SOCCA 2020 Annual Meeting and Critical Care Update

Abstracts and Medically Challening Case Reports

Scientific Abstracts

Airway Management

Airway Management-1 Preoperative airway assessment: a prospective study to evaluate the association between voice parameters and Mallampati classification.

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Introduction: Difficult airway management still lacks an accurate predictor and subjective parameters such as the modified Mallampati test may hamper its prediction leading to misclassification [1,2]. Objective measurements, on the other hand, have been shown to enhance the accuracy of any test [1]. In this field, voice parameters have been proved to be associated with upper airway anatomy besides been deemed to predict difficult airway management [3-8]. This way, some voice parameters such as formant frequencies (Figure 1) are supposed to improve, as objective parameters, the preoperative airway assessment by better evaluating the upper airway anatomy. Therefore, we aimed at observing whether voice parameters would be associated with Mallampati classification so that they could improve the assessment of upper airway anatomy.

Methods: A prospective study with 453 patients scheduled for elective surgery under general anesthesia was performed. At transitional waiting hall before transport to the operating room, we collected data on sex, age, weight, height, ASA physical status, Body Mass Index, modified Mallampati test, and acoustic parameters from voice. Uni and multivariable analyses were conducted. Two logistic regression models and their predictive performances were determined.

Results: Of a total of 467 initially eligible patients, 453 were submitted to statistical analysis, with 14 being excluded because of missing data. The Mallampati I was present in 161 patients (35.5%), the II in 158 (34.9%), the III in 94 (20.7%), and the IV in 40 (8.9%). The main result was the association found between formant if5 (p=0.00) and modified Mallampati test. ASA physical status and age were also related to Mallampati classification. Obesity, sex, weight, height, and BMI did not show any association with the Mallampati test. The AUC for the regression model containing all formants together was 65.0%, whereas the AUC for the model containing only three formants (af2, af4, and if5) after a stepwise was 60.2%.

Conclusion: Voice formants are objective measurements associated with both upper airway anatomy and Mallampati classification. Such as, voice analysis may improve the upper airway assessment performed by the conventional modified Mallampati test.

Reference(s):

1. Assessment Before Airway Management. 2015; 33: 257–78.

2. Inter-observer reproducibility of 15 tests used for predicting difficult intubation. 2011; 155: 275–81.

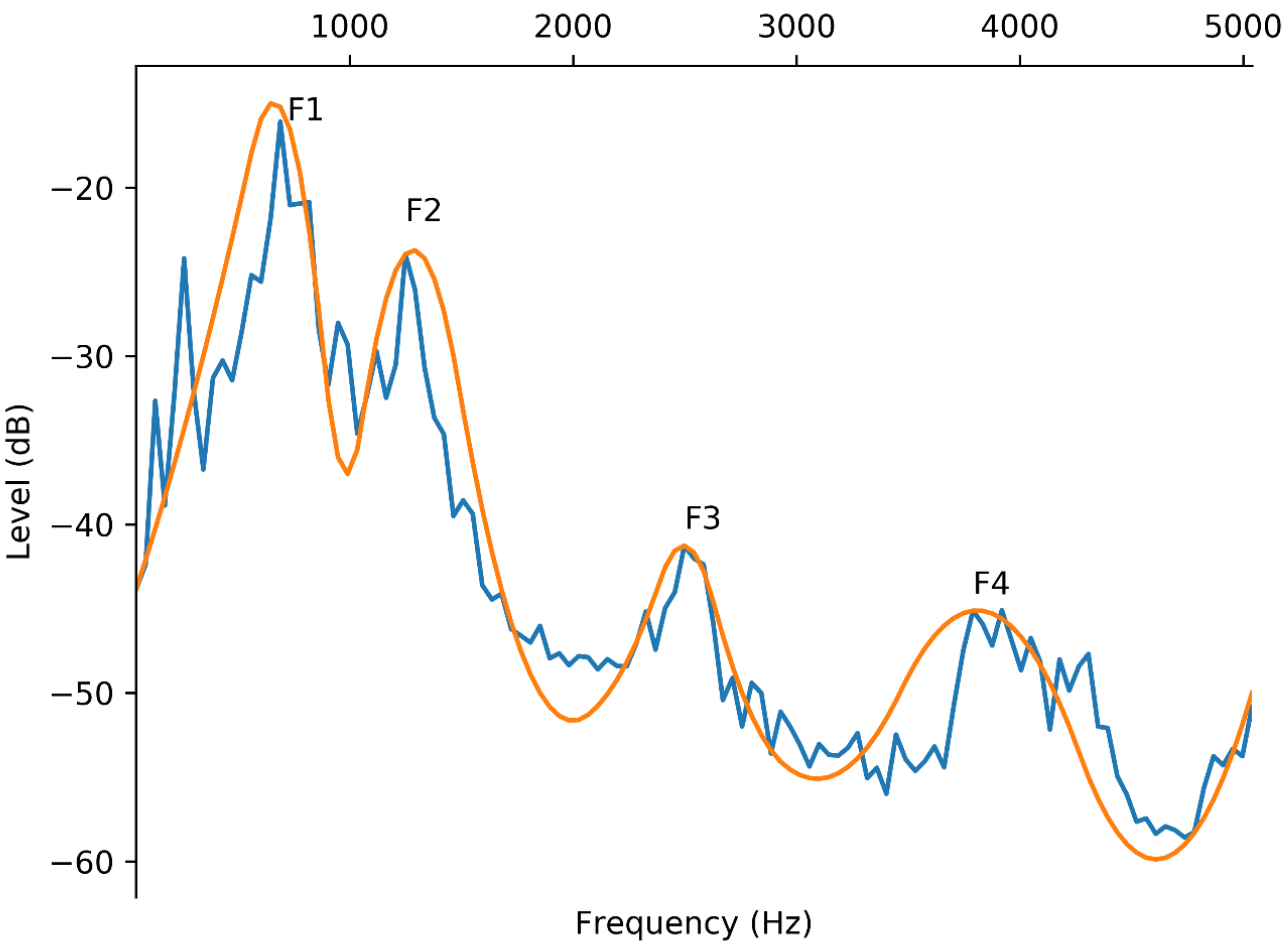
3. Pre-operative voice evaluation as a hypothetical predictor of difficult laryngoscopy. 2019; 74: 1147-52

4. A Formant Range Profile for Singers. 2017; 31: 382.e9-382.e13.

6. Acoustic pharyngometry measurement of minimal cross-sectional airway area is a significant independent predictor of moderate-to-severe obstructive sleep apnea. Acoustic pharyngometry and vowel formants. 2015; 138:833–45.

7. Influence of vocal tract geometry simplifications on the numerical simulation of vowel sounds. 2016;140:1707–18.

8. The singer's formant and the laryngeal adjustments used to realize it: a descriptive review. 2010; 21: 43-50.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−40
−50
−60
Level (dB)
Frequency (Hz)

Airway Management-2 Creating a Cognitive Aid to Improve the Efficiency and Safety of Out of OR Intubation

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Introduction: Out of operating room (OOR) intubations are critical care events that remain associated with significant morbidity and mortality. (1) These intubations are time-sensitive, cognitively demanding, and require rapid preparation of equipment as well as succinct but thorough report of patient information between teams that work together infrequently. Cognitive aids have been employed in similar situations to reduce information omission during passoff (2), improve adherence to protocols during intraoperative crises (3), and improve outcomes during intubations by pulmonary medicine fellows (4). At our institution critical airway events throughout the hospital are managed by a team involving an in-house critical care anesthesiologist, fellow, and resident who also serve as the responding clinicians in our largest surgical ICU, so timely equipment preparation and information report is essential not only for the safety of the patient in question but also the well-being of the other critically-ill ICU patients. We sought to develop a cognitive aid aimed at improving preparation for the arrival of our airway management team and increasing efficiency while decreasing omission of important information during communication of patient medical history.

Methods: A focus group consisting of critical care trained anesthesiologists identified an initial set of information and equipment necessary for preparing a safe OOR intubation, and this list was subsequently refined through a modified Delphi approach with the attending anesthesiologists of the OOR airway management service. An initial round was performed asking participants to identify additions to the initial list followed by a second round presenting the initial list with all recommended additions to solicit items for removal. Disagreements about which items to remove were resolved by majority opinion. The refined document was next brought to nursing leadership, providers from other departments, and our institution's committee in charge of overseeing critical care events for input regarding additional information to include in the cognitive aid and the optimal form to ensure easy use by registered nurses and responding clinicians at our hospital ranging from intern and attending physicians to licensed professionals such as nurse practitioners and physician's assistants. With the assistance of a graphic designer at our institution and a clinical business analyst specializing in content creation within our electronic medical records system, a handheld printed form and electronic form of the cognitive aid were created.

Results: The final cognitive aid included information about how to contact the OOR airway management team, what necessary equipment and medications to prepare while waiting for the team's arrival, and what relevant medical history to present. Clinicians and registered nurses both expressed desire to have a physical cognitive aid to use during critical airway events, though clinicians also showed support for an electronic form. There was consensus among the airway management team's anesthesiologists regarding necessary equipment and medications as well as the desire to be informed of the patient's one-line summary, code status, most recent transthoracic echocardiogram results, and information from prior intubation notes. There was disagreement about the need for presentation of the patient's NPO status and functional status prior to admission. Further discussion with anesthesiologists who disagreed on the necessity of these items revealed varying opinions on whether the use of a non-rapid sequence induction or succinylcholine, respectively, would be considered during an OOR intubation.

Conclusion: The use of a focus group followed by modified Delphi approach was effective to determine the desired equipment and medical history for an OOR intubation by the anesthesiologists of our airway management service, and collaboration with other healthcare professionals anticipated to use the cognitive aid revealed valuable insights to its form and content. The efficacy of this cognitive aid remains to be evaluated, though there are plans to compare changes in frequency of missing equipment at time of team arrival, rates of omission of important past medical history, and time from team arrival to intubation before and after the release of the cognitive aid.

Reference(s):

1. Cardiac Arrest and Mortality Related to Intubation Procedure in Critically Ill Adult Patients: A Multicenter Cohort Study. Crit Care Med. 2018;46(4):532-539.

2. Changes in medical errors after implementation of a handoff program. N Engl J Med. 2014 Nov 6;371(19):1803-12.

3. Operating Room Emergency Manuals Improve Patient Safety: A Systemic Review. Cureus. 2019;11(6):e4888.

4. A program to improve the quality of emergency endotracheal intubation. J Intensive Care Med. 2011;26(1):50–56.

RICU Consult Checklist

for use after decision is made to call RICU

Use Epic dot phrase ".RICU" in blank note

RICU x63333

- **INDICATE** "STAT" or "Non-Urgent" **WITH** clinician cell #
- **EVALUATE** patient's code status for appropriateness
- **STATE** patient last name and location

IMPORTANT: Informed clinician must be at patient's bedside when RICU arrives.

Please have computer logged in to patient chart.

WHAT TO PREPARE

- ☐ Respiratory Therapist present
- ☐ CO_2 detector & PEEP valve
- ☐ Ventilator (& AMBU bag)
- ☐ Working IV with free flowing IV bag attached
- ☐ Vasopressor and propofol
- ☐ Suction on and connected w/ tubing
- ☐ Video laryngoscope (if available)
- ☐ Leave HFNC or NIV in place

WHAT TO PRESENT

- **Code Status**
- **One-Liner:** major cardiac, pulm, ENT, acuity of decompensation
- **Last Echo:** EF, RV function, RVSP, valves
- **Prior Intubations:** "chart review" → "anesthesia," leave open
- **Allergies**
- **Access**
- **NPO Status:** last meal, major GI issues
- **Status:** functional status & weight [kg]

IF PATIENT REQURES EMERGENCY SURGICAL AIRWAY

Dial x**63333.** State the need for **"emergency surgical airway, [current location]."**

Airway Management-3 A Difficult Airway Early Warning System in Patients at High Risk for Clinical Decompensation

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Introduction: Predicting floor patients who will require emergency airway management and will be a difficult intubation may improve safety. With advanced warning, time is available to formulate an airway plan and optimize patients, potentially averting complications that contribute to high morbidity and mortality. We hypothesized that a trained rapid response team applying an abbreviated airway exam would effectively predict emergency airway management and difficult intubation.

Methods: Our hospital's rapid response team was taught to identify known or suspected difficult airway patients during bedside patient evaluations using an abbreviated airway exam. Known or suspected difficult airway patients were added to an electronic medical record 'patient list' to be seen by an anesthesiologist who would independently perform an airway exam. Patients evaluated by the rapid response team were retrospectively analyzed over the eight-months following implementation to measure the incidence of emergency intubation, difficult airway and quantifiable 'early warning.' A difficult airway was defined as an intubation requiring more than two attempts by direct laryngoscopy by a senior anesthesia resident (PGY-3 and above) or attending and/or the use of adjunctive airway equipment (e.g. video laryngoscopy, fiberoptic bronchoscopy). We excluded patients with an existing tracheostomy, Do-Not-Intubate / Do-Not-Resuscitate care plans, non-anesthesia intubations and unclear airway documentation from our final analysis.

Results: 45 (3.2%) of the total 1387 patients assessed by the rapid response team were identified as a potential difficult airway of which 7 were excluded from final analysis. 57.9% (22/38) identified patients required an emergency intubation during hospitalization of which 81.8% (18/22) had a documented difficult airway. This was in contrast to 1342 patients assessed that were not identified as difficult airways of which 15 were excluded from final analysis. 14.9% (198/1327) patients required emergency intubation during hospitalization, of which 28.8% (57/198) had a difficult airway. Patients were emergently intubated on average 1.86 days from the time they were placed on the 'patient list' to intubation (median 1 day, most common day 0).

Conclusion: Incorporating an airway exam during a rapid response evaluation identified patients where over half required emergency intubation and over 80% were difficult intubations. These patients were identified on average 1.86 days prior to intubation. The early warning provided in this high risk cohort may allow for improved patient safety during intubation for which future studies are needed.

Reference(s):

1. Mort TC. Complications of emergency tracheal intubation: immediate airway-related consequences: part II. J Intensive Care Med. 2007;22(4):208-15.

2. Mort TC. Emergency tracheal intubation: complications associated with repeated laryngoscopic attempts Anesth Analg. 2004;99(2):607-13. 3. Martin LD, Mhyre JM, Shanks AM, Tremper KK, Kheterpal S.

3,423 emergency tracheal intubations at a university hospital: airway outcomes and complications. Anesthesiology. 2011;114(1):42-8.

4. Schmidt UH, Kumwilaisak K, Bittner E, George E, Hess D. Effects of supervision by attending anesthesiologists on complications of emergency tracheal intubation. Anesthesiology. 2008 Dec;109(6):973-7.

Airway Management-4 3D Cric Trainer and Silicone Skin: A Novel Approach to Emergency Airway Simulation.

Jeffrey Huang[1], Charles R Sims[1]

[1]Mayo Clinic Rochester, Rochester, MN

Introduction: Surgical cricothyrotomy is a life-saving skill with rare opportunities to improve competency given the low incidence (Ref 1). While a systematic review comparing needle versus surgical cricothyrotomy failed to demonstrate superiority of either approach (Ref 2), low-quality evidence suggests a simple technique for surgical cricothyrotomy may be advantageous. Simulation models in the literature include pig tracheas, cadavers, and mannequins - each with limitations. Pig tracheas are cheap and realistically simulate human anatomy (Ref 3 & 4) but the ethics have been called into question by animal advocacy groups, leading institutions to pursue alternatives. 3D printing offers a cheap sustainable alternative, but evidence is limited comparing efficacy for skills training. We hypothesized that the 3D Cric Trainer is not inferior to a pig trachea for improving competency and confidence levels in anesthesia trainees.

Methods: The publicly-available 3D Cric Trainer (Ref 5) was printed by our institutional engineering department (Pictures 1-3; NB: the green tape was omitted in this study). Pig trachea models were obtained from Hormel by our simulation center. To simulate the cricothyroid membrane, Hy-Tape (Picture 4, left side) was applied to the 3D model. Skin and fat was simulated using a silicone pad created by combining Smooth-On Ecoflex 00-20, Smooth-On Ecoflex Gel, power mesh fabric, and peach and yellow acrylic paints (Picture 4). After institutional IRB exemption (IRB #19-008949), a randomized prospective pilot study was performed. Participants were randomized into the pig trachea arm (control) or the 3D model arm (intervention). After a brief didactic, and instructor demonstration of the scalpel-finger-bougie technique (Ref 6) on both models, participants were assessed on time to cricothyrotomy completion by the instructor using a stopwatch. The instructor then ensured procedure success and quality. After this pre assessment, participants practiced five repetitions on their assigned model, followed by post assessment timing and a post-survey. Paired student's t-tests were performed to determine mean difference and confidence intervals between pre/post assessments between the individual control and intervention groups. A Wilcoxon ranked sums test was applied comparatively for the two groups to determine non-inferiority. Power calculation: 28 participants are necessary to achieve a β cutoff of 20% to detect the probability of type II error.

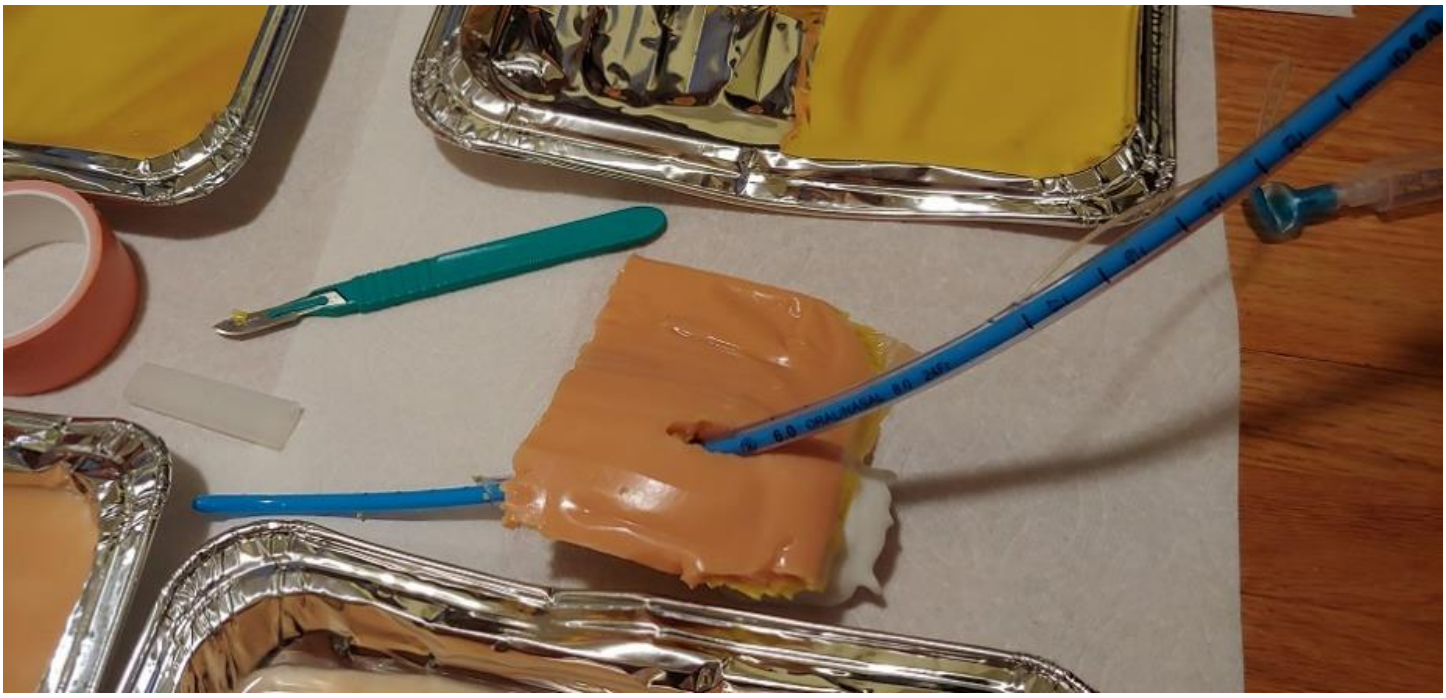
Results: Thirteen participants were included (Table 1). Six randomized to the 3D arm, and seven to the pig trachea arm. No participants had performed or witnessed a cricothyrotomy. At baseline, 23% (3/13) felt confident in performing the procedure, while 15.4% (2/13) strongly doubted their ability. After training, 92.3% (12/13) agreed or strongly agreed they would be confident in performing the procedure. 100% felt this training contributed to their education and should continue as part of a formal curriculum. Technique was satisfactory during 100% of the assessments. For the 3D Cric Trainer arm, the mean time pre-training was 36.33 seconds and post-training was 28 seconds (mean diff 8.33, CI, 1.8-14.86), p= 0.01). For the pig trachea arm, the mean time pre-training was 38.14 seconds and post-training was 32.29 seconds (mean diff 5.86, CI -8.51 - 20.23, p = 0.18). Comparing the two groups with a Wilcoxon Ranked Test given unequal variances, the mean time pre-training was 37.24 seconds, post-training 30.15 seconds (mean diff 7.09, CI -8.67 - 22.85, p = 0.99). See Table 1 for complete data.

Conclusion: The 3D Cric Trainer is cheap, reusable, and does not involve either animal or human components. We were successfully able to show the use of the 3D Cric Trainer for emergency airway simulation of a surgical cricothyrotomy was not inferior to a pig trachea model. We found significant pre-to-post improvement within the 3D-printed group, and observed no significant change in the control group. Confidence levels significantly improved among participants, with unanimous satisfaction among participants. Limitations include the small sample size, which will be addressed by enrolling additional participants over two repeat sessions to achieve the expected power to complete this pilot study. This work provides a foundation for future modifications to simulate and practice on challenging airway anatomy. It provides a framework for simulation training of other care providers involved in airway management.

