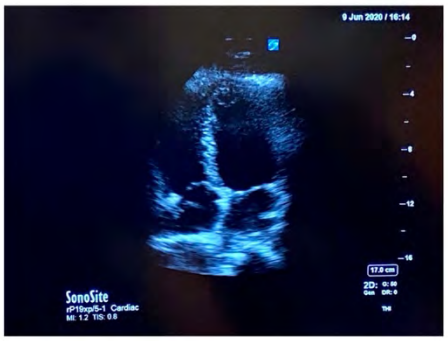
Subject ID_____

Examples of Somewhat (0.5) views:



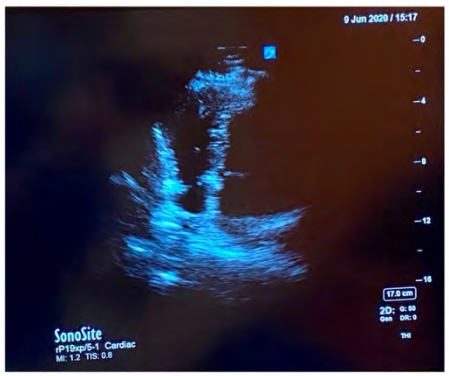
Comment: Incomplete views of RV, RA, TV, Atrial Septum (Total = 6 Structures)

Subject ID_____



Comments: All 4 chambers visualized

Subject ID_____



Comment: Incomplete views of LV, LA, RV, RA, TV, MV. (Total = 5 structures)

Subject ID_____

OSCE Pulmonary Views Scoring Guidelines

Scoring Guidelines
≥4 (≥80%) of Listed Structures = Yes (1)
3 (≥60%) of Listed Structures = Somewhat (0.5)
≤2 (<60%) of Listed Structures = No (0)
All or none, no ½ structures

Lung view for PTX Structures

1. 1 Rib
2. 2 Ribs
3. Lung Parenchyma
4. Pleural Line
5. Intercostal Muscles

Lung view for Pleural Effusion Structures

1. Liver
2. Diaphragm
3. Lung Parenchyma
4. Pleural Line
5. A Lines

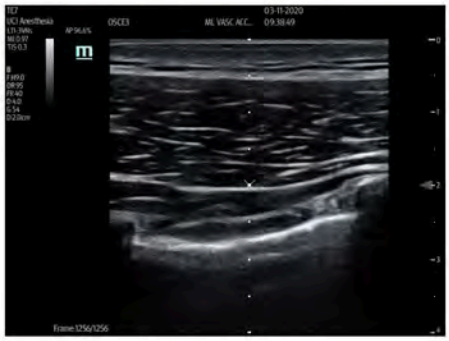
Disclaimer: Due to the fact that not all aspects of the ultrasound exam can always be captured in one image, examiners are allowed to make on the spot decisions regarding image scoring. The comments section should be used to justify captured image discrepancies that deviate from standard scoring.

Subject ID_____

Pulmonary Image Scoring Examples

PTX Examples:

Examples of Yes (1) views:



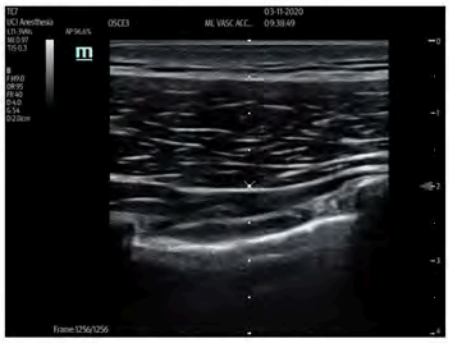
Comments: Excellent view with 2 rib shadowing

Subject ID_____

Pulmonary Image Scoring Examples

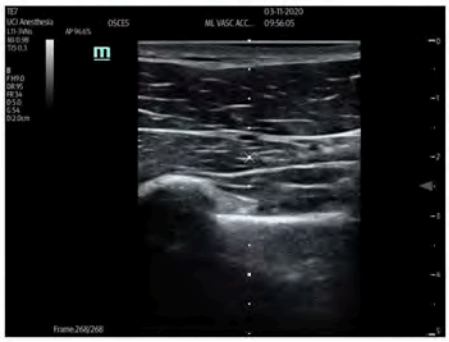
PTX Examples:

Examples of Yes (1) views:



Comments: Excellent view with 2 rib shadowing

Subject ID_____

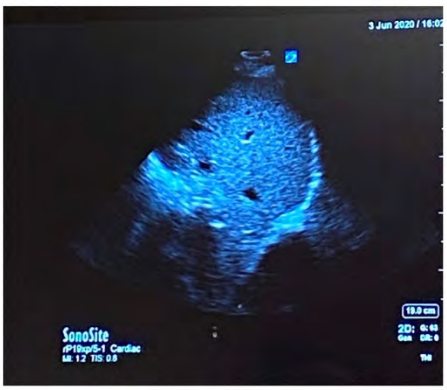


Comments: Acceptable view with 1 rib shadowing

Subject ID_____

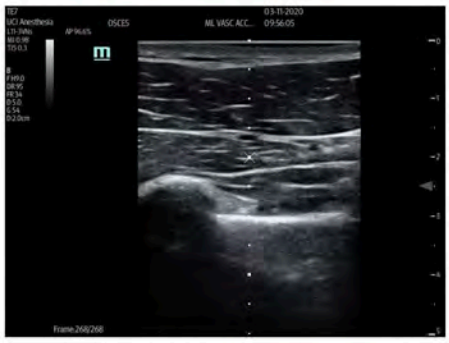
Pleural Effusion Examples:

Examples of Yes (1) views:



Comments: Acceptable view with Liver, Diaphragm, and lung parenchyma in view but no Pleural Line

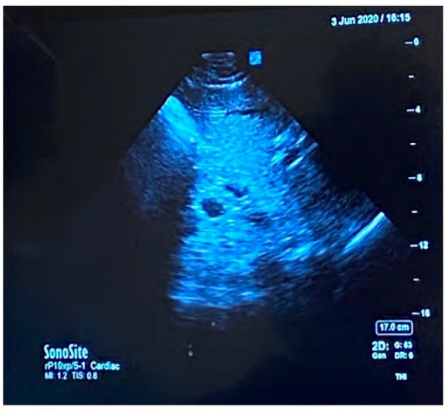
Subject ID_____



Comments: Acceptable view with 1 rib shadowing

Subject ID_____

Examples of Somewhat (0.5) views:



Comments: No Diaphragm or Pleural Line.

Subject ID_____

POCUS OSCE Pre-Survey

	Strongly Disagree 1	Disagree 2	Undecided 3	Agree 4	Strongly Agree 5
1. I feel that POCUS is an important aspect of my training.					
2. I feel that a structured POCUS Curriculum is important to anesthesia resident education					
3. I feel that practicing on live models and patients is helpful to learning POCUS					
4. I feel that consistent assessment of my POCUS skills would be helpful to my training.					
5. I have had prior experience with OSCE examinations.					
6. I feel that OSCE Examinations are helpful to skills assessment.					
7. I feel that skills assessment through OSCEs would be helpful to me in learning POCUS.					
8. Having scheduled OSCE examinations would encourage me to practice my POCUS skills.					

Subject ID_____

POCUS OSCE Post-Survey

	Strongly Disagree 1	Disagree 2	Undecided 3	Agree 4	Strongly Agree 5
The following questions pertain to the pre-examination instructions sheet.					
1. The pre-examinations instructions sheet was easy to read and understand.					
2. I had enough time to read the pre-examination instructions sheet.					
3. The pre-examination instruction sheet gave me a good understanding of what to expect from the OSCE scenarios.					
The following questions pertain to the ultrasound machine and facilities used to administer the OSCE.					
4. I was familiar with how to operate the provided ultrasound machine.					
5. I was able to adjust ultrasound settings appropriately (depth, gain, ect).					
6. The ultrasound machine functioned properly.					
7. The ultrasound probes functioned properly.					
8. The facilities used was appropriate for test administration.					
The following questions pertain to the ultrasound model used for examination.					
9. The ultrasound model's body habitus was appropriate.					
10. The ultrasound model had standard anatomy.					
11. The ultrasound model behaved appropriately throughout the exam.					

Subject ID:_____

Sample Test Form D
Apical 4 Chamber View

***** Please set US Machine to probe selection screen prior to starting exam prompt *****

Doctor,

Please position the patient for a cardiac scan in the apical 4 chamber view and then select the appropriate ultrasound probe. Please let me know when you are ready and you will have 3 minutes to complete the exam once your probe touches the patient.

- Please obtain an apical 4 chamber view and when you are happy with your view I will freeze the image for you ***(SAVE IMAGE HERE)***
- Please identify the interventricular septum
- Please identify the mitral valve.
- Explain how you would adjust your ultrasound probe to change this view to an apical 2 chamber view.

Subject ID:_____

Sample Test Form D
Apical 4 Chamber View

OSCE EVALUATOR'S CHECKLIST:

	Skill / Keywords	Yes (1)	Somewhat (0.5)	No (0)
1.	Demonstrated appropriate patient positioning (Left Lat = Yes, Supine = Somewhat)			
2.	Obtained an acceptable apical 4 chamber view(See Grading Rubric)			
3.	Identified the interventricular septum		[redacted]	
4.	Identified the mitral valve.		[redacted]	
5.	Explained how to obtain a 2 chamber view		[redacted]	

OSCE Total Score: (_)

Total Score Possible (5)

Time it took to complete exam: >1min left <1min left Did not finish

In my overall opinion, this resident demonstrated competency in this exam.

1 2 3 4 5

Did the resident exhibit professionalism during the exam?

Yes No

Evaluator Comments:

Subject ID:_____

Sample Test Form D Pulmonary Evaluation for Pneumonia

*** Please set US Machine to probe selection screen prior to starting exam prompt ***

Doctor,

Please position the patient appropriately for a lung exam to rule out pneumothorax and then select the best probe for the exam. Please let me know when you are ready and you will have 3 minutes to complete the exam once your probe touches the patient.

- Please obtain a view of the lung where you would access the patient for a pneumonia ***(SAVE IMAGE HERE)***
- Please identify an area of rib shadowing.
- Please obtain an M-Mode image and identify the pleural line in M-Mode ***(SAVE IMAGE HERE)***
- Explain what you would see in if there was an air bronchogram.

Subject ID:_____

Pulmonary Evaluation for Pneumonia Grading Rubric

OSCE EVALUATOR'S CHECKLIST:

	Skill / Keywords	Yes (1)	Somewhat (0.5)	No (0)
1.	Selected the correct Probe. (Linear Probe = no, Phased-Array or curvilinear = Yes)			
2.	Obtained an appropriate image of the lung to evaluate for Pneumonia			
3.	Correctly identified an area of rib shadowing		[redacted]	
4.	Identified the pleural line in M-Mode		[redacted]	
5.	Described what an air bronchogram would look like		[redacted]	

OSCE Total Score: (__)

Total Score Possible (5)

Time it took to complete exam: >1min left <1min left Did not finish

In my overall opinion, this resident demonstrated competency in this exam.

1 2 3 4 5

Did the resident exhibit professionalism during the exam?

Yes No

Evaluator Comments

Perioperative Anesthesia - 34

Intraoperative low driving pressure ventilation and loss of independent living after surgery in older patients: A retrospective multicenter cohort study.

Tim M Tartler[1], Luca J Wachtendorf[2], Aiman Suleiman[1], Michael Blank[1], Felix C Linhardt[1], Friederike C Althoff[1], Guanqing Chen[1], Peter Santer[3], Alexander Nagrebetsky[4], Matthias Eikermann[2], Maximilian S Schaefer[1]

[1]Center for Anesthesia Research Excellence (CARE), Beth Israel Deaconess Medical Center, Boston, MA, United States of America, [2]Department of Anesthesiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, United States of America, [3]Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, United States of America, [4]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, United States of America

Introduction: Loss of independent living after surgery is dreaded by older patients and their families. While comprehensive instruments to identify patients at risk of loss of independent living have been established [1, 2], few interventions are known to prevent this unfavorable outcome. In this study, we hypothesized that intraoperative ventilation maintaining lower driving pressures is associated with a lower risk of a patient's loss of previous independent living after surgery through a reduction in postoperative respiratory complications [3].

Methods: Patients aged 60 years or older who lived at home prior to elective, non-cardiothoracic surgery at two tertiary academic healthcare networks in Massachusetts, USA between 2006 and 2018 were included in this hospital registry study. The primary exposure was the median driving pressure (plateau pressure - positive end-expiratory pressure) during general anesthesia and the primary outcome was the loss of independent living, defined as postoperative discharge to a skilled nursing facility, long-term nursing home or hospice. Multivariable logistic regression analysis adjusted for a priori defined factors including patient demographics, comorbidities and intraoperative factors was applied. Path mediation analysis was conducted to examine whether the association between lower driving pressure ventilation and loss of independent living after surgery was mediated by a reduction in postoperative respiratory complications, defined as reintubation within 7 days or hemoglobin oxygen saturation below 90% within 10 minutes after extubation.

Results: Among 87,407 patients (Figure 1), 12,584 (14.4%) lost the ability to live independently after surgery. Patient characteristics are provided in Table 1. The median (interquartile range) driving pressure during general anesthesia was 16.0 cmH2O (13.0-19.5) in patients who lost the ability to live independently after surgery and 14.7 cmH2O (12.0-18.0) in patients who did not. There was variability for using low (<15 cmH2O) driving pressures among individual anesthesia providers (Figure 2). In adjusted analyses, a lower driving pressure was associated with a reduced risk of postoperative loss of independent living (adjusted odds ratio [aOR] 0.91 per every 10 cmH2O decrease [95% confidence interval [CI] 0.88 to 0.96]; p<0.001; Figure 3). This association was in part mediated by a reduction in postoperative respiratory complications (7.8% mediation [95% CI 5.5 to 38.3%]; p<0.001). A high baseline risk to lose the ability to live independently after surgery, defined as a Discharge Prediction for Patients Undergoing Inpatient Surgery (DEPENDENSE) [2] score ≥41, magnified this association (aOR 0.80 per every 10 cmH2O decrease [95% CI 0.76 to 0.84]; p<0.001; p-for-interaction<0.001), while there was no association in patients with a low baseline risk (aOR 1.05 per every 10 cmH2O decrease [95% CI 0.96 to 1.16]; p=0.29). The primary findings were confirmed through instrumental variable analysis in a homogeneous subgroup of patients undergoing general or orthopedic surgery, using the hospital network as instrument (coefficient -0.71 [95% CI -0.85 to -0.58]; p<0.001).

Conclusion: A lower intraoperative driving pressure is associated with a decreased risk of losing independent living after surgery in high-risk patients of advanced age. These results support preoperative risk assessment and targeted intraoperative ventilation strategies utilizing low driving pressures to avoid

postoperative respiratory complications and improve discharge disposition.

References: [1] Clin Orthop Relat Res. 2021,1;479(3):546-547. [2] Acta Anaesthesiol Scand. 2021, 65(5):607-617. [3] Lancet Respir Med. 2016, 4(4):272-80.

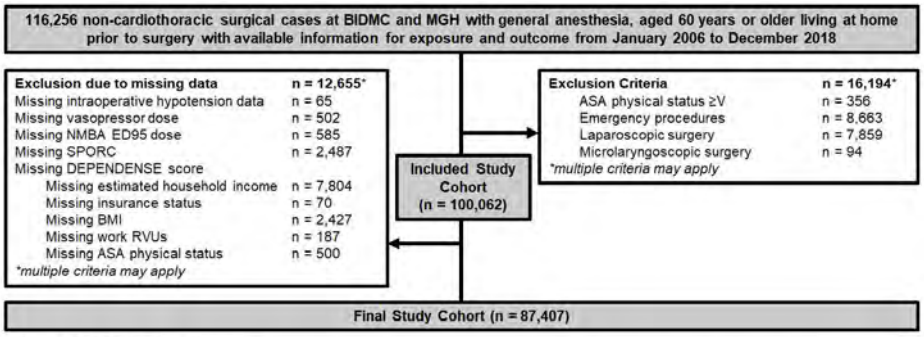


Figure 1. Study flow diagram.
ASA: American Society of Anesthesiologists; BIDMC: Beth Israel Deaconess Medical Center; BMI: Body Mass Index; DEPENDENSE: Discharge Prediction for Patients Undergoing Inpatient Surgery score; ED95: median effective dose required to achieve a 95% reduction in maximal twitch response from baseline; MGH: Massachusetts General Hospital; NMBA: neuromuscular blocking agents; SPORC: Score for Prediction of Postoperative Respiratory Complications; work RVUs: work Relative Value Units.

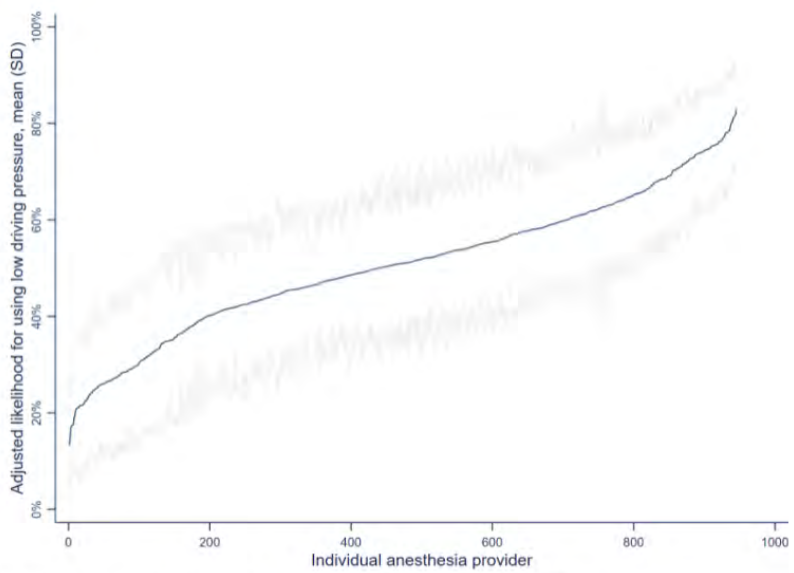


Figure 2. Adjusted likelihood for using mean low driving pressures.

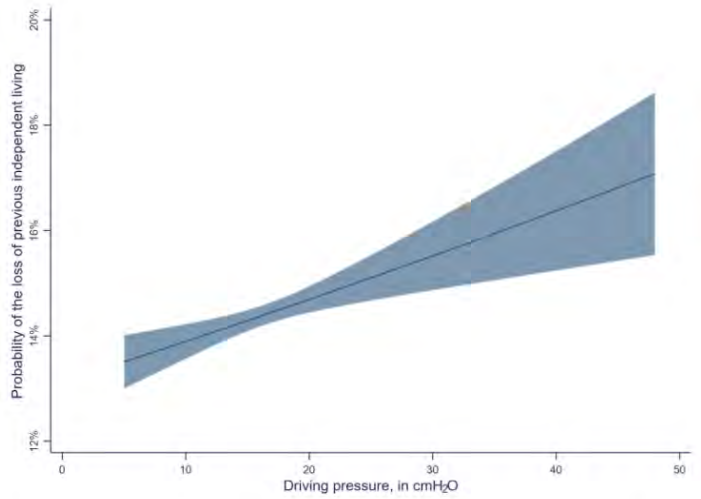


Figure 3. Intraoperative driving pressure and the probability of the loss of previous independent living.

Table 1. Patient characteristics and distribution of variables.

	Driving pressure ≥15 cmH₂O N = 44,921	Driving pressure <15 cmH₂O N = 42,486	Standardized difference
Demographics			
Age, years	68.0 (64.0 - 74.0)	69.0 (64.0 - 75.0)	-0.093
Sex (female)	25,107 (55.9%)	20,048 (47.2%)	0.175
BMI, kg/m²	29.3 (25.8 - 33.7)	25.8 (23.1 - 28.8)	0.695
ASA physical status	3.0 (2.0 - 3.0)	2.0 (2.0 - 3.0)	0.234
Admission type			
Ambulatory admission	9,752 (21.7%)	14,761 (34.7%)	-0.293
Comorbidities			
DEPENDENSE score*	39.0 (28.0 - 51.0)	35.0 (25.0 - 45.0)	0.237
SPORC ≥7	1,718 (3.8%)	1,235 (2.9%)	0.051
Intraoperative factors			
Duration of surgery, min	159.0 (109.2 - 231.0)	126.7 (80.8 - 196.0)	0.280
Mean arterial pressure below 55 mmHg, min	1.0 (0.0 - 4.0)	0.0 (0.0 - 3.0)	0.091
Vasopressor dose, mg norepinephrine equivalents	0.0 (0.0 - 0.3)	0.0 (0.0 - 0.2)	0.002
Crystalloid and colloid infusion, ml	1250.0 (900.0 - 2000.0)	1000.0 (700.0 - 1700.0)	0.193
Short acting opioid dose, mg OME	37.5 (25.0 - 62.5)	37.5 (25.0 - 62.5)	0.008
Long acting opioid dose, mg OME	8.5 (0.0 - 17.0)	3.2 (0.0 - 15.0)	0.199
Non-depolarizing NMBA, ED95	2.1 (0.9 - 3.2)	1.8 (0.0 - 3.1)	0.130
Age-adjusted mean alveolar concentration of inhalational anesthetics	1.0 (0.9 - 1.2)	1.0 (0.8 - 1.1)	0.195
Neostigmine dose, mg/kg	2.0 (0.0 - 3.0)	0.0 (0.0 - 3.0)	0.315
Units of packed red blood cells	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.047
Ventilatory parameters			
Tidal volume, ml/kg predicted body weight	9.1 (8.0 - 10.3)	7.5 (6.5 - 8.5)	0.949
Positive end-expiratory pressure, cmH₂O	4.1 (2.0 - 5.0)	5.0 (2.0 - 5.0)	-0.084
Standardized compliance, (ml/kg)/cmH₂O	29.0 (24.5 - 33.6)	40.8 (35.2 - 47.5)	-1.418
Plateau pressure, cmH₂O	22.0 (20.0 - 25.5)	16.0 (13.5 - 18.0)	2.027

Data are expressed as frequency (prevalence in %), mean ± standard deviation, or median (interquartile range [25th-75th percentile]).

ASA: American Society of Anesthesiologists; BMI: Body Mass Index; ED95: median effective dose required to achieve a 95% reduction in maximal twitch response from baseline; NMBA: neuromuscular blocking agents; OME: oral morphine equivalents; SPORC: Score for Prediction of Postoperative Respiratory Complications.
**DEPENDENSE (Discharge Prediction for Patients Undergoing Inpatient Surgery) score. Patients with emergency surgery were excluded. Therefore, emergency surgery was not considered as part of the DEPENDENSE score.*

Perioperative Anesthesia - 35 Association of Anesthesiologist Staffing Ratio with Postoperative Morbidity and Mortality

Michael L Burns[1], Leif Saager[2], Ruth Cassidy[1], Graciela Mentz[1], Sachin Kheterpal[1]

[1]University of Michigan Medicine, Ann Arbor, MI, [2]Universitaetsmedizin Goettingen, Goettingen, Germany

Introduction: While anesthesia staffing research has focused on provider type (independent nurse anesthetist versus anesthesiologist), little attention has been paid to evaluating the impact of varying staffing ratios of anesthesiologists across multiple operating rooms. Literature suggests no difference in quality based on anesthesia provider type1,2 yet improved patient outcomes with anesthesiologist involvement3. Anesthesiologists may operate as (1) a solo provider in a procedural room, or (2) in anesthesia care teams - overseeing multiple procedural rooms concurrently, each continuing a single nurse anesthetist, anesthesia assistant, or resident. There are presumed benefits of working in care teams, including cost reduction efforts targeting high fixed-cost anesthesiology services. These efforts assume increasing anesthesiologist responsibilities are non-inferior to lower staffing ratios1. Understanding potential effects of these efforts on patient care is necessary to inform clinical care staffing decisions. In this study, we used multicenter data from a national electronic perioperative health record registry to evaluate the association between varying anesthesiologist staffing ratios and operative patient morbidity and mortality.

Methods: Participants: Data was obtained from the Multicenter Perioperative Outcomes Group (MPOG) database, a comprehensive perioperative patient registry from over 50 hospitals4. Cases were selected for patients greater than 18 years of age who underwent surgery between 1/1/2010 and 10/31/2017. The ratio of anesthesiologist to the number of rooms covered is called their 'staffing ratio'. It can reach to 1:4 without resident involvement, above which care is considered medical supervision. For that reason, staffing ratios are commonly less than or equal to 1:4. Electronic health record anesthesiologist sign in/out times were used to determine staffing ratios. Cases with invalid data, including irreconcilable concurrencies, were excluded from analysis, as were cases with historically fixed staffing ratios: cardiac, liver transplant, cataract, organ procurement, and labor epidural procedures. Exposure measure (Staffing Ratio): Sign in/out times between anesthesia start and end were used to calculate a single staffing ratio for each operative case, using the time-weighted average of the individual staffing ratios as a continuous variable. This staffing ratio was categorized into 4 levels used in our regression models: 1, 1< Staffing Ratio <=2, 2< Staffing Ratio <=3 and 3< Staffing Ratio <=4. Primary Outcome: A composite of six major morbidities and in-hospital mortality. Morbidities are composed of cardiac, respiratory, gastrointestinal, urinary, bleeding, and infection ICD-9 groupings based on the U.S. Agency for Healthcare Research and Quality's single-level Clinical Classifications Software categories for International Classification of Diseases, 9th Revision, Clinical Modification diagnosis codes and manually crosswalked to ICD-10 codes within MPOG5. Statistical Analysis: Propensity score matching methods were applied to create a balanced sample with respect to patient, procedure, and hospital level confounders. A sequential modeling approach used logistic regression in which propensity scores were estimated for two staffing ratio levels at a time, using 1<staffing ratio<=2 as the reference group. Cases were matched on propensity scores, using a radius method with radius of 0.016. After matching, the association between staffing ratio group and the collapsed composite primary outcome was assessed using a multivariable conditional logistic regression modeling.

Results: Propensity matched samples consisted of 578,815 patients across 23 institutions. Compared to patients receiving care from an anesthesiologists covering between 1-2 cases, those exposed to an anesthesiologist covering between 2-3 and 3-4 overlapping cases showed a 5% and 13% increase in risk adjusted mortality/morbidity (5.27% vs 5.50%, aOR 1.05 [95% CI 1.01-1.08], p=0.005) and an observed composite rate of 5.27% vs 5.93%, aOR 1.13 [95% CI 1.08-1.19], p-value <0.001).

Conclusion: Increasing anesthesiologist staffing ratios was associated with an increase in risk-adjusted morbidity and mortality. These findings should be considered when considering clinical coverage efforts. These data quantify a potential patient and safety risk associated with increasing staffing ratio and highlight effects of anesthesiologist responsibilities in perioperative team models.

References: 1. Negrusa B, Hogan PF, Warner JT, Schroeder CH, Pang B. Scope of practice laws and anesthesia complications. Med Care. 2016;54(10):913-920. 2. Smith AF, Kane M, Milne R. Comparative effectiveness and safety of physician and nurse anaesthetists: a narrative systematic review,Ä†. Br J Anaesth. 2004;93(4):540-545. 3. Silber JH, Kennedy SK, Even-Shoshan O, et al. Anesthesiologist direction and patient outcomes. Anesthesiology. 2000;93(1):152-163. 4. Colquhoun DA, Shanks AM, Kapeles SR, et al. Considerations for Integration of Perioperative Electronic Health Records Across Institutions for Research and Quality Improvement: The Approach Taken by the Multicenter Perioperative Outcomes Group. Anesth Analg. 2020;130(5):1133-1146. 5. AHRQ, HCUP. Clinical Classifications Software Refined (CCSR). Accessed March 25, 2018. https://www.hcup-us.ahrq.gov/toolssoftware/ccsr/ccs_refined.jsp 6. Fraeman KH, Evidera B. A General SAS® Macro to Implement Optimal N: 1 Propensity Score Match

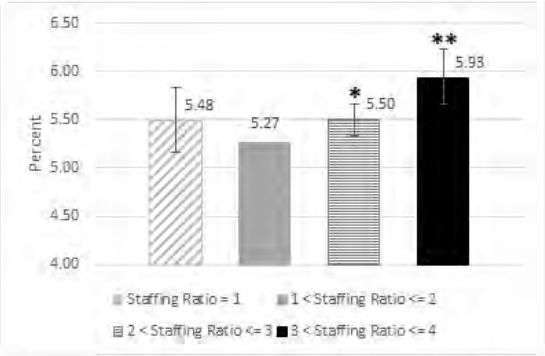


Figure: Adjusted Composite Morbidity/Mortality Rate. Values are shown composite morbidity/mortality percentage for four time-weighted average staffing ratio groups. *p-value=0.005. **p-value<0.001.

Regional Anesthesia

Regional Anesthesia - 1 Regional versus general anesthesia for hip fracture: a propensity-score matched analysis of the National Surgical Quality Improvement Program

Nicolas Salvatierra[1], Robert White[1], Tiffany Tedore[1], Roniel Weinberg[1], Richard Boyer[1]

[1]Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY

Introduction: Orthopedic surgery for hip fractures is a common procedure with an anticipated increase in incidence over the coming years given an aging population (1). These surgeries carry significant perioperative morbidity and mortality that are affected by a variety of factors, e.g., age, preexisting medical conditions and type of surgical procedure. One modifiable factor among these is the selected anesthetic technique, which include regional anesthesia - usually in the form of a spinal or epidural to induce surgical anesthesia - or general anesthesia. Multiple studies, including the recent REGAIN multicenter trial, have been performed comparing the effect of regional versus general anesthesia for hip fracture surgery (2). However, these past studies have shown conflicting results on whether there is a benefit of one anesthetic technique over the other, with some showing no statistical difference while others show regional anesthesia has advantages over general anesthesia in certain outcomes. Our study utilized the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database to evaluate patients undergoing hip fracture surgery between the years 2016-2019, with the aim of comparing the effect of regional anesthesia versus general anesthesia on postoperative morbidity and mortality.