Reference(s): Ref 1: Br J Anaesth. 2011 May;106(5):617-31. Ref 2: Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2013, 21:43. Ref 3: Emerg Med J. 2008 Nov;25(11):732-4. Ref 4: Rev Col Bras Cir. 2015 Jun;42(3):193-6. Ref 5: Can J Anesth/J Can Anesth (2017) 64:1079–1081. http://www.airwaycollaboration.org/3d-cric-trainer-1 Ref 6: EMCrit Podcast 131 - Cricothyrotomy - Cut to Air: Emergency Surgical Airway.

Table 1: 3D Model Arm Compared to Pig Model Arm for Pre and Post-training Completion Times.

3D Model Arm				
	Pre-Time (sec)	*Post-Time (sec)*	*Descriptive Statistics*	
n	6	6	Mean Diff	8.33
Mean	36.33	28	Std Dev	6.22
Variance	99.87	63.2	CI (95.0%)	6.53
P(T<=t) one-tail	0.01			
t Critical one-tail	2.02			
Pig Model Arm				
	Pre-Time (sec)	*Post-Time (sec)*	*Descriptive Statistics*	
n	7	7	Mean Diff	5.86
Mean	38.14	32.29	Std Dev	15.54
Variance	125.14	231.90	CI (95.0%)	14.37
P(T<=t) one-tail	0.18			
t Critical one-tail	1.94			
Wilcoxon Ranked Test	0.99			



Airway Management-5 Correlation between voice parameters and number of intubation attempts: a prospective study

Clístenes C de Carvalho[1], Danielle M da Silva[2]

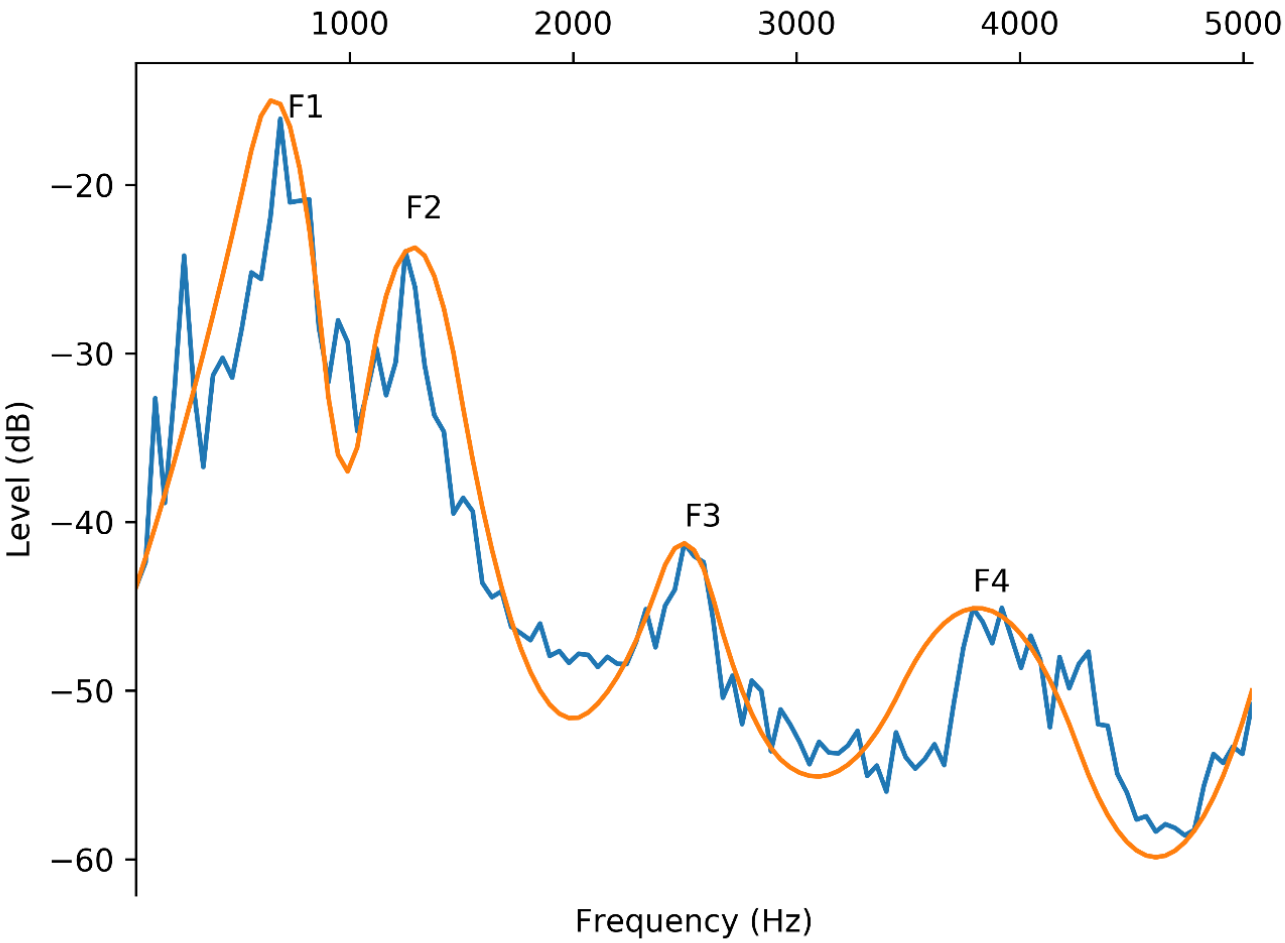
[1]Universidade Federal de Campina Grande, Campina Grande, Paraíba, [2]Hospital da Clínicas da UFPE, Recife, Pernambuco

Introduction: Predicting difficult airway management remains challenging so far. All predictors available to the present moment feature just a poor performance to anticipate problems over the airway manipulation. In this field, voice parameters have been proved to be associated with upper airway anatomy besides being deemed to predict difficult airway management. These conceptions led us to investigate the correlation between the formant frequencies (Figure 1) and the number of intubations attempts.

Methods: We performed a prospective study involving 453 patients who underwent elective surgeries under general anaesthesia with tracheal intubation. Before transporting the patients to the operating room, we collected their data on sex, age, weight, height, ASA physical status, Body Mass Index (BMI), and acoustic parameters from five phonemes (/a/, /e/, /i/, /o/, /u/). In the operating room, during the airway management maneuvers, the number of attempts to successfully allocate the orotracheal tube was noted. The Spearman correlation test was performed among the quantitative variables.

Results: The number of intubation attempts were correlated to the formants ef2 (r=-0.123, p=0.016); of2 (r=0.097, p=0.037); and of4 (r=0.114, p=0.014). Age, weight, height, and BMI did not show any correlation to the number of intubations attempts.

Conclusion: Voice formants were correlated to number of intubations attempts and may constitute an alternative tool for preoperative upper airway assessment.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−40
−50
−60
Level (dB)
Frequency (Hz)

Airway Management-6 Predictive value of combined Mallampati and Sternomental distance for difficult laryngoscopy: a prospective study.

Clístenes C de Carvalho[1], Danielle M da Silva[2], Flávia A de Orange[1]

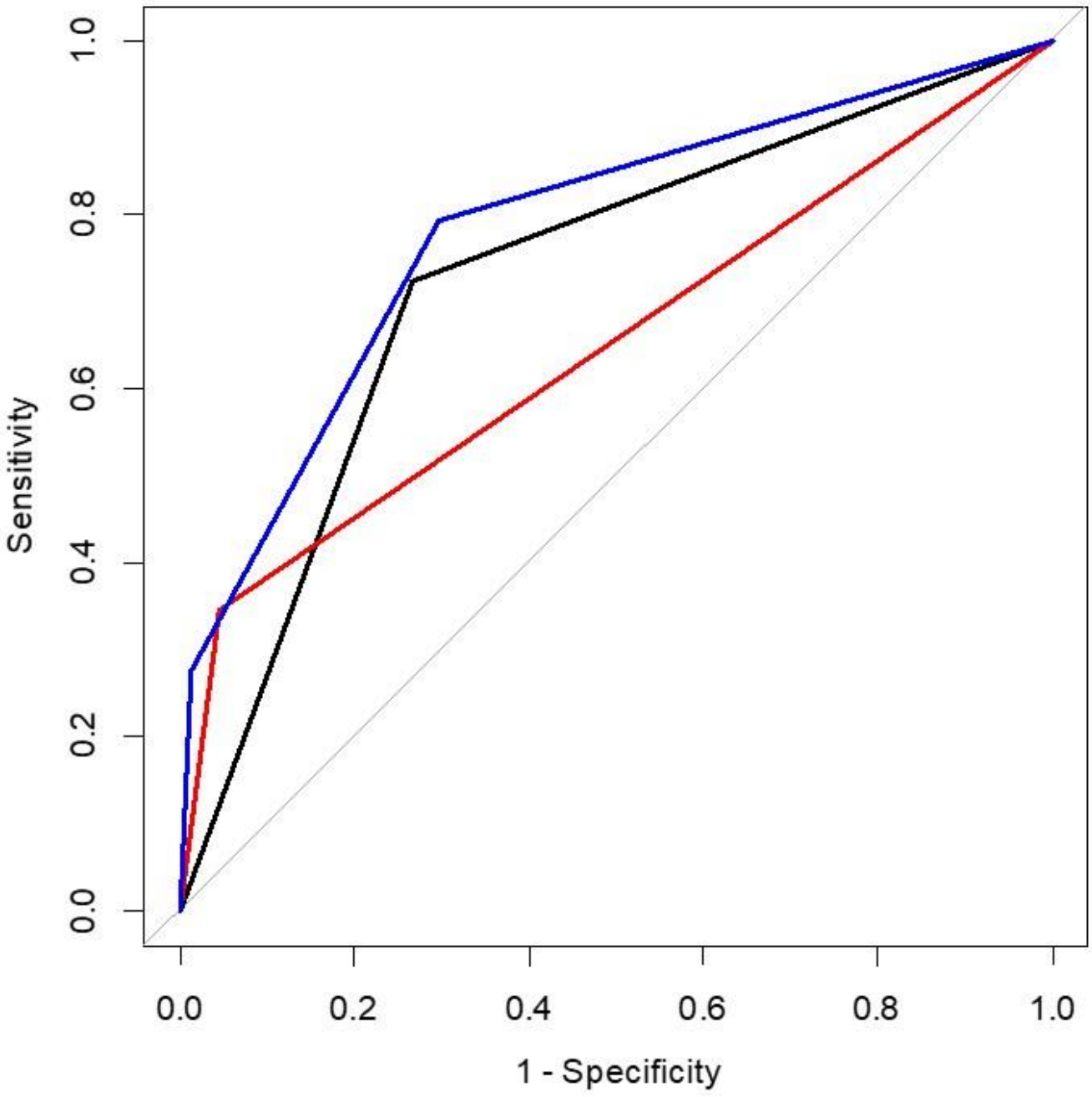
[1]Instituto de Medicina Integral Professor Fernando Figueira, Recife, Pernambuco, [2]Hospital da Clínicas da UFPE, Recife, Pernambuco

Introduction: Difficult airway prediction remains a challenging task as none of the predictors reported so far has featured satisfactory accuracy. Much of this poor accuracy may be due to the inability of predictors to assess the diverse anatomic structures involved in difficult airway management. This led us to investigate whether the Mallampati test, a parameter that assesses the upper region of the airway, along with the sternomental distance, a parameter which evaluates the lower region of the airway, would improve the preoperative airway assessment when bound together.

Methods: A prospective study with 453 patients scheduled for elective surgery under general anesthesia was performed. At transitional waiting hall before transport to the operating room, we collected data on sex, age, weight, height, ASA physical status, Body Mass Index, modified Mallampati test, and sternomental distance. In the operating room, after the induction of the anesthesia, direct laryngoscopies were performed by the assistant anesthesiologists who take note of the Cormack-Lahane classification. Uni and multivariable analyses were conducted and three logistic regression models were obtained.

Results: Of a total of 467 initially eligible patients, 453 were submitted to statistical analysis, with 14 being excluded because of missing data. Difficult laryngoscopy was present in 29 patients (6.4%). Mallampati classification (OR=7.17; p=0.000) and sternomental distance (SMD) (OR=11.08; p=0.000) were both associated with difficult laryngoscopy. The OR was 25.95 (p=0.000) when both Mallampati and SMD were indicative of difficult intubation. Three logistic regression models were evaluated (Figure 1) and their AUC defined as follows: Mallampati alone 72.88%; SMD alone 65.0%; Mallampati and SMD together 78.51%.

Conclusion: Mallampati test and sternomental distance have better predictive performance when evaluated together. Additionally, the chances of facing a real difficult airway are highly increased when both are indicative of difficulty.


Sensitivity
0.0
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1 - Specificity
0.0
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0.8
1.0

Anesthetic Pharmacology

Anesthetic Pharmacology-1 Propofol Toxicity in Cardiomyocyte Mitochondria of Developing Mice: A Novel Mechanism of Pediatric Propofol Infusion Syndrome?

Matthew Barajas[1], Sarah Brunner[2], Aili Wang[3], Richard J Levy[3]

[1]Columbia - New York Presbyterian, Brooklyn, NY, [2]Childrens Mercy Hospital, Kansas City, United States of America, [3]Columbia University, New York, NY

Introduction: Propofol infusion syndrome (PRIS) is a life-threatening condition characterized by metabolic acidosis, arrhythmias, cardiac failure, lactatemia, and fever.[1] Risk factors include young age and high cumulative doses. Prior studies suggest that propofol interferes with various components of the electron transport chain (ETC), including complexes I and IV and coenzyme Q (CoQ).[2] However, the exact mechanism of toxicity remains unknown. In addition, little is known regarding age-dependent vulnerability and few studies have assessed appropriate tissues of interest. Thus, we aimed to identify the mechanism of propofol toxicity within developing cardiomyocyte mitochondria in mice. We hypothesized that propofol would induce discrete defects within immature mitochondria.

Methods: 10-day old male C57BL6 mice were utilized to model a timepoint in human infancy. Ventricular myocardium was harvested and mitochondria isolated via differential centrifugation. Rates of oxygen consumption were measured polarographically prior to and following in vitro exposure to propofol. ETC enzyme kinetics were assessed via spectrophotometry. Substrate oxidation, ATP turnover, and proton leak were quantified relative to membrane potential. The source of proton leak was determined using specific inhibitors. 3-5 animals were evaluated per cohort. Data were analyzed using ANOVA and Tukey's post hoc analysis. Significance was set at $P < 0.05$.

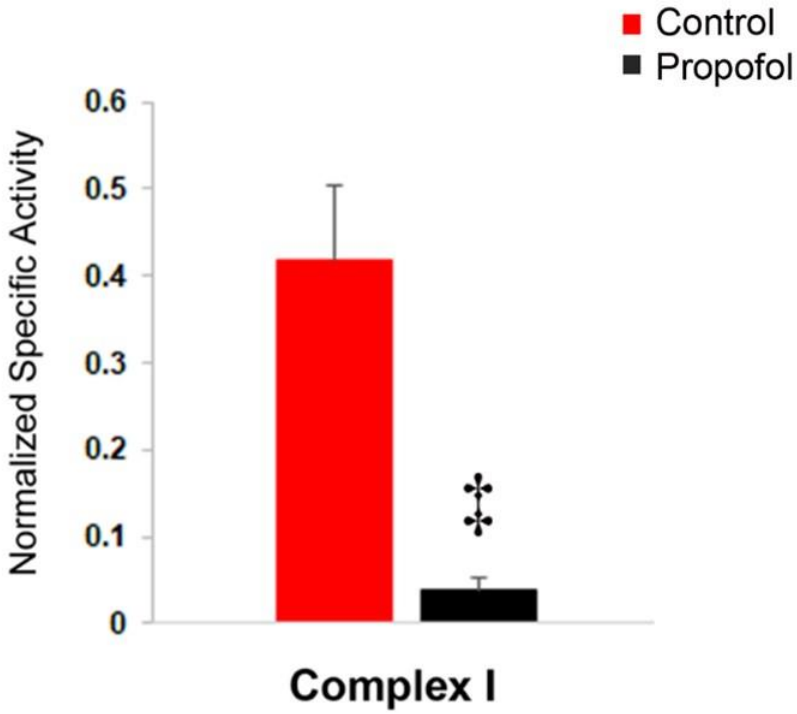
Results: Propofol had minimal effect on state 3 respiration, however, caused significant dose-dependent increases in state 4 and oligomycin-induced state 4 respiration (proton leak). (Fig.1) ETC inhibition was only seen at Complex I with the highest concentration of propofol. (Fig 2.) Propofol-mediated excessive leak was cyclosporin (CsA) sensitive, indicating the mitochondrial permeability transition pore (mPTP) as a major source of pathological leak. (Fig 3.) As such, CsA abrogated the inefficient futile proton leak caused by propofol and fully repolarized the mitochondrial membrane potential. (Fig 4.)

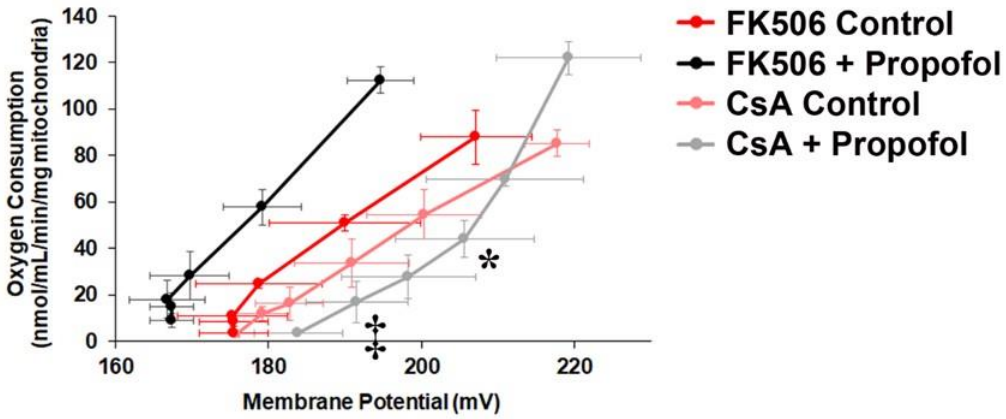
Conclusion: Propofol uncouples immature cardiac mitochondria in a dose-dependent manner leading to excessive proton leak via the mPTP. Uncontrolled opening of the mPTP causes mitochondrial inefficiency, dissipates the mitochondrial membrane potential, and leads to apoptosis or necrosis. Such a novel mechanism could underlie the toxicity of propofol and may highlight a previously unknown therapeutic target; the mPTP. Future work will, therefore, focus on developing novel agents to prevent pediatric PRIS.

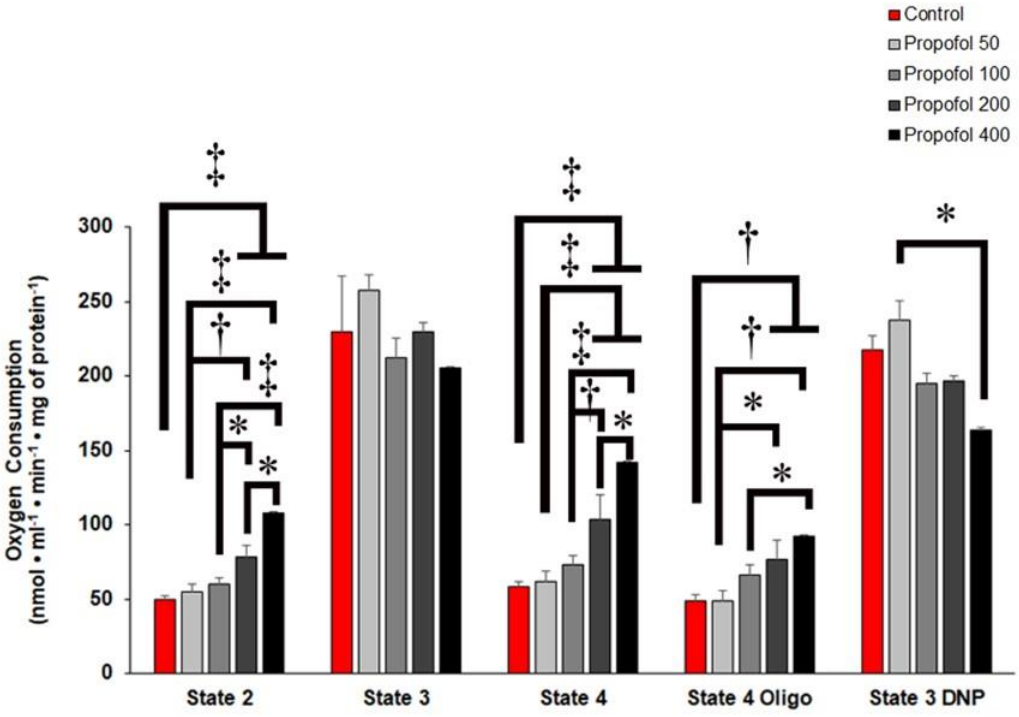
Reference(s):

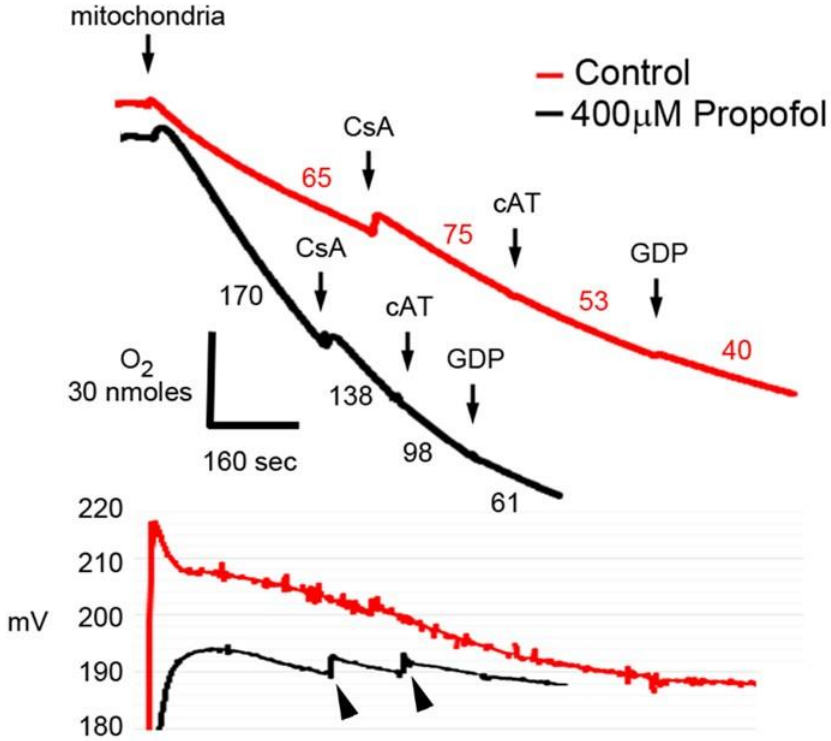
1. Kam, P. & Cardone, D. Propofol infusion syndrome. Anaesthesia 62, 690-701 (2007).