Methods: This study evaluated 96,713 patients who underwent surgery for hip fracture in the ACS NSQIP database between 2016 and 2019. All patients scheduled for hip fracture repair surgery with CPT codes 27125, 27235, 27236, 27244 or 27245 were included. Propensity scores were calculated with a logistic regression model that included all clinically relevant covariates that met a crude univariate chi-square or t-test $p < 0.50$ and had <15% of cases missing data. Nearest neighbor matching was performed 1:1 with a caliper of 0.001 and without replacement. The primary outcome of interest was combined 30-day myocardial infarction, stroke or death. Secondary outcomes of interest were operative time and 30-day adverse events. Outcome analysis was performed using conditional logistic regression for binary variables and Wilcoxon signed-rank test for continuous variables.

Results: Among the 3,035,119 total surgical cases in the 2016-2019 ACS NSQIP database, 96,713 patients met our CPT inclusion criteria, of which 69,385 (71.7%) had general anesthesia and 27,328 (28.3%) had primary regional or neuraxial anesthesia. Using propensity score matching, 10,839 regional or neuraxial cases were successfully matched to a general anesthetic case. Covariate balance was confirmed with a maximum absolute standardized mean difference between groups of 0.02. The odds ratio for combined 30-day myocardial infarction, stroke or death for general anesthesia was 1.21 [1.09, 1.34] with Bonferonni-adjusted p-value <0.001. Additional significant findings included 30-day death (OR 1.21, $p < 0.001$), 30-day cardiac arrest requiring CPR (OR 1.65, $p=0.004$), 30-day unplanned reintubation (OR 1.58, $p=0.001$), and 30-day DVT (OR 1.37, $p=0.02$).

Conclusion: Our propensity matched analysis suggests that general anesthesia as compared to regional or neuraxial anesthesia is associated with an increase in postoperative morbidity and mortality in patients undergoing hip fracture surgery.

References: 1. Veronese N, Maggi S. Epidemiology and social costs of hip fracture. Injury. 2018 Aug;49(8):1458-1460. doi: 10.1016/j.injury.2018.04.015. Epub 2018 Apr 20. PMID: 29699731. 2. Neuman MD, Feng R, Carson JL, Gaskins LJ, Dillane D, Sessler DI, Sieber F, Magaziner J, Marcantonio ER, Mehta S, Menio D, Ayad S, Stone T, Papp S, Schwenk ES, Elkassabany N, Marshall M, Jaffe JD, Luke C, Sharma B, Azim S, Hymes RA, Chin KJ, Sheppard R, Perlman B, Sappenfield J, Hauck E, Hoeft MA, Giska M,

Ranganath Y, Tedore T, Choi S, Li J, Kwofie MK, Nader A, Sanders RD, Allen BFS, Vlassakov K, Kates S, Fleisher LA, Dattilo J, Tierney A, Stephens-Shields AJ, Ellenberg SS; REGAIN Investigators. Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults. N Engl J Med. 2021 Oct 9. doi: 10.1056/NEJMoa2113514. Epub ahead of print. PMID: 34623788.

Regional Anesthesia - 2 The effect of peripheral nerve block anaesthesia on postoperative opioid use in ankle fracture surgery: a retrospective cohort study

Taehoon Kim[1], Heloise Hayakawa[2], Nicholas Gormack[2], Rachel Sara[2], Nicholas J Lightfoot[2]

[1]University of Auckland, Auckland, New Zealand, [2]Counties Manukau Health, Auckland, New Zealand

Introduction: Orthopaedic procedures are associated with significant postoperative pain and over-prescription of opioids, increasing the risk of persistent opioid use (1). Peripheral nerve blocks (PNB) are commonly used at the time of surgery following injuries such as ankle fracture to reduce perioperative pain and opioid consumption (2, 3). Limited standards exist to guide analgesia during and after traumatic lower extremity surgery (4). The purpose of this study is to determine the impact of PNBs on postoperative opioid use in patients undergoing acute, traumatic ankle fracture surgery.

Methods: Following ethical and hospital locality approval, all patients who underwent acute unilateral post-traumatic open reduction and internal fixation (ORIF) of the distal fibula and/or tibia at our institution, between 1st January-31st December 2019, were retrospectively identified. Patients with unilateral ankle mortice fractures, which were uni-, bi- or tri-malleolar were eligible for inclusion. Surgeries exceeding 4 hours in duration and patients with multiple injury sites were excluded. Eligible patients were stratified into two groups by use or avoidance of PNB at the time of surgery (PNB or reference group). Linked data from departmental and institutional health databases was used to obtain demographic, anaesthetic, surgical and pharmaceutical data. The primary outcome was cumulative opioid consumption during the first 48 hours postoperatively. In addition, we compared the proportion of patients dispensed strong opioids, either morphine or oxycodone, at 30-day intervals until 3 months post-discharge. All opioid doses were converted to Oral Morphine Equivalents (OMEs). Ancillary secondary outcomes included postoperative length of hospital stay, and Days Alive and Out of Hospital at 30-days (DAOH-30). Data was analysed using Chi Square and Mann Whitney U tests. A two-tailed p-value of <0.05 defined statistical significance.

Results: Two-hundred and eleven patients were eligible for inclusion. The PNB group were older (42.5 vs 35.0 years) and had a greater Charlson score when compared to the reference group, although neither were statistically significant. Patients receiving PNBs had more bi- or tri-malleolar fractures (p=0.023). Māori and Pacific patients were disproportionately overrepresented in our sample, compared to the ethnic composition of our hospital's catchment. Cumulative opioid consumption measured at 6-hourly intervals postoperatively showed the PNB group consumed significantly less opioid at 24 hours (p=0.002), and continued to consume less opioid at 36 and 48 hours although this was not statistically significant (p=0.06; p=0.11 respectively). Postoperatively during hospital stay, the PNB group had significantly lower daily average opioid use (23.8 [IQR 8.7–53.4] vs 40.2 mg OME [11.3–62.3], p=0.049). After discharge, there was no significant difference in opioid dispensing between the two groups. Dispensing of tramadol and codeine was greater in the PNB group at two-months (p=0.045; p=0.055 respectively). Overall, the incidence of outpatient strong opioid use in our sample was low, with all patients ceasing morphine or oxycodone use after 60 days following discharge. The PNB group had a longer hospital stay following surgery by 4.8 hours (1.20 [IQR 0.92-2.12] vs 1.00 days [0.88-1.87] , p=0.007) and had reduced DAOH-30 (p=0.0003).

Conclusion: Single-shot peripheral nerve blocks can provide opioid-sparing analgesia up to 48 hours following surgery for acute traumatic ankle fractures. PNBs alone are unlikely to impact persistent opioid use. Although, the reduction of inpatient opioid consumption may decrease long-term opioid dispensing (5). Further studies are needed to explore the effects of perioperative pain interventions on hospital length of stay and persistent opioid use following lower extremity procedures.

References: 1. Injury. 2018;49(6):1003-7. 2. British Journal of Anaesthesia. 2021;02:02. 3. Pain rep.

2021;6(1):e900. 4. Foot & Ankle Orthopaedics. 2018;3(3):247301141876446. 5. J Orthop Trauma. 2018;32(10):e408-e14.

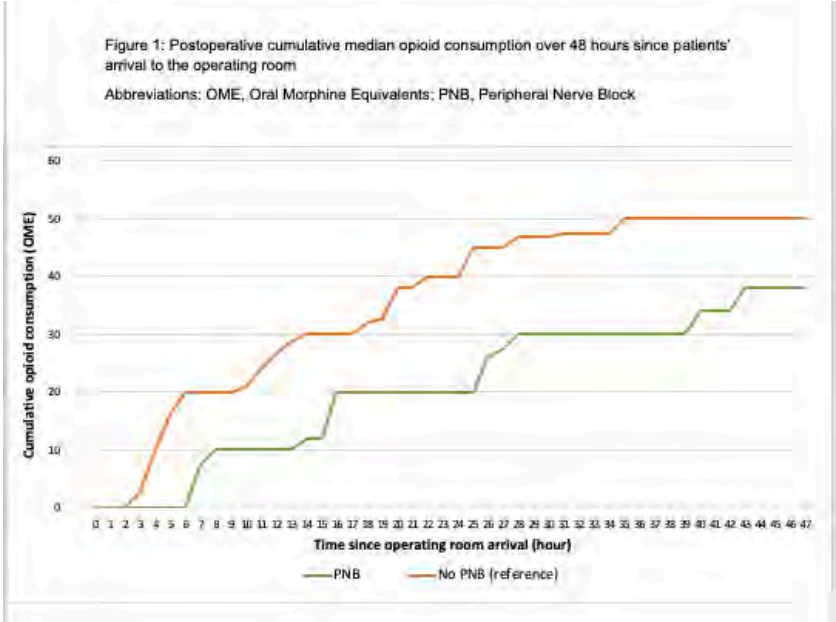


Figure 1: Postoperative cumulative median opioid consumption over 48 hours since patients' arrival to the operating room

Abbreviations: OME, Oral Morphine Equivalents; PNB, Peripheral Nerve Block

Table 1: Comparison of perioperative opioid consumption

	Total (n=211)	PNB group (n=132)	Reference group (n=79)	p-value
Intraoperative opioid use (OME)	50 (35-70)	40 (30-55.5)	70 (46-80)	**<0.0001**
Cumulative postoperative opioid use (OME)				
6 hrs	10 (0-26)	0 (0-20)	16.5 (0-36)	**0.0004**
12 hrs	20 (0-33)	10 (0-28)	24 (6.8-52.8)	**0.0001**
18 hrs	20 (0-46)	20 (0-40)	30 (14-60)	**0.0007**
24 hrs	30 (0-60)	20 (0-49.75)	40 (10-70)	**0.0096**
36 hrs	39.5 (10-72)	30 (10-72)	50 (20-73)	0.056
48 hrs	40 (15-82.5)	38 (10-81)	50 (21.3-86)	0.11
PACU opioid consumption in 48 hrs (OME)	0 (0-20)	0 (0-20)	6 (0-30)	**0.022**
Postoperative opioid use (OME)				
POD 0	30 (0-60)	20 (0-49.75)	40 (10-70)	**0.0096**
POD 1	10 (0-30)	10 (0-35)	0 (0-22.5)	0.17
POD 2	10 (0-37.5)	7.5 (0-35)	15 (0-37.5)	0.54
POD 3	10 (0-30)	10 (0-30)	5 (0-38.5)	0.81
Average inpatient postoperative opioid use (up to POD 7) (OME/day)	28.9 (9.0-57.0)	23.8 (8.7-53.4)	40.2 (11.3-62.3)	**0.049**

Results expressed as median (interquartile range).
p-values are two-tailed with a threshold of <0.05 used to define significance.
Abbreviations: OME, Oral Morphine Equivalents; PNB, Peripheral Nerve Block; PACU, Post Anaesthetic Care Unit; POD, Postoperative Day

Regional Anesthesia - 3 Social Determinants of Regional Anesthesia Use for Patients Undergoing Hemodialysis Vascular Access Procedures

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Introduction: Healthcare disparities exist in access to regional anesthesia (RA) in pediatric and obstetric anesthesiology.[1,2] To date there has been no investigation on whether these disparities persist in the end-stage renal disease population, which is disproportionately composed of patients from marginalized backgrounds.[3] RA is suggested to improve the success of hemodialysis (HD) vascular access surgeries via venodilation and improved fistula patency, blood flow, and maturation time.[4,5] This study aims to determine whether disparities in the use of RA for HD vascular access surgeries exist based on patient factors at a single academic hospital.

Methods: We performed a retrospective review of anesthetics for HD vascular access surgeries including arteriovenous (AV) fistula creation, AV graft, and AV transposition. Data was collected from one academic hospital in northern Boston from April 2016 to August 2021. 250 patients were reviewed. Associations between the use of RA and patient factors including race/ethnicity, language, estimated income, substance use disorder, chronic pain, and anticoagulation were determined via multiple logistic regression.

Results: The study cohort was made up of 250 patients, of which 42.4% received RA, 40.0% were minorities (non-white and/or Hispanic), 14.8% required interpreters, and 28.4% had low estimated incomes (median household income ≤ $65,000 for their zip code). Within subgroups, the percentages that received RA were 58.7% of minorities versus 85.2% of non-minorities, 68.2% of non-English speakers versus 74.5% of English speakers, and 77.4% of low-income versus 72.1% of high-income patients. Multiple logistic regression adjusting for confounders did not find statistically significant associations between the use of RA and language or income, but did find a lower odds ratio based on minority status (adjusted odds ratio = 0.35, 95% confidence interval = 0.14 – 0.86, p = 0.03). Findings were validated by sensitivity analyses. Review of platelet and coagulation parameters did not suggest any difference in subgroup eligibilities for RA, and the disparity was observed after controlling for anticoagulant use.

Conclusion: This study identifies a racial/ethnic disparity in the use of RA in HD vascular access surgeries at one academic hospital, with minority patients being less likely to receive RA. There was no significant difference in the use of RA based on language or income. The lack of language-based disparities may represent the success of institutional use of in-person and videophone interpreters. Given no observed physiologic differences between subgroups, differences in education on RA (e.g., regarding the need to hold anticoagulant drugs) may be a factor leading to the observed disparity. Quality improvement initiatives regarding RA education should be pursued. Further studies are needed to clarify the etiology of the racial/ethnic disparity and determine whether these trends persist among additional samples.

References: 1.) King MR, De Souza E, Rosenbloom J, Wang E, Anderson TA. Association Between Race and Ethnicity in the Delivery of Regional Anesthesia for Pediatric Patients: A Single-Center Study of 3189 Regional Anesthetics in 25,664 Surgeries. Anesth Analg. 2020;131:255-262. // 2.) Butwick AJ, Blumenfeld YJ, Brookfield KF, Nelson LM, Weiniger CF. Racial and Ethnic Disparities in Mode of Anesthesia for Cesarean Delivery. Anesth Analg. 2016;122:472-479. // 3.) Young EW, Mauger EA, Port FK, Wolfe RA. Socioeconomic Status and End-Stage Renal Disease in the United States. Kidney International. 1994;45(3):907-911. // 4.) Lo Monte AI, Damiano G, Mularo A, Palumbo VD, Alessi R, Gioviale MC, Spinelli G, Buscemi G. Comparison between local and regional anesthesia in arteriovenous fistula creation. J Vasc Access 2011;12(4):331-5. // 5.) Malinzak EB, Gan TJ. Regional anesthesia for vascular access surgery. Anesthesia Analgesia. 2009;109(3):976-980.

Table 1: Measured Factors Stratified by Procedure Type

	Procedure type				
	AV Fistula (n=166)	AV Graft (n=58)	AV Transposition (n = 26)	N	P-Value*
Age (yr)					
< 45	13 (7.8%)	10 (17.2%)	3 (11.5%)	10.4%	0.429
45-64	61 (36.7%)	23 (39.7%)	11 (42.3%)	38.0%	
65-74	47 (28.3%)	15 (25.9%)	6 (23.1%)	27.2%	
≥ 75	45 (27.1%)	10 (17.2%)	6 (23.1%)	24.4%	
Sex					
Male	112 (67.5%)	29 (50.0%)	21 (80.8%)	64.8%	0.0111
Female	54 (32.5%)	29 (50.0%)	5 (19.2%)	35.2%	
Race					
White	107 (64.5%)	33 (56.9%)	17 (65.4%)	62.8%	0.0274
Black	19 (11.4%)	16 (27.6%)	6 (23.1%)	16.4%	
Asian	20 (12.0%)	2 (3.4%)	0 (0.0%)	8.8%	
Other	20 (12.0%)	7 (12.1%)	3 (11.5%)	12.0%	
Ethnicity					
Hispanic	25 (15.1%)	7 (12.1%)	3 (11.5%)	14.0%	0.793
Non-Hispanic	141 (84.9%)	51 (87.9%)	23 (88.5%)	86.0%	
Primary Language					
English	138 (83.1%)	51 (87.9%)	24 (92.3%)	85.2%	0.378
Non-English	28 (16.9%)	7 (12.1%)	2 (7.7%)	14.8%	
Estimated Income†					
≤$65,000	47 (28.3%)	17 (29.3%)	7 (26.9%)	28.4%	0.974
>$65,000	119 (71.7%)	41 (70.7%)	19 (73.1%)	71.6%	
BMI					
<18.5	1 (0.6%)	4 (6.9%)	2 (7.7%)	2.8%	0.0387
18.5-24.9	45 (27.1%)	18 (31.0%)	8 (30.8%)	28.4%	
25.0-29.9	70 (42.2%)	15 (25.9%)	7 (26.9%)	36.8%	
>30.0	50 (30.1%)	21 (36.2%)	9 (34.6%)	32.0%	
ASA Class					
2	7 (4.2%)	2 (3.4%)	0 (0.0%)	3.6%	0.443
3	140 (84.3%)	47 (81.0%)	20 (76.9%)	82.8%	
4	19 (11.4%)	9 (15.5%)	6 (23.1%)	13.6%	
Substance Use Disorder					
Yes	11 (6.6%)	1 (1.7%)	3 (11.5%)	6.0%	0.182
No	155 (93.4%)	57 (98.3%)	23 (88.5%)	94.0%	
Diabetes Mellitus					
Yes	96 (57.8%)	33 (56.9%)	14 (53.8%)	57.2%	0.928
No	70 (42.2%)	25 (43.1%)	12 (46.2%)	42.8%	
Chronic Pain					
Yes	22 (13.3%)	11 (19.0%)	5 (19.2%)	15.2%	0.483
No	144 (86.7%)	47 (81.0%)	21 (80.8%)	19.2%	
Use of anticoagulants					
Yes	29 (17.5%)	12 (20.7%)	2 (7.7%)	17.2%	0.34
No	137 (82.5%)	46 (79.3%)	24 (92.3%)	82.8%	
Use of Nerve Block					
Yes	41 (24.7%)	41 (70.7%)	24 (92.3%)	42.4%	<0.0001
No	125 (75.3%)	17 (29.3%)	2 (7.7%)	57.6%	

Data presented as n (%). BMI = Body mass index.
*Chi-square test for categorical variables, t test for continuous variables.
†Estimated by median income for a household of 4 within the patient's zip code.

Table 2: Models of Correlations Between Patient Factors and Use of Regional Anesthesia

	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Race/Ethnicity*								
Non-minority	Reference		Reference		Reference		Reference	
Minority	0.69 (0.41—1.15)	0.160	0.52 (0.24—1.09)	0.0899	0.44 (0.18—1.01)	0.0598	0.35 (0.14—0.86)	0.0272
Language								
English	Reference		Reference		Reference		Reference	
Non-English	0.91 (0.44—1.85)	0.817	2.10 (0.80—5.58)	0.134	2.26 (0.77—6.70)	0.141	2.28 (0.76—6.99)	0.147
Income†								
High	Reference		Reference		Reference		Reference	
Low	1.07 (0.61—1.87)	0.812	NA	NA	1.08 (0.46—2.48)	0.868	1.23 (0.51—2.96)	0.661
Age (yr)								
	1.01 (0.99—1.03)	0.381	1.02 (0.98—1.05)	0.193	1.01 (0.98—1.03)	0.533	1.01 (0.98—1.04)	0.515
Sex								
Female	Reference		Reference		Reference		Reference	
Male	0.95 (0.56—1.61)	0.864	0.98 (0.51—1.88)	0.947	0.93 (0.46—1.92)	0.863	0.85 (0.41—1.77)	0.674
BMI								
	0.98 (0.95—1.02)	0.450	NA	NA	0.98 (0.93—1.03)	0.456	0.99 (0.93—1.05)	0.734
ASA Class								
2	Reference		Reference		Reference		Reference	Reference
3	0.82 (0.21—3.40)	0.792	0.39 (0.09—1.78)	0.216	0.52 (0.10—2.82)	0.443	0.50 (0.09—1.05)	0.860
4	1.79 (0.40—8.38)	0.463	0.71 (0.14—3.89)	0.703	1.11 (0.18—7.35)	0.917	1.28 (0.19—8.85)	0.812
Substance Use Disorder‡								
No	Reference		Reference		Reference		Reference	
Yes	0.32 (0.07—1.04)	0.0952	NA	NA	NA	NA	0.15 (0.02—0.86)	0.0575
Diabetes Mellitus								
No	Reference		Reference		Reference		Reference	
Yes	1.02 (0.62—1.71)	0.931	NA	NA	NA	NA	1.02 (0.48—2.14)	0.970
Chronic Pain								
No	Reference		Reference		Reference		Reference	
Yes	0.76 (0.37—1.53)	0.465	NA	NA	NA	NA	0.41 (0.13—1.16)	0.106
Use of anticoagulants								
No	Reference		Reference		Reference		Reference	
Yes	0.77 (0.38—1.50)	0.462	NA	NA	NA	NA	0.68 (0.26—1.70)	0.424

OR = Odds Ratio. CI = Confidence Interval.

* Non-minority defined as non-Hispanic white. Minority defined as non-white race and/or Hispanic ethnicity.

† Income estimated by median income for a household of 4 within the patient's zip code. High income is defined as cases where this value is ≥$65,000. Low income is defined as cases where this value is <$65,000.

‡ Substance use disorder defined as a diagnosis of any substance use disorder including alcohol, opiate, and polysubstance use disorders.

[a]Model 1: Unadjusted.

[b]Model 2: Adjusted for race/ethnicity, language, age, sex, ASA physical status, and procedure.

[c]Model 3: Adjusted for race/ethnicity, language, income, age, sex, ASA physical status, procedure, BMI, and surgeon.

[d]Model 4: Adjusted for race/ethnicity, language, income, age, sex, ASA physical status, procedure, BMI, surgeon, substance use disorder, chronic pain, diabetes mellitus, and anticoagulant prescription.

Regional Anesthesia - 4 Clonidine Prolongs Pediatric Spinal Blockade but May Increase the Risk of Airway Obstruction, Hiccups, and Apnea

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Introduction: Spinal anesthesia (SA) allows anesthesia providers to avoid general anesthesia (GA) during pediatric urological or lower abdominal surgery. Avoiding general anesthesia has implications for future neurological development, post-anesthesia apnea, and PACU length of stay. Adoption of SA has been limited by concerns for inadequate duration of blockade and spinal adjuvants like clonidine (SAC) have been increasingly used to prolong neuraxial blockade1. However, clonidine may impact intraoperative breathing mechanics.

Methods: This is a single institution, prospective cohort study. All patients aged ≤10.0 months receiving spinal anesthesia as their primary anesthetic were considered for inclusion in the present study (n=57). Patients received intrathecal bupivacaine (1mg/kg) with or without clonidine (1mcg/kg) at the anesthesia provider's discretion. Patients receiving alternative intrathecal dosing (n=4) or combined spinal and caudal epidural anesthesia (n=6) were excluded.

Results: 47 patients are included in the present analysis. Demographics including age, weight, ASA classification, and rate of prematurity were similar in the two groups (Table 1). A chi square test was performed for categorical variables. Intraoperatively, SAC patients had higher rates of hiccups (SAC: 30%, SA: 0.0%, p=0.01) and mild airway obstruction (SAC: 33.3%, SA: 0.0%, p<0.01). SAC patients also trended towards higher rates of apnea (SAC: 30.0%, SA: 11.8%, p=0.16) and oxygen desaturation (SAC: 26.7%, SA: 5.9%, p=0.08) though these outcomes did not reach significance. Rates of conversion to GA were similar in both groups (SAC: 3.3%, SA: 5.9%, p=0.68) (Table 2). Spinal to end-of-procedure times and PACU lengths of stay were not normally distributed and had unequal independent sample sizes and variances. Therefore, Mann-Whitney U-tests were performed for these outcome variables. SAC patients experienced longer times from spinal-placement to end-of-procedure (W=360.5, p=0.02) but had shorter PACU lengths of stay (W=128.5, p=0.02) (Table 2). The PACU time analysis included 44 patients, as 3 patients were planned inpatients. Analyses were conducted in R (R Core Team, 2018).

Conclusion: Results from this analysis demonstrate that SAC patients experienced longer spinal to end-of-procedure times without prolonging PACU length of stay. SAC patients also experienced a higher rate of hiccups and mild airway obstruction than patients receiving SA and trended towards higher rates of apnea and oxygen desaturation. These findings confirm that the addition of clonidine to spinal anesthesia impacts breathing mechanics within our study population. However, these findings did not result in an increased rate of conversion to general anesthesia.

References: Anesth Analg. 2004;98(1):56-59

Table 1: Patient Demographics

Classification	Without Clonidine (n=17)	With Clonidine (n=30)
Post-Menstrual Age (days) mean (+/-SD)	398.3 (78.2)	391.4 (72.7)
ASA Classification		
Mean	1.4 (0.57)	1.4 (0.58)
ASA 1 (n, %)	n=12 (70.6%)	n=19 (63.3%)
ASA 2 (n, %)	n=5 (29.4%)	n=8 (26.7%
ASA 3 (n, %)	n=0 (0.0%)	n=3 (10%)
Prematurity (y/n) (%)	n=3 (17.6%)	n=5 (16.7%)
Weight (kg) mean (SD)	6.4 (2.0)	6.4 (2.0)

Table 2: Procedure Outcomes

Outcome	Without Clonidine	With Clonidine	p-value
Apnea (n, %)	n=2 (11.8%)	n=9 (30.0%)	0.16
Desaturation (n, %)	n=1 (5.9%)	n=8 (26.7%)	0.08
Hiccups (n, %)	n=0 (0.0%)	n=9 (30.0%)	**0.01**
Airway Obstruction (n, %)	n=0 (0.0%)	n=10 (33.3%)	**0.007**
Conversion to General Anesthesia (n, %)	n=1 (5.9%)	n=1 (3.3%)	0.68
Time: Spinal Placement to Procedure End (min) mean (SD)	61.9 (17.8)	77.2(22.3)	0.02
PACU Time (min) mean (SD)	43.5 (29.7)	27.4 (42.5)	0.02

Respiration

Respiration - 1 Oxygen Administration Practices during Surgery in the United States

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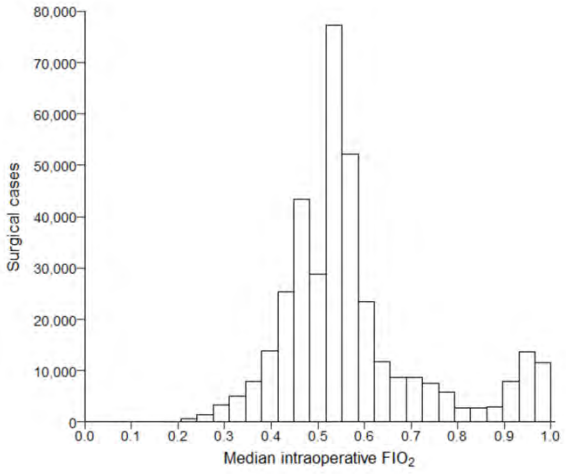
Introduction: Anesthesiologists administer supplemental oxygen to nearly all patients during surgery. Determinants of intraoperative oxygen administration practice patterns are unclear. We sought to describe current intraoperative oxygenation practices and characterize the relative contributions of patient, procedure, medical center, and anesthesia provider factors.

Methods: In 42 medical centers across the United States participating in the Multicenter Perioperative Outcomes Group data registry, we analyzed surgical cases of 120 minutes or longer in adult patients who received general anesthesia with endotracheal intubation and were admitted to the hospital after surgery between January 2016 and November 2018. We measured patient, procedure, medical center, anesthesiologist, and in-room anesthesia provider factors and compared these factors to the median intraoperative fraction of inspired oxygen.

Results: The cohort comprised 367,841 cases (median age [interquartile range], 59 [47-69] years; 51.1% women) managed by 3,836 anesthesiologists and 15,381 in-room anesthesia providers (nurse anesthetists, residents, fellows). Median fraction of inspired oxygen was 0.55 (interquartile range, 0.48-0.61) and the median pulse oximetry hemoglobin saturation was 99% (interquartile range, 98-100)(Figure 1). Multivariable linear mixed-effects regression revealed significant heterogeneity in oxygen administration among medical centers, anesthesiologists, and in-room providers. For example, independent of patient and procedure factors the median fraction of inspired oxygen ranged from 0.41 (95% confidence interval, 0.40-0.43) to 0.80 (0.79-0.82) across medical centers and from 0.27 (0.22-0.32) to 0.87 (0.83-0.92) across anesthesiologists (Figure 2). Patient factors explained 3.5% (95% confidence interval, 3.5-3.5) of the variability in oxygen administration, procedure factors 4.4% (4.3-4.6), medical center 23.3% (22.8-23.8), anesthesiologist 7.7% (7.3-8.1), and in-room provider 8.1% (7.6-8.5)(Figure 3). Individual patient factors independently associated with higher oxygen administration included age (0.05 % higher per year [95% confidence interval, 0.04-0.05]), female sex (0.36 [0.24-0.49]), body mass index (0.11 % per kg/m2 [0.10-0.11]), cardiac and pulmonary comorbidities, preoperative measurement of troponin (2.19 [1.93-2.45]), and American Society of Anesthesiology physical classification 4 or greater (4.11 [3.90-4.33]). Dominant procedural factors included emergency surgery (0.78 [0.61-0.95]), open heart surgery (10.18 [9.69-10.66]), and intraoperative transfusion (0.87 [0.65-1.08]).

Conclusion: Among adults undergoing surgery with general anesthesia in the United States, oxygen administration varied significantly, with more of the variability explained by the medical center and anesthesia provider than by patient or procedure factors.