2. Vanlander, A. V. et al. Possible pathogenic mechanism of propofol infusion syndrome involves coenzyme q. Anesthesiology: The Journal of the American Society of Anesthesiologists 122, 343-352 (2015).


Control
Propofol
Normalized Specific Activity
0.6
0.5
0.4
0.3
0.2
0.1
0
Complex I


Oxygen Consumption (nmol/mL/min/mg mitochondria)
140
120
100
80
60
40
20
0
160
180
200
220
Membrane Potential (mV)
FK506 Control
FK506 + Propofol
CsA Control
CsA + Propofol


Control
Propofol 50
Propofol 100
Propofol 200
Propofol 400
Oxygen Consumption
(nmol • ml-1 • min-1 • mg of protein-1)
300
250
200
150
100
50
0
State 2
State 3
State 4
State 4 Oligo
State 3 DNP


mitochondria
Control
400μM Propofol
CsA
65
cAT
75
CsA
GDP
53
170
cAT
40
O2
30 nmoles
GDP
138
160 sec
98
61
220
210
mV
200
190
180

Anesthetic Pharmacology-2 Effects of subanesthetic ketamine on breathing and electroencephalography in intubated, spontaneously breathing ICU patients

Ronny Munoz-Acuna[1], Peter Santer[2], Maximilian Hammer[3], Sandra Rumyantsev[1], Shinichiro Kato[1], Lorenzo Berra[4], Matthias Eikermann[3]

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Introduction: During weaning from mechanical ventilation, the use of respiratory depressants, such as propofol, benzodiazepines and opioids, is often required to achieve anxiolysis and pain control. Preclinical data suggest that low-dose ketamine, unlike other anesthetics, stimulates breathing(1). In this pharmaco-physiological interaction trial, we tested whether low-dose ketamine stimulates breathing while providing sedation(2). Hypothesis: Continuous infusion of ketamine at a subanesthetic dose is associated with increased inspiratory flow, as well as a ketamine-typical increase in EEG gamma power.

Methods: Adult patients admitted to a surgical ICU at two academic medical centers in Boston, MA, who required mechanical ventilation, were deemed suitable to undergo spontaneous breathing trials, and were maintained on a constant infusion rate of propofol were included. Eligible patients received a subanesthetic infusion of ketamine at 5 mcg/kg/min for 1hr (low dose) followed by 10 mcg/kg/min for 1hr (high dose). Measurements were performed during brief spontaneous breathing trials (1 min duration) at baseline and hours 1, 2 and 5. Respiratory flow and pressure were recorded using a pneumotachometer and pressure transducer, respectively. Changes in the EEG power spectrum derived from four frontal electrodes were recorded using a Masimo SedLine monitor. Statistical comparisons were performed using ANOVA. Changes in EEG gamma-power were analyzed using an established empirical bootstrap approach(3)

Results: A total of 12 patients were enrolled; 11 patients were included in the analysis. Ketamine increased maximum inspiratory flow (mean±SEM) by 10.55%±6.16% at low-dose and 9.89%±8.12% at high-dose infusion compared to baseline ($p=0.038$). Minute volume ventilation remained unchanged. The I:E ratio (MEAN±SEM) increased from 0.53±0.05 at baseline to 0.56±0.05 and 0.60±0.05 at low- and high-dose infusion, respectively. ($p=0.009$). EEG gamma power (29-42 Hz) was increased ($p<0.05$) when compared to baseline, indicating typical power spectrum changes of ketamine.

Conclusion: In mechanically ventilated, spontaneously breathing ICU patients, subanesthetic doses of ketamine during propofol sedation increased maximum inspiratory airflow and IE ratio while also increasing the gamma spectral power similarly to the reported effects of ketamine-induced unconsciousness. These results confirm that ketamine has respiratory stimulating properties and might represent an alternative to other sedating medications such as propofol, opioids or benzodiazepines when used in the ICU setting.

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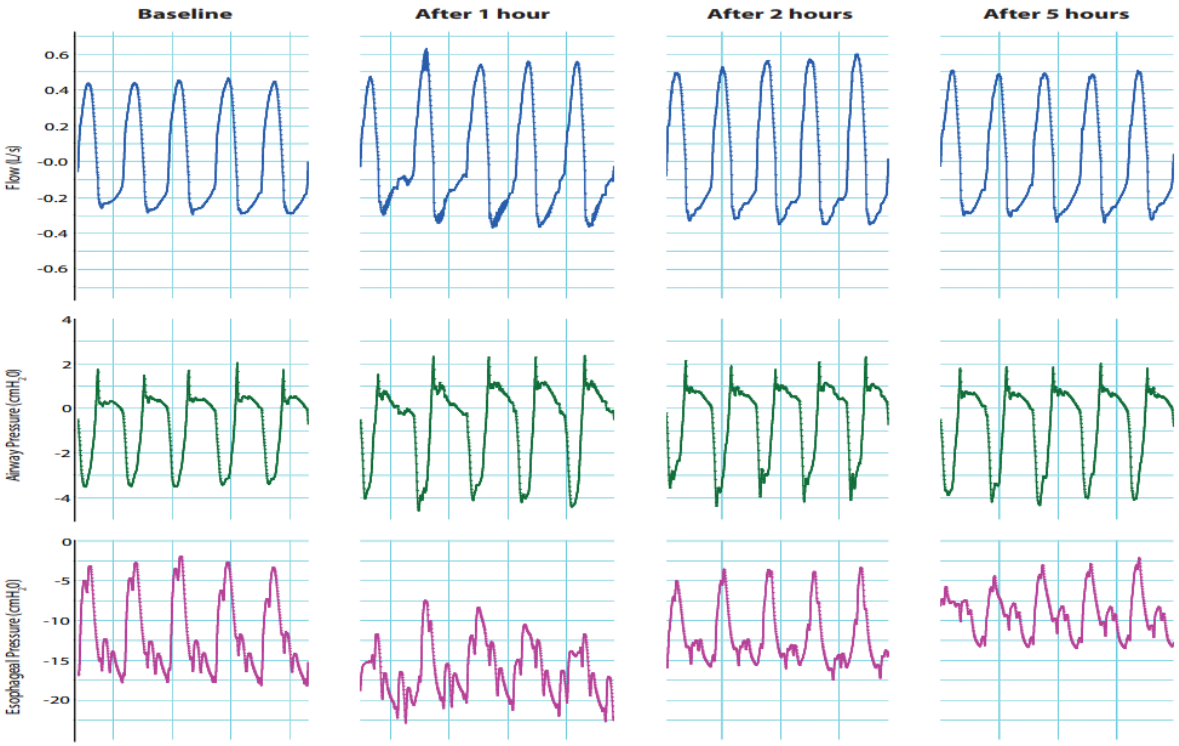
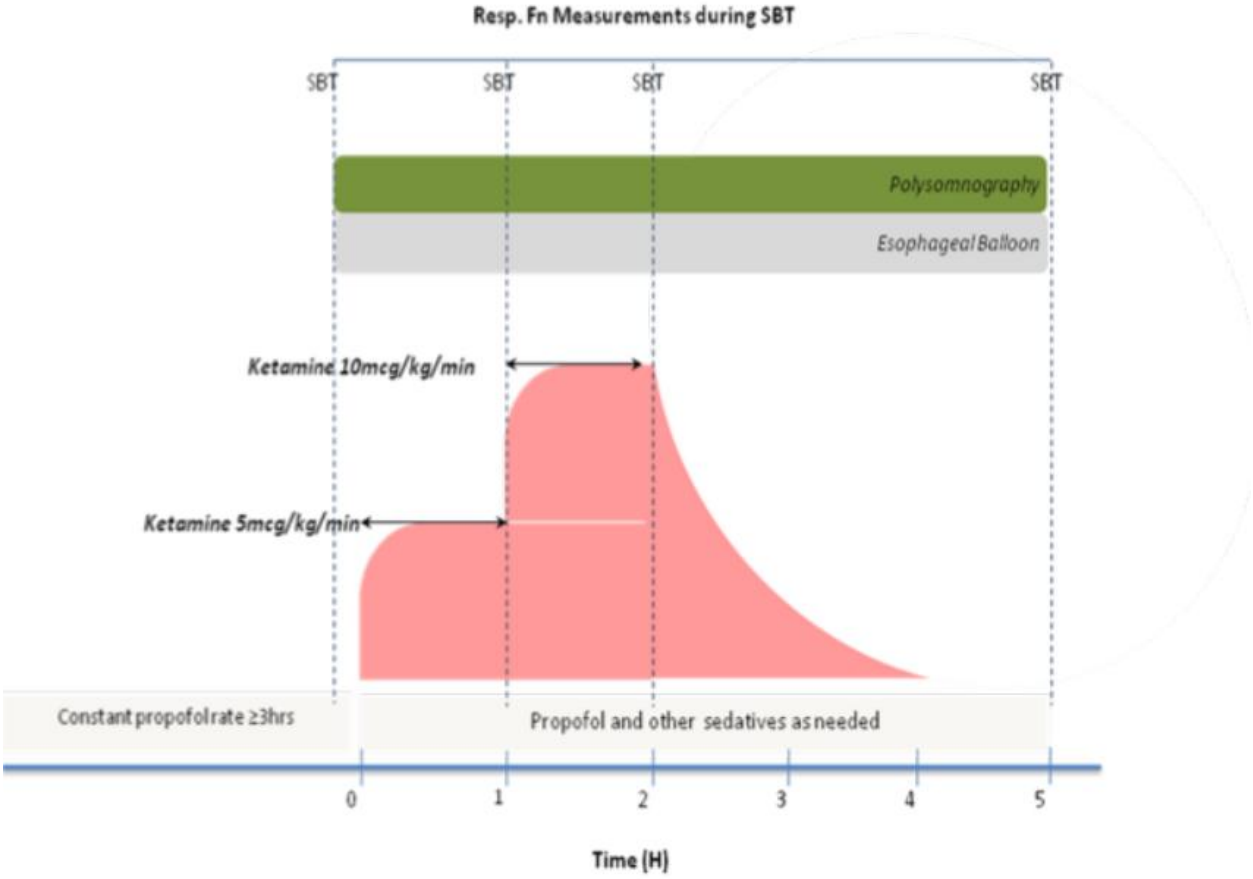
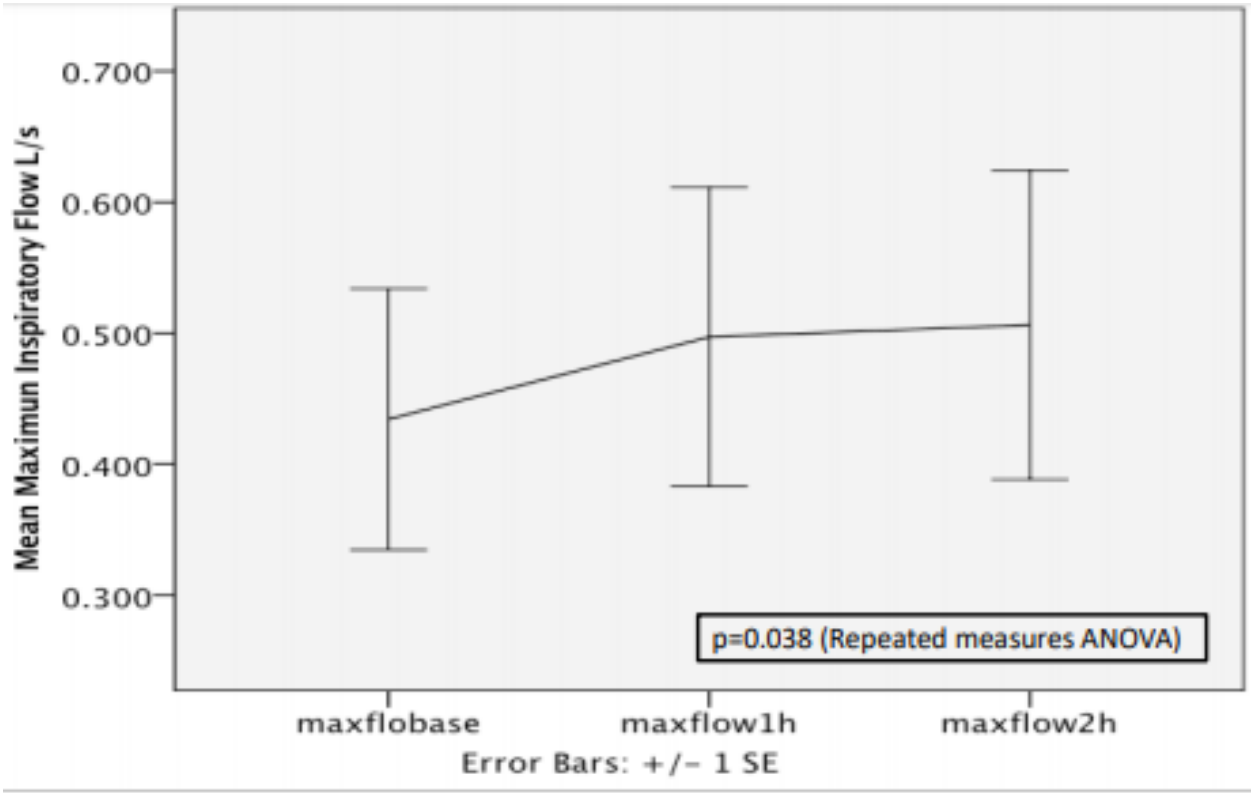
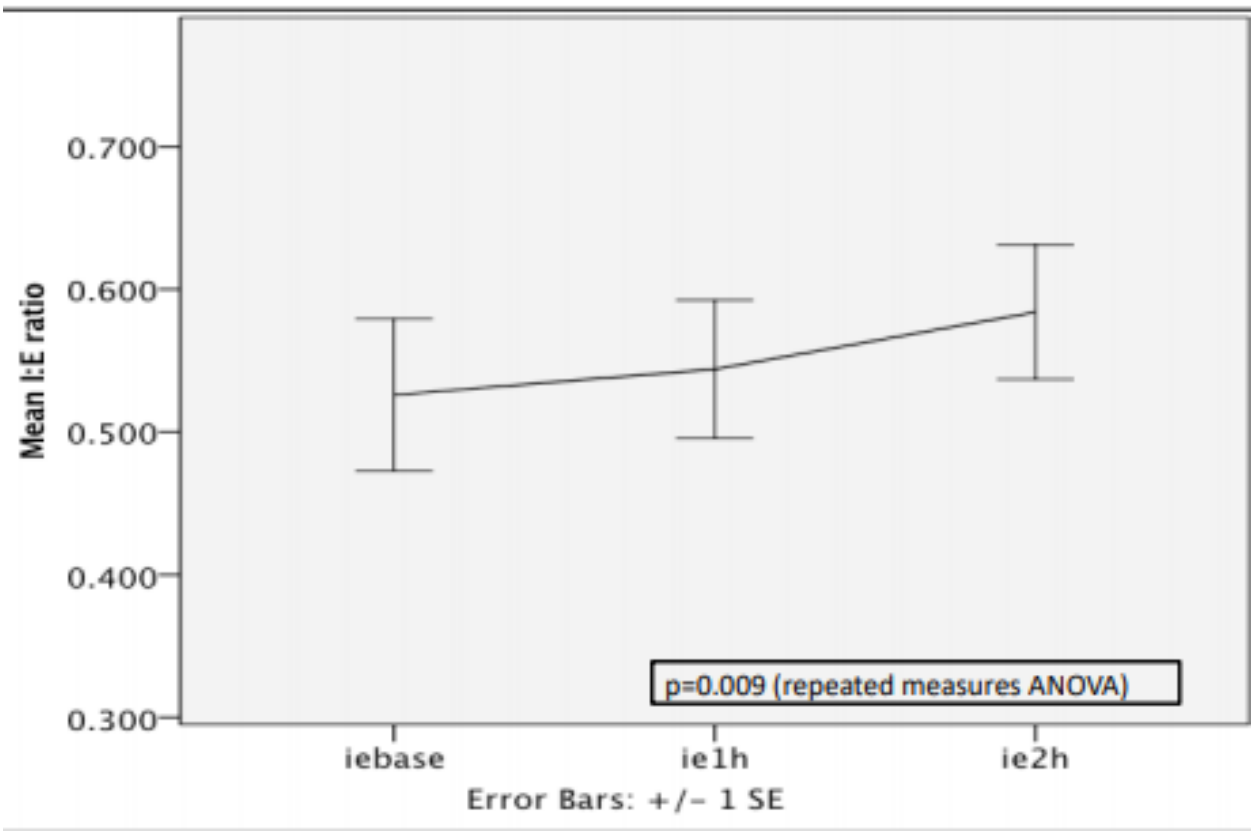
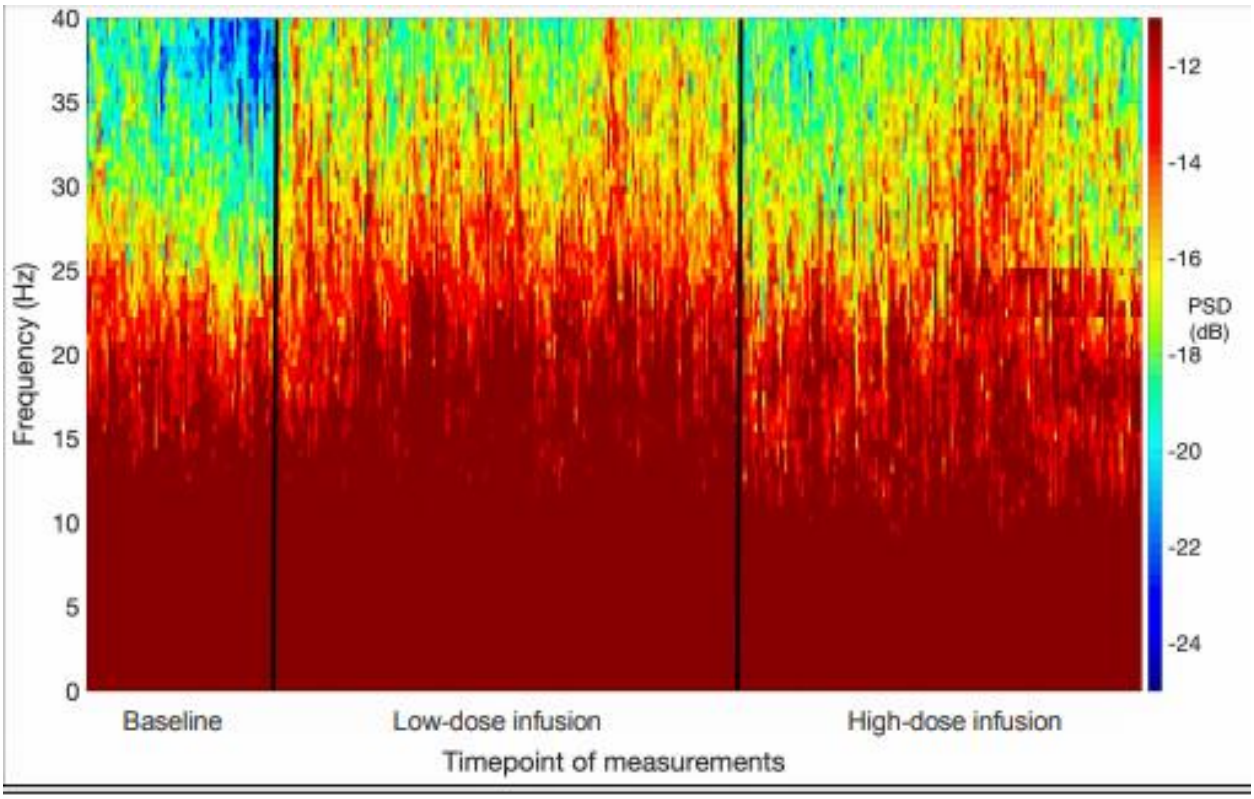
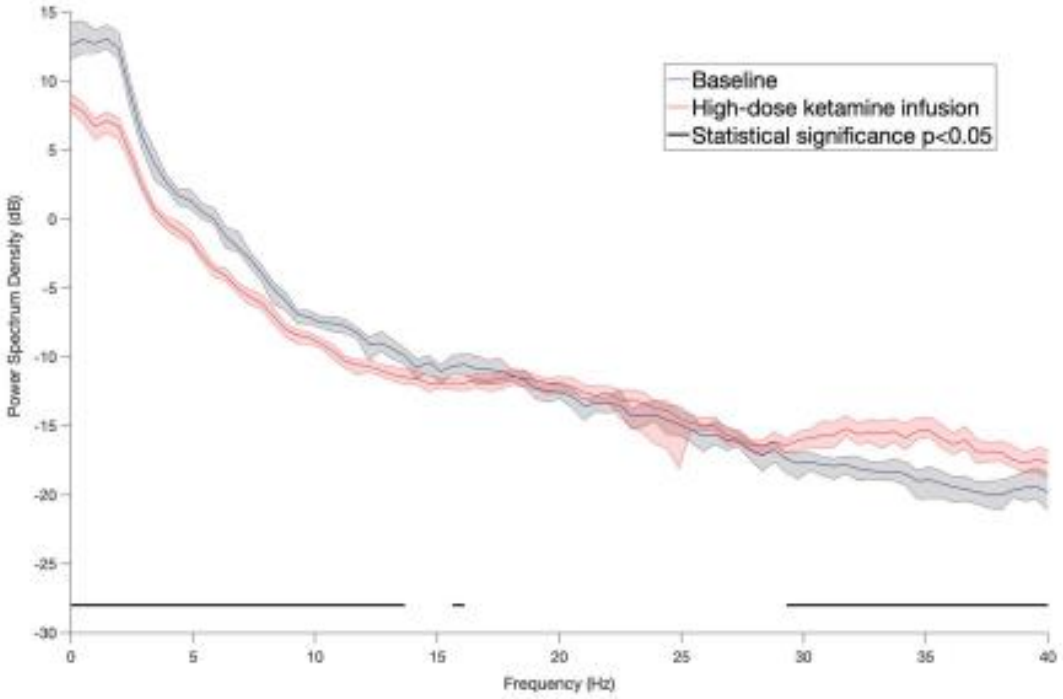