Surgical cases
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60,000
50,000
40,000
30,000
20,000
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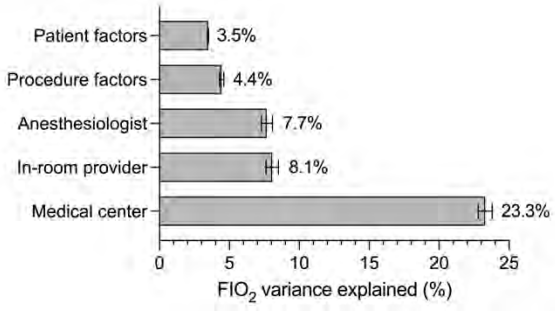
Median intraoperative FIO2


Patient factors
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Procedure factors
4.4%
Anesthesiologist
7.7%
In-room provider
8.1%
Medical center
23.3%
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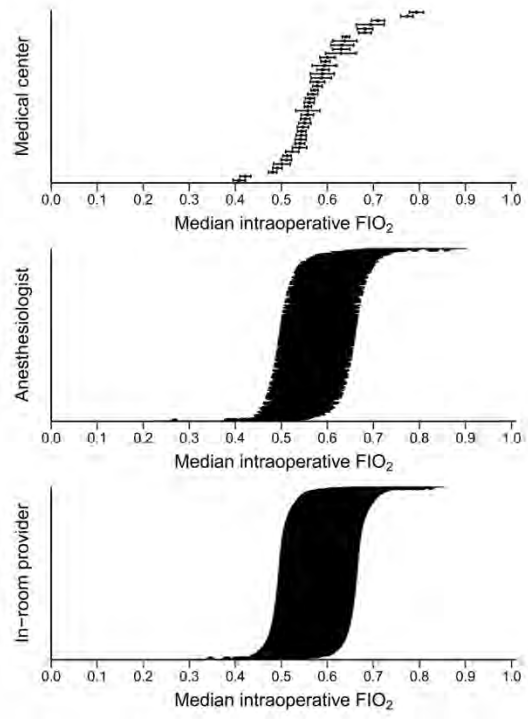
FIO2 variance explained (%)


Medical center
Anesthesiologist
In−room provider
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
Median intraoperative FIO2

Respiration - 2 Mechanical power in ventilated patients - Agreement between calculations from bedside formulae and continuous recordings

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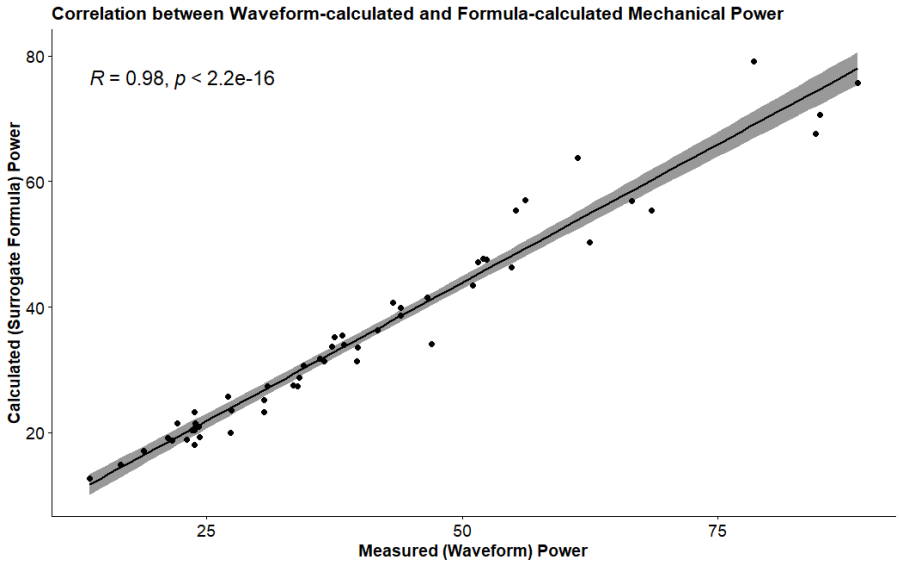
Introduction: Mechanical Power (MP) unifies physical forces exerted on the respiratory system during positive pressure ventilation(1) under the postulation that the applied energy is a primary driving factor of ventilator-induced lung injury. A high MP is associated with increased mortality in the intensive care unit (ICU).(2,3) MP is ideally calculated from continuous measurements of inspiratory flow and pressures, however, an abbreviated formula has been proposed for use in epidemiological studies and daily clinical use.(4) There is, however, a paucity of evidence with regard to the granularity of the surrogate formula to reflect MP calculated from continuous recordings based on 'real-world' clinical data.

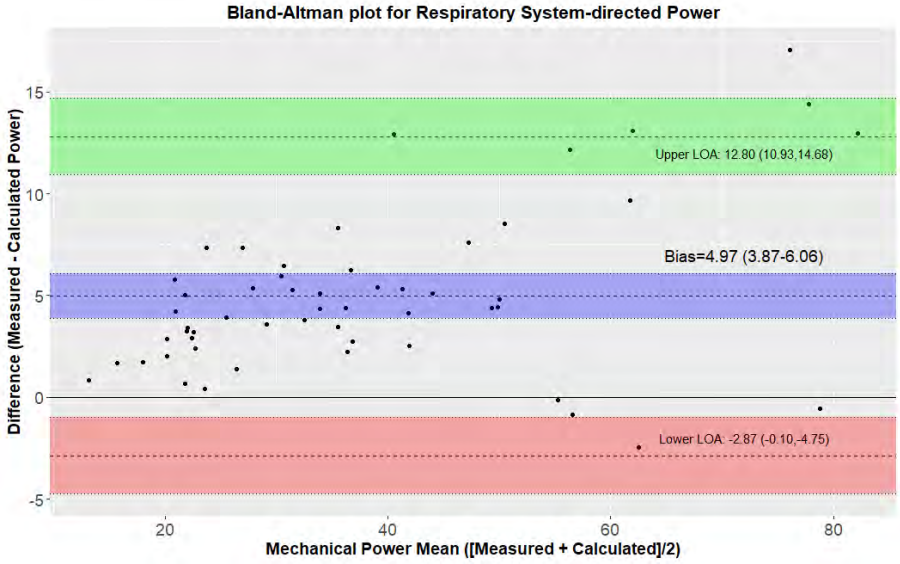
Methods We investigated the agreement between mechanical power calculated either based on the surrogate formula 0.098*RR*VT*[PEEP + ½(Pplat−PEEP) + (Ppeak−Pplat) or continuous recordings of inspiratory pressure and flow from data recorded in mechanically ventilated patients with acute respiratory distress syndrome during the EPVent study.(5) From continuous recordings, MP in J/min was derived from inspiratory work, calculated for each breath as the area under the inspiratory limb of the pressure/volume curve multiplied with the respiratory rate, and application of a conversion factor (0.098).(5) In a secondary analysis, we compared driving power after exclusion of the static (PEEP) component. Paired t-tests, Standard difference of means, Pearson's correlation, and Bland Altman analyses were used to evaluate agreement between measured and calculated MP. Alpha was set to 0.05. Julia (v1.6.3) within Microsoft Visual Studio Code (v1.61.2) and R (v4.1.1), "Kick Things", 2021-08-10 in RStudio 1.4.1106 were used.

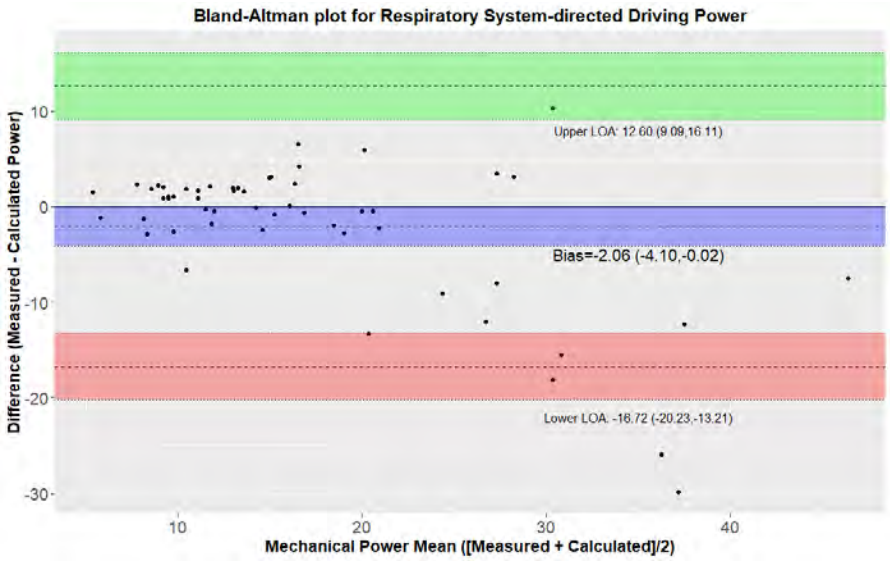
Results: Continuous flow and pressure recordings were available in 54 patients with an average sampling rate of 18.6 +-6.4Hz. The average MP was 40.3 +-18.3J/min, calculated from continuous recordings versus 35.3 +-16.5J/min, calculated from the surrogate formula ($p<0.001$). There was a strong correlation between both methods (Fig 1, R=0.98, 95%CI 0.96-0.99, $p<0.001$). Bland-Altman analysis (Fig 2) revealed an overall bias of 4.97 J/min (95% CI 3.87- to 6.06 $p<0.001$) and evidence of proportional bias with aggravation at MP>50J/min. Driving power displayed similar agreement (Fig 3) with a bias of -2.06 (95% CI -4.10 to -0.02), though aggravation of bias was noticed at DP>25J/min, suggesting aggravation of underestimation through the surrogate formula.

Conclusion: While MP calculated from continuous recordings and estimated from an abbreviated formula correlate closely, MP may be underestimated when the abbreviated formula is applied. Calculations of MP should be attempted based on continuous recordings in patients ventilated with high MP, for example through high respiratory rates or driving pressures.

References: 1. Ventilator-related causes of lung injury: the mechanical power. Intensive Care Med. 2016 Oct 1;42(10):1567-75. 2. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. Intensive Care Med. 2018 Nov 1;44(11):1914-22. 3. Mechanical power normalized to predicted body weight as a predictor of mortality in patients with acute respiratory distress syndrome. Intensive Care Med. 2019 Jun 1;45(6):856-64. 4. Bedside calculation of mechanical power during volume- and pressure-controlled mechanical ventilation. Crit Care. 2020 Jul 11;24(1):417. 5. Comparison of mechanical power estimations in mechanically ventilated patients with ARDS: a secondary data analysis from the EPVent study. Intensive Care Med [Internet]. 2020 Oct 19; Available from: https://doi.org/10.1007/s00134-020-06282-1


Correlation between Waveform-calculated and Formula-calculated Mechanical Power
R = 0.98, p < 2.2e-16
Calculated (Surrogate Formula) Power
Measured (Waveform) Power
80
60
40
20
25
50
75


Bland-Altman plot for Respiratory System-directed Power
Upper LOA: 12.80 (10.93,14.68)
Bias=4.97 (3.87-6.06)
Lower LOA: -2.87 (-0.10,-4.75)
Difference (Measured - Calculated Power)
Mechanical Power Mean ([Measured + Calculated]/2)
15
10
5
0
-5
20
40
60
80


Bland-Altman plot for Respiratory System-directed Driving Power
Upper LOA: 12.60 (9.09,16.11)
Bias=-2.06 (-4.10,-0.02)
Lower LOA: -16.72 (-20.23,-13.21)
Difference (Measured - Calculated Power)
Mechanical Power Mean ([Measured + Calculated]/2)
10
0
-10
-20
-30
10
20
30
40

Sleep Medicine

Sleep Medicine - 1 Examination of EEG Sleep Patterns in Post-Operative Cardiac Surgery Patients

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Introduction: Post-operative sleep alterations have been shown to play a role in the development of postoperative cognitive dysfunction and delirium [1,2,3]. Recently, postoperative delirium has been shown to be an independent predictor for the development of dementia within 5 years following cardiac surgery [4,5]. To date, few studies have examined continuous EEG monitoring in the post-operative period and its association with delirium with fewer studies examining patients in the postoperative intensive care unit or following cardiac surgery [1,6]. We designed a study that utilized a user-friendly single-lead EEG device to monitor sleep at home and also post-operatively in the ICU after cardiac surgery in the same group of patients. We aimed to determine the prevalence and severity of sleep disturbance following cardiac surgery using EEG data as well as qualitative sleep questionnaires to determine how these changes were associated with the development of postoperative delirium. We hypothesized that following cardiac surgery, total sleep and quality of sleep (measured by time in deep sleep and REM sleep) would be significantly decreased and that patients with sleep disturbances would be more likely to develop postoperative delirium. As a secondary aim of this study, we analyzed the raw EEG waveforms in our patient population pre-operatively while sleeping at home and compared them to post-operative EEG sleep data to determine whether we could uncover any changes in EEG signatures between baseline sleep and post-operative sleep.

Methods: This was a prospective observational study of adult patients (≥18 years of age) who were scheduled for cardiac surgery utilizing cardiopulmonary bypass. Any patients with a pre-existing sleep disorder, adhesive allergy, or inability to consent were excluded. EEG data was collected using ZMachine Insite [General Sleep, Cleveland, OH], an FDA-approved device that uses single-channel EEG to determine sleep state information including sleep stages. In patients able to use the device at home, a total of up to 5 consecutive nights of baseline sleep at home were collected to determine a representative sample of baseline sleep patterns. Following cardiac surgery, discontinuation of sedation, and extubation, patients underwent EEG monitoring with the same ZMachine device for the duration of their post-operative hospital stay up to a total of 5 consecutive postoperative nights. Light sleep, deep sleep, REM sleep, total sleep time, and sleep efficiency were collected for each day. Data from patient's who had significant sleep disturbances, did not use the EEG device correctly at home, had poor EEG data, or had significant amount of data missing were excluded from the final analysis.

Results: A total of 91 patients were included in the analysis. Baseline data for 15 patients were obtained. EEG data are described in Table 1. Self-reported questionnaire data suggest the postoperative period is associated with a reduction in the perceived amount of sleep. This perceived sleep disturbance is associated with post-operative EEG findings consistent with a reduction in sleep quality (reduced deep and REM sleep) as opposed to actual time spent sleeping (light sleep and total sleep) which was increased in the post-operative period. Our results revealed that although patients appeared to have an adequate amount of sleep post-operatively, most of their time sleeping was in light sleep and deep sleep and REM sleep were actually decreased from baseline. EEG spectrograms in these patients were analyzed pre and post-operatively to identify specific changes in EEG patterns post-operatively from baseline and will be displayed at the time of presentation.

Conclusion: Our data suggests that overall, patients have perceptibly poorer quality sleep in the post-operative period following cardiac surgery compared to cohort baseline which was confirmed with quantitative EEG data. The novelty of our study was in that we were able to observe direct changes in each individual patient's post-operative sleep from baseline sleep patterns and plan to evaluate individual EEG patterns with the objective to identify changes in EEG patterns in these patients. We hope that our study can improve the understanding of post-operative sleep

disturbances using quantitative EEG as well as qualitative data and help pave the way to uncovering the effects of surgery and anesthesia, in particular cardiac surgery, on postoperative delirium.

References: 1. Postoperative sleep disturbances: mechanisms and clinical implications. Br J Anaesth 1996;76:552-9 2. Postoperative sleep disturbance: influences of opioids and pain in humans. Sleep. 2001;24:39-44. 3. Preoperative Sleep Disruption and Postoperative Delirium. J Clin Sleep Med. 2015;11(8):907-13. 4. Pilot prospective study of post-surgery sleep and EEG predictors of post-operative delirium. Clinical Neurophysiology. 2017;128:1421-5. 5. Quantitative analysis of rest- activity patterns in elderly postoperative patients with delirium: support for a theory of pathologic wakefulness. J Clin Sleep Med. 2008;4:137-42. 6. Sleep in the surgical intensive care unit: continuous polygraphic recording of sleep in nine patients receiving postoperative care. British Medical Journal 1985; 290: 1029-1032. 7. EEG in delirium. Semin Clin Neuropsychiatry. 2000;5:86-92.

Table 1. Average amount of REM, deep, light and total sleep for baseline sleep and postoperative days 1 -5 (POD1 - POD5) sleep, p values comparing postoperative sleep to the baseline sleep.

Days	REM Sleep		Deep Sleep		Light Sleep		Total Sleep	
	Mean ± SD (hours)	p value	Mean ± SD (hours)	p value	Mean ± SD (hours)	p value	Mean ± SD (hours)	p value
Baseline Sleep	1.51± 0.78		1.98± 0.67		2.10± 0.85		5.59± 1.49	
POD1	0.91± 1.11	0.011	0.51± 0.76	<0.001	6.55± 2.14	<0.001	7.97± 2.71	<0.001
POD2	0.99± 1.25	0.021	0.91± 0.78	<0.001	6.14± 2.39	<0.001	8.04± 2.84	<0.001
POD3	1.05± 1.01	0.02	0.83± 0.71	<0.001	5.14± 2.56	<0.001	7.02± 2.75	<0.001
POD4	0.91± 0.98	<0.001	0.75± 0.61	<0.001	4.51± 2.01	<0.001	6.17± 2.61	<0.001
POD5	1.01± 0.96	0.004	0.69± 0.54	<0.001	4.61± 2.01	<0.001	6.31± 2.22	<0.001

Sleep Medicine - 2 The use of waist circumference instead of neck circumference in the STOP-Bang questionnaire and B-APNEIC score to screen for severe obstructive sleep apnea.

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Introduction: We have previously shown that neck circumference (NC) is the most important parameter to screen for severe obstructive sleep apnea (OSA) when using the STOP-Bang questionnaire or B-APNEIC score.1 However, NC is seldom measured during routine medical care. While more common anthropometric measures, such as waist circumference (WC), have been proposed as an alternative to NC for OSA screening tools, their validity has remained underexplored. Therefore, our goal was to compare the utility of WC to NC when using the STOP-Bang questionnaire and B-PANEIC score to screen for severe OSA.

Methods: Following Institutional Review Board approval, we retrospectively assessed data from a prospective cohort of patients referred for overnight polysomnography (PSG). Severe OSA was diagnosed based on criteria set by the American Academy of Sleep Medicine.2 We measured WC using 3 different methods: 1) at the level of the umbilicus; 2) the National Institutes of Health (NIH) method;3,4 and 3) the World Health Organization (WHO) method.4 First, locally weighted scatterplot smoothing (LOWESS) curves were generated to graphically represent the relationship between NC as well as all 3 WC measurements and the likelihood of severe OSA. Then, receiver operating characteristic (ROC) curves were generated for the STOP-Bang questionnaire as well as B-APNEIC score using NC and WC, and their areas under the curve (AUC) were compared using the DeLong method.

Results: Of the 275 patients in the main study cohort, 239 patients had complete data points for the present analysis. 33% (n=78) of patients were diagnosed with severe OSA. LOWESS curve analysis demonstrated a near linear relationship between NC as well as all 3 WC measurements and likelihood of severe OSA (Figure 1). Pearson correlation between NC and WC were: 1) Umbilicus, r=0.54; 2) NIH, r=0.46; and 3) WHO, r=0.62. Since NC and WC-WHO demonstrated the highest correlation, STOP-Bang questionnaire and B-APNEIC scores were tabulated using these two measurements. The traditional cut-off value for NC (40 cm) is in the center of the distribution of measurements and therefore we used similar approach to derive a cutoff value of 125 cm for WC-WHO (Figure 1). ROC curves (Figure 2) demonstrated that AUC for the original vs modified STOP-Bang questionnaire were 0.75; 95%CI 0.68-0.81 vs 0.74; 95%CI 0.68-0.80 (p=0.55), respectively. Similarly, AUC for the original vs modified B-APNEIC score were 0.75; 95%CI 0.68-0.81 vs 0.72; 95%CI 0.66-0.78 (p=0.27), respectively. Sensitivity, specificity, and accuracy data for the original and modified screening tools are shown in Table 1.

Conclusion: Our data suggest that WC-WHO may be an acceptable substitute for NC when screening for severe OSA using either the STOP-Bang questionnaire or B-APNEIC score. Further studies are needed to validate our findings and to prospectively assess the accuracy of OSA screening using alternative anthropometric measures such as WC.

References: 1. The B-APNEIC score: distilling the STOP-Bang questionnaire to identify patients at high risk for severe obstructive sleep apnoea. Anaesthesia. Published online September 2, 2021. doi:10.1111/anae.15571. 2. International Classification of Sleep Disorders, Third Edition. Darien, IL: American Academy of Sleep Medicine, 2014. 3. The Practical Guide to the Identification, Evaluation and Treatment of Overweight and Obesity in Adults. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute, NHLBI Obesity Education Initiative, North American Association for the Study of Obesity, 2000. 4. Waist

circumference and waist-hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008. Geneva, Switzerland: World Health Organization, 2011.

Figure 1. Locally weighted scatterplot smoothing curves to graphically represent the relationship between: (A) NC = neck circumference; (B) WC-Umbilicus = waist circumference - umbilicus method; (C) WC-NIH = waist circumference - National Institutes of Health method; as well as (D) WC-WHO = waist circumference - World Health Organization method and the likelihood of severe obstructive sleep apnea (OSA). Dotted line in (A) represents the original cut-point (<40cm vs ≥40cm) for NC in the STOP-Bang questionnaire and B-APNEIC score. Dotted line in (D) represents the proposed cut-point (<125cm vs ≥125cm) for WC-WHO for the STOP-Bang questionnaire and B-APNEIC score.

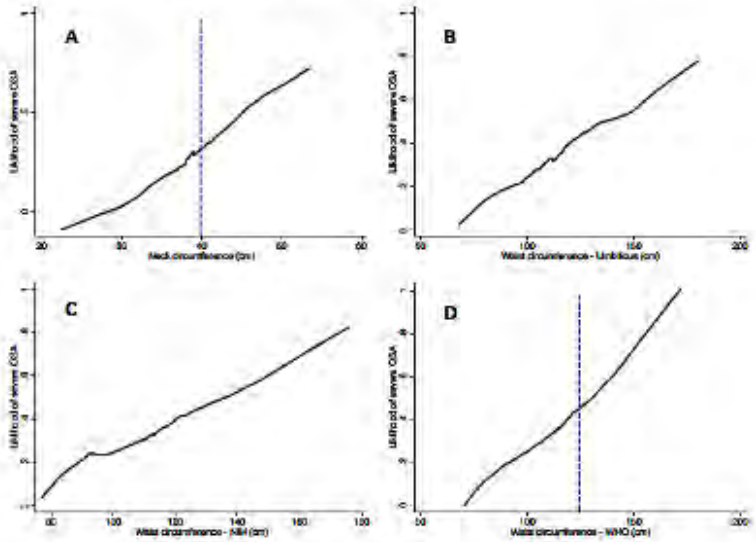

Figure 2. Receiver operating characteristic curves comparing: (A) original STOP-Bang questionnaire using neck circumference versus modified tool using waist circumference for severe obstructive sleep apnea (AUC 0.75; 95%CI 0.68-0.81 vs 0.74; 95%CI 0.68-0.80: p=0.55, respectively), and (B) original B-APNEIC score using neck circumference versus modified tool using waist circumference for severe obstructive sleep apnea (0.75; 95%CI 0.68-0.81 vs 0.72; 95%CI 0.66-0.78: p=0.27, respectively).

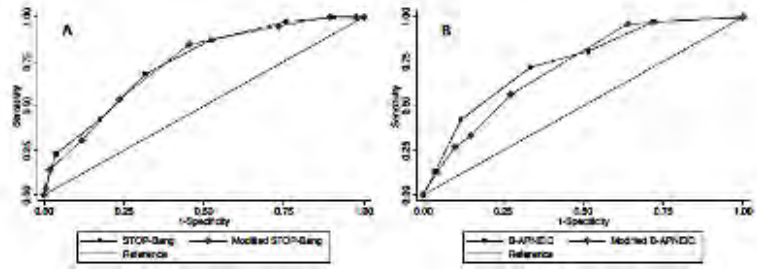

Table 1. Sensitivity, specificity, and accuracy of the STOP-Bang questionnaire and B-APNEIC score using neck circumference versus modified screening tools using waist circumference.

Screening Tool	Sensitivity (%)	Specificity (%)	Accuracy (%)
STOP-Bang (<5 vs ≥5)	68	68	68
Modified STOP-Bang (<5 vs ≥5)	54	76	69
B-APNEIC (<3 vs ≥3)	72	67	68
Modified B-APNEIC (<3 vs ≥3)	56	73	67

Sleep Medicine - 3 Postoperative outcomes in polysomnography diagnosed obstructive sleep apnea patients undergoing non-cardiac and cardiac surgeries: A meta-analysis of prospective cohort studies

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Introduction: Identifying surgical patients with obstructive sleep apnea (OSA) may assist with risk stratification, anesthetic management, and monitoring to minimize postoperative complications.[1] Our aim was to investigate the effect of OSA, diagnosed by objective measures such as polysomnography (PSG) or home sleep apnea testing (HSAT), on postoperative outcomes in cardiac and non-cardiac surgical patients. Therefore, we designed this systematic review and meta-analysis (SRMA) of prospective cohort studies using trial sequential analysis to minimize the risk of type 1 error in evaluating the impact of OSA on postoperative outcomes in surgical patients.

Methods: Multiple databases were systematically searched to identify prospective studies related to OSA patients undergoing surgery and postoperative outcomes. OSA patients were diagnosed by PSG or HSAT. Outcomes included: (1) total postoperative complications; (2) systemic complications: cardiovascular, respiratory, neurological, renal, and infectious; and (3) specific complications: atrial fibrillation, myocardial infarction, ICU admission, and mortality. The SRMA was conducted to examine pooled odds ratios (OR) of postoperative complications using inverse-variance random-effects model.

Results: The systematic search resulted in 12,717 articles and 20 prospective cohort studies, enrolled from 11 different countries, were included for meta-analysis (non-cardiac surgeries n=9; cardiac surgeries n=11). Total of 3,756 patients were screened for OSA using PSG or HSAT with 2,127 patients diagnosed with OSA and 1,629 control patients without OSA. Mean age of patients with OSA: 63.7±9.5 years; BMI of 29.5±9.1 kg/m^2; 65.0% male. Mean age of non-OSA patients: 58.5±10.3 years; BMI of 26.5±3.1kg/m^2; 49.1% male. Overall, postoperative complications were higher in the OSA than in the non-OSA group, with OR of 1.92 (95%CI: 1.52 - 2.42, P<0.05) and an absolute risk increase of 6.97% in OSA patients. For non-cardiac surgeries: OR of 1.97 (95%CI: 1.31 - 2.96, P<0.05) and absolute risk increase of 7.34% in OSA patients. For cardiac surgeries: OR of 1.89 (95%CI: 1.43 - 2.49, P<0.05) and absolute risk increase of 7.80% in OSA patients. There was also a significant increase in postoperative cardiovascular OR of 1.56 (95%CI: 1.20-2.02, P<0.05) and respiratory OR of 1.91 (95%CI: 1.39-2.62, P<0.05) complications in OSA patients. Other findings include increased neurological complications, hospital readmissions

Conclusion: OSA was associated with a nearly two-fold increased risk of total postoperative complications in patients undergoing either non-cardiac or cardiac surgeries compared with patients without OSA. This increased risk emphasizes the importance of preoperative screening of OSA, especially with newly diagnosed OSA patients. Future investigation needed to assess whether interventions can modify risk of OSA for cardiac and non-cardiac surgeries.

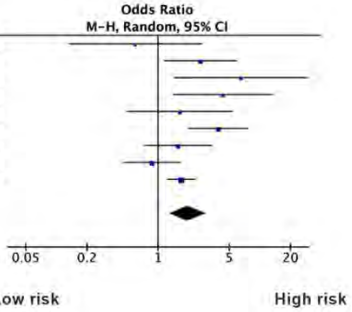
References: 1. Journal of Clinical Investigation. 2014;124(4):1454-7

A) Postoperative complications: non-cardiac surgeries

Study or Subgroup	OSA Events	OSA Total	Non-OSA Events	Non-OSA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ahmad et al. 2008	10	31	4	9	5.5%	0.60 [0.13, 2.71]	2008
Chung et al. 2008	40	147	8	64	11.8%	2.62 [1.15, 5.97]	2008
Hwang et al. 2008	15	98	2	74	5.5%	6.51 [1.44, 29.42]	2008
Flink et al. 2012	8	15	19	91	8.3%	4.33 [1.39, 13.45]	2012
Schumann et al. 2016	6	29	7	51	7.6%	1.64 [0.49, 5.45]	2016
Devaraj et al. 2017	30	70	18	112	13.9%	3.92 [1.96, 7.82]	2017
Bamgbade et al. 2017	20	80	14	80	12.7%	1.57 [0.73, 3.38]	2017
Hudson et al. 2018	23	66	38	100	14.6%	0.87 [0.46, 1.67]	2018
Chan et al. 2019	179	823	56	395	20.2%	1.68 [1.21, 2.33]	2019
Total (95% CI)		**1359**		**976**	**100.0%**	**1.97 [1.31, 2.96]**	
Total events	331		166				

Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 17.88$, $df = 8$ ($P = 0.02$); $I^2 = 55\%$

Test for overall effect: $Z = 3.28$ ($P = 0.001$)



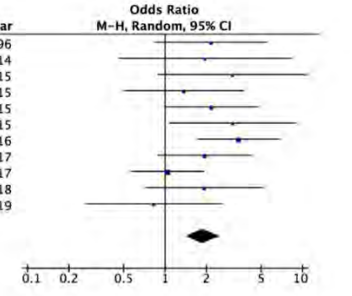
Bayesian model:
Absolute risk increase: 24.35 - 17.00 = 7.34%
Predictive intervals: 0.64 to 6.01

B) Postoperative complications: cardiac surgeries

Study or Subgroup	OSA Events	OSA Total	Non-OSA Events	Non-OSA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Mooe et al. 1996	25	78	7	39	8.2%	2.16 [0.84, 5.55]	1996
Roggenbach et al. 2014	41	83	3	9	3.6%	1.95 [0.46, 8.33]	2014
Zhao et al. 2015	31	128	3	32	4.8%	3.09 [0.88, 10.84]	2015
Foldvar-Schaefer et al. 2015	32	45	18	28	7.3%	1.37 [0.50, 3.74]	2015
Kua et al. 2015	22	75	12	75	11.5%	2.18 [0.99, 4.81]	2015
Uchoa et al. 2015	18	37	7	30	6.6%	3.11 [1.07, 9.02]	2015
Ding et al. 2016	41	54	84	175	14.9%	3.42 [1.71, 6.82]	2016
Mason et al. 2017	21	57	15	65	11.6%	1.94 [0.88, 4.28]	2017
Rupprecht et al. 2017	48	151	21	68	18.3%	1.04 [0.56, 1.94]	2017
Tafelmeier et al. 2018	10	23	18	63	7.5%	1.92 [0.72, 5.17]	2018
Tafelmeier et al., 2019	5	37	11	69	5.7%	0.82 [0.26, 2.58]	2019
Total (95% CI)		**768**		**653**	**100.0%**	**1.89 [1.43, 2.49]**	
Total events	294		199				

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 10.46$, $df = 10$ ($P = 0.40$); $I^2 = 4\%$

Test for overall effect: $Z = 4.49$ ($P < 0.00001$)



Bayesian model:
Absolute risk increase: 38.28 - 30.47 = 7.80%
Predictive intervals: 1.27 to 2.79

Sleep Medicine - 4 The SANDMAN Study: Sleep Apnea, Neuroinflammation, and Cognitive Dysfunction Manifesting After Non-cardiac surgery

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Introduction: Up to 40% of older surgical patients develop postoperative delirium (POD) and/or postoperative cognitive dysfunction (POCD)-objective cognitive deficits occurring 1-12 months after surgery. Although POCD and POD are both associated with decreased quality of life, increased mortality, and long-term cognitive decline, there are few interventions to prevent them. One potentially modifiable POD and POCD risk factor is poor sleep quality, due to obstructive sleep apnea (OSA), a frequently undiagnosed disorder characterized by repetitive breathing interruptions and hypoxia during sleep. Although OSA has been connected to long-term cognitive decline and earlier dementia onset, it is unknown whether untreated OSA is associated with POD, POCD, or increased neuroinflammation-a potential mechanism underlying POD and POCD. SANDMAN aims to determine the relationship between untreated OSA, POD, POCD, and neuroinflammation.

Methods: SANDMAN is an IRB-approved sub-study of the NIH-funded INTUIT study, in which 200 patients age>60 undergoing non-cardiac surgery complete blood and cerebrospinal fluid sampling before, 24 hours, and 6 weeks after surgery. POD is assessed up to 5-days postoperatively with 3D-CAM, and a cognitive testing battery is performed before, 6-weeks, and 1-year after surgery. SANDMAN patients underwent preoperative home sleep apnea testing (HSAT) to diagnose OSA and quantify its severity by measuring the apnea-hypopnea index (AHI). Preoperative subjective sleepiness, a marker of sleep quality, was assessed with the Epworth Sleepiness Scale (ESS), categorized as normal, mild, and moderate/severe excessive. The relationship of OSA severity and ESS scores with POD incidence and severity change was assessed in multivariable models adjusting for age, sex, and baseline POD severity score.

Results: 145 INTUIT patients were screened for SANDMAN inclusion, and 101 eligible patients underwent preoperative HSAT (Figure 1). We obtained valid HSAT data on 97 subjects, of whom 91 completed POD assessments. 60% of the SANDMAN patients who completed HSAT were diagnosed with OSA, of whom 36% had mild OSA, 14% had moderate OSA, and 9% had severe OSA (Table 1). There was no significant relationship between OSA severity (AHI) and POD incidence (OR 0.99; 95% CI 0.93-1.04, p=0.97) or severity (OR 0.98, 95% CI 0.95-1.01, p=0.32; Figure 2). ESS was not associated with POD incidence, but moderate-severe sleepiness (ESS,â•13) was associated with increased POD severity (OR 3.98; 95% CI 1.10-14.37, p=0.035; Figure 3).

Conclusion: These results suggest no relationship between OSA and POD incidence or severity, although increased preoperative subjective sleepiness was associated with POD severity. This suggests that sleep deficits, perhaps unrelated to OSA, could play a role in POD. Future work is warranted on the role of perioperative sleepiness and sleep dysfunction in POD.

Table 1. Baseline summary table by physician diagnosis of OSA severity. Variables summarized with mean (SD) or median [Q1, Q3] and compared with ANOVA or Kruskal Wallis tests

	None (N=39)	Mild OSA (N=35)	Moderate OSA (N=14)	Severe OSA (N=9)	p value
Age	67.54 (6.21)	68.17 (5.17)	70.71 (6.94)	68.78 (4.52)	0.377
Gender (Male)	14 (35.9%)	14 (40.0%)	7 (50.0%)	9 (100.0%)	0.005
AHI	2.19 (1.49)	9.68 (4.27)	18.56 (2.84)	48.97 (16.79)	<0.001
ODI					<0.001
Mean (SD)	3.08 (1.98)	11.50 (5.27)	18.96 (7.69)	49.72 (23.79)	
Median	2.70	10.80	18.45	41.90	
Q1, Q3	1.40, 4.50	8.50, 15.50	15.10, 21.30	37.10, 59.90	
HSAT days to surgery	-4 [-6, -2]	-3 [-8, -3]	-4 [-7, -3]	-3 [-7, -1]	0.782
Duration of Recording (min)	439 [356, 544]	438 [360, 508]	455 [387, 532]	403 [357, 420]	0.341
Baseline Delirium	0	0	0	0	--
Baseline 3D-CAM severity Score	0 [0, 0]	0 [0, 1]	0 [0, 1]	0 [0, 0]	0.318
Epworth Sleepiness Score	8 [5, 9]	6 [4, 8]	6 [3, 10]	7 [5, 13]	0.366

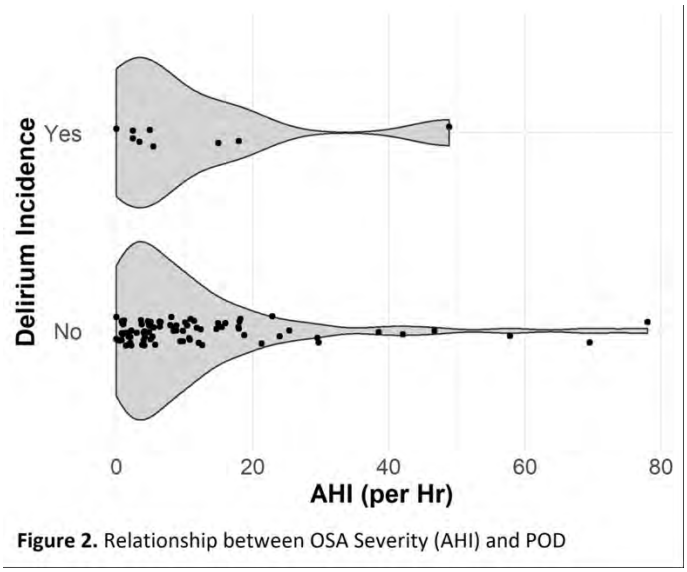

Figure 2. Relationship between OSA Severity (AHI) and POD

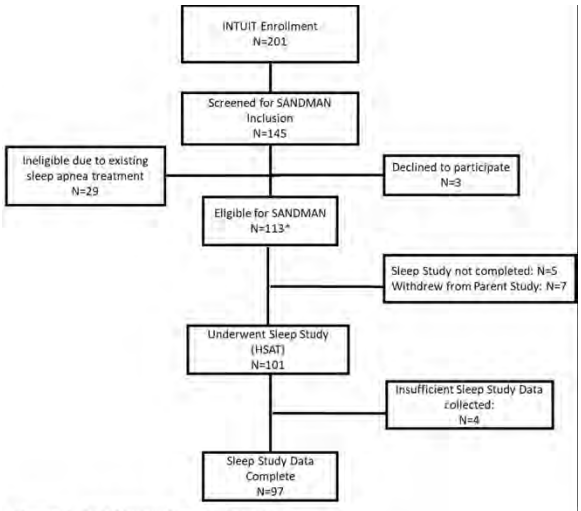

Figure 1. SANDMAN Consort Diagram

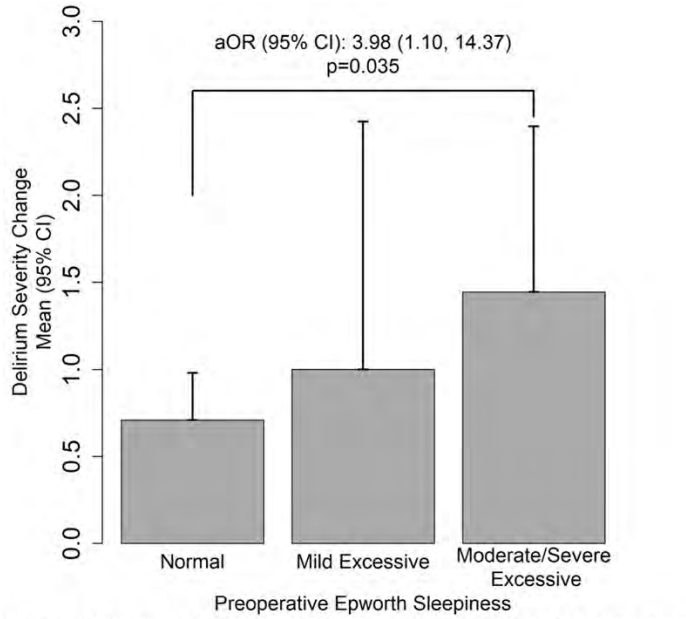

Figure 3. Relationship between sleepiness (ESS score) and POD severity

Technology, Computing and Simulation, Equipment Monitoring - 1 Use of Simulation-based Mastery Learning Curriculum to Improve Breaking Bad News Skills Amongst Pediatric Anesthesiologists: A Pilot Study

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Introduction: Breaking bad news is one of the most stressful duties that a physician must undertake. Unfortunately, pediatric anesthesiologists must often disclose bad news with very little training during residency or fellowship. Anesthesiologists who lack the necessary communication skills required for such a task may suffer from increased burnout after a bad event. We developed a breaking bad news simulation-based mastery learning (SBML) curriculum to determine whether the communications skills of pediatric anesthesiologists could be improved.

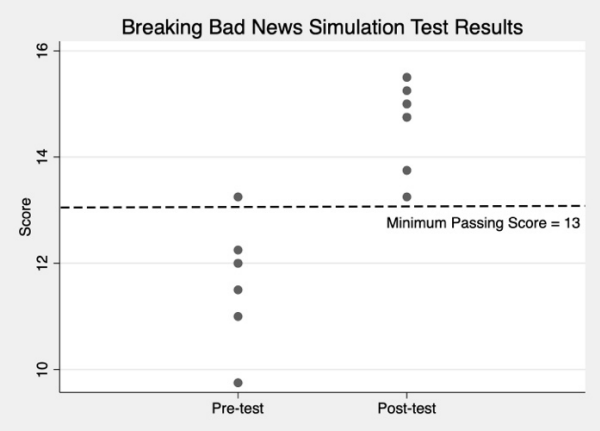
Methods: Using the modified Delphi technique, an expert panel consisting of ten board-certified physicians (six pediatric anesthesiologists, one pediatric anesthesiologist/intensivist, one pediatric intensivist, and two internists) reached consensus on a 16-item skills checklist (Table 1). The minimum passing standard (MPS) was set at 13 out of 16 (81%) using the modified Angoff method. A pre-test/post-test study design was used to evaluate pediatric anesthesiologists' performance using the skills checklist. Participants completed a two-hour curriculum consisting of a pre-test, didactic session, deliberate practice with immediate feedback, and a post-test. The pre-test and post-test were simulated scenarios where the participant had to inform a parent actor that their child died in the operating room. Participants were required to meet or exceed the MPS to pass the course. Prevalence and bias adjusted Kappa (PABAK) coefficients were calculated to determine inter-rater reliability. We report descriptive summaries of collected data as medians with interquartile ranges for continuous data and counts and frequencies for categorical data. The Wilcoxon rank sign test was used to test whether there was a significant difference between pre-test and post-test scores and pre-course and post-course confidence, scored from 1 to 5.

Results: Approval for this study was granted by the Institutional Review Board of the Ann & Robert H. Lurie Children's Hospital of Chicago (IRB # 2020-3469). Five pediatric anesthesiology attending physicians and five pediatric anesthesiology fellows were enrolled at a tertiary care children's hospital between February and September 2021. A summary of participants' demographic data is presented in Table 2. The median years of clinical experience was 6.5 (IQR 5-12.5) with approximately 70% of participants reporting breaking bad news in the past. The skills checklist inter-rater reliability was substantial with a PABAK of 0.76. At pretest, 2/10 (20%) of participants were able to meet or exceed the minimum passing standard. The median score on the pretest was 12/16 (75%) skills checklist items correct, which improved to 15/16 (94%) at post-test, p=0.02. All study participants achieved the MPS on their first post-test (Figure 1). Confidence improved from 3/5 to 4/5, p=0.02. Course satisfaction was high among participants.

Conclusion: Our pilot study demonstrates that a breaking bad news SBML curriculum for pediatric anesthesiologists significantly improved communication skills and confidence in a simulated environment. Since only two participants met the minimum passing score prior to training, our results suggest pediatric anesthesiologists could benefit from further education to gain effective communication skills and SBML training may be effective to achieve this result.

	Yes	
Creates initial rapport when first walking into room (e.g. introduces self/introduced by someone)		
Sits down		
Assumes a comfortable interpersonal distance		
Assesses family's perception or understanding of medical situation before breaking news (e.g. "tell me what you understand")		
Asks permission before giving the news (e.g. "I would like to discuss what happened")		
Gives a clear and concise "warning shot" (e.g. "I have some serious news")		
Pauses after delivering bad news		
Delivers bad news within the first minute of the conversation		
Delivers an empathic statement (e.g. "I know this is not what you expected to hear today")		
Suggests a plan for the next step		
Ensures family understanding (e.g. "It sounds like …")		
Avoids medical jargon (uses technical language without clarifying what it means)		
Gives information in small chunks (e.g. no more than 1 chunk of information before allowing family to process)		
Avoids giving information while family very emotional		
Avoids providing reassurances to family's emotion (e.g. avoid saying something like "it's ok")		
Listens attentively		

	Fellow (n=5)	Attending (n=5)	Overall (n=
Clinical Experience (yrs, IQR)	5 (5-5)	13 (11-36)	6.5 (5-12.5
Experience breaking bad news (%)	2 (40%)	5 (100%)	7 (70%)
# of times breaking bad news			
Never	3 (60%)	0	1 (10%)
<3	2 (40%)	0	3 (30%)
3-8	0	2 (40%)	2 (20%)
>10	0	3 (60%)	3 (30%)
Formal training in difficult conversations	2 (40%)	3 (60%)	5 (50%)
When did you receive education?			
None	3 (60%)	2 (40%)	5 (50%)
Medical School	2 (40%)	0	2 (20%)
Residency	1 (20%)	2 (40%)	3 (30%)
Attending	N/A	1 (20%)	1 (20%)
Pre-course Confidence (IQR)	2 (1-2)	3 (3-4)	3 (2-4)
Post-course Confidence (IQR)	4 (3-4)	4 (4-4)	4 (3.25-4
Overall satisfaction (IQR)	5 (4-5)	5 (4-5)	5 (4.25-5



Technology, Computing and Simulation, Equipment Monitoring

Technology, Computing and Simulation, Equipment Monitoring - 2 Validation of an Intensive Care Unit Data Mart for Research and Quality Improvement

Christina Boncyk[1], Robert Freundlich[1], Karen McCarthy[1], Pamela Butler[1]

[1]Vanderbilt University Medical Center, Nashville, TN

Introduction: The acceptance and adoption of findings from observational studies based on data derived from the electronic health record (EHR) is frequently limited by the perception that these data are inadequately validated and inherently inferior to data collected through more traditional means. We sought to create a structured, rigorously validated intensive care unit (ICU) data mart based on data automatically and routinely derived from the EHR, inclusive of data elements commonly used for quality improvement and research purposes, including high-quality outcomes data.

Methods: Key variables were identified by study investigators and faculty critical care physicians. Physicians worked closely with analysts using a structured approach. First, the presence of data in routine clinical practice was confirmed using chart review. Next, algorithmic definitions were created for complex data elements, including most outcomes, leveraging existing literature, when available. Data analysts worked to identify the location of variables within the data architecture underlying the EHR. Test patients were extracted and algorithms were iteratively refined. Once shown to be reproducible in a broad cohort of patients, structured query language (SQL) was used to extract, transform, and load data from the EHR into a relational database housed on a departmental server. The sensitivity and specificity of algorithmic definitions was formally assessed.

Results: A total of 459,465 patient ICU encounters were identified and included within the ICU data mart. These patients include over 460,000,000 individual laboratory results and 4,610,776 vital signs (with q1 minute fidelity in the first 24-hours of admission). We currently have 26 validated outcomes, structured within 19 tables, all of which have a sensitivity and specificity of greater than 95%. These data can be joined to 215 validated variables included within 125 tables comprising an existing anesthesiology perioperative data warehouse (PDW) for perioperative patients.

Conclusion: We propose a methodology for building a robust and highly granular ICU data mart, leveraging the synergistic expertise of clinicians and data analysts. Work to further identify and validate additional patient variables remains a core component of future quality improvement and research processes.

Technology, Computing and Simulation, Equipment Monitoring - 3 Development and Deployment of a ROTEM Clinical Decision Support App

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Introduction: At busy Trauma 1 Centers, there is a critical need for coagulation assays to delivery timely and accurate results during early trauma to improve the treatment of coagulopathies and allow for directed therapies to correct sources of bleeding in critically ill patients. This need has prompted the use of thromboelastography (TEG ®) and rotational thromboelastometry (ROTEM®)(1,2), respectively, in order to better classify the hemostatic process and status in individual patients. At the University of Utah School of Medicine we routinely utilize ROTEM in the perioperative and intraoperative period to direct therapies, however knowledge of ROTEM and confidence in result interpretation is limited by user frequency. This has thus limited the uptake and utilization of ROTEM by non-cardiac specialist faculty even during Trauma 1 activations. In order to realize the benefits of ROTEM in a broader set of physicians and care teams at our institution and others, we developed a smartphone app to ease the interpretation of ROTEM and assist in guiding therapy. We describe, herein, the development and deployment of the ROTEM Clinical Decision Support (RCDS) App.

Methods: The RCDS app was developed through an iterative process in collaboration with Anesthesiology faculty, Information Technology management, Clinical Informatics, and anesthesia technicians. The process to develop the app took part in stages, including a literature review, review of current apps available in the Apple iOS App Store and Android Google Play stores, informal end user consultations, and beta testing with both clinical experts and ROTEM technicians. Our further plans include usability testing, an iterative development process planned in iOS TestFlight for Winter 2021, and solicitation of formal user ratings on usability and clinical relevance of the app. Given the infrequent and sporadic need for ROTEM in trauma situations, we will undertake a formal monitoring process to determine adequate length of testing prior to public availability.

Results: At the time of submission we have developed a beta version of the RCDS app, which includes a clinical algorithm to interpret ROTEM in a step-wise visual manner (Figure 1). Our review of the iOS App store yielded n=3 apps, with one app having not been updated for five years, one app based on Australian guidelines, and one app that covered TEG but not ROTEM. The review of Android Play Store only yielded n=1 app that similarly covered TEG and not ROTEM, and had not been updated since 2018. Early feedback suggests the App is clinically useful and easy to use. The incorporation of Anesthesia Technicians in our test group has also been well received. Ongoing iterations are being tested from December 2021 - February 2021 in TestFlight, prior to publishing the app to the public via the iOS App Store.

Conclusion: The use of smartphones for clinical decision support is a feasible manner to simplify complex decision making and improve patient care. In addition, our search of the Android and iOS app stores found there is a dearth of clinical decision support for both TEG ® and ROTEM ®. The cost of smartphone app development continues to fall, making it a worthwhile investment for institutions. It is also worth mentioning that the incorporation of staff and technicians in the development process has both encouraged use and increased uptake of the app as well as improved the design and usability.

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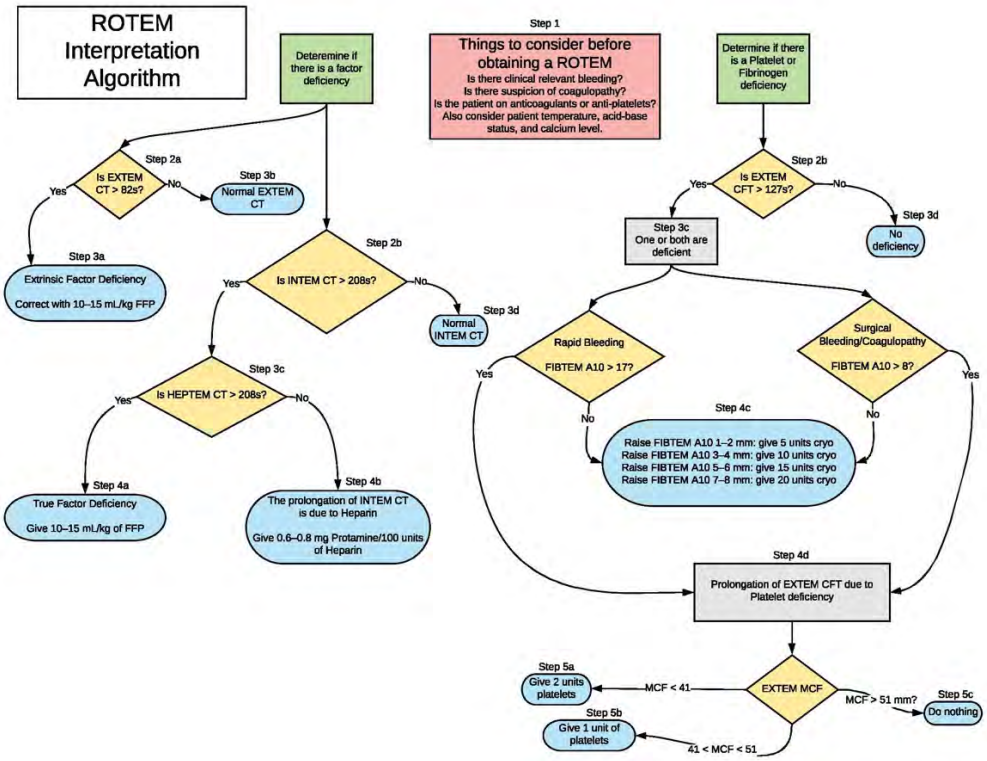
PMID: 25261079; PMCID: PMC4206701.



Technology, Computing and Simulation, Equipment Monitoring - 4 A Sim Ops Guide to Setting Up Pediatric Anesthesia Oscillator Training Simulations

Tanna J Boyer[1], Johnny F Cartwright[1], Daniel Germeroth[1], Sally A Mitchell[1]

[1]Indiana University School of Medicine, Indianapolis, IN

Introduction: High Frequency Oscillatory Ventilation (HFOV) is often used in Pediatric and Neonatal Intensive Care Units across the United States. Unfortunately, pediatric anesthesia fellows tend to have limited experience and education on how to manage HFOV. We present a new way to simulate HFOV in a micro-preemie for high-fidelity simulation scenario training for pediatric anesthesia fellows. This simulation could also be useful in the training of pediatricians, neonatologists, and pediatric intensivists.

Methods: We have successfully used a micro-preemie low-fidelity mannequin with a real oscillator, and a high-fidelity lung simulator, for interprofessional simulations with our pediatric anesthesia fellows, faculty, and respiratory therapy for the past three years. Training groups have included three to five fellows per year with two to three faculty and a respiratory therapist each year. The micro-preemie mannequin can be connected directly to the oscillator via a 2.5 uncuffed endotracheal tube or via a high-fidelity lung simulator. Vital signs including heart rate and rhythm, blood pressure, SpO2, temperature, and FiO2, can be viewed via the patient monitor function on simulation platform.

Results: With this setup, the mannequin is able to display chest wiggle similar to a real premature neonate and the settings on the oscillator can be changed appropriately for the case. Picture one shows our respiratory therapist teaching the group about HFOV and how to use an oscillator. Picture two shows the micro-preemie mannequin with the 2.5 endotracheal tube and the oscillator tubing connected. Picture three shows the output seen on the high-fidelity lung simulator when used in conjunction with the micro-preemie mannequin, 2.5 endotracheal tube, and oscillator.

Conclusion: HFOV can be effectively simulated using a micro-preemie mannequin, which opens many opportunities in HFOV training for pediatric anesthesia fellows, pediatric residents, neonatology fellows, and pediatric intensive care fellows. In theory, this same simulation set up would work with a toddler, child, or adult-sized mannequin as well.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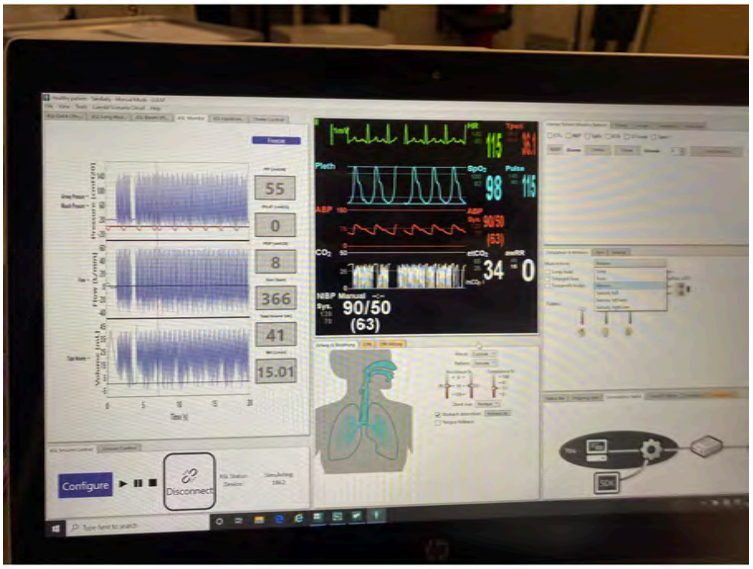
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Technology, Computing and Simulation, Equipment Monitoring - 5 A prospective, observational study of Non-Invasive Venous waveform Analysis (NIVA) for the detection of low volume blood loss in humans

Bret Alvis[1], Dawson C Wervey[2], Jenna Helmer Sobey[3], Romy Pein[2], Marisa Case[1], Meghan Breed[1], Philip Leisy[1], Colleen Brophy[4], Kyle Hocking[3]

[1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, United States of America, [3]Vanderbilt University Hospital, Nashville, TN, [4]Vanderbilt University Hospital, Nashville, United States of America

Introduction: Accurate non-invasive monitoring for early diagnosis of hemorrhage is an unmet need in the acute care setting.1,2 Heart rate (HR) and blood pressure (BP) are the most common data points used to clinically diagnose acute hemorrhage.1-3 However, they have routinely been shown to be unreliable requiring approximately 25-35% of blood loss before alteration in HR and BP occur.1-3 Non-invasive Venous waveform Analysis (NIVA) has demonstrated significant sensitivity in detecting acute hemorrhage of only 8-10% blood volume loss.3 In this prospective observational study, using a more optimized NIVA device prototype than prior studies3, we hypothesize that a quantifiable change in the venous waveform would be associated with less than 8% blood loss in healthy adult subjects donating whole blood.

Methods: 55 human blood donors were enrolled at an American Red Cross (ARC) donation center, of this data 39 subjects had waveforms clean enough for analysis. An optimized venous waveform capturing prototype with improved signal processing was secured to the volar aspect of the wrist in human subjects prior to the initiation of blood removal. Waveforms were recorded for the duration of the whole blood donation and then transformed from the time to the frequency domain. The ratio-metric power contribution of the cardiac frequencies were used to calculate a representative of volume status value- the NIVA score. The volume of whole blood removed was measured by an ARC digital flow device per ARC protocol.

Results: A significant average change in the NIVA score was observed after 200 mL (3-4% blood volume) of whole blood donation (0.4, SD 1.8, $p < 0.05$). A ROC curve for the ability of the change in the NIVA score to detect 200 mL of blood loss demonstrated an area under the curve (AUC) of 0.65.

Conclusion: There remains a large unmet need in accurate and timely detection of acute hemorrhage. This study supports the potential application of NIVA in detection of low volume human blood loss. NIVA is a novel technology that uses previously undetectable, low frequency signals of the cardiac pulse that may prove useful for more accurate and early detection of acute hemorrhage.

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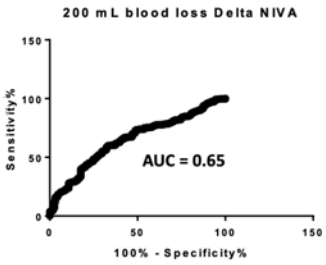

Technology, Computing and Simulation, Equipment Monitoring - 6

Demonstration of Artificial Intelligence Enabled Personalized Control of Hemodynamics (PCH) for High-Risk Surgery Patients in a Rat Model

Jinyoung Brian Jeong Jeong[1], Michael Zargari[2], Daniel Garcia[1], Chih-Ming Ho[1], Jacques Neelankavil[1], Maxime Cannesson[3], Jure Marijic[1], Soban Umar[2]

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Introduction: In surgery, even short periods of hypotension have been linked with increased incidence of complications such as acute kidney injury and myocardial infarction, leading to increased mortality and hospitalization. Despite substantial diversity among the 42 million surgery patients in the United States each year, management of hemodynamics currently uses a dose titration method, which is unable to precisely account for this diversity [1] (Fig. 1). An artificial intelligence (AI) platform, which is personalized based on a response surface of phenotypic variables and does not require large training datasets (AI-PRS), has been successfully used in the therapeutic intervention of organ transplants, cancers and infectious diseases [2,3,4]. By analyzing patients' unique hemodynamic response to medications with this platform, our AI-enabled Personalized Control of Hemodynamics (PCH) system can quickly customize drug dosing for a specific patient based on their individual physiology and biochemical profile [5,6]. Using this tool, hemodynamics such as blood pressure (BP) can be guided within a narrow and appropriate range. Here, we describe the preclinical testing and validation of the automated PCH in controlling BP of a rat model.