Baseline
After 1 hour
After 2 hours
After 5 hours
Flow (L/s)
Airway Pressure (cmH2O)
Esophageal Pressure (cmH2O)


Resp. Fn Measurements during SBT
SBT
SBT
SBT
SBT
Polysomnography
Esophageal Balloon
Ketamine 10mcg/kg/min
Ketamine 5mcg/kg/min
Constant propofol rate ≥3hrs
Propofol and other sedatives as needed
0
1
2
3
4
5
Time (H)


Mean Maximun Inspiratory Flow L/s
0.700
0.600
0.500
0.400
0.300
p=0.038 (Repeated measures ANOVA)
maxflobase
maxflow1h
maxflow2h
Error Bars: +/- 1 SE


Mean I:E ratio
0.700
0.600
0.500
0.400
0.300
p=0.009 (repeated measures ANOVA)
iebase
ie1h
ie2h
Error Bars: +/- 1 SE


Frequency (Hz)
40
35
30
25
20
15
10
5
0
-12
-14
-16
-18
-20
-22
-24
PSD (dB)
Baseline
Low-dose infusion
High-dose infusion
Timepoint of measurements


Baseline
High-dose ketamine infusion
Statistical significance p<0.05
Power Spectrum Density (dB)
15
10
5
0
-5
-10
-15
-20
-25
-30
0
5
10
15
20
25
30
35
40
Frequency (Hz)

Anesthetic Pharmacology-3 Oral dexmedetomidine is systemically available and promotes non-rapid eye movement sleep in healthy volunteers

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Introduction: The administration of dexmedetomidine is limited to highly monitored care settings largely because it is only available as an intravenous medication. An oral formulation of dexmedetomidine may broaden its use and benefits (e.g., delirium sparing, sedation)[1-3] to all care settings. Therefore, we investigated whether a capsule-based oral dosage formulation of dexmedetomidine is systemically available in a phase I dose-finding study. We also investigated the effect of a capsule-based oral dosage formulation of dexmedetomidine on polysomnography sleep quality and motor memory consolidation in a phase II study.

Methods: These studies were conducted under a Food and Drug Administration investigator-initiated Investigational New Drug Application and was registered on clinicaltrials.gov. First, we performed a single-site, open-label, phase I dose-escalating study of a solid oral dosage formulation of dexmedetomidine in healthy volunteers (n = 5, 300 mcg; followed by n = 5, 500 mcg; followed by n = 5, 700 mcg). The primary outcome for the Phase I study was hemodynamic stability. Mean arterial pressure and heart rate data were analyzed with polynomial mixed-effects models using time as a fixed predictor and subjects as random predictors. Plasma dexmedetomidine concentrations were determined by liquid chromatograph-tandem mass spectrometry. Next, we performed a single-site, placebo-controlled randomized, cross-over, double-blind phase II nighttime sleep study of oral dexmedetomidine (700 mcg) in healthy volunteers (n = 15). The primary outcome for the Phase II study was polysomnography sleep quality. Polysomnography data were recorded using the Somté PSG (Compumedics, Charlotte, NC) and scored using a validated automated sleep scoring software. [4] The motor sequence task and sleep questionnaires were also administered.

Results: In the Phase I study, we found that oral dexmedetomidine was systemically available and was associated with decreased heart rate and mean arterial pressure. However, these decreases did not meet our threshold for hemodynamic instability. The calculated elimination half-lives for the 300 mcg, 500 mcg, and 700 mcg groups were 2.7 hours, 2.5 hours, and 3.1 hours, respectively (Fig. 1). In the Phase II study, we found that oral dexmedetomidine increased the duration of non-rapid eye movement (non-REM) stage 2 sleep by 63 [95% CI: 19, 107] minutes (p = 0.010) (Fig. 2) and decreased the duration of REM sleep by 42 [5, 78] minutes (p = 0.031) (Table 1). We did not find any significant differences in measures of sleep latency, sleep stage switching, or subjective sleep quality (Table 2). Overnight motor memory consolidation improved after placebo sleep (7.9%, p = 0.003) but not after oral dexmedetomidine-induced sleep (-0.8%, p = 0.900) (Fig. 3).

Conclusion: We conclude that an oral capsule-based formulation of dexmedetomidine is systemically available in humans. Further, this formulation of dexmedetomidine promoted non-REM 2 sleep. The clinical significance of our motor memory consolidation findings are unclear. Overall, our results demonstrate the feasibility of developing oral dexmedetomidine as a non-REM sleep-promoting medication.

Reference(s):

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4. Sleep 2018; 41(5)

Table 1. Sleep metrics derived from polysomnography

	Placebo (STD)	Dexmedetomidine (STD)	Diff (95% CI)	P value
Total dark time (mins)	600 (0.3)	600 (0.4)	0.1 (-0.5, 0.2)	0.422
Total sleep time (mins)	523 (40)	544 (33)	-16 (-43, 11)	0.207
Sleep Efficiency (%)	87 (7)	91 (5)	-3 (-7, 2)	0.211
WASO (mins)	53 (39)	42 (29)	5 (-19, 29)	0.639
Wake duration (min)	77 (40)	56 (33)	16 (-11, 43)	0.212
N1 (mins)	24 (13)	24 (19)	0.3 (-10, 11)	0.953
N2 (mins)	256 (46)	326 (69)	-63 (-107, -19)	0.010
N3 (mins)	122 (32)	108 (34)	5 (-7, 18)	0.362
REM (mins)	120 (27)	86 (53)	42 (5, 78)	0.031
N1 TST (%)	5 (3)	5 (4)	0.2 (-2, 2)	0.881
N2 TST (%)	49 (6)	60 (11)	-10 (-16, -4)	0.005
N3 TST (%)	24 (6)	20 (6)	2 (-0.2, 4)	0.071
REM TST (%)	23 (6)	16 (11)	8 (1, 15)	0.026

WASO, wake after sleep onset; N1, non-rapid eye movement stage 1; N2, non-rapid eye movement stage 2; N3, non-rapid eye movement stage 3; REM, rapid eye movement stage; TST, total sleep time. Diff, differences in the mean of the groups.

Fig. 1

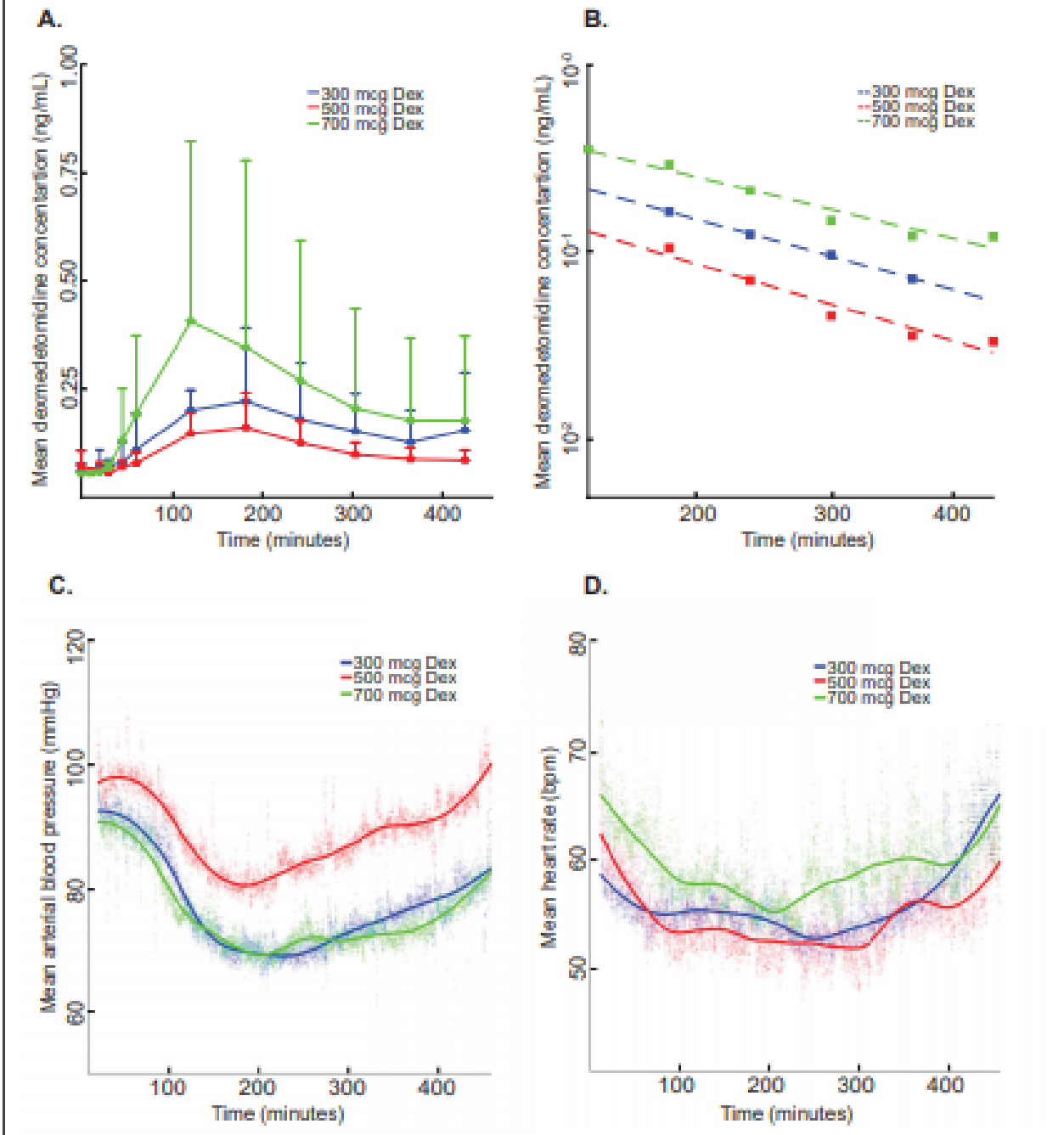

Fig. 1. Dexmedetomidine plasma concentration, mean arterial blood pressure, and heart rate. (A) Mean dexmedetomidine plasma concentration measured by liquid chromatograph-tandem mass spectrometry. The mean plasma concentration for the 500 mcg group was lower than the 300 mcg and 700 mcg groups at all time points beginning 30 minutes after drug administration. Vertical error bars represent the standard deviation. (B) We fit a line to the concentration (logarithmic) versus time (linear) starting at the peak plasma concentration. The slopes of the fitted lines were used to calculate the half-lives. (C) Group level mean arterial blood pressure. The line represents a smoothed best fit line to the data. Shaded colored bubbles represent the mean of arterial pressure over each group. (D) Group level mean heart rate. The line represents a smoothed best-fit line to the data. Shaded colored bubbles represent the mean of heart rate over each group. Blue color represents the 300 mcg group (n = 5), red color represents the 500 mcg group (n = 5), and the green color represents the 700 mcg (n = 5).

Table 2. Sleep latencies, fragmentation and administered sleep questionnaires

Sleep latencies derived from polysomnography

	Placebo (STD)	Dexmedetomidine (STD)	Diff (95% CI)	P value
Sleep latency (mins)	23.8 (18.4)	12.6 (7.5)	11.1 (-2.6, 24.7)	0.101
Wake duration (min)	77.0 (40.2)	55.6 (32.5)	16 (-10.9, 42.9)	0.212
Sleep latency to N1 (mins)	24.8 (18.6)	13.0 (7.4)	10.6 (-3.2, 24.4)	0.117
Sleep latency to N2 (mins)	28.3 (18.4)	21.0 (12.8)	5.5 (-8.4, 19.4)	0.395
Sleep latency to N3 (mins)	49.5 (27.0)	34.8 (21.4)	-10.7 (-2, 23.4)	0.089
Sleep latency to REM (mins)	70.6 (56.6)	74.3 (88.4)	-7.4 (-96.1, 81.2)	0.837
Switch	173.9 (44.7)	170.2 (64.0)	5.8 (-26.3, 38)	0.690
Switch index (per min)	0.3 (0.1)	0.3 (0.1)	0.02 (-0.03, 0.1)	0.404
Sleep fragmentation	59.1 (15.5)	58.7 (20.4)	1.9 (-10.7, 14.5)	0.746
Sleep fragmentation index (per min)	0.1 (0.01)	0.1 (0.04)	0.0 (-0.02, 0.03)	0.588

N1, non-rapid eye movement stage 1; N2, non-rapid eye movement stage 2; N3, non-rapid eye movement stage 3; REM, rapid eye movement stage; switch, number of stage shifts; sleep fragmentation, number of shifts to a lighter stage; Diff, differences in the mean of the groups.

Sleep metrics derived from questionnaire

	Placebo (STD)	Dexmedetomidine (STD)	Diff (95% CI)	P value
Total sleep (mins)	521.3 (62.2)	531.6 (59.5)	-16.9 (-44.2, 10.5)	0.203
Sleep latency (mins)	36.3 (27.3)	33 (24.4)	5.9 (-10.3, 22.2)	0.435
Times awakened (n)	3.7 (3)	3.2 (2.6)	0.9 (-1.1, 3.1)	0.315
Total time awake (mins)	23 (21.3)	24 (21)	-2.5 (-12.1, 17.1)	0.719
Overall sleepiness (1-Awake, 7-Not Awake)	2.6 (1.1)	2.6 (1.2)	-0.1 (-0.8, 1)	0.826
Quality of sleep (1-Bad, 4-Excellent)	2.5 (0.8)	2.6 (0.6)	-0.3 (-0.8, 0.2)	0.230

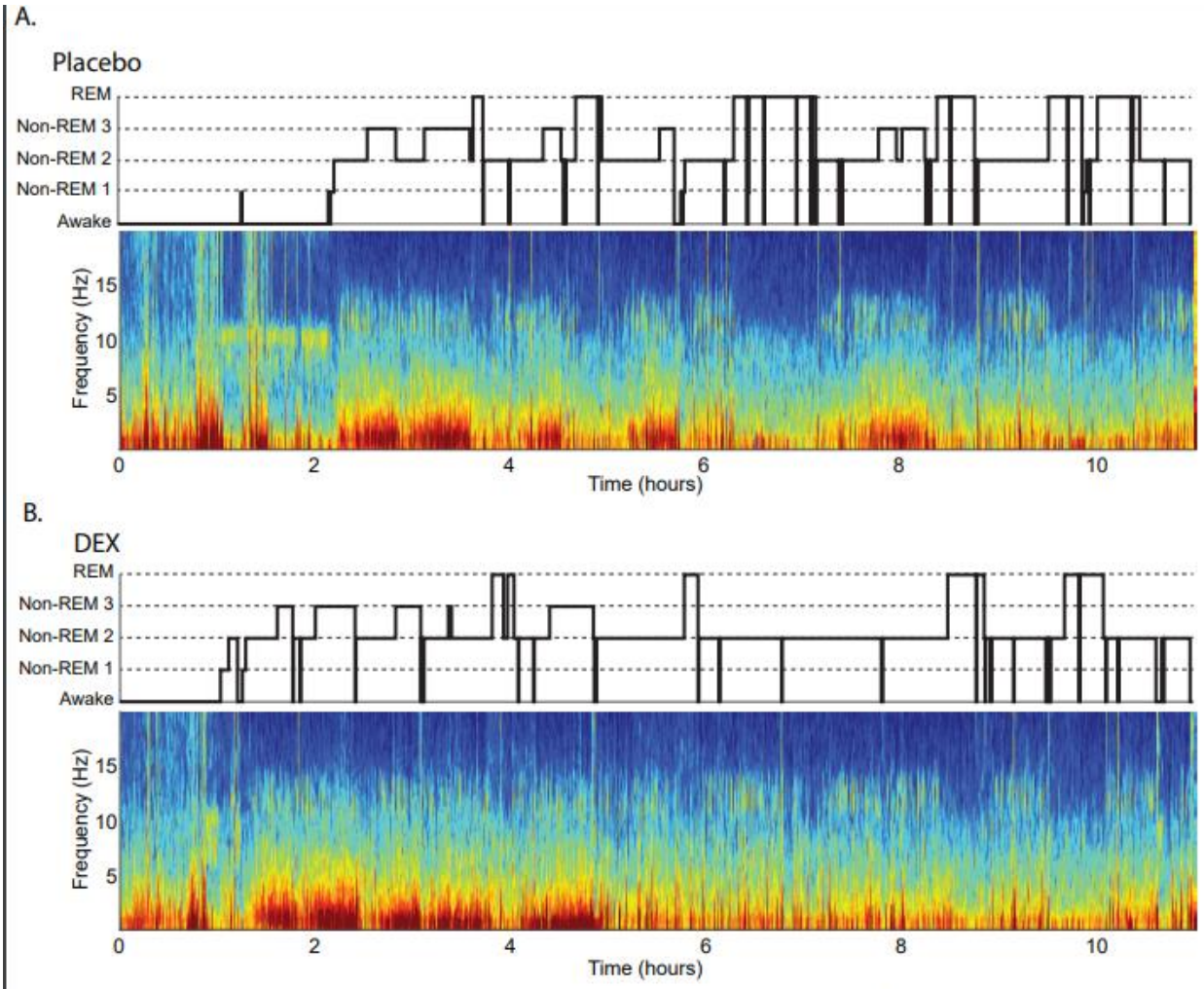

Fig. 2. Overnight sleep-wake profile of an illustrative subject during (A) Placebo visit and (B) 700 mcg oral-dexmedetomidine visit. Oral-dexmedetomidine administration is associated with an increased non-REM stage 2 sleep as compared to placebo visit.

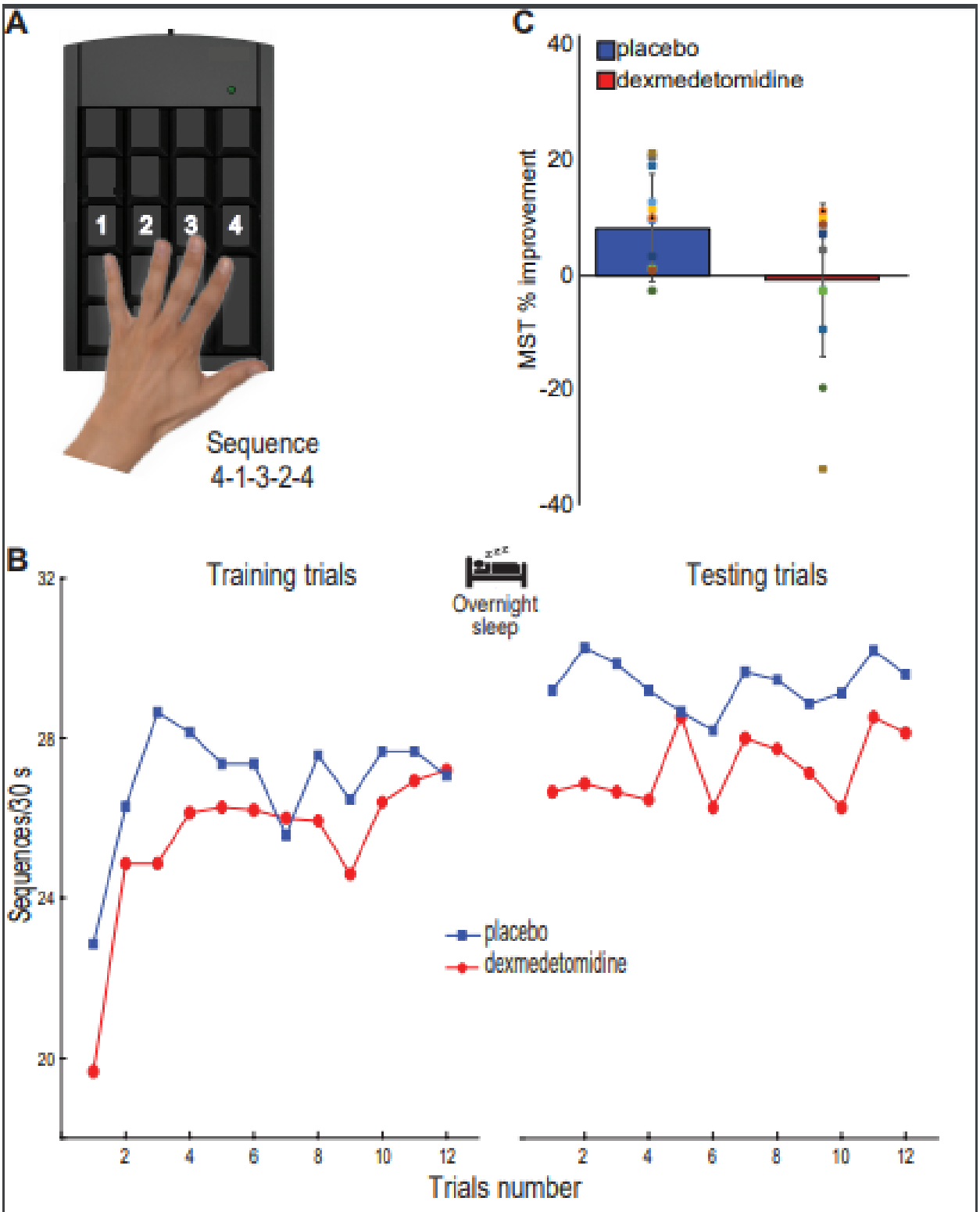

Fig. 3. MST performance. (A) The Motor Sequence Task (MST) involves typing a 5-digit sequence (4-1-3-2-4) as quickly and correctly as possible for 12 rounds of 30 second intervals. (B) MST performance during both the placebo and dexmedetomidine study visits. Placebo visits showed visibly improved overnight performance (average of first three testing sequences - average of last three training sequences), whereas oral dexmedetomidine immediate performance appeared similar between training and testing sessions. (C) Improvement in MST performance (%) met our threshold for statistical significance for the placebo (7.9%, p=0.003) but not for the dexmedetomidine (-0.8%, p=0.900) study visits. There were no statistically significant differences in immediate (p = 0.078) performance between groups.

Blood Management

Blood Management-1 Effect of preoperative ferric carboxymaltose injection on perioperative transfusion in patients undergoing total hip arthroplasty: A retrospective, propensity-score matched study

heijin Lee[1], Hyun-Jung Shin[1]

[1]Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do

Introduction: Despite ongoing efforts to reduce perioperative transfusion, there is still a high chance of transfusion in total hip arthroplasty (THA). We investigated the requirement and incidence of red blood cell (RBC) transfusion according to the administration of preoperative ferric carboxymaltose (FCM), which is one of the intravenous irons, in patients undergoing THA.

Methods: This retrospective study examined medical records of the patients who received FCM (FCM group) or did not (non-FCM group) in unilateral THA at a single tertiary care academic hospital from November 2014 to July 2018. To balance the two groups for analysis, a propensity-score matching method was used. The primary endpoint was the difference in the amounts of RBC transfused between the two groups. The secondary endpoints were the association between the FCM use and the requirement and incidence of RBC transfusion in the perioperative period.

Results: This study included 1032 cases of THA for final analysis, and the cases were divided into the FCM group (n = 568) and non-FCM group (n = 464). Propensity matching produced 389 patients in each group. In the FCM group showed significant lower amount (0.4 vs. 0.6 units) and incidence (21% vs. 31%) of RBC transfusion compared with non-FCM group (P = 0.035 and P = 0.003, respectively). Also, FCM administration was associated with lower requirement (coefficient -0.145, 95% CI -0.253 to -0.036, P = 0.009) and lower incidence (OR 0.492, 95% CI 0.317–0.765, P = 0.002) of RBC transfusion.

Conclusion: Preoperative intravenous iron administration may reduce the needs of RBC transfusion in patients undergoing THA.

Cardiovascular Anesthesiology

Cardiovascular Anesthesiology-1 Snail Knockdown is a Novel Therapeutic Strategy for Inhibiting Endothelial-to-Mesenchymal Transition in Right Ventricular Failure Secondary to Pulmonary Hypertension

Varina R Clark[1], John Park[1], Nicole Yin[1], Michael Zargari[1], Emma Said[1], Christian Makar[1], Jacqueline Agopian[1], Darnell Bagsik[1], Jason Hong[1], Gregory A Fishb

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Introduction: Right ventricular failure (RVF), the main cause of death in pulmonary hypertension (PH) patients, is associated with distinct structural remodeling which is poorly understood [1,2]. We performed transcriptome analysis of RV remodeling in two clinically relevant rat models of PH using RNASeq and investigated the role of transcription factor Snail in mediating Endothelial-to-Mesenchymal Transition (EndMT) [3-6] in rats and explanted human RV tissue. We also performed in vivo knockdown of Snail as a therapeutic strategy for RVF.

Methods: Adult male Sprague Dawley rats (250-300g) received either a single s.c. injection of Monocrotaline (MCT, 60mg/kg, n=4; followed for 30-days) or Sugen (SU5416 20mg/kg, n=4; 10% O2 hypoxia for 3-weeks followed by normoxia for 2-weeks) or PBS (CTRL, n=4). For in vivo Snail knockdown, MCT-rats either received Snail-siRNA (n=6; 5nM/injection every 3-4 days; 4-injections) or scramble (n=7) through tail vein from day 14-30 after MCT. Echocardiography and RV-catheterization were performed terminally. RVs were stained with Trichrome and EndMT markers. RNASeq was performed on rat RV tissue. Differential expression analysis was conducted. Gene expression was assessed by RT-PCR. Human RV sections (CTRL n=3; PAH n=7) were stained with Trichrome and Snail antibody. ANOVA and Student's t-test were used for statistical analysis. Values are mean±SEM.

Results: PH was confirmed by increased RVSP (mmHg) in MCT (97.6±6.6) and Su/Hx (85.26±15.6) vs CTRL (37.1±1.3; $p<0.05$). RV hypertrophy index was significantly increased in MCT (0.82±0.07) and Su/Hx (0.61±0.1) vs CTRL (0.27±0.01; $p<0.05$). MCT and Su/Hx had significant RV dilatation vs CTRL (RVID diastolic: MCT 3.5±0.3mm, SuHx 2.5±0.2 vs CTRL 1.3±0.1; $p<0.05$). PH patients had significantly elevated RVSP (80.7±9.9 mmHg) and reduced RV-function. MCT, Su/Hx rats and PH patients had increased RV-fibrosis. Double immunolabeling of RVs demonstrated colocalization of endothelial and smooth muscle markers, illustrating EndMT in RVs of MCT, Su/Hx and humans. RNASeq demonstrated EndMT as the top upregulated pathway in both MCT and Su/Hx RVs. Snail was significantly increased (~2-fold) in MCT and Su/Hx ($p<0.05$) and demonstrated increased nuclear immunolabeling (activation) in humans. Other known EndMT-transcription factors Snai2, Twist1, and Zeb1 were unchanged. Based on RNASeq, we propose that increased TGFβ (~2-fold), CDKN2B (~3-fold) and PRSS23 (~2-fold) upregulate Snail that recruits LOXL2 (~2-3-fold increase), causing HistoneH3 oxidation (~1.5-fold decrease) and CBX5 (~1.5-fold decrease) release leading to chromatin reorganization resulting in EndMT. Finally, MCT-rats treated with Snail-siRNA demonstrated decreased Snail expression (~3-fold), RVSP (45±1.6 vs 60±3.9 in scramble; $p<0.05$) and RV hypertrophy index (0.41±.01 vs 0.81±.06; $p<0.05$).

Conclusion: Pre-clinical and clinical PH-induced RVF is associated with EndMT mediated via Snail. Targeting Snail is a novel therapeutic strategy for PH-associated RVF.

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Cardiovascular Anesthesiology-2 Deletion of miR-155 in motor neurons protects from aortic cross clamping-induced paralysis in mice

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Introduction: Spinal cord (SC) injury after aortic aneurysm repair surgery is one of the most feared and devastating complication post-surgery, with 5-15% of patients experiencing paraparesis or paraplegia (1). Using our mouse model of paralysis induced by transient aortic cross-clamping (ACC) we had found that microRNA miR-155 is up-regulated in the SC after ischemia-reperfusion, in two compartments of the neurovascular unit, endothelial cells (ECs) and motor neurons (MNs). We had also found that mice with global miR-155 deletion present with reduced central cord edema and gray matter damage, and suffer roughly 35% less paralysis than wild-type mice. The aims of this study were: (1) to investigate the roles of miR-155 in these two compartments of the SC; and (2) to identify key miR-155-target genes in ECs and MNs.

Methods: To investigate the cell specific contribution of miR-155 in MN and EC in SC injury after ACC, we developed four strains of mice: Two knock-out (KO) strains: Mice that specifically lack miR-155 expression either in MNs (MN-miR-155-KO) or in ECs (EC-miR-155-KO); and two knock-in (KI) strains: Mice that over-express miR-155 specifically in MNs (MN-miR-155-KI) or in ECs (EC-miR-155-KI). The KO and KI strains were respectively produced by mating miR-155 fl/fl mice (that allow miR-155 deletion upon CRE expression) or Rosa-26-lox-stop-lox-miR-155-KI mice (where miR-155 expression is induced after the stop codon is eliminated upon CRE expression) to either ChAT-Cre transgenic mice (that express Cre in MNs) or Tie-Cre transgenic mice (that express Cre in ECs). The effects of ACC surgery on mice of these four strains were then compared to those on WT mice by recording the rate of paralysis and by measuring the volume of central cord edema using MRI. Additionally, we used Affymetrix MTA-Mouse total transcriptome profiling arrays to compare gene expression in SCs from WT mice and SCs from both MN-miR-155-KI and EC-miR-155-KI mice.

Results: We found that miR-155 activity in MNs is instrumental in the initiation of molecular malfunctions leading to paralysis in our mouse ACC model. Namely, specifically deleting miR-155 in MNs provided a level of protection against paralysis that is very similar to the level of protection provided by the global deletion of the miR-155 gene. In agreement with this result, MN-miR-155-KI developed more paralysis than the WT mice. Our finding suggests the urgency to focus on analyzing miR-155 intrinsic effects on neuron homeostasis and survival, at least in the context of our ACC model and thoracic-abdominal aneurism repair by open surgery. Interestingly, although EC-miR-155-KO mice developed less central cord edema than WT mice, that did not translate in protection from paralysis after ACC.

Conclusion: The deletion of miR-155 in MNs but not in ECs reduces the initial response to ischemia, thus limiting the spreading of inflammation and reducing the intensity of secondary SC damage.

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Cardiovascular Anesthesiology-3 Utility of pulmonary artery pulsatility index (PAPi) in estimation of RV ejection fraction

Ellesse Credaroli[1], Ahmed El-Assal[2], Paul M Heerdt[1]

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Introduction: The pulmonary artery (PA) pulsatility index (PAPi) has been proposed as a preload-adjusted metric for right ventricular (RV) function. Calculated as the ratio of PA pulse pressure to right atrial pressure (RAP) (1), PAPi has been shown to have prognostic value in the setting of acute inferior wall myocardial infarction (1) and utility for predicting RV failure in the setting of left ventricular mechanical support (2). Ultimately, performance of the RV as a pump is largely determined by the balance or 'coupling' between contractility and afterload; when relative afterload progressively exceeds contractile reserve, the system becomes uncoupled and the RV fails. In this context, PAPi has been found to correlate with RV:PA coupling metrics derived intermittently from snap shots of stroke volume and data provided by offline modeling of the RV pressure waveform (3). How PAPi relates to RV ejection fraction (RVEF), a summary of contractility/afterload balance clinicians are especially familiar with, remains unclear. Recent data demonstrate that RVEF can be estimated without measurement of ventricular volume based upon characteristics of the RVP waveform (4), and methodological refinements have now made it possible to perform this analysis on a beat-to-beat basis coincident with PAPi. The present pilot study was designed to test the hypothesis that using continuous data a relationship can be defined for predicting RVEF from PAPi.

Methods: Archived RV and PA pressure data previously acquired under IACUC-approved protocols in ~50 kg swine were used for the study. Data had been recorded in digital format during increasing isoflurane doses and subsequent barbiturate overdose (progressive depression of contractility, n=5), or sequential pulmonary embolization (progressive increase in afterload, n=4). Beat-to-beat PAPi was calculated as pulse pressure/RV end-diastolic pressure for which RAP is a surrogate. RVEF was simultaneously determined as previously described (3), with methods adapted to the pressure-volume module of LabChart (ADInstruments). For each variable, the median over a 10 second interval was defined and recorded for several minutes before and after an intervention. PAPi was plotted as a function of RVEF and the relationship analyzed as a standard curve using a 4 parameter logistic regression forced through 0 to solve for RVEF ranging from 0.45 (commonly regarded as the lower limit of normal) to 0.1.

Results: The PAPi vs RVEF relationship over 917 simultaneous measurements is shown in Figure 1 with the standard curve regression solutions superimposed. This analysis suggests that for RVEF < 0.45 the relationship with PAPi is essentially linear. Accordingly, RVEF can be predicted from the straight line y = 7.5703x - 0.1329 although appropriate confidence intervals remain to be defined.

Conclusion: Multiple studies have demonstrated utility of PAPi in prediction of impending right heart failure through hemodynamic parameters such as Ees:Ea and RAP:PCWP. However none to date have examined PAPi's utility in predicting the RVEF, a hemodynamic parameter that is more familiar to clinicians. The relationship was investigated by comparing PAPi and RVEF values collected through RVP waveform analysis in two pathophysiological models; reduced contractility by volatile anesthetic and barbiturate overdose and increased afterload by induced pulmonary embolism. Results of the current experimental study indicate that once RVEF declines below the low end of normal there is a linear relationship with PAPi. If this relationship is confirmed clinically, it may be possible to continuously predict RVEF from PAPi values obtained at the bedside, assess a gradual decline in RV function, and recognize the need for intervention earlier. This is especially significant for patients unable to undergo immediate cardiac imaging or where cardiac imaging may be distorted due to postoperative changes or body habitus. Further human studies need to be performed to learn more about this relationship and its application to a clinical picture.

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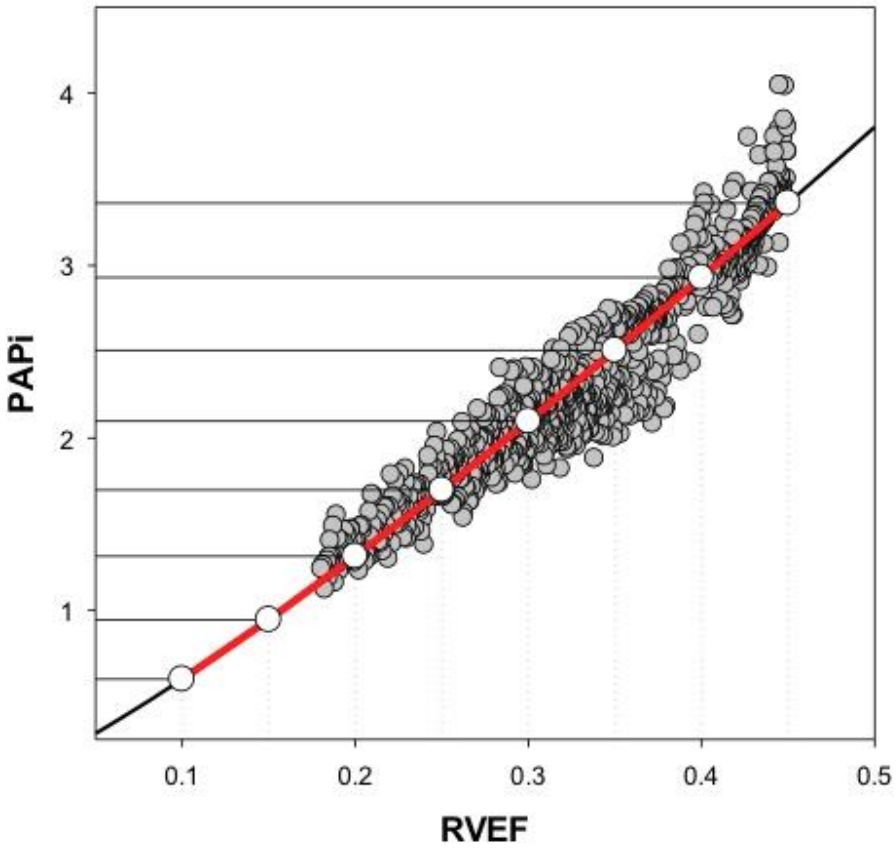
PAPi
4
3
2
1
0.1
0.2
0.3
0.4
0.5
RVEF

Cardiovascular Anesthesiology-4

Echocardiographic Assessment of Left Ventricle Function During Ex Vivo Heart Perfusion using Pump Supported and Passive Afterload Working Mode prior to transplant.

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Introduction: Heart transplant remains the gold standard for the treatment of end stage heart failure but it is limited by an increasing gap between available donor organs and recipients. As a result, many centers are introducing donation after circulatory death (DCD) to increase the donor pool. Ex vivo heart perfusion (EVHP) was created to decrease cold ischemia time and allow metabolic and functional assessment of donor hearts prior to transplantation. However, current clinical platforms do not allow functional evaluation of hearts. Echocardiography is a validated non-invasive imaging modality to assess heart function. We developed an EVHP system to allow functional donor heart evaluation in 2 working modes: Pump Supported (PSWM) and Passive Afterload Working Mode (PAWM). PSWM enables an antegrade flow to the left atrium, and a retrograde flow into the aorta. In systole, the LV must overcomes the aortic backpressure that in diastole provides retrograde coronary perfusion. PAWM is an alternative to PSWM to closer simulate systemic vascular resistances. In PAWM the ascending aorta is connected to a Windkessel-based afterload module. In this report, we performed echocardiographic evaluation of LV function during this two different working modes.

Methods: After approval of local ethics board, 4 Yorkshire male pigs underwent general anesthesia for heart harvesting. The hearts were procured after injection of cardioplegia solution and subsequent cardiac arrest. They were put in cold storage for 15 minutes to allow cannulation and were then mounted on our custom EVHP circuit. The reperfusion protocol consisted of Langherdorf mode (LM) for 30m, PSWM for 1h, PAWM for 4h, and PSWM for 1h. LV function was assessed using echocardiography in vivo, during PSWM1, PAWM and PSWM2. Echocardiography included the main standard LV views to quantify LV function according to current guidelines. We measured: EF, fractional shorting (FS), fractional area change (FAC), global longitudinal strain (GLS), global circumferential strain (GCS) and radial strain (RAD).

Results: During EVHP, our 3D custom setup was able to provide good quality images comparable to standard transthoracic and transesophageal views which allowed for measurements of functional cardiac assessment (Figure 1). The global systolic function of the LV (represented by EF, FAC, FS) was reduced over the course of the experiment (Figure 2). In addition, GLS and GCS increased while RAD strain decreased over the course of the experiment (Figure 3)

Conclusion: Heart transplantation after DCD is a viable option to increase the number of viable available organs, however DCD hearts are invariably exposed to warm ischemia that leads to a variable degree of LV dysfunction. It is of critical importance to assess DCD heart function to determine organ suitability before transplantation. Epicardial echocardiography assessment during EVHP in bi-PSWM and bi-PAWM was feasible with our system and provides high quality images to assess the cardiac function as per current guidelines. Echocardiography may be included as a diagnostic modality during the working mode in EVHP. Further experiments of transplant after PSWM and PAWM are needed to compare both preservation modalities.

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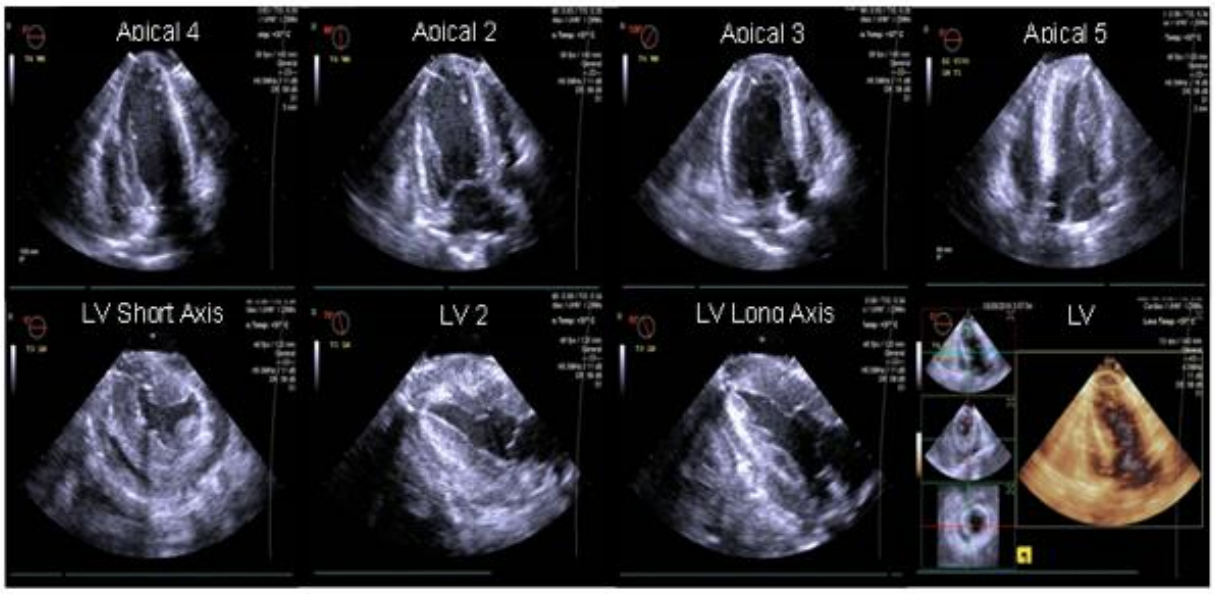

Figure 1: Modified epicardial echocardiography views acquired with a 3 D custom made setup
LV: left ventricle.