Methods: Rats were anesthetized with isoflurane and placed on mechanical ventilation via a tracheostomy. Venous access for drug administration was obtained via femoral vein, and the left ventricular systolic pressure (LVSP) was continuously measured with a catheter that was placed directly into the left ventricle after sternotomy. Cardiac events were simulated by increasing the concentration of isoflurane to lower BP, or administering phenylephrine (PE) to raise it. LVSP was noted at baseline, and following bolus doses of medications to increase (with PE) or decrease (with nitroglycerin: NG) it, and analyzed to determine a population-averaged sensitivity. Syringe pumps and a pressure monitoring catheter were interfaced with a computer, and software was programmed to automate the system. AI-guided partial doses of PE and NG based on previously determined population-averaged profiles were given to dynamically calibrate individualized sensitivities, which were used to determine dosing to target LVSP (Fig. 2). LVSP readings were collected with PowerLabs from ADInstruments and all code was written in MATLAB. All experiments were conducted with IRB approval.

Results: The preclinical PCH experiments were successful in controlling LVSP, from both hypotensive and hypertensive situations. The rats had varying responses to PE and NG, but by utilizing the calibrated individualized sensitivities, PCH brought the LVSP into target range with two boluses for most cases. Changing sensitivities to the medications, due to effects such as tachyphylaxis, were accounted for by the AI.

Conclusion: The emergence of AI has created a new paradigm for personalized and data-driven patient management. PCH greatly improves and simplifies BP management by utilizing dynamic personalized dosing. Our proof-of-concept experiments and analysis served as an initial step in validating the PCH for clinical use (patent pending). Ultimately, we will aim to develop the PCH platform to assist anesthesia providers in maintaining tight hemodynamic control with speed and precision.

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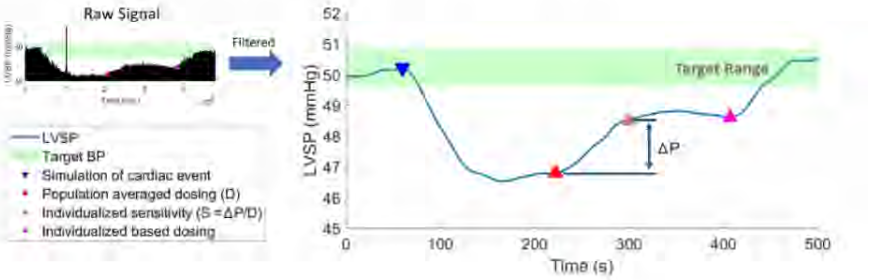
Figure 1. Mean Arterial Pressure (MAP) management during surgery. *This retrospective data of a MAP recording during a coronary artery bypass graft illustrates that with current practices, keeping a patient's BP within a narrow range is a major challenge for anesthesiologists. The green area shows the safest range of MAP. Red boxes mark periods of time where the patient is hypotensive, which can increase the likelihood of complications.*

Figure 2. PCH system brings the LVSP of a rat into target range. *After decreasing LVSP by increasing isoflurane concentration (blue triangle), the rat is dosed with a partial dose of phenylephrine based on the population average (red triangle). Feedback is used to calculate an individualized sensitivity (brown triangle), which determines the remaining dose to target (pink triangle). Following the total dose, LVSP is in target range (green area).*



Technology, Computing and Simulation, Equipment Monitoring - 7 Using Motion Analysis to Assess Skill Acquisition in Anesthesiology Interns Practicing Central Venous Catheter Placement

Vincent Baribeau[1], Arjun Bose[1], Aidan Sharkey[1], Kadhiresan Murugappan[1], Vanessa Wong[1], Dustin Lin[1], Jeffrey Weinstein[1], Robina Matyal[1], Feroze Mahmood[1], John D Mitchell[2]

[1]Beth Israel Deaconess Medical Center, Boston, MA, [2]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

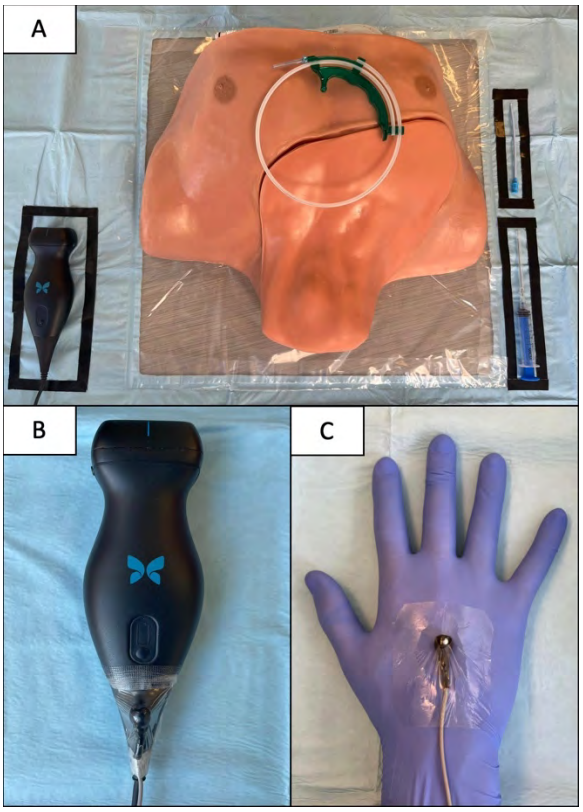
Introduction: Motion analysis involves the recording of hands and medical instruments using sensors. These recordings allow for objective comparison of certain metrics, including total distance travelled (path length), movements performed (translational motions) and time [1]. These metrics can be analyzed further to establish thresholds of performance, and potentially track skill acquisition in clinical procedures such central venous catheter (CVC) placement. We hypothesized that a combination of previously used and novel (rotational sum) motion metrics could be used to analyze performance trends of anesthesiology interns practicing central venous catheter placement in the simulation setting. We also hypothesized that segmentation of motion recordings would identify specific areas either exhibiting significant improvement or requiring deliberate practice.

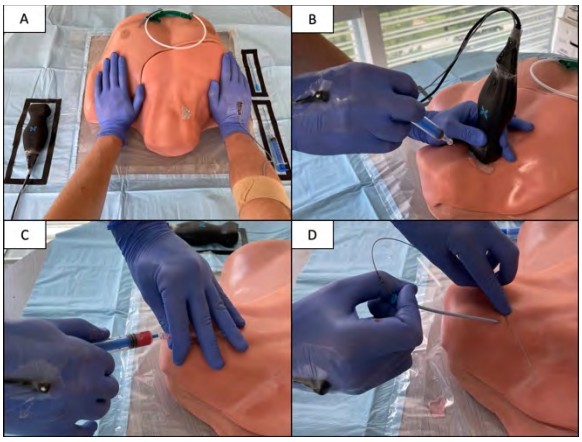
Methods: Twelve anesthesiology interns (novices) underwent a two-day training course in which they performed a total of nine central venous catheter placements each. They were equipped with motion sensors on the dorsum of their dominant hand and ultrasound probe (Figure 1). An additional five attending anesthesiologists (experts) performed 3 trials each in order to establish metric thresholds for comparison. Trials were recorded in order to precisely segment the motion recordings and assess metrics by procedural checkpoint (Figure 2). We analyzed the trend of each metric (path length, translational motions, rotational sum and time) for each sensor (dorsum of dominant hand and ultrasound probe) across all trials using generalized estimating equations (GEE). We also calculated the Pearson correlation coefficient between rotational sum and each other metric.

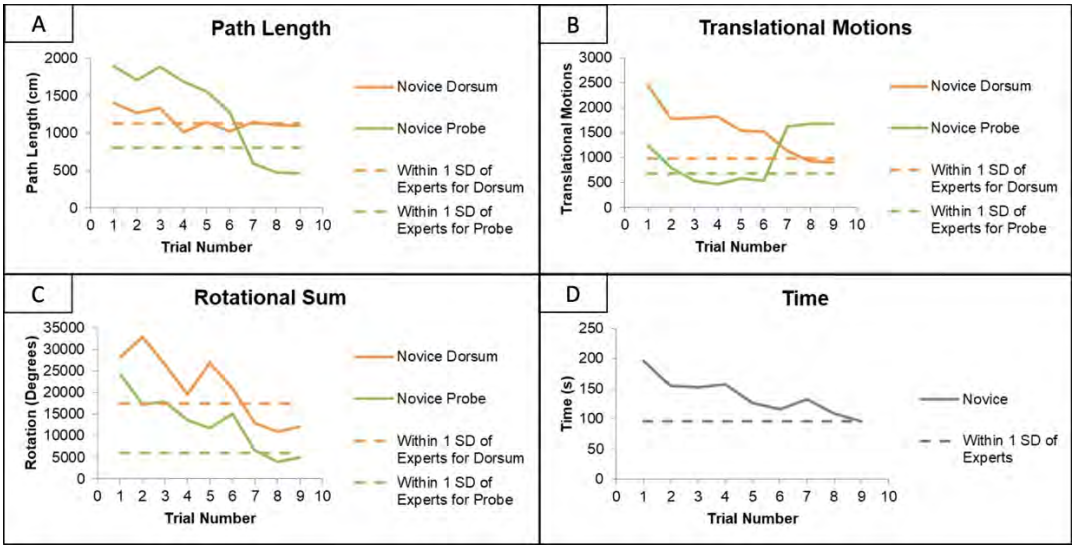
Results: On average, novices exhibited a negative trend in path length, translational motions, rotational sum, and time ($p \leq 0.001$) with the exception of translational motions of the ultrasound probe (Figures 3, 4). Interns reached within one standard deviation of the expert average by trials 7-8 for most metrics. Rotational sum exhibited a moderate to strong positive correlation with previously explored metrics ($p < 0.001$). Segmentation revealed significant improvement in all metrics for each checkpoint describing the novice average, except for the path length of the dorsum in checkpoint 3 ($p = 0.130$).

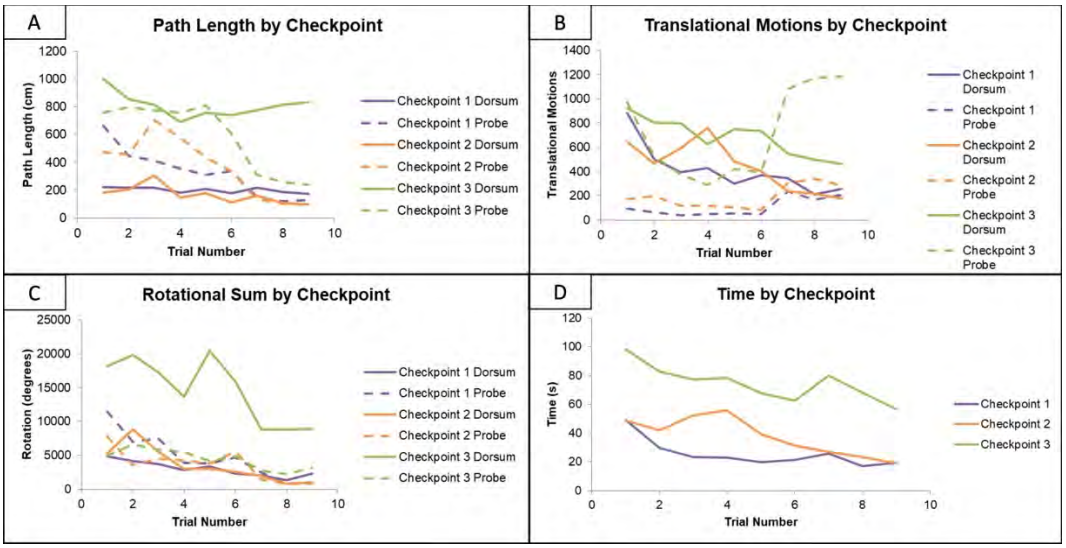
Conclusion: It was determined that a comprehensive series of motion metrics, including path length, translational motions, rotational sum, and time, is able to track progression in novice performance of CVC placement in the simulation setting. Rotational sum may be used as a supplementary metric to assess performance in CVC placement. Segmentation provides detailed insight into skill acquisition in particular checkpoints of CVC placement, and can inform deliberate practice.

References: [1] Motion-Tracking Machines and Sensors: Advancing Education Technology. Online ahead of print. 2021


A
B
C


A
B
C
D


A
Path Length
Path Length (cm)
Trial Number
Novice Dorsum
Novice Probe
Within 1 SD of Experts for Dorsum
Within 1 SD of Experts for Probe
B
Translational Motions
Translational Motions
Trial Number
Novice Dorsum
Novice Probe
Within 1 SD of Experts for Dorsum
Within 1 SD of Experts for Probe
C
Rotational Sum
Rotation (Degrees)
Trial Number
Novice Dorsum
Novice Probe
Within 1 SD of Experts for Dorsum
Within 1 SD of Experts for Probe
D
Time
Time (s)
Trial Number
Novice
Within 1 SD of Experts


A
Path Length by Checkpoint
Path Length (cm)
Trial Number
Checkpoint 1 Dorsum
Checkpoint 1 Probe
Checkpoint 2 Dorsum
Checkpoint 2 Probe
Checkpoint 3 Dorsum
Checkpoint 3 Probe
B
Translational Motions by Checkpoint
Translational Motions
Trial Number
Checkpoint 1 Dorsum
Checkpoint 1 Probe
Checkpoint 2 Dorsum
Checkpoint 2 Probe
Checkpoint 3 Dorsum
Checkpoint 3 Probe
C
Rotational Sum by Checkpoint
Rotation (degrees)
Trial Number
Checkpoint 1 Dorsum
Checkpoint 1 Probe
Checkpoint 2 Dorsum
Checkpoint 2 Probe
Checkpoint 3 Dorsum
Checkpoint 3 Probe
D
Time by Checkpoint
Time (s)
Trial Number
Checkpoint 1
Checkpoint 2
Checkpoint 3

Technology, Computing and Simulation, Equipment Monitoring - 8 Comparison of Onset of Neuromuscular Blockade with Electromyographic and Acceleromyographic Monitoring: A Prospective, Randomized Trial

Harold E Chaves-Cardona[1], Eslam A Fouda[2], Vivian Hernandez-Torres[2], Klaus Torp[3], J. Ross Renew[2]

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Introduction: Neuromuscular blocking agents (NMBAs) are a group of medications used in anesthesia to facilitate endotracheal intubation and optimize surgical conditions [1]. Reliable devices that quantitatively monitor the level of neuromuscular blockade (NMB) are crucial. Electromyography (EMG) and acceleromyography (AMG) are the two monitoring modalities used in the clinical practice. TetraGraph (Senzime AB, Sweden) is an EMG-based quantitative monitor that measures electrical activity within the muscle following stimulation. In comparison, TOFScan (Draeger Medical Inc., Telford, PA) is an AMG-based quantitative monitor that measures the muscle group of interest [2]. This study compares the onset of action of NMB, defined as a train-of-four count (TOFC) equal to 0, between the two devices while evaluating intubation conditions.

Methods: After IRB approval, 15 adult patients scheduled for elective surgery requiring NMB were screened and enrolled after written informed consent. Prior to induction of anesthesia, TetraGraph and TOFScan electrodes were placed separately over the ulnar nerve and the thumb randomly assigned to their dominant or non-dominant hand. Intraoperative NMBA dose was standardized to 0.5 mg/kg of rocuronium. After baseline measurements were obtained, objective measurements were recorded every 20 seconds and intubation was performed using GlideScope only either device displayed a TOFC=0. The anesthesia provider was then surveyed about intubating conditions. Shapiro-Wilk statistics were used to conduct normality test. Results showed that data was not normally distributed, for that reason non-parametric tests were performed. The mean time difference between devices was determined with Wilcoxon rank sum test and chi-square statistic was performed for intubating conditions.

Results: Eight males and seven females (58 ¬± 9 yr) (Table 1) were enrolled in the study. The onset time of NMB was 164 ¬± 54 (SD=98) seconds in TetraGraph, and 152 ¬± 34 (SD=61) seconds in TOFScan (p=0.563). TetraGraph displayed a TOFC=0 in 4 patients (26.7%) before TOFScan, while TOFScan displayed a TOFC=0 first in 7 patients (46.7%). Both devices reached TOFC=0 at the same time in 4 patients (26.7%) (p=0.549) (Table 2). During intubation, jaw relaxation was easy in 12 patients (80%) and fair in 3 (20%) (p=0.020). Vocal cord position was abducted in 14 patients (93.3%) and intermediate in 1 (6.7%) (p=0.001). Vocal cord movement was seen only in 1 patient (6.7%) (p=0.001). We did not detect patients with airway reaction or movement of the limbs during intubation (Table 3).

Conclusion: This study demonstrated that TOFScan measured a TOFC=0 in more patients before TetraGraph, however there was no significant difference between them. Significant variability exists between patients following a standardized dose of rocuronium, demonstrating the need for quantitative monitoring. A TOFC=0 in either device was a useful indicator for intubating conditions.

References: 1. Neuromuscular monitoring in the perioperative period. Anesthesia & Analgesia 2018; 126, 464-468. 2. Quantitative neuromuscular monitoring: Current devices, new technological advances, and use in clinical practice. Current Anesthesiology Reports 2018; 8, 134-144.

Table 1. Demographics.

Variables	Categories		
Gender	Male	8	53.3%
	Female	7	46.7%

	Mean	Std. Dev.
Weight	84.08 ±8.95	16.15
BMI	28.13 ±2.88	5.20
Wrist Circumference	18.27 ±1.52	2.75
Age	58.67 ±9.51	17.17

Table 2. Number of times each device first reached zero.

	Frequency	%	p-value
TG	4	26.7	
TS	7	46.7	0.549
Both Devices	4	26.7	

TG: TetraGraph; TS: TOFScan.

Table 3. Intubating conditions assessment.

	Easy	Fair	Difficult	p-value
Jaw relaxation	12 (80%)	3 (20%)	0 (0%)	0.020
	Abducted	Intermediate	Closed	p-value
Vocal cord position	14 (93.3%)	1 (6.7%)	0 (0%)	0.001
	None	Moving	Closed	p-value
Vocal cord movement	14 (93.3%)	1 (6.7%)	0 (0%)	0.001
	None	Diaphragm	Sustained	p-value
Airway reaction	15 (100%)	0 (0%)	0 (0%)	0.000
	None	Slight	Vigorous	p-value
Movement of the limbs	15 (100%)	0 (0%)	0 (0%)	0.000

Technology, Computing and Simulation, Equipment Monitoring - 9 Generalizing Machine Learning Models from Medical Free Text

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Introduction: Research of medical applications using machine learning (ML) models have become increasingly common, but investigation into optimal methods of development for use outside of the institution on which they were trained is sparse[1]. Generalizability can theoretically improve with higher quality and more standardized model inputs. As medical free text data is often fraught with spelling, translational, grammatical, and copy-forward errors, improvement of this data's quality is considered critical for optimal ML model performance. While medical free text may contain 10% spelling error rates[2], studies of pre-processing are limited in both scope and size[3]. Understanding data discrepancy could help guide ML adoption at outside institutions. In this study, we investigate generalizing ML models using medical free text for anesthesiology Current Procedural Terminology (CPT) code prediction. First, we analyze the utility of text preprocessing using the medically focused preprocessing method cSpell[4]. Second, we use probability distributions and clustering techniques to group and predict ML performance at external institutions prior to expanded model implementation. Finally, we evaluate optimal pathways for implementing models at new sites with considerations on when to retrain on new data.

Methods: Data: Utilizing data from the Multicenter Perioperative Outcomes Group, we identified all operative cases from 44 participating U.S. institutions[5-6]. Text Processing: Misspelled words were identified using context insensitive word correction by NIH Unified Medical Language System (UMLS) cSpell. 'Minimal' cleaning consisted of lowercasing, stripping excess white space, normalizing numbers, and removing punctuation and special characters. 'Maximal' cleaning included all of minimal cleaning and in addition included replacing identified misspelling with tool automated suggestions. 'Acronym' cleaning consisted of expanding physician-validated medical acronyms identified by the UMLS Specialist lexicon tool. Machine Learning (ML) Models: We created deep neural network ML models to predict anesthesiology CPT codes using procedural text [7]. Five-fold cross validation was used and models were evaluated with holdout testing data accuracy. A composite Kullback-Leibler Divergence (KLD) value was created for each institution using CPT code and procedural text distributions. K-medioid clustering and multidimensional scaling were then used to create a comparative 2-dimensional representation of KLD between institutions (Figure 1). Generalization by Institution: Independent ML models were trained and tested using each cleaning method by training on one or more institutions and testing on one or more remaining institutions.

Results: From an initial 3,564,947 cases, 48 anesthesia CPT codes were shared across all 44 institutions, resulting in a final dataset of 1,607,393 cases. Within this dataset, approximately 64,248 unique terms were used in procedural texts, 10% of which were identified as misspelled. Nine percent of cases contained text with at least one misspelled word. Vocabulary varied considerably between institutions with an average overlap of 44.2% (9.0 - 93.2%, median 45.0%) (Figure 2). Preprocessing using 'maximal' cleaning reduced vocabulary size by 20% with a 7% increase in vocabulary match between any two institutions, though ML model accuracy was not substantially affected (+0.2%, IQR [-0.35%, 0.71%] average improvement). 'Maximal' + 'Acronym' preprocessing showed a pairwise ML performance improvement of +0.5% (IQR [-0.32%, 1.06%]).There was a negative correlation between accuracy and KLD for 100% of institution pairs (-3.5% average accuracy per KLD distance from the training institution, +/- 1.5%), with an overall trend of -5.0% (Figure 3). Adding institutional data to training improved accuracy 12.7% +/- 6.8% at that site, while adding other sites showed minimal change (0.1% +/- 0.3%).

Conclusion: Cleaning medical free text prior to ML model development may not yield significant improvement in model performance. Single institution ML models show greatest generalizability to external institutions by retraining with data from that external site. When retraining is infeasible or prohibitive, the strong correlation between KLD and accuracy suggests that measures of probability distributions and clustering techniques can aid identifying model performance apriori and provide a path for creating ML models with aspirations of expansion to external sites.

References: 1.'Clinical documentation variations and NLP system portability...' Journal of the American Medical Informatics Association 25.3 (2018): 353-359 2.'Using lexical disambiguation and named-entity recognition to improve spelling correction in the electronic patient record.' Artificial intelligence in medicine 29.1-2 (2003): 169-184 3.'Automated misspelling detection and correction in clinical free-text records.' Journal of biomedical informatics 55 (2015): 188-195 4.'The unified medical language system (UMLS)...' Nucleic acids research 32.s_1 (2004): D267-D270 5.'Perioperative effectiveness research using large databases.' Best Practice & Research Clinical Anesthesiology 25.4 (2011): 489-498 6.'Clinical research using an information system: the multicenter perioperative outcomes group.' Anesthesiology clinics 29.3 (2011): 377-388 7.'Classification of current procedural terminology codes from electronic health record data using machine learning.' Anesthesiology 132.4 (2020): 738-749

Figure 2: Institutional Vocabulary Overlap. Heat map showing vocabulary overlap between individual institutions (x and y axes). Intersections depict a heat map translation of the % overlap in vocabulary between institutions as: (number unique vocabulary in x-axis institution that matches to y-axis institution vocabulary) / y-axis institution vocabulary.

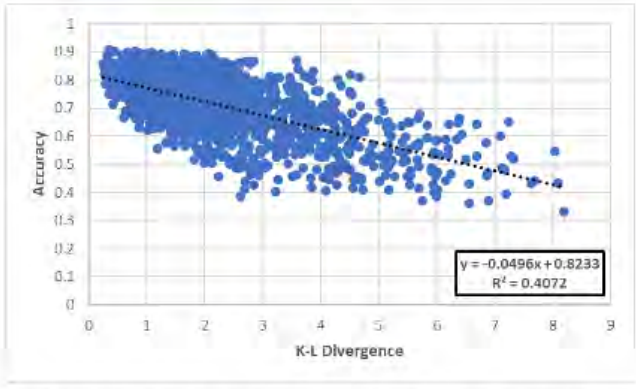

Figure 3: Single Institution Pairwise Comparison vs KLD. Each dot represents the performance of an ML model trained on an institution A and tested on a different institution B. This process was repeated for all pairs of institutions (except where A = B). This figure shows a negative correlation between performance and KL-Divergence between the institution pairs.

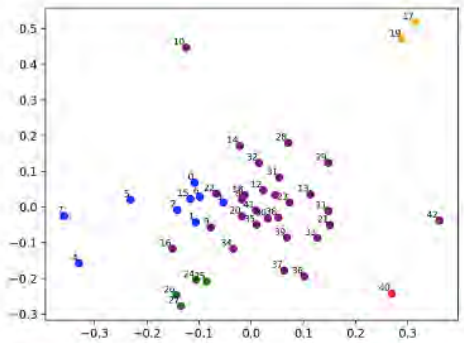

Figure 1: K-medoid Institutional Clustering. Each dot represents a single institution. The composite KLD score between institutions is represented in a 2D-cartesian plane utilizing multidimensional scaling. K-medoid clustering yields 5 distinct clusters identified by color. Institutions that are far apart have a large KLD indicating significant anesthesiology CPT and/or vocabulary differences.

Technology, Computing and Simulation, Equipment Monitoring - 10 Effectiveness of a Covid-19 Aerosol Box in protecting healthcare workers - A Computational Fluid Dynamic Study (CFD)

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[1]Duke Health, Durham, NC, [2]Western Health, Footscray, Australia, [3]University of Melbourne, Parkville, Australia

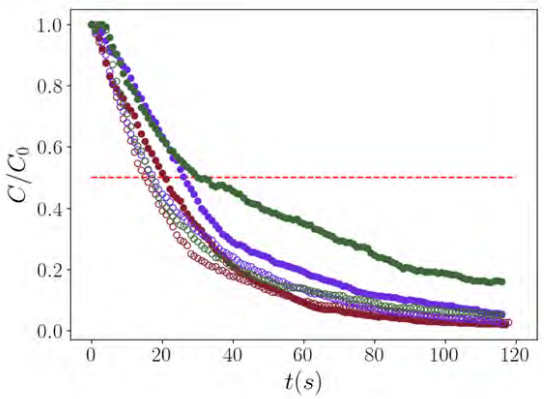
Introduction: Many variations of the COVID-19 Aerosol Box have been theorized and produced.[1, 2] However, there is a paucity of scientific evidence regarding the effectiveness of such design alternatives. In light of this, we assess the effectiveness of a variation of the aerosol box using Computational Fluid Dynamics.[3]

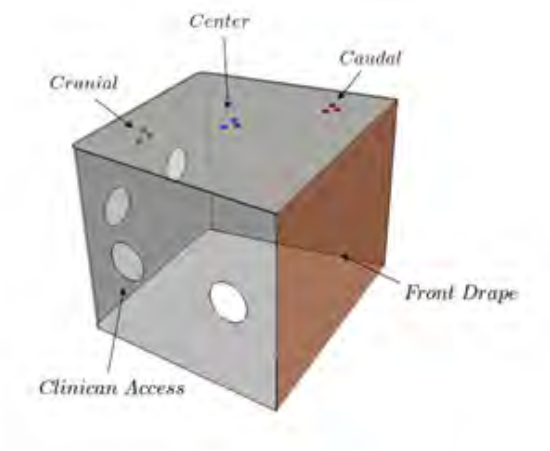
Methods: An aerosol box designed by the Medical Pantry was used in this simulation. This open source design incorporated a trapezoid shape whereby the cranial aspect was more narrow Using OpenFOAM (OpenCFD Ltd) and basing our equations on previously validated data by Bourouiba et al, we tested a trapezoidal shaped aerosol box and examined the fate of particles from a single a cough over 120 seconds. We examined the fate of particles from a cough in a supine patient in the following scenarios: no aerosol box, aerosol box with an open foot-facing side, and a sealed aerosol box while varying the number and position of wall suction ports. Variations on suction included 1 or 3 suction holes, and positions at either the cranial, center, or caudal aspect of the box. Particle fate at any given timepoint was classified as having collided with the box interior, having been suctioned, having remained floating inside the box, or having escaped the box. Finally, confederates, representing healthcare workers were placed cranially, to the right and the foot-end, and their particle exposure was assessed.

Results: We found that the closed design with the drape on the foot-facing side reduced the number of escaped particles. Regardless of suction port outlet positioning, escaped or floating particles ranged from 4.6% to 5.6% by 30 seconds post-cough and this proportion remained the same by 100 seconds post-cough. Increasing the number of suction outlets significantly improved the efficiency of the aerosol box at clearing floating particles. Confederate exposure to particles was significantly reduced, with the exception of those positioned lateral to the patient in scenarios with aerosol box with an open foot-facing side.

Conclusion: We conclude that a modified, enclosed aerosol box with a trapezoid shape reduces the probability of floating or escaped particles in a simulated software environment and suggest further examination in a practical environment before widespread use in the COVID-19 environment.

References: 1. Lai H. Aerosol box - design [Available from: https://sites.google.com/view/aerosolbox/design 2. Fried EA, Zhou G, Shah R, Shin DW, Shah A, Katz D, et al. Barrier Devices, Intubation, and Aerosol Mitigation Strategies: Personal Protective Equipment in the Time of Coronavirus Disease 2019. Anesth Analg. 2021;132(1):38-45. 3. Price C, Ben-Yakov M, Choi J, Orchanian-Cheff A, Tawadrous D. Barrier enclosure use during aerosol-generating medical procedures: A scoping review. The American journal of emergency medicine. 2021;41:209-18.

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Technology, Computing and Simulation, Equipment Monitoring - 11 Assessment Of The Pulmonary Gas Exchange Efficiency and Cardiac Output By An Online Volumetric Capnography In Anesthetized Rabbits

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[1]Facultad de Medicina, Hospital de Clínicas, Universidad de la República, Montevideo, Uruguay, [2]Facultad de Veterinaria, Universidad de la República,, Montevideo, Uruguay

Introduction: Assessment of exhaled CO2 has evolved into an essential component of patient monitoring in different clinical scenarios (1). Volumetric capnography (Vcap) allows a complete analysis of the global V/Q efficiency by comparing Bohr versus Enghoff approaches to physiologic dead space measurements (VDB and VDE, respectively), as it should also monitor cardiac output (CO) non-invasively (if minute ventilation and cellular metabolism are stable) (2-4). We developed a wireless online capnograph to determine the correlation between the intrapulmonary shunt fraction (Qs/Qt) and (VDE-VDB) and the correlation between pulmonary flow (PF) and minute expiratory CO2 (VCO2) (5) during normobaric acute global hypoxia (Hx) in a rabbit model.