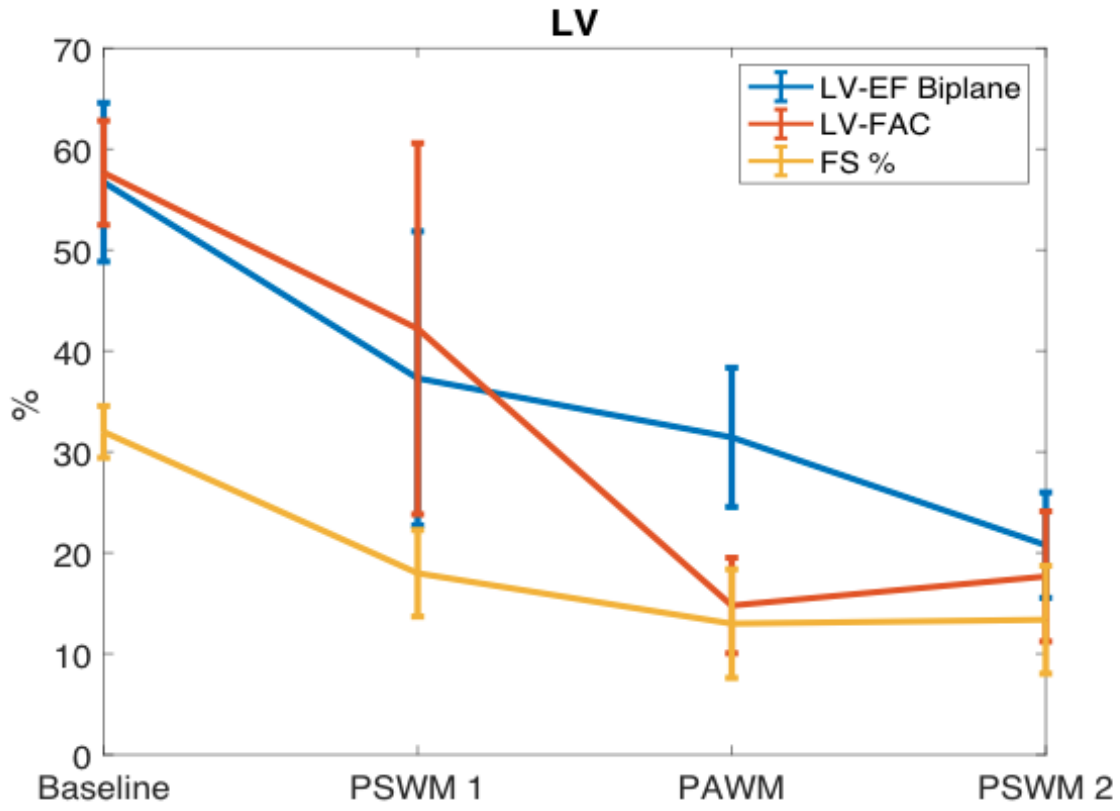

Figure 2: Trend of EF, FAC, FS during the experiment
PSWM: Pump Supported Working mode. PAWM Passive Afterload Working Mode EF: ejection fraction. FAC: fractional area change. FS: fractional shorting GCS: global circumferential strain. GLS: global longitudinal strain. LV: left ventricle.

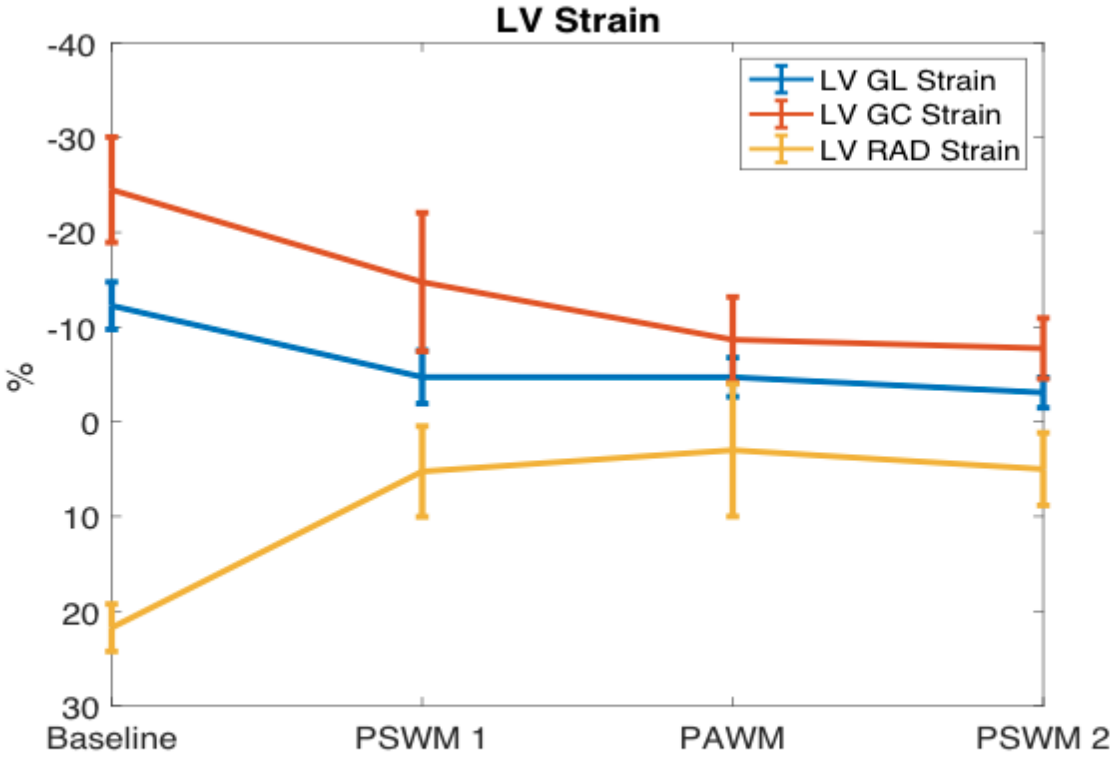

Figure 3: Trend of GLS, GCS, RAD during the experiment
PSWM: Pump Supported Working mode PAWM Passive Afterload Working Mode GCS: global circumferential strain. GLS: global longitudinal strain. RAD: radial LV: left ventricle.

Cardiovascular Anesthesiology-5

Perioperative multimodal general AnesTHesia FocusINg on specific CNS targets in patients undergoing carDiac surgERies: The PATHFINDER study

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Introduction: The current practice of balanced anesthesia generally uses intravenous propofol to induce and inhaled ethers to sustain unconsciousness, midazolam for amnesia, muscle relaxants for immobility and opioids for antinociception (1,2). However, recent advances in the understanding of specific neural circuits involved in antinociceptive and arousal pathways have made it possible to use medications synergistically to achieve proper levels of antinociception and unconsciousness. Evidence suggests that the selection of multiple classes of intravenous medications allows for a reduction in overall dosing requirement when compared to dosing each medication individually (3). Multimodal general anesthesia (MMGA) is a strategy designed to utilize known central and peripheral neurophysiology in designing a rational and explicit mechanism to control levels of unconsciousness and antinociception during anesthetic practice. MMGA uses a combination of multiple agents with specific central nervous system targets at low doses to maximize therapeutic benefit while minimizing the potential side effects of each agent. MMGA improves on the practice of balanced anesthesia by using multiple antinociceptive agents which act at different parts of the nociceptive system. These medications also contribute to unconsciousness by decreasing arousal and limit the amount of opioids necessary to manage nociception intraoperatively and pain postoperatively (4).

Methods: In the PATHFINDER pilot study, a rational strategy of multimodal general anesthesia with EEG-based neuromonitoring was employed in a group of 18 elderly patients undergoing cardiac surgery, a high risk population for hemodynamic instability, delirium, and post-operative cognitive dysfunction (5, 6 ,7). Antinociception was achieved by a combination of remifentanil, ketamine, dexmedetomidine, bupivacaine, and magnesium. The state of unconsciousness was achieved primarily by propofol; however, the chosen antinociceptive agents have secondary effects in decreasing levels of arousal (2). Image/ Chart Captions: Table 1: Demographics of study cohort. Table 2: Flowchart of multimodal general analgesia protocol.

Results: Quantitative data was collected (data collection ongoing) with a primary outcome of postoperative delirium and secondary outcomes of intraoperative hemodynamic stability (via area under the curve of hypotension and blood pressure coefficient of variation) and post-operative analgesic requirements. Qualitative observations include a) smooth wake-ups in the ICU (per nursing); b) stable hemodynamics in the operating rooms (per anesthesiologists); and c) a comprehensive use of the raw EEG waveforms, density spectral array, and patient state index to ensure adequate levels of unconsciousness states. Image/ Chart Captions: Figure 1: Incidence of burst-suppression in EEG of patients. Burst-suppression is an EEG waveform seen during medically induced coma that is undesirable during surgical unconsciousness. (A, B) Computed EEG spectrograms for a selected control and experimental group patient during cardiac surgery with labeled timepoints of surgical incision (S), sternotomy (ST), heparin bolus (H), bypass begin (BB), bypass end (BE), and sternal closure (CS) before ICU transfer. Suppression epochs are visible in the multitaper spectrograms and, suppressions were identified computationally as 2s epochs with EEG amplitude >5uV. Identified suppression epochs are plotted below each spectrogram. (C) Selected raw EEG samples comparing waveforms during general anesthesia versus a waveform of burst suppression. (D) Fraction of time spent in burst suppression from induction to closing of the sternum during cardiac surgery under multimodal anesthesia. Figure 2: Graphical representation of the area under the curve (AUC) of mean arterial pressure < 65 using trapezoidal rule (median = 911.03), time-weighted average of AUC adjusted to the length of surgery (TWA, median = 3.47), and mean arterial pressure coefficient of variation (CV, median = 0.345) during cases under the multimodel anesthesia paradigm.

Conclusion: By using multiple medications with specific CNS targets at low doses, it is possible to operationalize a strategy in cardiac anesthesia to optimize therapeutic benefit and minimize potential side effects of each agent.

Reference(s):

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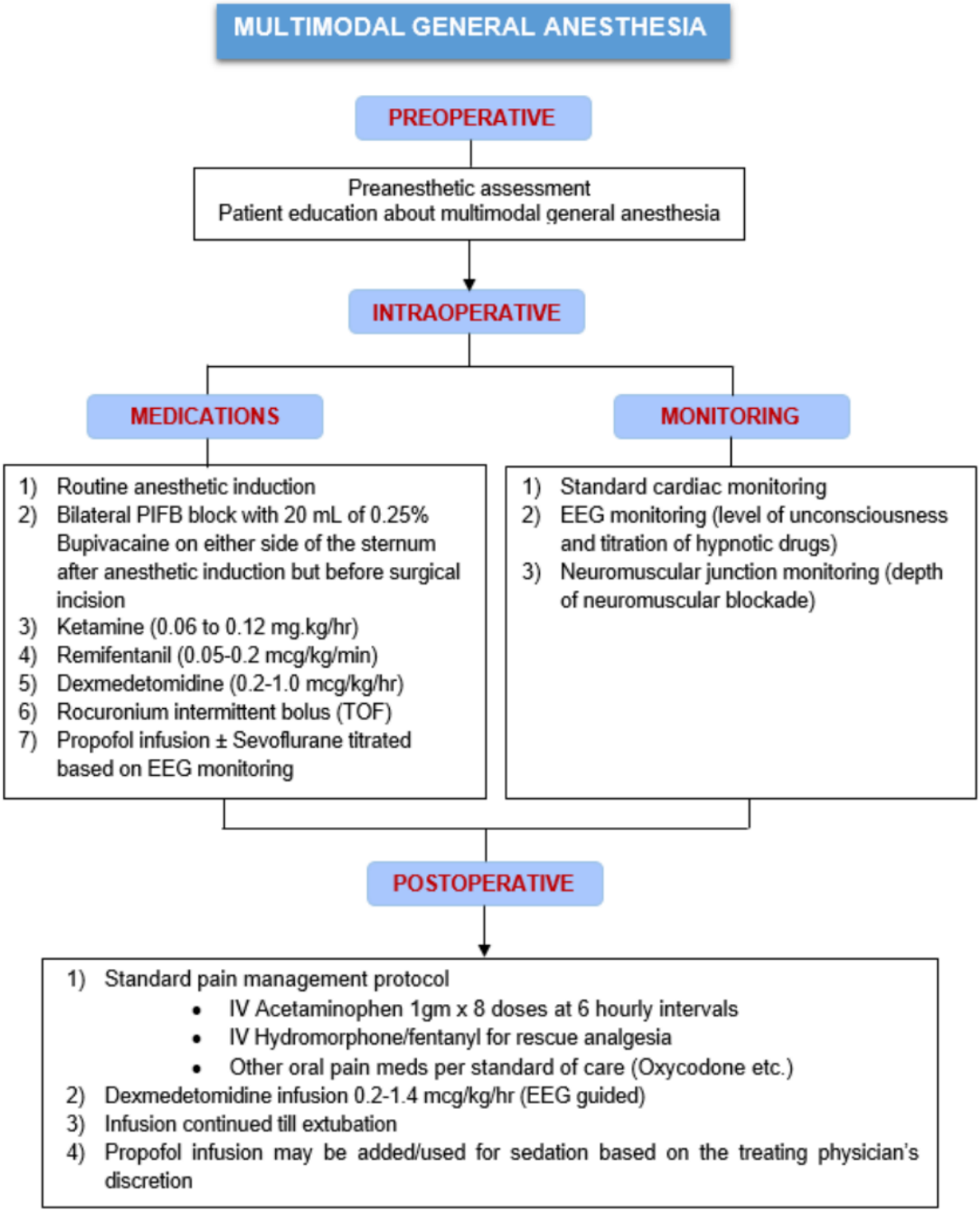
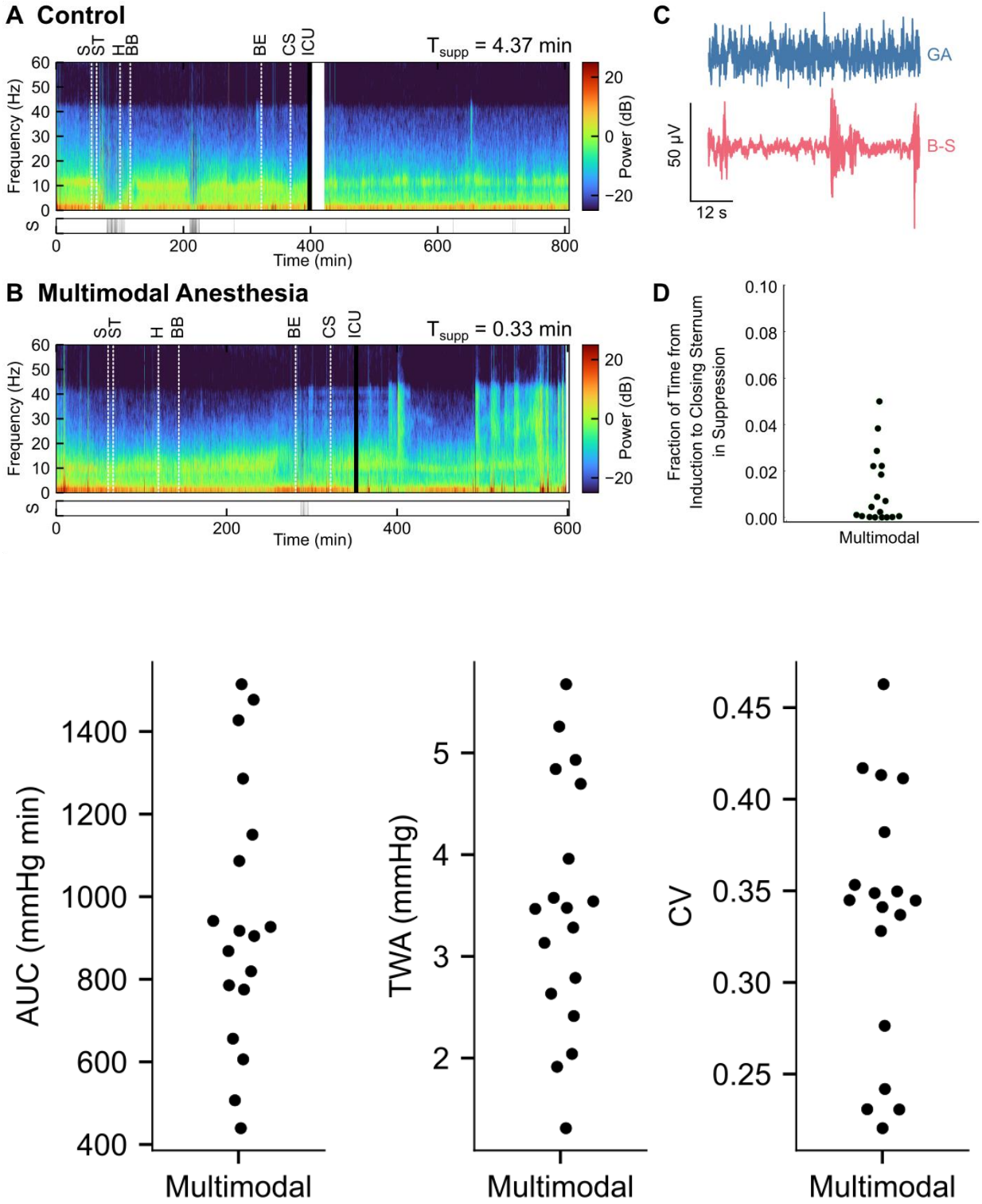
Table 1: Baseline Characteristics of Study Participants

Demographics:	Control (n=2)	Experimental (n=18)
Sex, no (%)		
Male	1 (50)	13 (72.2)
Female	1 (50)	5 (27.7)
Age, mean (SD)	67 (9.9)	72.7 (5.2)
Weight, mean (SD), kg	88.4 (0.3)	82.1 (17.6)
Height, mean (SD), cm	166.4 (1.8)	170.7 (9)
ASA status, no (%)		
3	1 (50)	9 (50)
4	1 (50)	9 (50)
Length of Surgery, mean (SD), min	338.5 (123.7)	346.5 (100.4)
Type of Surgery, no (%)		
Isolated CABG	1 (50)	8 (44.4)
Isolated valve	1 (50)	4 (22.2)
CABG + valve		5 (27.8)
Other		1 (5.6)


MULTIMODAL GENERAL ANESTHESIA
PREOPERATIVE
Preanesthetic assessment
Patient education about multimodal general anesthesia
INTRAOPERATIVE
MEDICATIONS
MONITORING
1) Routine anesthetic induction
2) Bilateral PIFB block with 20 mL of 0.25% Bupivacaine on either side of the sternum after anesthetic induction but before surgical incision
3) Ketamine (0.06 to 0.12 mg.kg/hr)
4) Remifentanil (0.05-0.2 mcg/kg/min)
5) Dexmedetomidine (0.2-1.0 mcg/kg/hr)
6) Rocuronium intermittent bolus (TOF)
7) Propofol infusion ± Sevoflurane titrated based on EEG monitoring
1) Standard cardiac monitoring
2) EEG monitoring (level of unconsciousness and titration of hypnotic drugs)
3) Neuromuscular junction monitoring (depth of neuromuscular blockade)
POSTOPERATIVE
1) Standard pain management protocol
• IV Acetaminophen 1gm x 8 doses at 6 hourly intervals
• IV Hydromorphone/fentanyl for rescue analgesia
• Other oral pain meds per standard of care (Oxycodone etc.)
2) Dexmedetomidine infusion 0.2-1.4 mcg/kg/hr (EEG guided)
3) Infusion continued till extubation
4) Propofol infusion may be added/used for sedation based on the treating physician's discretion


A Control
S
ST
H
BB
BE
CS
ICU
T_{supp} = 4.37 min
Frequency (Hz)
Power (dB)
Time (min)
B Multimodal Anesthesia
T_{supp} = 0.33 min
C
GA
B-S
50 μV
12 s
D
Fraction of Time from Induction to Closing Sternum in Suppression
Multimodal
AUC (mmHg min)
TWA (mmHg)
CV
Multimodal
Multimodal
Multimodal

Cardiovascular Anesthesiology-6

Comparative Analysis of Right Ventricular Transcriptome in Pulmonary Arterial Hypertension Animal Models

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Introduction: Right ventricular (RV) dysfunction is a significant prognostic determinant of morbidity and mortality in pulmonary arterial hypertension (PH). However, the underlying molecular mechanism of RV dysfunction secondary to PH remains unclear. To better understand its pathobiological characteristics, PH animal models have been used to study human PH. Here, we compare the RV transcriptome of two clinically relevant PH rat models with maladaptive RV remodeling.

Methods: Adults male Sprague Dawley rats received either a single subcutaneous injection of pulmonary endothelial toxin Monocrotaline (MCT group, 60mg/kg, n=7, followed 30-days), VEGF-receptor antagonist Sugen with 3-weeks of hypoxia (10% oxygen), followed by 2-weeks of normoxia (SU5416, 20mg/kg, SuHx group, n=7), or PBS for control (Ctrl, n=7). PH and RV failure were confirmed by echocardiography and RV-catheterization. RNA sequencing was performed on rat RV tissue, followed by differential expression and pathway analysis using a threshold of 0.05 for statistical significance (p-value). The p-value was corrected for multiple comparisons using false discovery rate and Bonferroni. Pathway analysis was done with hallmark gene sets. Real-time quantitative polymerase chain reaction (qRT-PCR) was used to confirm the RNA sequencing results.

Results: Both MCT and SuHx rats had severe PH, RV hypertrophy and RV dilation compared to Ctrl. RNA sequencing revealed 7,842 and 3,146 differentially expressed genes (DEG) in RV from MCT and SuHx groups compared to control, respectively, with significant overlap. The overlapping DEGs in RV exhibited a strong correlation between both animal groups. In addition, pathway enrichment analysis of DEGs in the RV from MCT and SuHx groups according to hallmark gene sets revealed 32 and 30 significant pathways, respectively, and 25 overlapping pathways. More specifically, both groups showed similar significant up-regulation of epithelial mesenchymal transition and TNFα signaling pathways, and down-regulation of fatty acid oxidation and oxidative phosphorylation pathways. We validated the RNA-sequencing with qRT-PCR by selecting several key dysregulated genes from epithelial mesenchymal transition (SPP1, CCN2), TNFA signaling (IL7R), oxidative phosphorylation (ACAT1, COX7B), fatty acid metabolism (DECR1, HSP90A), inflammation (C5AR1), and angiogenesis (S100A4). The qRT-PCR findings from RV tissue of independent MCT and SuHx groups (n= ≥6 rats per group) were consistent with sequencing results.

Conclusion: Our RV transcriptomic analysis of MCT and SuHx animal models identified similar patterns of gene expression changes. Targeting specific molecular mechanisms responsible for RV failure in both MCT and SuHx animal models may identify novel therapeutic strategies for PAH-associated RV failure.

Cardiovascular Anesthesiology-7

MicroRNA10b-5p Inhibition Rescues Severe Pulmonary Hypertensive Rats

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Introduction: Pulmonary hypertension (PH) is a fatal disease associated with pulmonary vascular remodeling that leads to right ventricular (RV) failure and death. While mir-10b-5p exerts pro-proliferative effects in various cancers via inhibition of its targets Cell Adhesion Molecule-1(CADM1) and Apoptotic Peptidase Activating Factor-1(APAF1), its role in PH is yet to be elucidated. We hypothesize that PH in rats is associated with upregulation of lung miR10b-5p and downregulation of its targets CADM1 and APAF1. Furthermore, inhibition of miR10b-5p may rescue pre-existing PH.

Methods: PH was induced in adult male Sprague Dawley rats (150-200 g) by either monocrotaline (MCT; 60 mg/kg single subcutaneous injection; n=4; followed for 30-days) or Sugen/Hypoxia (SU5416; 20 mg/kg single subcutaneous injection and 10% O2 hypoxia for 3-weeks followed by normoxia for 2-weeks; n=3). In vivo inhibition of miR10b-5p was performed from day 14-30 after MCT (5 intratracheal injections of miR10b-5p antagomir every 3-4 days; 5nM per injection; n=3). PBS treated MCT rats served as controls (n=5). Rats were followed via echocardiography. RV catheterization was performed terminally and RV hypertrophy index was calculated. MicroRNA microarray was performed to assess miR10b-5p levels in MCT rat lungs. Lungs were stained with trichrome to quantify pulmonary vascular remodeling. RT-PCR was performed to assess gene expression. Data is expressed as mean ± SEM. ANOVA was used to compare groups. P<0.05 was considered statistically significant.

Results: As expected, MCT and SU/Hx rats developed severe PH. MiRNA microarray data demonstrated a 3-fold increase in miR10b-5p levels in MCT rat lungs. RT-PCR demonstrated an increase in miR10b-5p in SU/Hx and MCT rat lungs. Furthermore, there was significant downregulation of miR10b-5p targets CADM1 (MCT 1.64-fold; Su/Hx 1.48-fold) and APAF1 (MCT 1.23-fold; Su/Hx 1.21-fold) in rat lungs. In vivo knockdown of miR10b-5p resulted in rescue of PH in MCT rats (RVSP: 50.7 ± 4.42 in antagomir vs. 95.81 ± 3.70 mmHg in placebo; p-value <0.005; RV hypertrophy index: 0.52 ± 0.02 in antagomir vs. 0.80 ± 0.07; p<0.05; RVID: diastolic 2.44 ± 0.68 in antagomir vs. 4.55 ± 0.42 mm; p<0.05). RT-PCR of lungs demonstrated 30% decrease in miR10b-5p expression of antagomir-treated rats. Histological analysis revealed that miR10b-5p antagomir treatment resulted in significantly decreased pulmonary arteriolar wall thickness (32.72 ± 1.12 in antagomir vs. 42.24 ± 3.26 % in placebo, p<0.005).

Conclusion: Pre-clinical PH is associated with an increase in miR10b-5p expression and decrease in its targets CADM1 and APAF1. MiR10b-5p inhibition rescues experimental PH and may serve as a novel therapeutic target.

Cardiovascular Anesthesiology-8 Proteomic Changes Associated with Cardiopulmonary Bypass for Coronary Artery Bypass Surgery

Justin C De Biasio[1], Shahzad Shaefi[1], Edward Marcantonio[1], Balachundhar Subramaniam[1], Puja Shankar[1], Towia A Libermann[1], Simon Dillon[1]

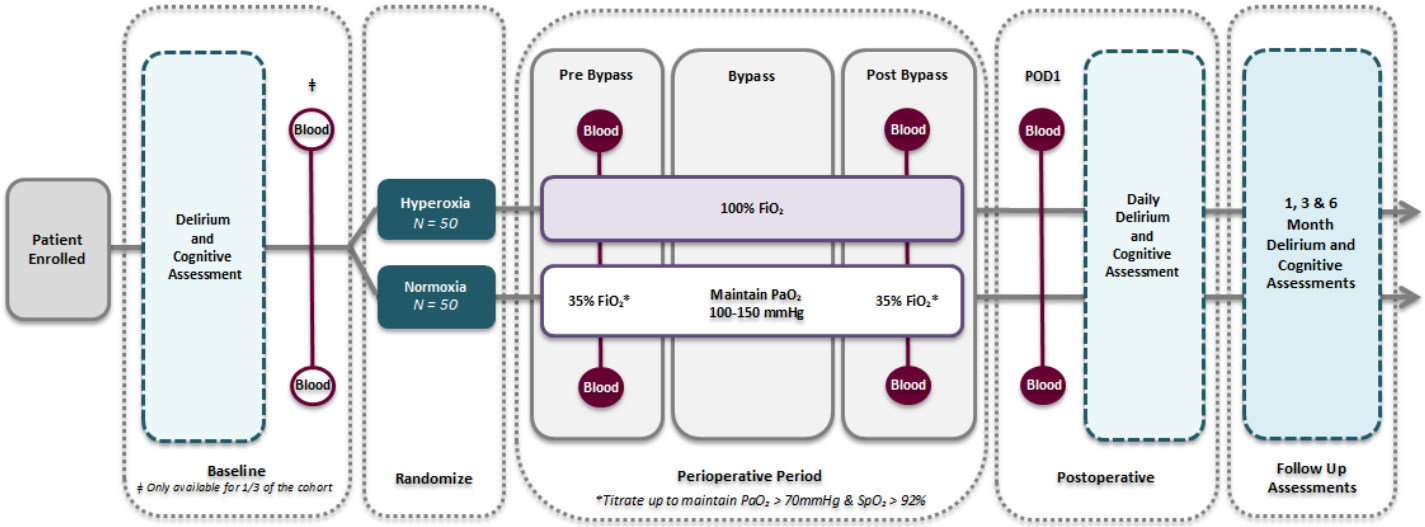
[1]Beth Israel Deaconess Medical Center, Boston, MA

Introduction: The physiologic consequences of cardiopulmonary bypass for coronary artery bypass and other cardiac surgical procedures are substantial. In particular, the Inflammatory and hemostatic changes of cardiopulmonary bypass are well recognized, and procedures utilizing cardiopulmonary bypass require the effective management of such anticipated effects. While it is understood that cardiopulmonary bypass causes substantial changes in general, a more thorough appreciation of these effects may be possible with a systematic analysis of the plasma proteome in this setting. Identifying proteomic changes associated with cardiopulmonary bypass for coronary artery bypass surgery may help to determine the pathophysiology of particular adverse outcomes associated with this procedure.

Methods: In a secondary study of a randomized controlled trial comparing higher and lower concentrations of inspired oxygen in patients undergoing coronary artery bypass surgery with cardiopulmonary bypass, we analyzed previously collected and stored plasma samples from a subset of the study population. A total of 48 sets of samples were analyzed; the subset was comprised of pairs of subjects with and without postoperative delirium matched by age, sex, and preoperative Telephone-Montreal Cognitive Assessment (t-MoCA) score. Each plasma sample was analyzed with the aptamer-based proteomics assay SOMAscan (SomaLogic Inc, Boulder, CO) to determine the plasma concentration of >1300 proteins before and immediately after cardiopulmonary bypass. To determine the impact of cardiopulmonary bypass, relative fold-change comparing post-bypass to pre-bypass plasma protein concentration was determined. Using the Wilcoxon rank-sum test with Benjamini-Hochberg correction for multiple hypothesis testing, statistical significance was evaluated. A p-value less than 0.01 was considered significant. Systems biology analysis was performed using Ingenuity Pathway Analysis (Ingenuity Systems, Redwood City, CA) to evaluate the pathways most significantly altered by cardiopulmonary bypass.

Results: Among those proteins with statistically significant change in concentration from pre-bypass to post-bypass, there were 48 proteins that exhibited a greater than 2-fold increase and 14 proteins that exhibited a greater than 2-fold decrease. Systems biology analysis of these proteins identified disproportionate involvement of a large number of inflammation- and hemostasis-related pathways.

Conclusion: Major changes in plasma protein concentrations occur during cardiopulmonary bypass in the context of coronary artery bypass surgery. These changes particularly reflect alterations in inflammatory and hemostatic pathways. The substantial number and degree of large changes in protein concentration observed in this context offer several candidate proteins for further evaluation that may ultimately offer improved prognostication and management of patients who undergo procedures that utilize cardiopulmonary bypass.


Patient Enrolled
Delirium and Cognitive Assessment
‡
Blood
Blood
Baseline
‡ Only available for 1/3 of the cohort
Hyperoxia N = 50
Normoxia N = 50
Randomize
Pre Bypass
Bypass
Post Bypass
Blood
Blood
Blood
Blood
100% FiO₂
35% FiO₂*
Maintain PaO₂ 100-150 mmHg
35% FiO₂*
Perioperative Period
*Titrate up to maintain PaO₂ > 70mmHg & SpO₂ > 92%
POD1
Blood
Blood
Daily Delirium and Cognitive Assessment
Postoperative
1, 3 & 6 Month Delirium and Cognitive Assessments
Follow Up Assessments

Critical Care

Critical Care-1 Functional Mobility predicts Readmission to the Surgical Intensive Care Unit

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Introduction: Readmission to the intensive care unit (ICU) is associated with a higher risk of in-hospital mortality, prolonged hospital stay and increased healthcare utilization.[1-3] We hypothesized that patients' functional mobility level in the ICU predicts ICU readmission.

Methods: This observational study examined adult surgical ICU patients hospitalized between 2015 and 2018 at an academic tertiary care center. Functional mobility was quantified by the maximum Johns Hopkins Highest Level of Mobility score (JH-HLM) during the ICU stay. The primary outcome was ICU readmission within the same hospitalization. We tested two primary hypotheses: We hypothesized that maximum functional mobility as well as a fast speed of functional mobility progress are associated with a lower risk of ICU readmission. Speed of functional mobility progress was based on daily maximum values. Further, we tested the secondary hypotheses that the speed of progress predicts readmissions to the ICU better than the maximum value and that these functional mobility measures have a higher predictive value than respective measures of the Glasgow Coma Scale (GCS) and the Medical Research Council Strength Score (MRC). With an exploratory intent to further understand the association of functional mobility and readmission, the endpoint was divided into predefined subcategories depending on the primary reason for readmission. Confounder-adjusted multivariable logistic regression and c-statistics were used for prediction of ICU readmission.

Results: In our cohort of 9,605 SICU patients, 401 (4.17%) got readmitted to the ICU (Table 1, Figure 1). Low compared to high maximum functional mobility and speed of functional mobility progress were independently associated with higher risk of ICU readmission (adjusted absolute risk difference for lowest compared to highest maximum functional mobility: 1.54 (0.42-2.66) %). The speed of progress was a better predictor than maximum functional mobility (AUC 0.65 [95% CI, 0.62-0.67] vs. 0.59 [95% CI, 0.57-0.62], p<0.001). Both functional mobility measures outperformed GCS and MRC measures (p<0.001, Figure 2). Low functional mobility was most strongly associated with respiratory-related ICU readmissions. (aOR 3.00 (1.42-6.33), p=0.004).

Conclusion: High maximum functional mobility and fast speed of functional mobility progress are associated with a lower risk of ICU readmission. Patients' functional mobility level in the ICU may be utilized as a marker of discharge readiness.

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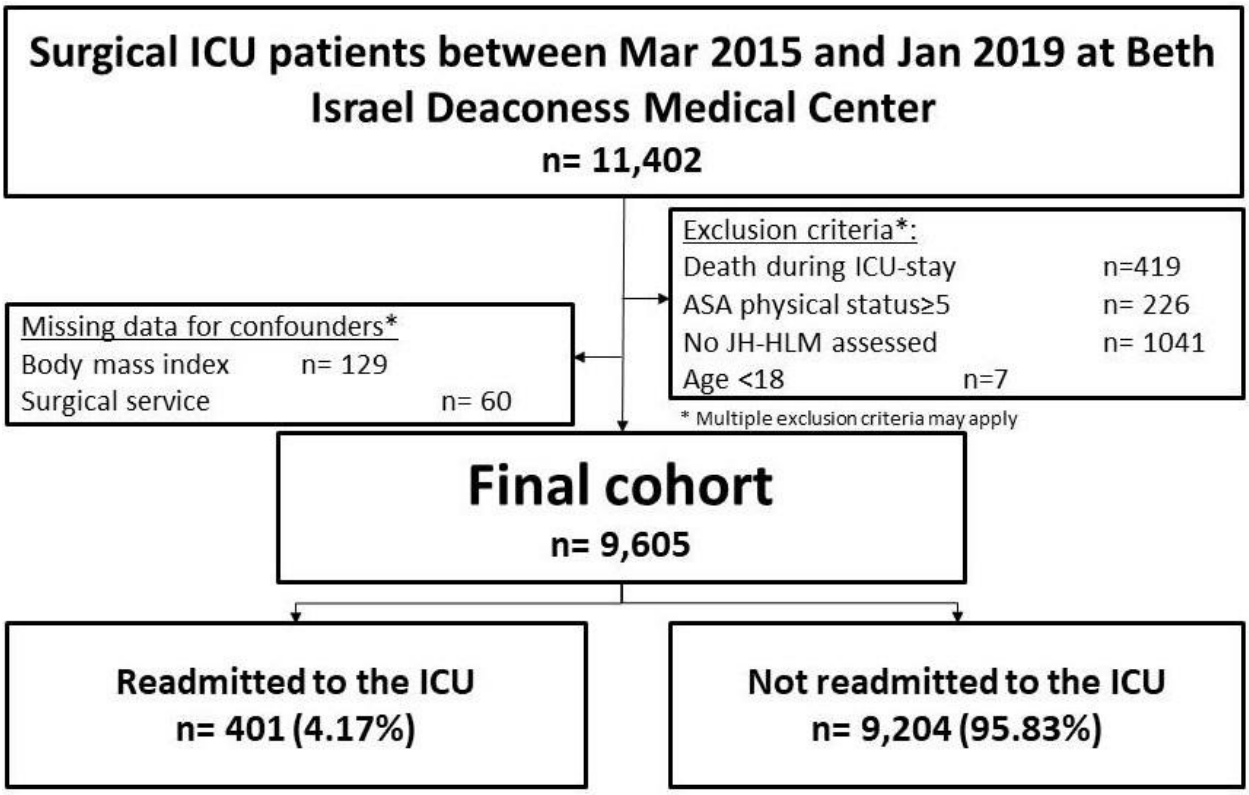
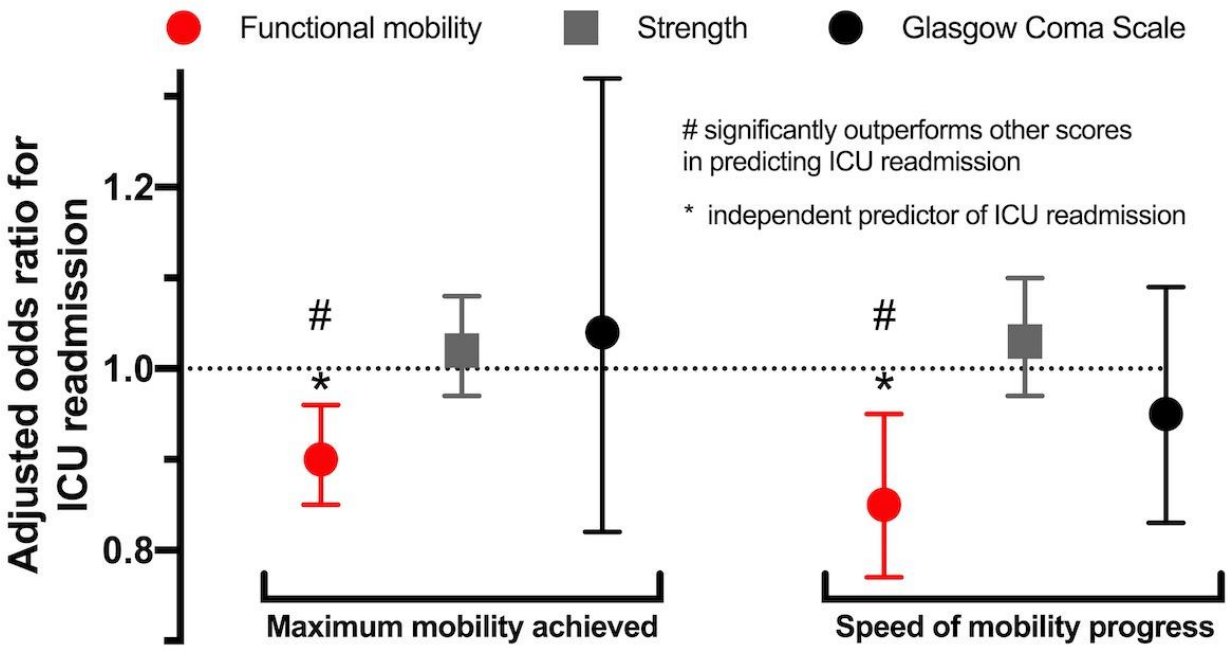


Table 1: Cohort Characteristics	Walk (JH-HLM 6-8)	Stand (JH-HLM 5)	Chair (JH-HLM 4)	Bed (JH-HLM 1-3)
N, (%)	3618 (37.7)	1982 (43.0)	2144 (22.3)	1861 (19.4)
ICU-readmission, (%)	100 (2.8)	92 (4.6%)	101 (4.7%)	108 (5.8%)
Demographics				
Age, mean ±SD	62.9 ± 14.8	65.5 ± 14.2	66.2 ± 14.0	63.9 ± 16.1
Male, (%)	2123 (58.7)	1264 (63.8)	1253 (58.4)	986 (53.0)
BMI, mean ±SD	28.43 ± 6.40	28.87 ± 6.61	28.96 ± 7.07	28.62 ± 7.60
APACHEII, mean ±SD	16.31 ± 6.00	18.24 ± 5.79	18.74 ± 6.00	16.64 ± 6.46
Frost et al. Score	27.0 ± 12.1	29.6 ± 12.9	30.41 ± 14.1	31.0 ± 13.1
Source of Admission				
Operating room, (%)	2544 (70.3)	1280 (64.6)	1386 (64.6)	877 (47.1)
Emergency department, (%)	494 (13.7)	292 (14.7)	353 (16.5)	494 (26.5)
Floor, (%)	406 (11.2)	286 (14.4)	258 (12.0)	332 (17.8)
Other Hospital, (%)	174 (4.8)	124 (6.3)	147 (6.9)	158 (8.5)
Emergency admission, (%)	589 (16.3)	393 (19.8)	466 (21.7)	519 (27.9)
Length of ICU stay, mean ± SD	4.26 ± 5.25	4.35 ± 6.55	5.33 ± 9.03	3.13 ± 4.34
Surgical and ICU-specific factors				
Acute renal failure, (%)	148 (4.1)	119 (6.0)	141 (6.6)	183 (9.8)
Delirium, (%)	841 (23.2)	620 (31.3)	761 (35.5)	695 (37.3)
Need of vasopressors, (%)	718 (19.8)	545 (27.5)	602 (28.1)	343 (18.4)
Mechanical ventil., (%)	1846 (51.0)	1263 (63.7)	1425 (66.5)	709 (38.1)
Abdominal, (%)	542 (15.0)	481 (24.3)	481 (22.4)	665 (35.7)
Cardiac, (%)	1435 (39.7)	861 (43.4)	866 (40.4)	154 (8.3)
Neurosurgery, (%)	463 (12.8)	91 (4.6)	153 (7.1)	177 (9.5)
Orthopedic, (%)	86 (2.4)	95 (4.8)	142 (6.6)	323 (17.4)
Other, (%)	208 (5.7)	147 (7.4)	166 (7.7)	167 (9.0)
Thoracic, (%)	215 (5.9)	115 (5.8)	84 (3.9)	59 (3.2)
Vascular, (%)	669 (18.5)	192 (9.7)	252 (11.8)	316 (17.0)

Figure 2


Functional mobility
Strength
Glasgow Coma Scale
significantly outperforms other scores in predicting ICU readmission
* independent predictor of ICU readmission
Adjusted odds ratio for ICU readmission
1.2
1.0
0.8
#
*
#
*
Maximum mobility achieved
Speed of mobility progress

Critical Care-2 Anesthesia resident preparedness for palliative care conversations in the ICU

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Introduction: There is a growing need for palliative or end of life (EOL) care in our aging population. While these conversations would ideally begin in the outpatient setting with primary care providers, there is not always time or a desire to have them. Families often find themselves dealing with EOL issues by surprise in the hospital setting. Anesthesiologists and anesthesia residents play a significant role in EOL care both in the operating room (OR) and as intensivists in the intensive care unit (ICU). , As a specialty, we have described the need for our presence during EOL conversations and management. , Despite this, there is little published literature describing anesthesia residents' preparedness, comfort, or training with EOL conversations and palliative care. The purpose of this study is to survey anesthesia residents to help better define their perceived confidence and deficiencies in EOL training.