Methods: Five female New Zealand rabbits (3.1 ¬± 0.2 Kg) were anesthetized and mechanically ventilated. A left thoracotomy was performed. Central venous (CVP) left atrial (LAP); and femoral arterial (AoP) pressures (fluid column catheter); and pulmonary arterial pressure (PAP, Millar); and PF (Transonic) were monitored (LabChart, 1KHz). Blood gas samples from central venous; arterial; and left atrial; and hemoglobin content were obtained. The Qs/Qt (Berggren equation) and HPV stimulus (PsO2, Marshall equation) were estimated (6,7). Vcap was obtained by an infrared mainstream CO2 sensor (QuRe, Treaton) clipped onto a neonatal digital flow meter (SFM3400, Sensirion) and airway pressure transducer (HSC series, Honeywell) (200 Hz). We designed dedicated hardware and software (Samay S24) (Fig. 1) which communicates via Wifi on a cell phone or tablet screen to display in real-time the temporal signals with Vcap and estimated parameters (minute VCO2, mean-expired PCO2 -PECO2-, end-tidal PCO2 -PetCO2-, and VDE) (Fig. 2). The S24 does not need the installation of any specific software, just a web browser, and it supports up to four monitors connected in simultaneously mode with a storage capacity of 1536 hours of registration. We estimated dead airway space (VDaw, Fowler), alveolar PCO2 (PACO2), VDB, and alveolar dead space (VDalv) off-line (Fig. 3). The animals were subjected to a FiO2 0.1 for 5 min.

Results: HPV stimulus obtained during Hx was 26 ¬± 3 mmHg. Hypoxic pulmonary vasoconstriction determined a significant increase in mean PAP and pulmonary vascular resistance without a significant change of the AoP (Table). VDaw was 4.6 ¬± 1 mL, and minute ventilation (MV) was 539 ¬± 101 (Basal) and 459 ¬± 86 mL/min (Hx) (NS). The PF correlated with the minute expired VCO2 normalized for the MV ($r = 0.56$; $P < 0.05$) (Fig. 3). Hx increases the VDE-VDB difference at the expense of the increase of VDE, coinciding with the increase in Qs/Qt ($P < 0.05$) (Table). Both, VDE-VDB and Qs/Qt were correlated ($r = 0.79$; $P < 0.01$) (Fig. 4).

Conclusion: We present the Samay S24 designed in our laboratory to monitor online expired CO2 parameters (wireless communication and web browser). Generalized HPV could impair circulatory efficiency, increasing the intrapulmonary shunt associated with the significant increase in VDE-VDB. Under stable CO2 metabolism conditions, PF was correlated with normalized minute expiratory VCO2.

References: 1. Resp Care 2016; 61:1397-1416 2. Int Care Med 2011; 37:870-74 3. Crit Care 2016; 20:184 4. J Clin Monit Comput 2020; 34:7-16 5. J Clin Monit Comput 2012; 26:183-90 6. Int Care Med 1994; 20:291-97

Figure 1. Volumetric capnograph SAMAY 24 (S24)

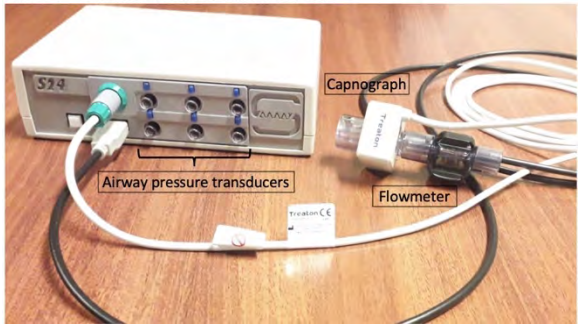


Table: Changes in hemodynamic, gasometric and capnographic data values during hypoxia

	Basal	Hx
Mean AoP, mmHg	55±12	56±15
Mean PAP, mmHg	7.2±1.3	8.8±1.7*
PF, mL/min	214±56	208±69
PVR, Wu	22.4±5	43±14*
pH	7.40±0.06	7.36±0.06
PaO_2, mmHg	371±34	33±6
$PaCO_2$, mmHg	34±1.4	34±3
Lactate, mEq/L	1.7±0.4	1.7±0.9
VCO_2, mL/min	11.2±2.2	11.8±2.0
$PetCO_2$, mmHg	31±5	33±5
VD_B, %	26.9±6.6	27.7±5
VD_E, %	31.8±9.8	38±7.5
VD_E-VD_B, %	3.0±3.9	12±5*
VDalv, mL	1.3±0.9	1.6±1.5
Qs/Qt, %	4.2±3	14.8±9*

Mean ± SD. *P* <0.05 *vs. Basal (n = 5).

Figure 2. Online variables monitored by the SAMAY 24 (S24) on a cell phone screen. VCI, VCE: inspiratory and expiratory volume; TI, TE: inspiratory and expiratory time; FR: respiratory rate; $EtCO_2$: end-tidal CO_2; VCO_2: minute expiratory CO_2; $PECO_2$: mean-expired CO_2; VD/VT: Enghoff dead space; AwP: airway pressure; left loop: volumetric capnography; right loop: tidal volume-AwP loop (Temporal variables were subjected to a compression algorithm).

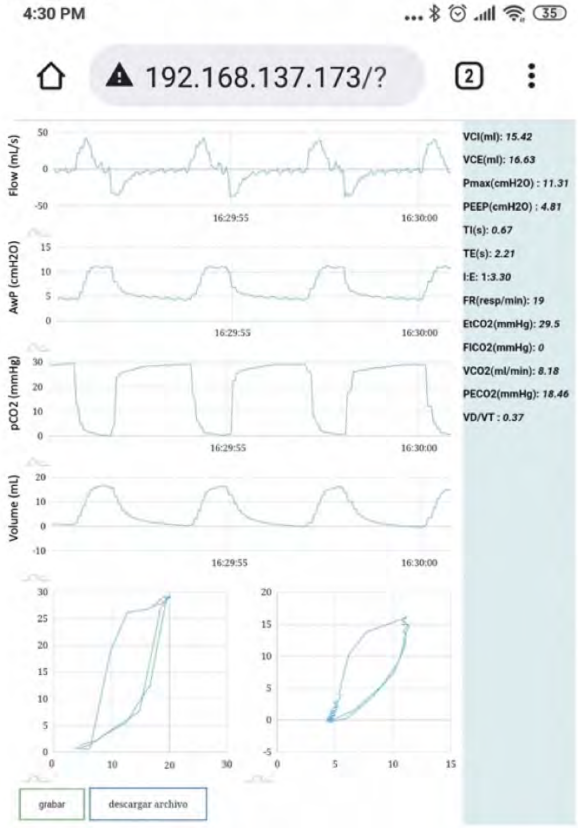


Figure 3: Representative volumetric capnogram (left) and temporal tracings of the online variables (right). Off-line estimated parameters in red italic font (PACO2, PaCO2, PECO2, and PetCO2: alveolar, arterial, mean-expired, and end-tidal PCO2, respectively; VD_{Alv}, VD_{AW}, VD_B, and VD_E: alveolar, airway, Bohr and Enghoff volume dead spaces; I: Inspiration; E: Expiration).

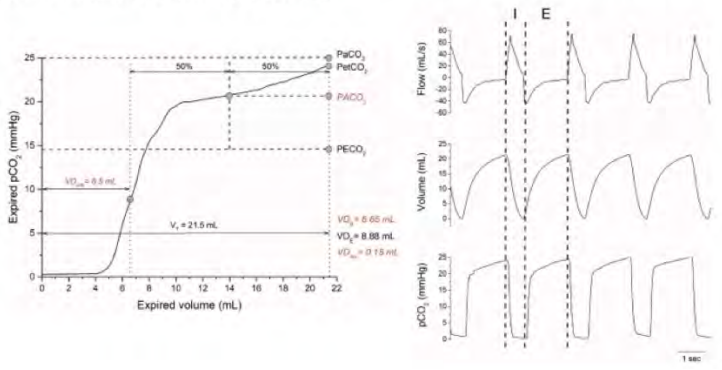
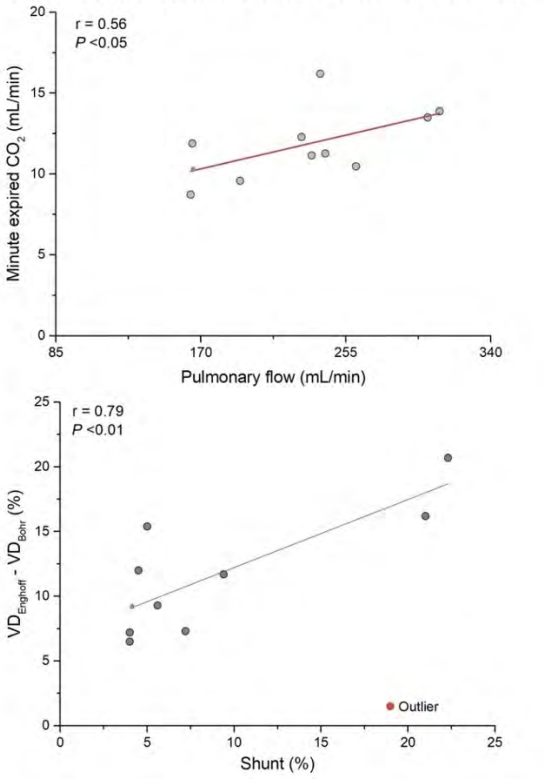


Figure 4: Scatter plots between the intrapulmonary shunt fraction and (VD_E-VD_B), and between pulmonary flow and minute expiratory CO_2



Technology, Computing and Simulation, Equipment Monitoring - 12 Pilot Validation of Airway Hemorrhage Simulation Scenarios

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Introduction: Airway hemorrhage is a challenging clinical situation faced by rapid response teams and emergency physicians, with an incidence of difficult airway intubation of 9-12% and complications that range from 4-28%. Simulation offers a teaching modality to facilitate education for high-risk, low frequency clinical situations. Creation of a simulator with airway hemorrhage capabilities in high fidelity airway scenarios (expanding post-surgical neck hematoma, oropharyngeal hemorrhage, posterior nasopharyngeal epistaxis) for interprofessional management with deliberate practice would lead to ability to discriminate between performance after debriefing and formative feedback.

Methods: We recruited trainees in Emergency Medicine and Critical Care Medicine. We had 2 confederates (ME, DS, or AA) serving as RT and RN during all scenarios, which ran 5 minutes. Each subject underwent 3 versions of a simulation scenario within in one of our 3 types of airway hemorrhage cases (either hematoma, oropharyngeal hemorrhage or posterior nasopharyngeal epistaxis) in 1 hour, with no debriefing after scenario 1 (baseline), formative debriefing after scenario 2 (learning), and summative debriefing after scenario 3 (assessment). Post-simulation feedback was obtained for confidence, key learning point, and feedback for our scenario fidelity. Two anesthesiology-critical care (TD, SA) expert raters rated scenario 1 and 3 to look for performance difference in global rating (pass/ low pass/ fail) and items derived from previously validated NOTSS/ ANTS rating scales of non-technical skills. Interrater reliability, percent agreement, and intraclass coefficient were calculated for each type of scenario and overall between scenario 1 (pre) and scenario 3 (post).

Results: A total of 11 trainees participated, with high ratings (5-point Likert) of overall clarity (4.9), realism (4.7), and usefulness (4.9). Interrater reliability (IRR) of entire rating scale by expert raters varied per scenario, with nasopharyngeal at 0.78, oropharyngeal at 0.78, and neck hematoma at 0.65. Majority of trainees were Pass or Low Pass for all scenarios, with only 4 instances of a global rating of Fail (out of 36 total assessments).

Conclusion: We piloted 3 airway hemorrhage simulation scenarios to determine the ability of the scenarios to discriminate between performance before and after formative debriefing feedback. We found for even highly complicated advanced airway simulation the benefit of deliberate practice and reflection on key cognitive, skills, and team performance related to airway hemorrhage. This pilot study validates these airway hemorrhage simulation scenarios as a modality for improving resident and fellow skills for complicated airway hemorrhage management through deliberate practice and reflection.

Technology, Computing and Simulation, Equipment Monitoring - 13 Differences Between Pulse Oximetry Readings from Finger vs. Ear Probe Locations in Anesthetized Patients

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Introduction: Pulse oximetry (PO) is a standard of care during the administration of anesthesia. During anesthesia, oxygen saturation (SpO2) sometimes decreases to levels that require diagnostic and/or therapeutic interventions by the anesthesiologist. When SpO2 decreases unexpectedly, the anesthesia provider will often place a second PO probe in a different location. During desaturation, we have seen ear probes placed that read higher SpO2 than finger probes placed initially. If the second probe confirms a higher saturation, it is usually interpreted as confirmation that the reading from the first location is falsely low. The goal of this study is to determine if there are significant differences between SpO2 readings obtained with PO probes on a finger vs. the ear.

Methods: With IRB approval and informed consent, we studied 99 adults receiving general anesthesia or MAC for non-cardiac diagnostic or surgical procedures. A disposable PO probe (Nellcor Max-N) was placed on a finger and an ear. It was placed on a finger in the standard fashion. To reinforce connection on the ear, a layer of silk tape was applied to supplement the band-aid design of the probe. Readings were recorded with a Phillips 1020a PO module. Paired saturation readings for the finger and ear probes were recorded every five minutes. We analyzed pairs with differences of 5% or more between SpO2 as this can be clinically significant. We assumed the higher SpO2 to better reflect safety of a patient's status (no reason to suspect carboxyhemoglobin or methemoglobin in study subjects), and therefore labeled the higher SpO2 the correct reading. We hypothesized there would be no difference in readings between the probes. One sample test of proportions was applied with p-value < 0.05 significant.

Results: 12,409 paired readings were recorded (see Table 1). The mean number (range) of paired readings per patient was 125.4 (19 - 456). A difference of 5% or more between SpO2 of the two probes occurred in 1,372/12,409 (11.06%) of paired readings. Of 1,372 paired SpO2 with differences of 5% or greater, the ear probe reported a higher SpO2 214/1,372 (15.6%) of the time, while the finger probe reported a higher SpO2 1,158/1,372 (84.4%) of the time; $p < 0.0001$. The data indicate a higher SpO2 is measured significantly more often on the finger vs. the ear, so we reject the null hypothesis.

Conclusion: When probes placed on the finger and ear provided SpO2 that differed by 5% or more, the higher SpO2 was generated on the finger 84.4% of the time. Still, 15.6% of the time the ear probe measured a higher SpO2. If SpO2 decreases, and stable vital signs and end-tidal carbon dioxide suggest no need for rapid or urgent measures, a reasonable course of action is to apply an SpO2 probe in a second location. One intriguing possibility remains; that both probes read accurately at their respective locations. A possible future study designed to determine if this is so will be described in a poster. A limitation of our work is that we used the same type of probe, one designed for the finger on the ear as well, with a layer of silk tape reinforcing the application, as we have found this better maintains this probe on the ear. Although not designed for the ear the PI has practiced at several centers that apply the finger probe to the ear in this manner, because these sites have not stocked probes designed for the ear. This data is representative of our clinical practice, but sites that have dedicated ear probes might repeat this work with the dedicated ear probe on the ear. Recent work suggests SpO2 may be elevated by 4% or more in Black patients with hypoxemia (1), thereby performing less well to detect hypoxemia. Additional analyses will be performed to assess paired SpO2 differences between finger and ear locations in

Caucasian vs. Black patients, in patients with vascular disease, and during periods of hypotension.

References: 1.NEJM 383:25, Dec. 17, 2020

Paired SpO2 Data of Finger and Ear Locations				
	Frequency	Percent	Cumulative Frequency	Cumulative Percent
I) SpO2 difference 7 % or greater, very large, clinically relevant, ear SpO2 higher	85	0.68	85	0.68
II) SpO2 difference 5 or 6 %, large, clinically relevant, ear SpO2 higher	129	1.04	214	1.72
III) SpO2 difference 3 or 4 %, moderate, may be clinically relevant, ear SpO2 higher	942	7.59	1156	9.32
IV) SpO2 difference 1 -2 %, "minimal, not clinically relevant	2805	22.60	3961	31.92
V) SpO2 difference of 0%	5874	47.34	9835	79.26
VI) SpO2 difference (-) 1% – (-) 2 %, "minimal, not clinically relevant	934	7.53	10769	86.78
VII) SpO2 difference (-) 3% - (-) 4 %, "moderate, may be clinically relevant, finger SpO2 higher	482	3.88	11251	90.67
VIII) SpO2 difference (-) 5% - (-) 6 %, "large, clinically relevant, finger SpO2 higher	332	2.68	11583	93.34
IX) SpO2 difference - 7 % or greater, very large, definitely clinically relevant, finger SpO2 higher	826	6.66	12409	100.00

Technology, Computing and Simulation, Equipment Monitoring - 14 Development of interprofessional crisis simulation for a hybrid magnetic resonance imaging operating-room suite.

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Introduction: Intraoperative magnetic resonance imaging (MRI) is a technology increasingly used for neurosurgical and other procedures (1,2). Operating in close proximity to a mobile magnetic field requires multiple changes and adaptations to normal equipment and workflow, making it a highly complex environment with potential for significant adverse events (3,4). In addition, the MRI operating room (MRI-OR) is often isolated from the regular operating rooms, either because it is located in a different part of the hospital, or because entry into the MRI-OR requires adherence to time-consuming MRI safety protocols (5). Our institution experienced several incidents in which corrective actions were delayed because external help arrived many minutes after a call for help. This resulted in an institutional review of our crisis response for the MRI-OR and the request to create mock code training. The intent was to define distinctive features of crisis management in the MRI-OR and to develop a realistic location-specific crisis simulation module for the MRI-OR.

Methods: An initial group of experts and stakeholders, including anesthesia, nursing, and MRI personnel, convened and discussed MRI-OR related barriers to effective crisis management and explored potential solutions. Next, a series of mock code scenarios were conducted over several months by a volunteer group of personnel directly involved in MRI-OR procedures, including anesthesia personnel, perioperative nurses and scrub technicians, and MRI technologists (Figure 1A). In an iterative process, we identified problems experienced during resuscitation efforts and addressed them, trialing various solutions. This effort led to a low-fidelity code simulation training that was offered to about 100 anesthesia and perioperative personnel over the course of 1 year as part of mandatory orientation training to the MRI-OR. Feedback from participants prompted minor adjustments to the training content as well as to organization of emergency equipment. In light of rising case volumes and increasing complexity of procedures in the MRI-OR, we subsequently developed several high-fidelity scenarios with a customized MRI-safe mannequin, to be able to realistically present a larger variety of crisis situations during neurosurgical procedures (Figure 1 B-D).

Results: The following areas of crisis management were identified as uniquely affected by the MRI-OR environment (see table 1): Calling for help, providing positive pressure ventilation and effective chest compressions, and accessing the code cart. Standard operating procedures and cognitive aids for these areas were then created, tested, and subsequently modified as needed. MRI-safe 'airway grab bags' and 'code medication trays' were assembled and are now available in the room at all times. Creation of a high-fidelity simulation required several workarounds. The following 2 were most significant: 1) Metal-containing simulation equipment cannot enter the MRI-OR. Therefore, simulation technicians customized an adult (upper body) mannequin by removing any metal screws and 3D printing them in plastic, resulting in an MRI-safe mannequin capable of being ventilated, intubated, auscultated, and to receive intravascular medication. 2) The computer/device on which the simulation software is controlled cannot be brought in the MRI-OR, nor can wireless signals be transmitted due to radio frequency shielding of MRI rooms. This made it initially difficult to project vital signs (and their dynamic changes) in the operating room. We ultimately positioned the simulation computer in the control room, hardwiring the 'anesthesia vital sign screen display' and the sounds of vital signs and alarms to equipment in the MRI-OR. Our final simulation module has several variations including lost airway or lost vascular access scenarios, with options to mimic intraoperative status (head in pins) and supine or prone positioning.

Conclusion: Creating realistic simulation scenarios for complex environments such as the MRI-OR is very resource-intensive, but feasible with several modifications to normal simulation set-ups (6). While simulation training has become established in multiple

different healthcare fields (7), the effectiveness and acceptance of this highly specific simulation training will need to be evaluated. If found to be useful, this training could be modified for multiple other complex non-operating room environments, including diagnostic MRI settings and cardiac hybrid operating rooms.

References: 1) J Neurooncol. 2021;151(3):479-490. 2) Neurosurg Clin N Am. 2017;28(4):477-485. 3) J Clin Anesth. 2019;54:89-101. 4) Curr Opin Anaesthesiol. 2016;29(5):563-567. 5) Anesth Analg. 2017;124(4):1044-1046. 6) Pediatr Qual Saf. 2019;4(6):e222. 7) Australas Emerg Nurs J. 2016;19(1):44-53

Table 1

Key feature of crisis management	Problem in MRI-OR setting	Solutions and workarounds	Discarded suggestions
Call for help	• remote • no personal cell/devices in MRI-OR • not every responder MRI-OR trained	• group page with cognitive aid • portable phone for covering attending for non-emergent communication	• overhead page system • phone call to main OR front desk • code blue button
Positive-pressure ventilation (PPV)	• head of patient inaccessible while in scanner • far away from machine - single provider can either be at head or ventilate	• Airway grab bag • Training of PST/circulator to "squeeze the bag"	• circulator obtaining specific airway equipment as per directions
Chest compressions (CPR)	• OR table swings, needs stabilizer • table too high for CPR	• Stabilizer pole • designated step stools	
General resuscitation	• Code cart is not MRI-safe	• Airway grab bag • Code drug kit	• MRI safe code cart

Abbreviations: CPR: cardiopulmonary resuscitation; MRI-OR: magnet resonance imaging operating-room suite; OR: operating room; PPV: positive pressure ventilation; PST: periprocedural services technologist.

Technology, Computing and Simulation, Equipment Monitoring - 15 Arterial line: how accurate is it?

Luiz gustavo moreira costa[1], Vikas Kumar[2]

[1]Augusta University, Augusta, GA, [2]Augusta University, augusta, GA

Introduction: Variability exists between accuracy of arterial line transducers that can create inconsistencies in the management of intraoperative, postoperative and ICU blood pressure through invasive measurements; especially when reusable transducers are used. The Philips Intellivue MX800 monitors allow for a correction factor to be applied to invasive blood pressure measurements to compensate for this (ranging from 180 to 220). We have discovered that this value was being incorrectly modified within our institution. This value can be easily changed by any healthcare personnel or be locked to an incorrect value by engineering departments. The purpose of this study was to identify the ideal settings for obtaining the most accurate blood pressure readings and to assess the prevalence of incorrect monitor configurations within our institution.

Methods: The validity of measurements from a monitor can be easily verified by using a sphygmomanometer connected to the transducer to raise the pressure to a desired level and confirming the reading on the screen. A monitor was calibrated with four disposable transducers at 200 mmHg of pressure; per instructions from the Phillips manual. A pressure reading was also tested in a Datex-Ohmeda monitor, which had no option for calibration. Furthermore, the settings of 52 monitors in the post anesthesia care unit (PACU) and preoperative holding area was verified.

Results: The mean calibration factor obtained from new disposable transducers was 205; all values we're within a 204.5 to 205.5 range. The Datex-Ohmeda monitor confirmed a reading consistent with one from a Phillips monitor with a calibration factor of 200. In the PACU and preoperative holding area, 10 monitors had inappropriately low calibration factors ranging from 180-195. A monitor set to a callibration factor of 180 showed readings about 12% lower than expected; with 200 as the factor, the results were 2% lower.

Conclusion: When the calibration factor in the Phillips monitor for the transducer is too low, the blood pressure reading is lower than the actual patients blood pressure; this can make an adequate mean arterial pressure appear too low and cause delays in discontinuation of supportive therapy and invasive monitoring. The converse happens when the value is too high. A hypotensive patient may therefore not receive adequate supportive therapy for maintenance of end organ perfusion; which can result in worse outcomes over the treatment of a large patient population. Therefore, inconsistencies in invasive blood pressure readings due to the configuration of monitors is worrisome. A value of 205 as a calibration factor seems to result in the most accurate readings for the transducers used in our institution. Considering that there are small variations in between transducers of the same model, using a value slightly lower, such as 200, could be appropriate. If a change in transducer model or monitor is made institutionally, confirmation of accuracy should be performed in a small sample size of disposable transducers to determine the correct monitor settings for these transducers and reliability of readings.

Technology, Computing and Simulation, Equipment Monitoring - 16 Using 'Plan, Do, Study, Act' (PDSA) Cycles to Improve an Ultrasound Guided Vascular Access Course

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Introduction: Establishing vascular access is a critical skill for anesthesiologists. With an increasing overweight patient population in the United States, ultrasound guidance is imperative for obtaining expedient arterial or venous access. Traditionally, trainees were only able to develop these proficiencies in the operating room which can limit skill acquisition. To address this, we developed and hosted a workshop focused on furthering the technical skill of ultrasound to establish vascular access. The ultrasound simulator was a mold made from ballistics gel and a 'Plan, Do, Study, 'Act model of process improvement was used to rapidly evaluate effects of the changes made in the simulator mold. The workshop consisted of two-parts the first being short 20-minute multi-media lecture that reviewed the basics of POCUS machines, discussed the advantages and disadvantages of short axis and long axis cannulation, and reviewed catheter length and target vessel depth. This was followed by approximately 70 minutes of unstructured time to allow learners to use various types and sizes of peripheral intravenous catheters, arterial catheters, and central lines on the homemade simulators made using ballistics gel. After each workshop, a survey was sent to the learners to solicit feedback about the workshop, the simulator molds, and the learning materials. Rapid changes to the workshop and simulator were rapidly implemented based on feedback from the learners.

Methods: Six workshops were held between July 2018 and December 2021 for incoming CA-1 residents and anesthesiologist assistant students. A total of 57 trainees filled out the post-course evaluation survey. 12 ranked questions and 3 free text questions were answered.

Results: There was a gradual improvement in the quality of the ultrasound simulator molds. This was expected due 'Plan, Do, Study, Act' process improvement model used for the simulator mold. Improvements over the study period include but not limited to changing the melting techniques to reduce the amount of air bubbles in the ballistics gel, changing the diameter of the vessels, trialing out different types of tubing, and adding dye to color the gel. The ultrasound models worked well (LIkert Scale 1=Strongly Disagree, 2=Disagree, 3=Neutral, 4=Agree, 5=Strongly Agree) 3.10 4.33 4.17 3.83 4.76 4.33 I would recommend this workshop to a colleague. 4.30 4.83 4.67 4.33 5.00 5.00

Conclusion: A 'Plan, Do, Study, Act' model of rapid process improvement can be an effective method in the development of ultrasound simulators for vascular access workshops. Future directions of the workshop would include the use of Butterfly iQ+ which allows for imaging in both long-axis and short-axis views at the same time. In addition, creation of the simulator mold that is longer in length to allow for full cannulation of the central venous catheters.

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Technology, Computing and Simulation, Equipment Monitoring - 17 Mask Ventilation Grip Device: A manikin study comparing the efficacy of a novel device to standard two-handed mask ventilation technique

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Introduction: During bedside airway emergencies, the nearest provider may have limited experience with delivering mask ventilation (MV) compared to anesthesiologists.1, 2 Therefore, investigating strategies to make MV easier to deliver for inexperienced providers is warranted. In challenging cases, two-handed techniques are required over one-handed techniques.3, 4, 5, 6, 7 The mask ventilation grip (MVG) device was designed to facilitate two-handed MV (Figure 1.)8 This study investigates whether use of the MVG device improves two-handed MV. Our primary objective was to test the hypothesis that performing two-handed MV with the MVG device in a manikin simulation setting results in greater average expired tidal volumes (TVavg) than standard two-handed MV technique (Standard;) and that if this effect is present, it is more pronounced in novice providers versus experts. Secondarily, we also investigated the perceived task load and fatigue of providers when performing two-handed MV with and without the MVG device.

Methods: This study has a repeated-measures cross over design and is powered sufficiently with a sample size of 32 subjects (16 novices and 16 experts) (Figure 2.) Novices were subjects without experience performing MV and consisted of interns and medical students; experts were subjects with more than 2 years of experience performing MV. Recruitment was conducted via email to University of Miami (UM) Miller School of Medicine clerkship directors and the Department of Anesthesiology. After obtaining written informed consent, subjects were randomized into order groups (Standard->MVG versus MVG->Standard) that indicated the order in which they would employ the techniques. TVavg values were obtained from subjects delivering two-handed MV to a manikin during separate sessions with each technique) in accordance with their order groups. Our primary outcome of interest, differences in mean TVavg, was analyzed for significance with respect to technique, expertise level, and order of techniques. Following each MV session, subjects completed the NASA-Task Load Index (NASA-TLX) and the Swedish Occupational Fatigue Inventory (SOFI,) instruments as a measure of subjective experience of task load and fatigue perceived with each technique. Differences in mean scores of items within both forms were analyzed with respect to technique, expertise, and order. All statistical analyses were performed with SPSS version 28. To test for the effect of within-subjects variables (Technique,) between-subjects variables (Order and Expertise) and their interactions, hypothesis testing was completed with a general linear model in the form of a mixed design with repeated measures. In addition to the calculated P values for each pairwise comparison, point estimation, and 95% confidence interval (CIs) were also calculated. Effect size is reported as the absolute difference between the means for each dependent variable across experimental conditions.

Results: The final dataset consisted of 16 novices and 13 experts after 3 experts were excluded due to technical issues. Performing two-handed MV with the MVG device increased TVavg compared to Standard technique (MD = +17.058 mL; P = 0.004; Table 1.) No significant effect was observed with respect to order or expertise (Table 1.) Mean scores for NASA-TLX items were overall higher with Standard technique than with the MVG device (MD = +9.161; P = 0.022; Figure 3.) Specifically, the mean item scores of 'Physical Demand' (MD = + 3.420; P = 0.0004) and 'Effort' (MD = + 0.2470; P = 0.011) were greater with Standard technique than with the device (Figure 3.) Similarly, mean scores for SOFI items, 'Lack of Energy' (MD = + 2.417; P = 0.002) and 'Physical Exertion' (MD = + 1.323; P = 0.015) were greater with Standard technique than with the device (Figure 4.) Expertise had an effect on scores in both psychometric instruments. Amongst NASA-TLX items, novices' mean scores for self-assessed 'Performance' (MD = +4.028; P = 0.0008; Figure 3) and 'Frustration' (MD = +4.143; P = 0.010; Figure 3) were higher than experts' respective scores. Within the SOFI items, novices'

mean scores for 'Physical Exertion' were higher than experts' (MD = +1.719; P = 0.039; Figure 4.)

Conclusion: The results demonstrate that the MVG device is an objective and subjective improvement of standard two-handed MV technique. This study also shows that gaps in expertise level may not present as objective differences but as subjective differences in perceived task load and fatigue.

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Figure 1

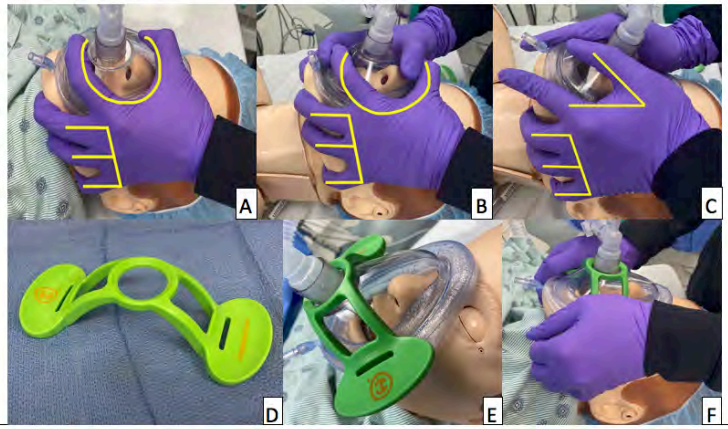

Figure 1: The one-handed C-E grip (E-C clamp) consists of the thumb and index finger of one hand forming a "C" shape as they hold the mask and apply downward pressure, as the the third, fourth, and fifth fingers (E) pull the mandible into the mask, collectively forms an air-tight seal (A.)[3] This one-handed grip technique enables the provider's free hand to squeeze a reservoir bag or perform other functions. In the 2-handed C-E technique, the thumb and index finger of each hand form a "C" shape as they grasp the mask from each side while while pushing down onto the face as the remaining fingers (the E) on both hands lift the mandible toward the mask (B.) In the 2-handed V-E technique, the thumb and thenar eminence of each hand are placed on the sides of the mask, forming a "V" with the second finger, which in addition to the remaining fingers is available to pull the mandible up into the mask. (C)* In both two-handed techniques, gas flow is supplied by mechanical ventilation or another provider.[3] The MVG grip device (D) is an add-on device that fits onto most anesthesia masks (E.) The "wings" of the device are designed to provide more lateral and lower-set leverage points for the provider to place their thumbs/thenar eminences, which creates a shorter distance for their other fingers to traverse and more comfortably grasp the mandible (F.)

Footnote: The index fingers of the provider in Figure 1C are extended outwards to demonstrate the potential to provide support over the mental protuberance in comparison to the 2-handed C-E grip.

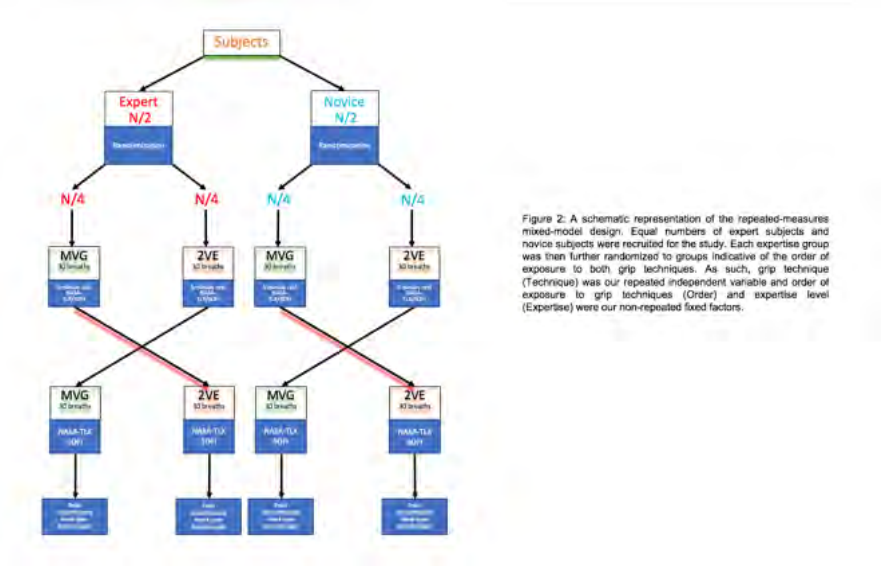

Figure 2: A schematic representation of the repeated-measures mixed-model design. Equal numbers of expert subjects and novice subjects were recruited for the study. Each expertise group was then further randomized to groups indicative of the order of exposure to both grip techniques. As such, grip technique (Technique) was our repeated independent variable and order of exposure to grip techniques (Order) and expertise level (Expertise) were our non-repeated fixed factors.

Table 1: TVavg

Independent factors	Observed Effect		Significance ($P < 0.05$)
	*Non-Standardized (mL)**	*Standardized (Partial Eta Squared)*	
Within-subjects			
Technique	**+17.058**	0.292	*P* = 0.004
Technique*Expertise		0.050	*P* = 0.263
Technique*Order		0.021	*P* = 0.473
Technique*Expertise*Order		0.002	*P* = 0.846
Between-Subjects			
Expertise	**-3.489**	0.002	*P* = 0.822
Order	**+21.787**	0.077	*P* = 0.162
Expertise*Order		0.015	*P* = 0.543

Figure 3

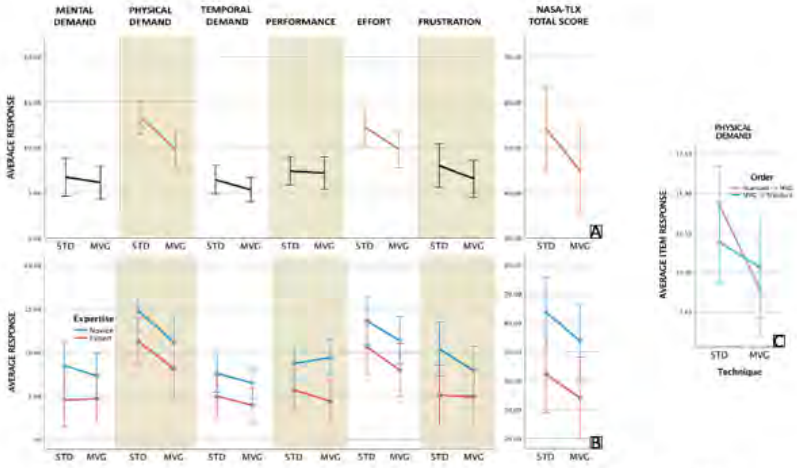

Figure 3: The difference in mean scores of "Physical Demand," "Effort," and "Nasa-TLX Total Score" were statistically significant with respect to Technique; this is highlighted in orange. Providing two-handed MV with MVG was perceived as less physically demanding and requiring less effort than Standard technique (A.)

Although only difference in mean scores of "Performance," "Frustration," and "NASA-TLX Total" demonstrated statistical significance with respect to Expertise, there were noticeable differences in mean scores between the expertise groups observed in all the items within the NASA-TLX assessment, which fell short of statistical significance (B.)

Subjects who belonged to the Order group "Standard→MVG," averaged "Physical demand" scores of 14.250 for MV with the Standard technique and 8.973 for MV with the MVG technique. Subjects belonging to the group "MVG→Standard" had average scores of 11.896 for the Standard technique and 10.333 for the MVG device (C.)

Figure 4

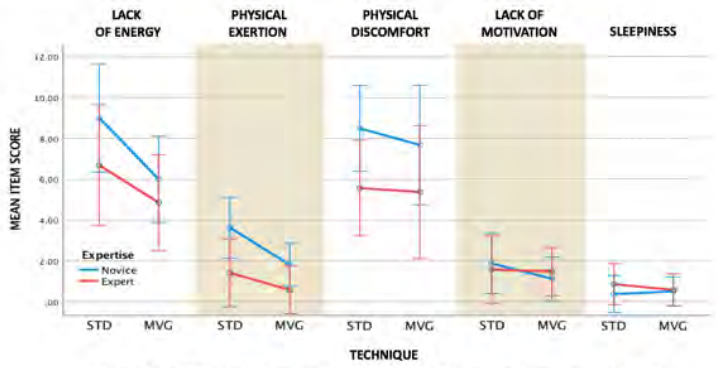

Figure 4: Average SOFI item scores for each expertise group with respect to Technique. Mean item scores are displayed with 95% confidence intervals. Technique had a significant effect on mean scores for the items "Lack of Energy" and "Physical Exertion." While there was no statistical difference with respect to Technique in the remaining items, the magnitudes of the "Physical Discomfort" item scores were high for both techniques, indicating that both techniques were uncomfortable to use. While Expertise had a statistically significant effect in mean scores for only the "Physical Exertion" item, there is a clear difference in novice score distributions and expert score distributions within the "Lack of energy" and "Physical discomfort" items as well.

Trauma

Trauma - 1 Integrated single-cell and plasma proteomic modeling to predict surgical site complications, a prospective cohort study

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Introduction: Surgical Site Complications (SSCs) may occur in up to 25% of patients undergoing bowel resection, resulting in significant morbidity and economic burden(1,2). However, the accurate prediction of SSCs remains clinically challenging. Leveraging high-content proteomic technologies to comprehensively profile patients' immune response to surgery is a promising approach to identify predictive biological factors of SSCs. The objective of this study is to determine whether single-cell and plasma proteomic elements of the host's immune response to surgery accurately identifies patients who develop a SSC after major abdominal surgery.

Methods: Forty-one patients undergoing non-cancer bowel resection at a major university hospital were prospectively enrolled. Blood samples collected before surgery and on post-operative day one (POD1) were analyzed using a combination of single-cell mass cytometry and plasma proteomics (Fig. 1a, 1b). The primary outcome was the occurrence of an SSC, including surgical site infection, anastomotic leak, or wound dehiscence within 30 days of surgery. We employed a stacked generalization (SG) predictive modeling approach(3,4) to determine whether differences in immune responses between patients with or without an SSC can be detected on POD1, which is before SSCs become clinically apparent. This approach integrates individual data layers into a single multivariate model (Fig. 1c). The SG model classified patients with high accuracy (AUC = 0.86, p = 2.5e-04, unpaired Mann-Whitney rank-sum test on the SG model cross-validated values, Fig. 1d). Additionally, single cell and plasma proteomic relationships were identified and explored (Fig. 1e).

Results: A multiomic model integrating the single-cell and plasma proteomic data collected on POD1 accurately differentiated patients with (n=11) and without (n=30) an SSC (AUC = 0.86). Model features included co-regulated pro-inflammatory (e.g. IL-6- and MyD88- signaling responses in myeloid cells) and immunosuppressive (e.g. JAK/STAT signaling responses in M-MDSCs and Tregs) events preceding an SSC. Importantly, analysis of the immunological data obtained before surgery also yielded a model comprising 17 features that accurately predict SSCs (AUC = 0.82, Fig. 2).

Conclusion: The multiomic analysis of patients' immune response after surgery and immune state before surgery revealed systemic immune signatures preceding the development of SSCs. Our results suggest that integrating immunological data in perioperative risk assessment paradigms is a plausible strategy to guide individualized clinical care.

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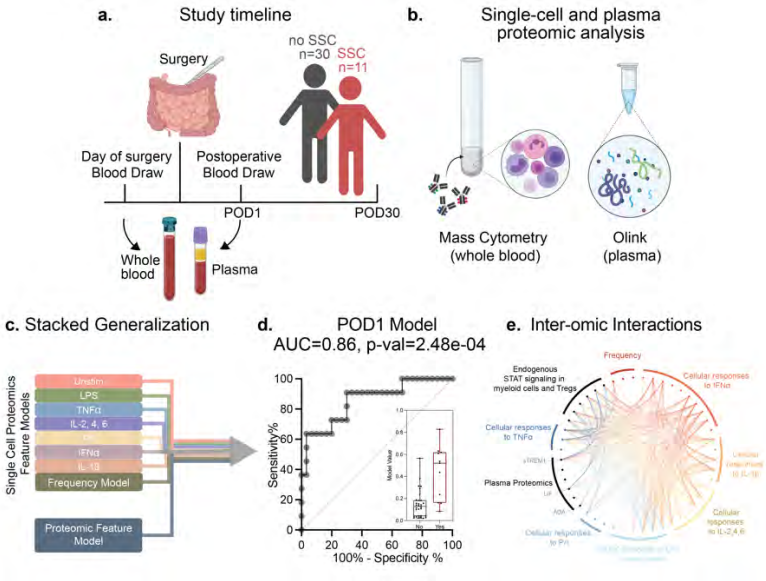
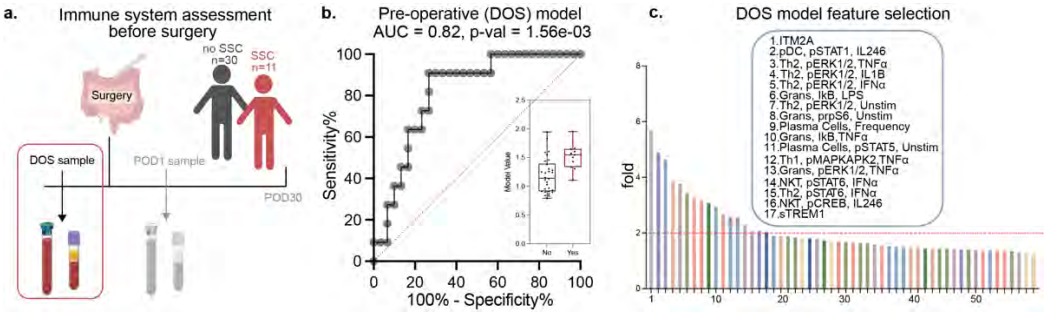

a. Study timeline
Surgery
no SSC n=30
SSC n=11
Day of surgery Blood Draw
Postoperative Blood Draw
POD1
POD30
Whole blood
Plasma
b. Single-cell and plasma proteomic analysis
Mass Cytometry (whole blood)
Olink (plasma)
c. Stacked Generalization
Single Cell Proteomics Feature Models
Unstim
LPS
TNFα
IL-2, 4, 6
IFNα
IL-1β
Frequency Model
Proteomic Feature Model
d. POD1 Model
AUC=0.86, p-val=2.48e-04
Sensitivity%
100% - Specificity %
e. Inter-omic Interactions
Frequency
Endogenous STAT signaling in myeloid cells and Tregs
Cellular responses to IFNα
Cellular responses to TNFα
sTREM1
Plasma Proteomics
LIF
ADA
Cellular responses to IL-2,4,6


a. Immune system assessment before surgery
Surgery
no SSC n=30
SSC n=11
DOS sample
POD1 sample
POD30
b. Pre-operative (DOS) model
AUC = 0.82, p-val = 1.56e-03
Sensitivity%
100% - Specificity%
c. DOS model feature selection
fold
1.ITM2A
2.pDC, pSTAT1, IL246
3.Th2, pERK1/2,TNFα
4.Th2, pERK1/2, IL1B
5.Th2, pERK1/2, IFNα
6.Grans, IkB, LPS
7.Th2, pERK1/2, Unstim
8.Grans, prpS6, Unstim
9.Plasma Cells, Frequency
10.Grans, IkB,TNFα
11.Plasma Cells, pSTAT5, Unstim
12.Th1, pMAPKAPK2,TNFα
13.Grans, pERK1/2,TNFα
14.NKT, pSTAT6, IFNα
15.Th2, pSTAT6, IFNα
16.NKT, pCREB, IL246
17.sTREM1

Trauma - 2 Outcomes and Biomarker Response Associated with Ketamine Administration after Traumatic Brain Injury: a Retrospective Study

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Introduction: As a major contributor to death and disability worldwide, traumatic brain injuries (TBIs) remain a serious public health issue with limited therapeutic options. Historically contraindicated in the context of head injuries due to its purported intracranial effects, ketamine is increasingly being utilized after TBIs despite a lack of efficacy and safety studies in this patient population [1].

Methods: We performed a retrospective analysis using data from the Tranexamic Acid for TBI (TXA for TBI) study, a national multicenter randomized controlled study in which TXA in 1 g, 2g and placebo dosing in the pre-hospital setting in patients who sustained TBI between May 2015 and November 2017 [2]. Our primary outcome was mortality within 6 months of TBI; our secondary outcomes included morbidity, vital signs responses and TBI biomarker response. Demographic variables and risk factors analyzed include age, sex, BMI, weight, Glasgow Coma Score (GCS), Injury Severity Score (ISS), seizure history, and intubation; Glasgow Outcomes Scale Extended (GOSE) and Disability Rating Scale (DRS) were used to assess morbidity at discharge and 6 months later. Statistical analysis consisted of propensity matched logistic regression analysis as well as a repeated measures analysis of biomarkers over time.

Results: 840 patients had ketamine exposure data recorded, with 131 patients receiving ketamine and 709 who were not administered ketamine. Patients who received ketamine had a lower GCS (6.7 (mean) ± 3.2 (SD) to 7.6 ± 3.5), worse ISS (20.7 ± 13.6 to 18.8 ± 13.1) and were more likely to be intubated than those patients who did not receive ketamine (88.6% to 44.3%), however these differences were not statistically significant. There was no significant difference in mortality (12.2% ketamine exposed vs 15.4% ketamine unexposed; $p > 0.05$) or required surgical intervention (6.9% ketamine exposed vs 11.1% ketamine unexposed; $p > 0.05$). The incidence of cardiac failure (1.5% ketamine exposed vs 0.8% ketamine unexposed) and seizure (3.1% ketamine exposed vs 1.0% ketamine unexposed) were too few to statistically analyze.

GOSE and DRS scores were compared between groups at time of discharge and at 6 months post-injury, with no significant differences at either time interval. Discharge GOSE (3.93 ± 2.08 ketamine exposed to 4.31 ± 2.41 ketamine unexposed); 6-month GOSE (5.35 ± 2.43 exposed to 5.40 ± 2.64 unexposed); discharge DRS (9.76 ± 9.70 exposed to 9.29 ± 10.26 unexposed); and 6-month DRS (8.01 ± 11.12 unexposed to 6.82 ± 9.94 exposed). Ketamine exposure was not associated with an increased risk of elevated ICP (50% ketamine exposed vs 82.4% ketamine unexposed). Similarly, there were no statistically significant differences in blood pressure extremes, heart rate extremes, temperature extremes or hypoxia between groups.

Serum biomarker levels of GFAP, MAP-2, and UCHL1 were compared between the ketamine exposed and unexposed groups at t = 0, 6-, 12-, 24-, and 48-hour intervals. There were no significant differences between groups for serum levels of MAP2 and UCHL1. Serum GFAP levels were significantly lower in the ketamine-exposed group at t = 6-, 12-, 24-, and 48-hour intervals as compared to the ketamine unexposed group ($p < 0.0001$).

Conclusion: Ketamine administration was not associated with increased mortality or worse recovery after TBI. Despite concern for ICP increases with ketamine use, no association was observed. Ketamine appears to have a differential effect on the astrocyte-specific biomarker GFAP than neuronal-related biomarkers MAP-2 and UCHL1.

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	Ketamine Unexposed (n = 709)	Ketamine Exposed (n = 131)	P-value
Age, Mean + SD (years)	42.1 ± 18.6	37.3 ± 16.9	> 0.05
Sex (% M)	74.0%	77.1%	0.950
BMI, Mean + SD (kg/m²)	26.3 ± 5.6	27.0 ± 5.8	0.264
GCS, Mean + SD	7.6 ± 3.5	6.7 ± 3.2	> 0.05
ISS, Mean + SD	18.8 ± 13.1	20.7 ± 13.6	> 0.05
Seizure History (%)	5.1%	3.8%	0.323
Intubated (%)	44.3%	88.6%	0.545
TXA Group (%)			
Placebo	36.4%	36.6%	
1g	31.7%	29.0%	
2g	31.9%	34.4%	

Table 1. Demographics

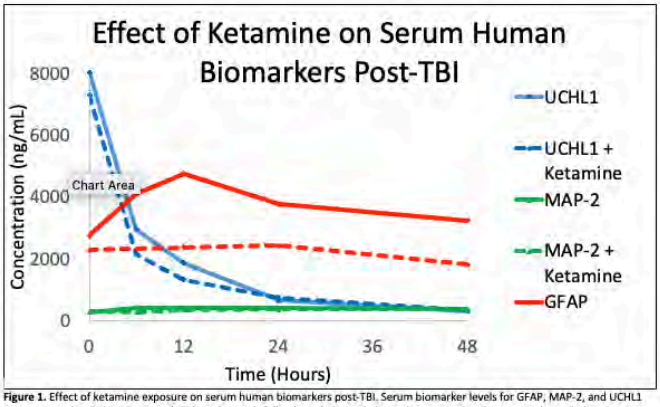

Figure 1. Effect of ketamine exposure on serum human biomarkers post-TBI. Serum biomarker levels for GFAP, MAP-2, and UCHL1 were assessed at 0, 12, 24, 36, and 48-hour intervals following admission in ketamine exposed and unexposed populations.

	Ketamine Unexposed (n = 709)	Ketamine Exposed (n = 131)	P-value
Death at any time (%)	15.4%	12.2%	0.4237
Seizure activity & timing (%)	1%	3.1%	-
Cardiac arrest and/or cardiac failure	0.8%	1.5%	-
Required surgical intervention	11%	7.0%	0.1675
GOSE at discharge	4.31 ± 2.41	3.93 ± 2.08	> 0.05
GOSE at 6 months	5.40 ± 2.64	5.35 ± 2.43	> 0.05
DRS at discharge	9.29 ± 10.26	9.76 ± 9.70	> 0.05
DRS at 6 months	8.01 ± 11.12	6.82 ± 9.94	> 0.05

Table 2. Morbidity and mortality outcomes

	Ketamine Unexposed	Ketamine Exposed	P-Value
ICP, % (n)			
>20mmHg	82.4% (103)	50.0% (8)	> 0.05
SaO_2, % (n)			
Hypoxemic (<95%)	46.5% (218)	37.3% (44)	> 0.05
PaO_2, % (n)			
Hypoxic (<80 mmHg)	42.6% (244)	39.7% (48)	> 0.05
Temperature, % (n)			
Hypothermic (≤ 35˚C)	7.8% (44)	19.7% (23)	> 0.05
Febrile (≥ 38˚C)	1.4% (8)	0% (0)	> 0.05
Heart Rate, % (n)			
Bradycardic (<60 BPM)	9.7% (69)	10.8% (14)	> 0.05
Tachycardic (>100 BPM)	45.1% (319)	46.2% (60)	> 0.05
Bradycardia & Tachycardia	2.7% (19)	3.1% (4)	> 0.05
Systolic Blood Pressure, % (n)			
Hypotensive (<90 mmHg)	9.7% (69)	12.2% (16)	> 0.05
Hypertensive (>180 mmHg)	18.5% (131)	14.5% (19)	> 0.05
Hypotensive & Hypertensive	0.4% (3)	1.5% (2)	> 0.05

Table 3. Vitals signs response

Trauma - 3 Spinal cord injury in aged mice exacerbates neuropathological changes in both spinal cord and brain leading to worsened neurological function

Zhuofan Lei[1], Yun Li[1], Rodney Ritzel[1], Hui Li[1], Alan I Faden[1], Junfang Wu[1]

[1]University of Maryland School of Medicine, Baltimore, MD

Introduction: Approximately 20% of all spinal cord injuries (SCI) occur in persons aged 65 years or older. Older patients with SCI have different features with regard to neurological characteristics after injury. Recent large-scale longitudinal population-based studies showed that patients with SCI are at higher risk of developing dementia than non-SCI patients, indicating that SCI is a potential risk factor for dementia. Age is known to potentiate inflammation and neurodegeneration at the injured site leading to impaired recovery from SCI. However, no research has been aimed at studying the mechanisms of SCI-mediated cognitive impairment in the elderly. The present study examined the long-term neurological function and the underlying mechanisms associated with advanced age in mice using a thoracic contusion SCI model.

Methods: Young adult (3-month-old) and aged (18-month-old) male C57BL/6 mice were subjected to moderate contusion SCI at T10 and their functional outcomes were evaluated for up to 2 months post-injury using a battery of neurobehavioral tests including motor function [Basso Mouse Scale (BMS)], cognition [Y-maze, novel object recognition (NOR)], and depression [novelty-suppressed feeding (NSF) and social recognition (SR)]. After completion of behavioral tests, injured spinal cord tissue and brain tissue (the somatosensory cortex and hippocampus) were dissected and processed for transcriptomic analysis using NanoString neuropathology panel, flow cytometry, and histology. Differential changes identified between young and aged groups were further validated by qPCR, western blotting, and microscopy.

Results: BMS assessment of locomotor function showed marked impairment in aged mice compared to young animals (Fig 1A), which were correlated with increased lesion volume (Fig 1B) and reduced spared white matter (Fig 1C). At 2 months post-injury, aged mice displayed worse performance in neurobehavioral tests, as evidenced by lower % of spontaneous alteration in Y-Maze task (Fig 1D), reduced novelty preference in NOR test (Fig 1E), increased sociability deficits in SR (Fig 1F), and elevated latency to detect food in NSF (Fig 1G), indicating exacerbated impairment of cognition and depressive-like behavior in aged mice compared to young animals. Flow cytometry demonstrated increased microglia and myeloid and lymphocytes infiltration at injured site from young mice which was exacerbated with age (Fig 1H). Moreover, SCI in aged mice altered microglial function (Fig 1I) and dysregulated autophagy function in both microglia (Fig 1J) and neurons (Fig 1K) of the brain, resulting in neurodegeneration (Fig 1L) compared to young animals. NanoString analysis with the neuropathology panel demonstrated increased pro-inflammatory genes and decreased expression of molecules related to neuroprotection in the aged/SCI mice compared to young/SCI animals (Fig 1M-N). These findings were further validated by qPCR, in which we observed significantly higher levels of pro-inflammatory cytokines.

Conclusion: Our data indicate that aging exacerbates neuropathological changes in both injured spinal cord and remote brain region that is associated with poorer functional outcome. Our studies provide innovative cellular and molecular perspectives on the pathophysiology of age-related deficits after SCI.

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Trauma - 4 Type I Interferons Contribute to Inflammation and Neurological Decline Following Experimental Traumatic Brain Injury in mice

James Barrett[1], Rebecca J Henry[1], Kari Ann Shirey[1], Stefanie Vogel[1], David J Loane[1], Alan I Faden[1], Bogdan A Stoica[1]

[1]UMB, Baltimore, MD

Introduction: Traumatic brain injury (TBI) causes primary tissue damage that results in activation of microglia and peripherally derived inflammatory macrophages leading to secondary injury. Recent evidence suggests that Type I Interferons (IFN-I) play a key role in the inflammatory response following central nervous system (CNS) injury and during age-related neurodegenerative disease (e.g., Alzheimer's disease). We previously demonstrated that IFN-I inhibition during the early recovery phase following TBI reduces secondary neuroinflammatory responses, neurodegeneration, and improves long-term neurological recovery. In the present study, we examined the impact of IFN-I signalling on microglial transcriptome and neurological function during the chronic phase of injury.

Methods: Young adult male C57BL/6J (wild-type) and IFN-β knockout (10–12-week-old) mice underwent controlled cortical impact (CCI, a well-established TBI model) or Sham surgery. Cognitive function was tested at 60-90 days post-injury (dpi) using the Y maze test (short-term spatial working memory), novel object recognition test (NOR, non-spatial declarative memory), and Morris water maze (MWM, hippocampal-dependent spatial learning and memory). Motor function was assessed using the beam walk test (fine motor coordination). At 90 dpi, microglia were isolated from ipsilateral cortex and hippocampi and were processed for mRNA/Nanostring transcriptome analysis.

Results: We demonstrate that TBI resulted in significant change in microglial transcriptome, including a significant upregulation in genes associated with the disease-associated microglia phenotype (DAM). We also observed increased expression of several genes associated with IFN-I responses (Isg15, Ifi204, Ifi30 and Cxcl10). CCI-induced increases in gene expression of several pro-inflammatory mediators, including viral response genes, were significantly attenuated in IFN-β KO mice when compared to wild-type CCI mice. TBI-induced cognitive impairments in the Y maze and NOR tasks were significantly reduced in IFN-β KO mice vs. wild-type. IFN-β-deficiency only transiently improved motor function recovery.

Conclusion: These data probing specific changes in the microglia cellular compartment demonstrate that TBI induces expression of genes associated with the DAM phenotype along with elevation of IFN-I related genes in wild-type experimental mice. Notably, IFN-β-deficient mice exhibit an attenuation of these responses with decreased expression of neurotoxic neuroinflammatory mediators. Moreover, IFN-β-deficiency was associated with improved neurological recovery after TBI. Thus, IFN-I pathways and, specifically, IFN-β may play a significant role in mediating neuroinflammatory responses during the chronic phase of TBI and represent an important therapeutic target for traumatic head injury.

Trauma - 5 Voluntary Exercise Attenuates Hippocampal Neuroinflammation after Experimental Traumatic Brain Injury in Mice.

Bogdan A Stoica[1], Rebecca J Henry[1], Alan I Faden[1], James P Barrett[1]

[1]UMB, Baltimore, MD

Introduction: Delayed secondary biochemical and cellular changes after traumatic brain injury continue for months to years and are associated with chronic neuroinflammation and progressive neurodegeneration. Increasing evidence suggests that secondary injury processes and neurological recovery after CNS injuries can be modulated by physical exercise. Our previous work has demonstrated that exercise reduced TBI-induced upregulation of key pro-inflammatory mediators, while concurrently increasing anti-inflammatory molecules and neurogenesis. The present study examined the effects of voluntary wheel running exercise on comprehensive TBI-induced transcriptomic changes in the cortex and hippocampus.

Methods: C57Bl/6 mice (n=8-10/group) underwent moderate controlled cortical impact (CCI, a well-established experimental TBI model) or sham surgery. TBI mice were randomly divided into two groups, 1) exercise beginning at 2 weeks post-trauma and lasting for 4 weeks (EX); or 2) no exercise (noEX). Exercise group mice were placed in cages equipped with running wheel (30.3 × 20.6 × 26 cm by L × W × H; Mini Mitter) to permit spontaneous voluntary exercise; non-exercised animals were housed in cages without running wheels. The number of wheel revolutions per hour was recorded by an automated computer monitoring system and software (Vital View Application software, Mini Mitter). Fine motor coordination was assessed throughout the duration of the study using the beam walk test. Following 2 weeks of exercise, cognitive function was assessed by the novel object recognition test (NOR) that probes declarative (non-spatial) memory. Cortical and hippocampal tissue was isolated for mRNA and protein analysis.

Results: Bulk RNAseq analysis of cortical and hippocampus tissue revealed that TBI resulted in widespread changes including upregulation of genes driving several key pathways involved in inflammatory processes and cell death. Remarkably, RNAseq and qPCR analysis of inflammatory markers in the hippocampus showed that exercise was associated with decreased expression of TNFa, IL-1b, Itgam and GFAP mRNA. The reduction in IL-1b was also associated with reduced expression of the inflammasome components ASC and Caspase1. Notably, the exercise-mediated reduction in these pro-inflammatory markers was accompanied with enhanced expression of the anti-inflammatory cytokine IL-13. Furthermore, analysis of neuronal markers also revealed that TBI resulted in significant decreases in NEFM, NEFH and Syn1 expression levels, indicative of neurodegeneration processes and that exercise reversed these brain trauma-induced effects. We observed no significant effects of exercise on TBI-induced deficits in fine motor and cognitive function.

Conclusion: These data demonstrate that exercise following experimental TBI is associated with a reduction in pro-inflammatory activity in the hippocampus that may contribute to improvements in long-term neurodegeneration. The exercise mediated increase in IL-13 may represent a novel anti-inflammatory pathway induced by post-traumatic exercise. Acknowledgements: Supported in part by NIH R01NS096002 (BS) and U.S. Veterans Affairs grant 1I01 RX001993 (BS)

Trauma - 6 Impairment of autophagy in microglia/macrophages exacerbates neuroinflammation after spinal cord injury in mice

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Introduction: Autophagy is a catabolic process that degrades cytoplasmic constituents and organelles in the lysosome, thus serves an important role in cellular homeostasis and protection against neurodegeneration. We have previously reported that defects in autophagy contribute to neuronal cell damage and are part of the secondary injury mechanism in traumatic spinal cord injury (SCI) [1, 2]. Recent data implicate autophagy in regulation of immune and inflammatory responses, with high levels of autophagy flux associated with anti-inflammatory, and low levels with pro-inflammatory phenotypes [3, 4]. The present study assessed if autophagy is involved in modulation of neuroinflammation after SCI.

Methods: Young adult male C57BL/6, autophagy hypomorph Becn1+/- mice and their wildtype (WT) littermates were subjected to moderate/severe thoracic spinal cord contusion. Neuroinflammation and autophagy flux in the injured spinal cord were examined by flow cytometry, immunohistochemistry (IHC), and NanoString technology. Motor function was evaluated using the Basso Mouse Scale (BMS) and Horizontal ladder test. Lesion volume and spared white matter were evaluated by unbiased stereology. To stimulate autophagy, trehalose or sucrose control was administered continuously in drinking water starting at 1d post-injury.

Results: Flow cytometry demonstrated temporal dysregulation of autophagic function in both microglia and infiltrating myeloid cells from injured spinal cord at 3d post-injury which was accompanied by increased pro-inflammatory cytokines. IHC in transgenic Cx3cr1-GFP mice confirmed accumulation of autophagosomes and inhibition of autophagy flux specifically in the activated microglia/macrophages. NanoString analysis with the neuroinflammation panel demonstrated increased pro-inflammatory genes and decreased expression of molecules related to neuroprotection in the Becn1+/- mice compared to WT at 3d SCI. These findings were further validated by qPCR, in which we observed significantly higher levels of pro-inflammatory cytokines. Western blot analysis showed higher protein expression levels for microglia/macrophages marker Iba-1 and autophagosome marker LC3 in Becn1+/- mice at 1d SCI, along with increased levels of the inflammasome marker NLRP3. Locomotor function showed poorer recovery in Becn1+/- mice, which correlated with increased tissue damage. Trehalose treatment significantly reduced expression levels of p62, accompanied by reduced expression of NOX2, Iba-1, NLRP3, and cell death marker Œ±-Fodrin at 3d post-injury. Finally, C57BL/6 mice treated with trehalose showed better recovery at 6 weeks post-injury.

Conclusion: Our data indicates that inhibition of autophagy in microglia/macrophages potentiates pro-inflammatory activation that is associated with poorer functional outcome following SCI. These findings highlight the importance of autophagy in resident immune cells of the CNS and further elucidates its role in secondary injury after SCI.

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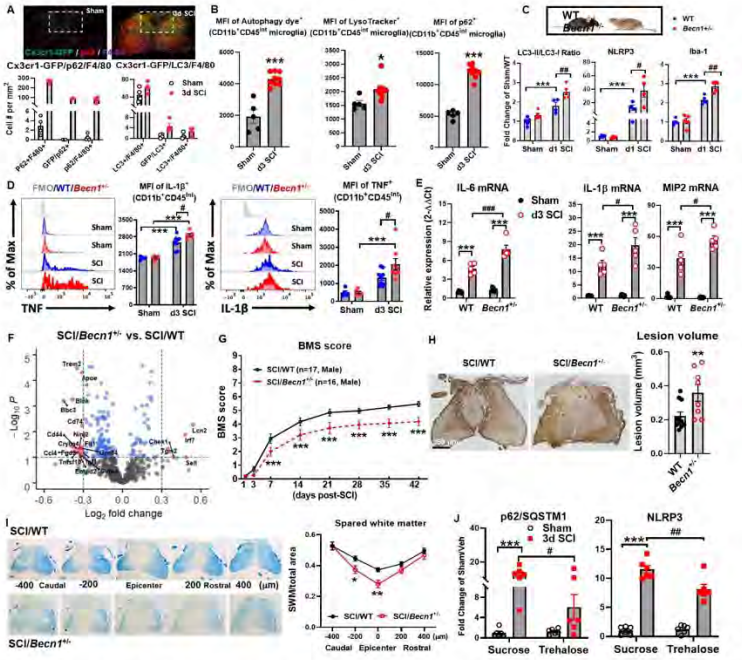

Figure. Impairment of autophagy in microglia/macrophages potentiates neuroinflammation after spinal cord injury (SCI). A) IHC staining of Cx3cr1-GFP mice showed LC3 and p62 accumulating in activated microglia and infiltrating macrophages at 3d post-injury. n=5 mice/group. **B)** Flow cytometry analysis showed increased autophagic marker in CD11b^{+}CD45^{int+} microglia at 3 d post-injury. n=5 (Sham) and 9 (SCI). **C)** Western blot analysis showed level of LC3-II/LC3-I ratio in autophagy hypomorph *Becn1*$^{+/-}$ mice at 1d post-injury, along with increased levels of inflammasome marker NLRP3 and Iba-1. n=5/group. **D)** Flow cytometry showed higher levels of IL-1β and TNF-α in *Becn1*$^{+/-}$ mice at 3d post-injury. n=5 (Sham/WT), 6 (Sham/*Becn1*$^{+/-}$), 9 (SCI/WT), and 8 (SCI/*Becn1*$^{+/-}$). **E)** qPCR analysis demonstrated higher levels of pro-inflammatory genes, IL-6, IL-1β and MIP2 in *Becn1*$^{+/-}$ mice at 3d post-injury. n=5/group. **F)** NanoString Assay showed robust changes of genes related to neuroinflammation in the injury site between SCI/WT and SCI/*Becn1*$^{+/-}$ at 3d post-injury. n=5/group. **G)** BMS score showed significantly worse locomotor functional recovery for *Becn1*$^{+/-}$ mice. n=16-17/group. **H)** GFAP-DAB staining showed significantly higher lesion volume after SCI for *Becn1*$^{+/-}$ mice. n=11 (SCI/WT) and 8 (SCI/*Becn1*$^{+/-}$). **I)** Luxol fast blue staining showed significantly lower levels of spared white matter in *Becn1*$^{+/-}$ mice. n=11 (SCI/WT) and 8 (SCI/*Becn1*$^{+/-}$). **J)** After treatment with 5% Trehalose (w/v), Western blot analysis showed restoration of autophagy flux and decreased inflammasomes at 3 d post-injury. n=6/group. *p<0.05, **p<0.01, ***p<0.001 vs Sham using Mann Whitney test or unpaired t test (B, H). *p<0.05, **p<0.01, ***p<0.001 vs WT/Sham, ##p<0.01, ###p<0.001 vs WT/TBI using 2-way ANOVA group analysis with Tukey's test for multiple comparisons (C-E, I-J) or repeated measurement (G).

Trauma - 7 Restraint-induced psychological stress increases oxidative stress, worsens blood-brain barrier disruption, systemic inflammation and behavioral deficits in rats

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Introduction: United States military service members suffer substantial psychological stress on the battlefield where more than 175, 000 of them suffered traumatic brain injury (TBI) during the Iraq and Afghanistan wars. Noticeably, prolonged psychological stress causes the neurotoxic accumulation of the amino acid homocysteine and other stress inducing biomolecules such as glucocorticoids. They trigger several TBI-associated pathological markers, including oxidative stress, blood-brain barrier (BBB) dysfunction, and inflammation. In the present study, we examined the hypothesis that chronic psychological stress alters homocysteine metabolism and exacerbates TBI pathological outcomes.

Methods: Male Sprague Dawley rats (250-300g, n=88) were subjected to stress via restraint (Rst) for 1hr daily for seven consecutive days. On day 8, they underwent surgery to induced mild TBI, which represents more than 80% of all TBI cases, by Controlled Cortical Impact (CCI) method or sham operation under anesthesia. Following CCI/sham surgery, some rats were assessed for anxiety, working memory and fine motor coordination (n = 12/group). Plasma and brain tissues were collected for histological and biochemical analyses. Statistical analysis was performed by one-way analysis of variance with Tukey-Kramer post-test analyses and results expressed as Mean ± SD.

Results: Restraint induced stress increased plasma homocysteine levels by 18% and 24.5% in Rst shams and CCI rats at days 1 and 7-pi compared to controls ($n = 6$, $p < 0.05$). Levels of oxidative stress markers 4-hydroxynenonal (4-HNE) were substantially increased in the prefrontal cortex (PFC) and hippocampus (HP) of Rst-sham and brain-injured rats at days 1 and 7 post-injury by up to 2.03-fold. Levels of BBB integrity proteins ZO-1 and occludin were decreased in Rst-sham in the HP by 30% on day 7-pi and was exacerbated to 41% in the HP of Rst-CCI rats (n =4/group). Similar effects were observed in the PFC. C-reactive protein, a marker of systemic inflammation, was significantly elevated in Rst-sham and CCI rats at day 1 post-injury compared to non-Rst rats. This difference was sustained in Rst-CCI rats on day 7 post-injury. Behavioral assessments showed significantly increased anxiety in shams rats on day 2 post-injury, which reduced their time in the maze by 32% compared to non-Rst-shams ($p < 0.05$). This deficit was intensified in rats subjected to mTBI and reduced their time in open arms of the maze by 51% compared to non-Rst rats ($p < 0.001$). This deficit persisted up to day 8-pi ($p < 0.05$). Fine motor activity was significantly impaired in Rst-rats up to 16-days post-trauma, resulting in significantly more foot faults during the Beam Walk task than non-Rst sham ($p < 0.01$).

Conclusion: In summary, Rst-induced stress increased plasma homocysteine concentration and elevated 4HNE and MDA. Besides, it worsened TBI induced decreased expression of ZO-1 and occludin and exacerbated TBI-induced behavioral deficits in mTBI rats. Grant support: U.S. Air Force FA8650-17-2-6H10

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Trauma - 8 Intra-Colon Cooling Significantly Prolongs Lethal Hemorrhage Survival Duration in Rats

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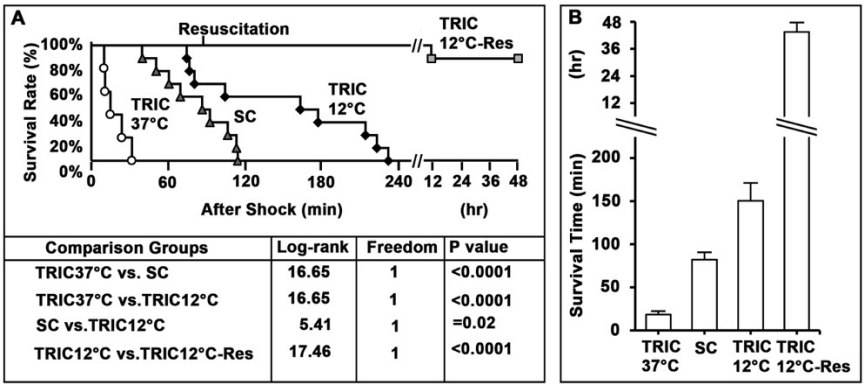
Introduction: The first line measure for reducing death of the hemorrhagic patients is to prolong the survival time, so that they can be transported to a trauma center for receiving care before developing irreversible tissue injury. Hypothermia is the most effective strategy currently known for protecting organs from hypovolemic shock. Previous studies show that core body temperatures of 10-15°C optimally preserve tissue and prolong the survival duration. Unfortunately, two major issues prevent the use of systemic deep hypothermia in hemorrhage patients: (i) rapid cooling of a human body to target temperatures is challenging; and (ii) body temperature at lower than 28°C itself can cause cardiac arrest or respiratory failure. The objective is to report a focal intra-colon cooling technique that can prolong the survival duration by 6-fold in a rat model of lethal hemorrhage.

Methods: Rats were subjected to class 4 lethal hemorrhage (via bleeding 46% of the total estimated blood volume over 25 min) with or without resuscitation. An inferior vena cava catheter line via the jugular vein in the neck was inserted to withdraw and return the blood. A novel TransRectal Intra-Colon (TRIC) temperature management device was placed in the descending colon, and activated from 10 min onwards after the start of bleeding to maintain an intra-colon temperature at 37°C or 12°C for a period of 240 min. The upper body temperature was maintained at as close to 37°C as possible in both groups. In body surface cooling experimental group, both the esophageal and rectal temperatures were maintained at the level that was the same as the esophageal temperature in the TRIC12°C group. In the TRIC12°C + Resuscitation group, rats with TRIC12°C were resuscitated at 90 min after the end of 25 min bleeding with the withdrawn shed blood and lactated Ring's solution to maintain blood pressure at above 70 mmHg. The proximal mean arterial blood pressure (pMAP) was monitored via the axillary artery, while the distal MAP (dMAP) via the tail artery. The blood samples were collected at 10 min before, and 30, 60, 120, and 180 min after HS for monitoring the Arterial Blood Gas (ABG), abdominal organ injury biomarkers, as well as pro-inflammatory and anti-inflammatory cytokines.

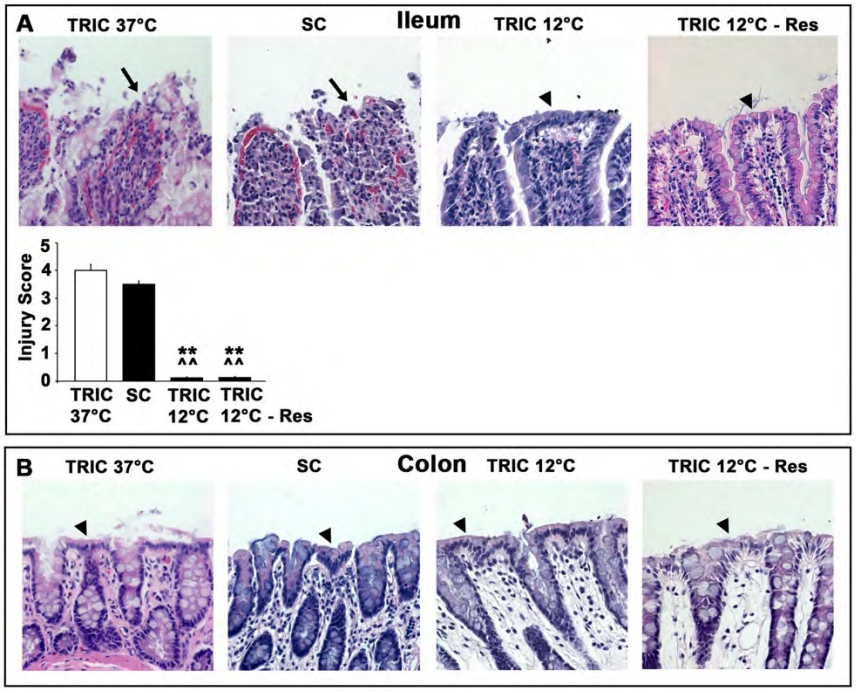
Results: An average survival time of rats after lethal hemorrhage was 18.4 +/- 9.4 min in intra-colon 37°C (TRIC37°C) group and 82 +/- 27.82 min in the body surface cooling group. In striking contrast, the average survival time was 150.2 +/- 66.43 min in intra-colon 12°C (TRIC12°C) group (Fig. 1). Among the ABG parameters, the potassium was increased dramatically in the TRIC37°C group and also, to a lesser degree, in the body surface cooling group, but was significantly lower in the TRIC12°C group. The MAPs tended to be higher in the TRIC12°C group, compared to the TRIC37°C and body surface cooling groups during the post-hemorrhage phase. The intestine was significantly damaged in the TRIC37°C and body surface cooling groups, but remain mostly intact in the the TRIC12°C group (Fig. 2). All rats had severe respiratory difficulties before death, suggesting these animals might die from cardiopulmonary failure. In the TRIC12°C + Resuscitation group, all post-hemorrhage rats (n=9) were successfully resuscitated at 90 min following the end of lethal hemorrhage. All resuscitated rats (but one) were fully recovered and survived to the endpoint (2 days). After resuscitation, the MAP was successfully maintained at 60-70 mmHg, the ABG parameters were significantly improved, and the levels plasma inflammatory cytokines and organ injury biomarkers are significantly recovered toward the normal level.

Conclusion: Intra-colon cooling with TRIC device at 12°C significantly prolonged the post-hemorrhage survival duration by more than 6-fold, compared to the normothermia, and 2-fold, relative to the body surface cooling group in the rat model of lethal hemorrhagic shock. All rats might die due to cardiopulmonary failure. All hemorrhagic rats (n=9) were successfully rescued at 90 min following the end of lethal hemorrhage. All hemorrhagic rats but one (n=8) were fully recovered from hemorrhage and survived to the

endpoint of the study. TRIC cooling offers at least 90 min prolonged time window for successfully rescuing the subjects with lethal hemorrhage.



Comparison Groups	Log-rank	Freedom	P value
TRIC37°C vs. SC	16.65	1	<0.0001
TRIC37°C vs.TRIC12°C	16.65	1	<0.0001
SC vs.TRIC12°C	5.41	1	=0.02
TRIC12°C vs.TRIC12°C-Res	17.46	1	<0.0001



Trauma - 9 Effects of air-evacuation-relevant hypobaria on ferrets following traumatic brain injury combined with hemorrhagic shock

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Introduction: Rats exposed to aeromedical evacuation (AE) relevant hypobaria within seven days after traumatic brain injury (TBI) alone or in combination with hemorrhagic shock (HS) exhibit greater neurologic injury and mortality than those maintained under normobaria (1-4). The applicability of these results to humans may be limited, however, by differences in brain neuroanatomy. Like humans, ferrets have a gyrencephalic brain. We therefore developed a ferret polytrauma (PT) model consisting of controlled cortical impact TBI (CCI) of moderate severity combined with mild HS. The objective was to determine if the deleterious effects of AE-relevant hypobaria observed in rats after TBI are also observed in a distinctly different species with a gyrencephalic brain.

Methods: The protocol was reviewed and approved by the U.S. Air Force Surgeon General's Office of Research Oversight and Compliance (AFOSR-2017-0017A) and by the University of Maryland, Baltimore Institutional Animal Care and Use Committee. Animal activities were conducted in compliance with all federal regulations governing the protection of animals and research. Anesthetized adult male ferrets (n=18) received CCI at a depth of 4 mm followed immediately by HS induced by withdrawing blood to maintain MAP 35-45 mm Hg for 30 minutes. Shams (n=4) received a craniotomy with no impact. Resuscitation with Hextend was followed one hr later by blood re-infusion. At 24 hr, ferrets were placed in a 'flight' chamber for 6 hr and exposed to normobaria (NB) (sea level, n=9) or to hypobaria (HB)(=8000 ft altitude, n=9) under normoxic conditions of 21-28% O2. MRI and MRS measurements were performed before injury and 2 days later. Cortical areas on T2 images appearing bright white were classified as 'hyperintensities' (HI) and areas appearing matte gray were classified as 'healthy'. Areas quantified with ImageJ from 1mm thick sections were summed to calculate cortical volumes (mm3). Spatial memory was evaluated with novel object location test before and 6 days after injury. Ferrets first spent time in an arena with two objects and then reintroduced to the arena once one object had been moved. Brains were perfusion-fixed on day 7, immunostained for IBA-1(microglia) and used for stereologic quantification of lesion volume and activated microglia near the site of cortical impact.

Results: Data was analyzed by t test (behavior) or ANOVA (all other data) with Fishers LSD post hoc test. In contrast to our rat PT model that results in 30–60% mortality, no ferret deaths occurred. Polytrauma impaired spatial memory in ferrets at 6 dpi. Sham ferrets explored the moved object significantly more than the unmoved object whereas PT ferrets showed no preference for either object. Hypobaria exposure did not exacerbate this deficit. The total cortical lesion volume (11.9 ± 3.7 vs 98.4 ± 8.3 mm3) induced by PT was not affected by HB (98.4 ± 8.3 vs 108.0 ± 9.6 mm3). MRS results obtained at 48hr indicate reduced cortical levels of creatine, N-acetyl aspartate, GABA and glutamate after PT which was not affected by HB. T2 image quantification revealed increased HI volume representing cortical edema at the site of impact following PT (4.6 ± 1.6 vs 149.5 ± 38.2 mm3). Hypobaria did not exacerbate this focal edema but did result in an overall decrease in cortical volume in both ipsilateral (27%) and contralateral (34%) hemispheres.

Conclusion: To our knowledge this is the first ferret polytrauma model combining TBI plus hemorrhagic shock. Although the extent of total cortical injury was similar in rats and ferrets, neuroinflammation was more extensive in the gyrencephalic species. Results indicate that hypobaria exposure in ferrets does not further exacerbate the impairment of spatial memory, the reduction in several key brain metabolites, or the increase in cortical edema and neuropathology, induced by polytrauma. Hypobaria after injury does, however, result in the acute reduction of cortical volumes in both injured and uninjured hemispheres. The lack of any improvement in neuroinflammation or behavior by exposure to hypobaria indicates that flying

within a few days after polytrauma should be avoided, if possible, for TBI patients. The views and opinions presented herein are those of the author(s) and do not necessarily represent the views of DoD or its Components. Supported by US AF FA8650-15-2-6D21.

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Trauma - 10 Flight Relevant Hypobaria Worsens Neuropathologic and Behavioral Outcomes in Rats Following the Combination of Under-Vehicle Blast plus Controlled Cortical Impact

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Introduction: US warfighters exhibit a very high incidence of traumatic brain injury (TBI) that often results in long term neurologic impairment. Most injuries are caused by exposures to blasts, either as an unmounted soldier or present within a vehicle targeted by a land mine. A small-scale model of 'under-vehicle' blast was developed for studying the effects of this blast paradigm on TBI alone, or in combination with other trauma (1-5). The current study utilized a new rat blast polytrauma model consisting of under-vehicle blast (B) followed by controlled cortical impact (CCI). This BCCI model extends our characterization of how exposure to aeromedical evacuation-relevant hypobaria can worsen neurologic outcomes (1-5). Hypothesis 1: Exposure to hypobaria (=8000 ft) one day following BCCI worsens cerebral cortex inflammation compared to no hypobaria or to 4000 ft hypobaria. Hypothesis 2: Exposure to moderate hyperoxia (50% O2) during hypobaria worsens outcomes compared to rats maintained normoxic. Hypothesis 3: Exposure to BCCI damages the cerebellum which is exacerbated by exposure to hypobaria.

Methods: The animal protocol was approved by the University of Maryland, Baltimore Institutional Animal Care and Use Committee (IACUC) and the U.S. Air Force Surgeon General's Office of Research Oversight and Compliance as protocol number FWR-2018-0002A. These studies were conducted in a facility accredited by AAALAC, in accordance with the Guide for the Care and Use of Laboratory Animals (NRC, 2011) and were performed in compliance with DODI 3216.1. The views and opinions presented herein are those of the author(s) and do not necessarily represent the views of DoD or its Components. Adult male rats were secured within restraints secured to a metal plate, simulating a vehicle. An explosive under the plate was detonated, causing 1800G acceleration. Rats were then anesthetized and subjected to the CCI model of TBI, thus simulating blast polytrauma caused by the combination of acceleration and head impact. At 24 hr after sham surgery or BCCI, rats were placed inside an altitude chamber under normobaric (sea level) or hypobaric (4000 or 8000 ft) pressures in the presence of either normoxic (21-28% O2) or hyperoxic (50% O2) conditions for 6 hr. Anxiety-like behavior was tested using time spent in the open zone of the elevated plus maze at 2, 7, and 14 days post injury (dpi). Anesthetized rats were euthanized by perfusion with paraformaldehyde at 2 or 14 dpi. Cortical inflammation was stereologically quantified using immunostained sections for activated macrophages (ED-1) or myeloperoxidase positive (MPO) neutrophils and astrocytes. Cerebellar injury was assessed in calbindin immunostained sections where Purkinje neurons were morphologically classified as healthy or injured.

Results: All data were analyzed by ANOVA or Repeated Measures ANOVA with Fishers LSD post hoc test. A single under-vehicle blast followed immediately by moderate CCI resulted in acute neutrophil activation (MPO) in the cortex which was not further exacerbated by exposure to hypobaria. Blast CCI injury resulted in a two-fold increase in MPO positive neutrophil populations at 2 days, returning to sham levels by 14 dpi. Peri-lesional astrocyte volumes increased acutely by 7-fold and were not significantly different from shams at 14 dpi. Post injury exposure to 8000 ft hypobaria increased both anxiety-like behavior and inflammation (ED1) in the potentially salvageable penumbra near the site of cortical impact at 14 dpi. Increased anxiety behavior and cortical inflammation were neither further exacerbated by hyperoxia, or alleviated by a change in ambient pressure to 4,000 ft. Although cerebellar injury increased following exposure to BCCI, as reflected by an increase in numbers of injured Purkinje neurons, it was not further exacerbated by exposure to hypobaria. BCCI rats exposed to hypobaria under 50% oxygen had fewer injured Purkinje neurons compared to when hypobaria was performed under 28% O2.

Conclusion: 1. Hypobaria exposure after BCCI increases post-acute cortical inflammation and anxiety behavior in rats. 2. Blast polytrauma induces an acute increase in cortical activated neutrophils and long term cerebellar injury which are not further exacerbated by hypobaria or moderate hyperoxia. These results raise further concern that exposure of trauma patients to hypobaria during aeromedical transport can worsen neurologic outcomes. Supported by US Air Force FA8650-17-2-6H13

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Trauma - 11 Trauma-Induced Massive Transfusion Effect on Mortality: a Systematic Review

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Introduction: Massive transfusion (MT) is defined as transfusion of ten or more units of packed red blood cells (pRBCs) in a 24-hour period.Trauma remains a major cause of hemorrhage often necessitating MT. In this review, we aim to investigate the literature on MTs in order to determine the relationship between number of blood units and patient mortality in the setting of trauma with the ultimate goal of identifying a point when additional units of blood could be harmful.

Methods: We performed a systematic review with a comprehensive search of Scopus, Cinahl Complete, Medline Complete, and PubMed databases from years 2000 to 2021 using a combination of keywords such as transfusion, blood, massive, mortality, etc. Inclusion criteria for studies was U.S. adult population, trauma as mechanism of injury, published in the English language, and includes information on the number of blood products administered and mortality rates.

Results: The review identified 2763 studies. 1133 were duplicates. Of the remaining 1630 studies, 166 studies underwent full-text review. Twelve studies met inclusion criteria, which analyzed an aggregate of 6717 patient records. Eight of the studies were retrospective, four were prospective, and zero were randomized controlled trials (RCTs). Quality assessment yielded four low quality studies, six moderate-low quality studies, and two moderate quality studies. We identified zero high quality studies. There was a broad range of patient populations, process indicators, and outcomes utilized by the different authors, including using acute respiratory distress syndrome (ARDS) as the primary outcome, plasma deficit versus plasma ratio as predictors of mortality, defining poor outcomes by hemoglobin oxygen saturation, among a few others. In addition, each of the studies defined a myriad of blood product use ranges as well as different proportions of trauma patients, rendering the systematic review inconclusive. Due to the limitations, no study was able to isolate the ceiling of blood transfusion that causes patient mortality without introducing significant confounders.

Conclusion: There is currently no comprehensive analysis on the number of blood units transfused and patient mortality when removing confounding variables. Further research on this topic is necessary to limit mortality and promote lifesaving interventions in trauma care.