Methods: We developed a twenty-question survey specific to the ICU from studies that have explored this topic in other physician populations. Residents were asked to provide their thoughts about their preparedness to handle palliative care conversations, and their attitudes toward EOL care and training. The survey was sent out to all of the anesthesia residency program directors across the nation via email, and subsequently distributed to residents via program listservs. Residents at all stages of training (CA-0 to CA-3) were included.

Results: We received a total of 105 responses to the survey, from 9 CA-0s, 36 CA-1s, 40 CA-2s, and 20 CA-3s. 63% were male and 36% were female. 35% of the respondents had cared for more than 20 dying patients, but 40% had only cared for 3-10 dying patients. 94% of the respondents had attended at least 1-2 family meetings during their ICU experiences, but 43% reported that they had never conducted a family meeting. Respondents were split evenly on their comfort level with leading a family EOL discussion, but responses clearly delineated the residents perceived need for more education and the importance of EOL skills to their future practice. (Fig) Logistic regression identified the number of previously attended EOL family discussion >3 as an independent predictor of increased comfort with leading an EOL discussion (OR 15.9, 05% CI 2.5 to 56.3) compared with attendance of < 1. Characteristics of the respondents including gender, level of training, race, ethnicity, religious beliefs, months rotating in ICU, and prior care of dying patients were not found to be significant predictors of increased comfort with initiating EOL discussions.

Conclusion: Although the distribution of responses between residents who were comfortable and uncomfortable with handling goals of care conversations in the ICU was relatively even, there was clear desire for more training and a feeling that EOL training in general was insufficient. Although we expected the level of comfort in handling EOL discussions would increase with the level of training, the primary predicator of increased comfort was the number of EOL discussions to which residents had been previously attended. Moving forward, we plan to increase exposure to EOL discussion as well as learning activities and provide feedback to trainees to help address these potential deficiencies identified in this study.

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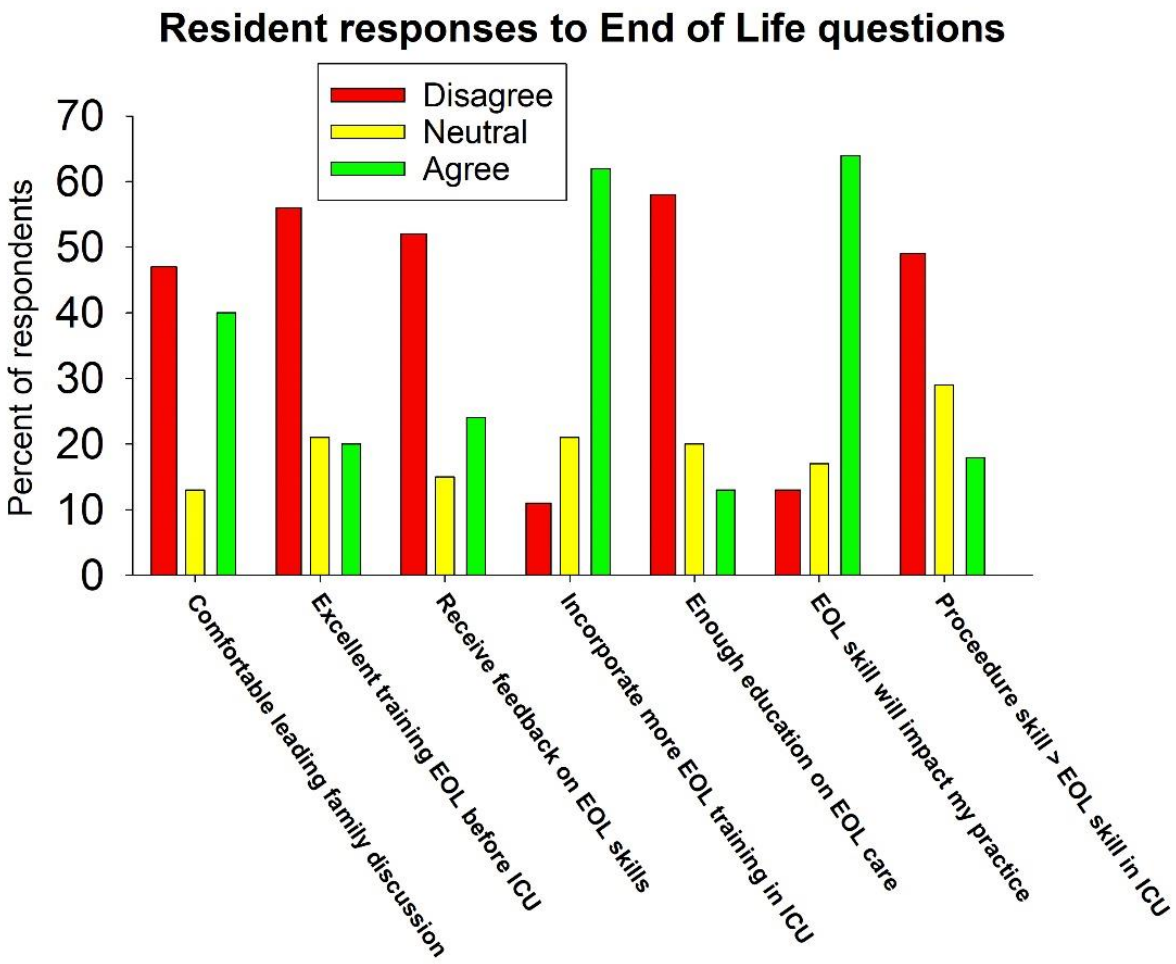
Resident responses to End of Life questions
Disagree
Neutral
Agree
Percent of respondents
70
60
50
40
30
20
10
0
Comfortable leading family discussion
Excellent training EOL before ICU
Receive feedback on EOL skills
Incorporate more EOL training in ICU
Enough education on EOL care
EOL skill will impact my practice
Proceedure skill > EOL skill in ICU

Critical Care-3 Inotropic and LVAD therapy for heart failure alter coherence between macro- and microcirculation

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Introduction: Studies have demonstrated incoherence between microcirculatory perfusion and macrovascular hemodynamics in both normal physiology and pathophysiologic states [1]. Hemodynamic coherence has not been well characterized in heart failure (HF) using modern techniques. The purpose of this study was to compare peripheral capillary perfusion with routine hemodynamic variables in healthy controls and a cohort of advanced HF patients receiving inotropic or left ventricular assist device (LVAD) support. We also explored the impact of LVAD pump settings on these circulatory parameters.

Methods: This was a prospective, observational, and single center study. Inclusion criteria were adult age and LVAD surgery. The main exclusion criterion was consent refusal. We recruited 14 HF patients who underwent HeartMate 3 LVAD implantation from 11/2018 - 6/2019. Sublingual microcirculation was studied using the Cytocam-IDF camera before and after LVAD surgery (mean 0.9 and 34 days, respectively). None of the patients were in shock and all but one were receiving inotropic therapy. Additionally, 7 healthy volunteers were separately studied as controls. Videos were analyzed using automated, validated software. Microvascular parameters included total vessel density (TVD), functional capillary density (FCD), proportion of perfused vessels, and mean red blood cell velocity (RBCv). Hemodynamic parameters included systolic, diastolic, and mean arterial blood pressure (MAP) as well as pulse pressure and heart rate (HR). Correlation was tested using linear regression analysis.

Results: There was a negative correlation between MAP and RBCv in healthy controls ($R2 = 0.6$; $p<0.05$) but not in HF or LVAD patients. There was also a positive correlation between HR and TVD in healthy controls ($R2 = 0.7$; $p<0.05$) and HF patients ($R2 = 0.5$; $p<0.01$) but not LVAD patients. A similar positive correlation between HR and FCD was noted only in HF patients ($R2 = 0.5$; $p<0.01$). No other hemodynamic parameters were associated with any other microvascular variables. Likewise, LVAD pump flow and RPM were not associated with either micro- or macrovascular parameters.

Conclusion: Microcirculatory and hemodynamic variables differentially correlated with one another between healthy controls and HF patients treated with either inotropic or LVAD support. Together with our previous observation of increased RBCv in HF patients, our finding of decreased RBCv with increased MAP only in healthy controls suggests that chronic cardiovascular disease, fluid overload, and/or advanced treatment is associated with a loss of micro- to macrocirculatory coherence and possibly autoregulation. This is in agreement with previous observations in compensated HF outpatients [2,3] and inpatients stabilized after cardiogenic shock [4]. The persistence of this hemodynamic incoherence in ready-for-discharge LVAD patients is a novel observation and may contribute to the increased incidence of adverse events like stroke and gastrointestinal bleeding [5].

Reference(s):

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Critical Care-4 Post heart surgery MO characteristic is pro-atherosclerotic at three months after elective coronary artery bypass surgery.

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Introduction: Coronary artery bypass graft (CABG) is performed frequently on a semi-elective basis to improve myocardial perfusion. However, the inflammation in the aftermath of the surgery does not resolve quickly as previously thought. In particular, monocyte (MO) exhibit altered responsiveness for several months after surgery. Consequently, their abnormalities in characteristic and performance profile may affect pivotal elements of the atherosclerotic process. A higher prevalence of inflammatory or atypical MOs supports the progression of atherosclerosis, especially if oxidized LDLs are present. Overall, these may create condition accelerating atherosclerosis and potentially limits benefits of CABG.

Methods: We explored the duration of immune activation up until three months after trauma by utilizing the longitudinal assessment of immune system response to quantify the insult of heart surgery. We conducted a study of the responsiveness of MOs obtained from humans (n=34) before (tbase), 24 hours (t24h), seven days (t7d), and three months (t3m) after elective heart surgery. Isolated MOs were stimulated with LPS (50ng/ml) and HMGB1 (200ug/ml) for 18 hours. Additionally, we analyzed the transcriptome activity of circulating MOs by RNA-seq. RT-PCR, flow cytometry, and ELISA were utilized to confirm RNA-seq results and define atypical, atherogenic MO (†‘†‘†‘M-CSF,†‘†‘†‘OLR1). Finally, we analyzed epigenetic changes in gene promoters using the bisulfite technique.

Results: Analysis of the RNA-seq data revealed that several genes involved in MO lipid processing and atherosclerosis were altered during the post-CABG aftermath, even at three months post-surgery (Figure). We demonstrated that the OLR1 receptor is particularly elevated three months after surgery (p=0.021). CD36 expression was elevated shortly after surgery and returned to the pre-CABG level at three months. Concomitantly, the serum level of OLR1 was elevated. Interestingly, the expression of OLR1 by MO in response to LPS unaltered at t3m depressed in response to HMGB1 at three months (Figure). In contrast, pre-surgery MOs responded to HMGB1 exposure with increased expression of LOR1 (Figure). M-CSF production was exaggerated at 3months in response to LPS (Me; M-CSFbase=68.72 vs M-CSFt+3m=319.90*; p=0.033) and HMGB1 (Me; M-CSFbase=19.72 vs M-CSFt+3m=128.35*; p=0.037). Uptake of oxLDL correlated with an increase in expression of the OLR1 receptor. Finally, changes in methylation of the studied gene promoters or gene's promoter persisted at 3 three months, suggesting a potential underlying reason for persistent expression.

Conclusion: Here, we demonstrated that conditions created in open-chest heart surgery with the application of a cardiopulmonary bypass machine results in a prolonged MO atherosclerotic condition extending beyond traditionally understood surgery. These characteristics can interfere with full benefits of surgery.

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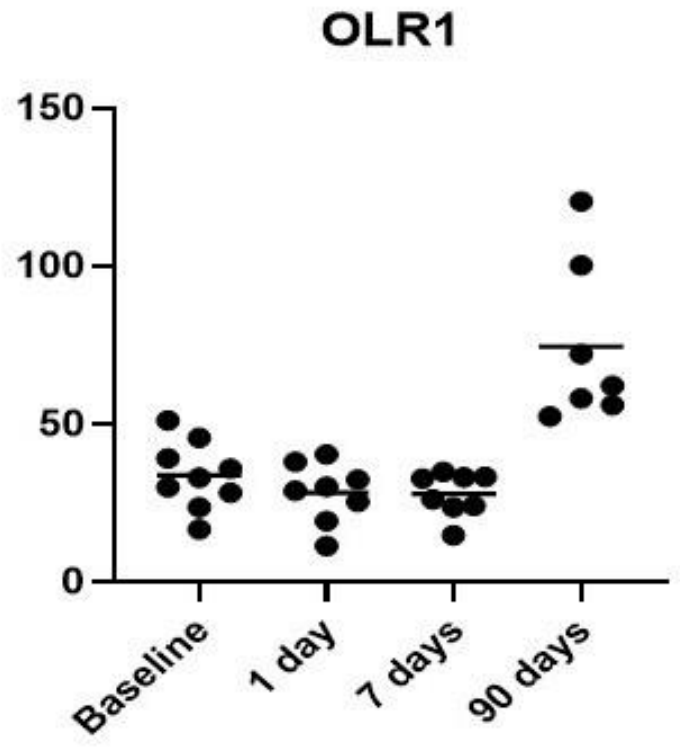
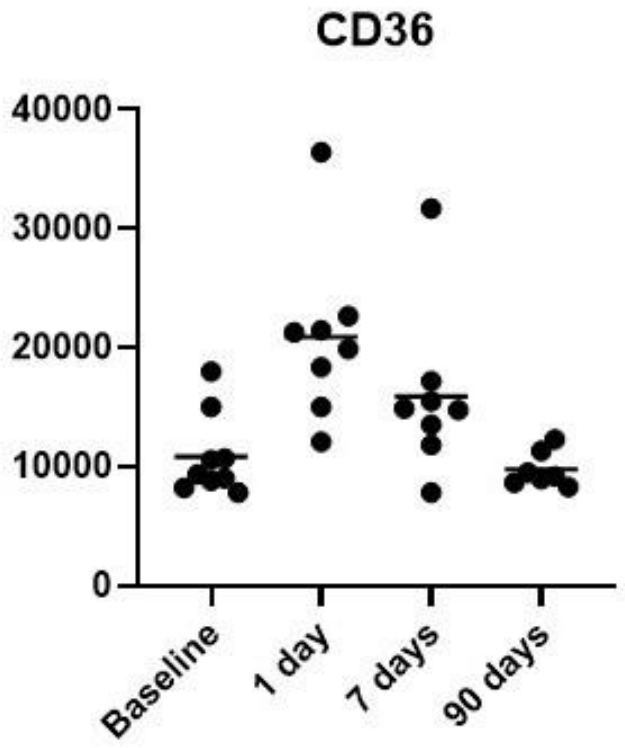
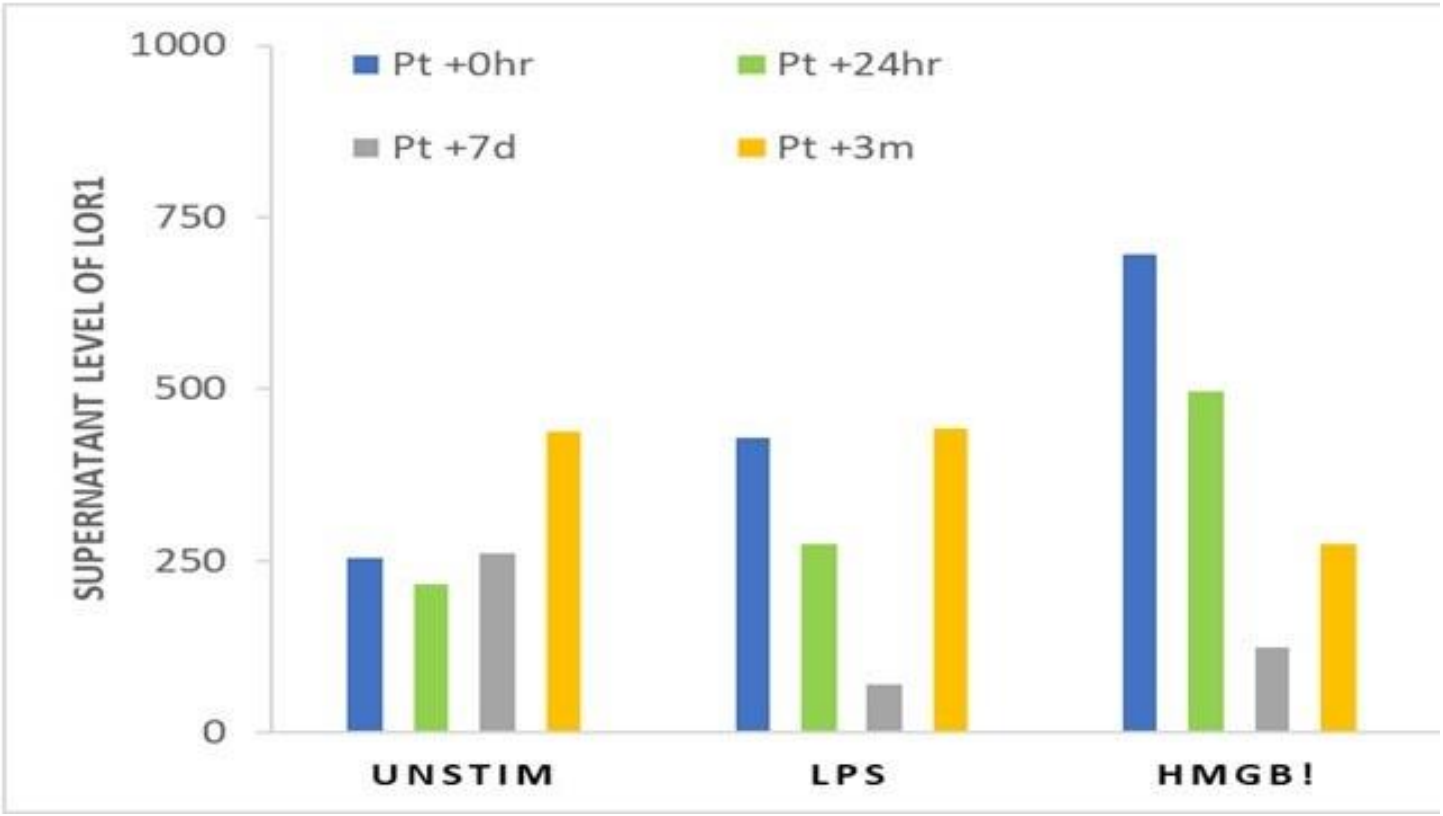

OLR1
150
100
50
0
Baseline
1 day
7 days
90 days


CD36
40000
30000
20000
10000
0
Baseline
1 day
7 days
90 days


1000
750
500
250
0
SUPERNATANT LEVEL OF LOR1
Pt +0hr
Pt +24hr
Pt +7d
Pt +3m
UNSTIM
LPS
HMGB!

Critical Care-5 Isoflurane and Ketamine Differentially Impact Survival, Inflammatory Lung Damage and Bacterial Counts in a Murine Model of Pseudomonas aeruginosa Pneumonia

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Introduction: The inhalational anesthetic isoflurane impacts immune system function1,2 and bacterial phenotypes3. Isoflurane can positively impact survival in bacterial peritonitis4,5 and shows protective effects on lung structure in inhaled lipopolysaccharide (LPS) challenge6, but the impact of different anesthetics on the course of infectious pneumonia is unknown6. Here we use a murine model of Pseudomonas aeruginosa pneumonia to determine the effect of two common anesthetics on survival and histopathological and microbiological measures of disease severity.

Methods: Studies were approved by the UC San Diego IACUC. Eight to 10-week-old outbred CD-1 mice were infected intratracheally with 2.7-5x107 colony-forming units (CFU) of logarithmic growth phase P. aeruginosa while receiving either ketamine anesthesia, isoflurane anesthesia (n = 16 mice over two experiments), or a combination of both (n = 8 mice); survival was measured for 4 days in 2 independent experiments with 8 mice in each group (total of 16 mice for the first and 24 mice for the second experiment). In a third experiment, mice were anesthetized with either ketamine/xylazine, isoflurane or a combination of both (n = 8 per group) and euthanized 12 h post infection, at which point lung tissue was harvested, with a portion selected for histopathology analysis scored by a blinded veterinary pathologist, while the remaining lung tissue was homogenized, diluted and plated for bacterial CFU enumeration. Blood was also analyzed for evidence bacterial dissemination.

Results: In the initial P. aeruginosa lung challenge experiment 7/8 mice died in the ketamine/xylazine group by the experimental endpoint (day 4), while 3/8 died in the isoflurane group. In a second P. aeruginosa challenge, all mice in the ketamine/xylazine group died within 24 h, while 3/8 survived for 4 days in the isoflurane group or the ketamine/xylazine plus isoflurane groups. When mice were euthanized 12 h post challenge, the isoflurane alone group showed significantly lower bacteria recovery in CFU/gm lung) compared to either ketamine alone, p = 0.0141) or the isoflurane plus ketamine/xylazine group, p = 0.0018); statistical analysis by Kruskal Wallis test. Moreover, bacteremia (blood) was also reduced in the isoflurane group compared to the ketamine/xylazine group p = 0.0165). Histopathological evaluation by a veterinanry pathologist blinded to treatment groups revealed significantly less inflammation, bacterial burden and tissue necrosis in the isoflurane group compared to the ketamine group.

Conclusion: We illustrate a potential differential impact of isoflurane vs ketamine/xylazine on murine survival, lung inflammatory damage and bacterial counts in murine P. aeruginosa pneumonia model. We are conducting follow-on studies to dissect the mechanism of this effect, which could include inhibitory effects of isoflurane or augmenting effects of ketamine on bacterial virulence and/or augmenting effects of isoflurane or inhibitory effects of ketamine on pulmonary innate immune functions. In the setting of rising antibiotic resistance, it is of utmost importance to optimize treatment conditions for our most critically ill patients suffering infections including the drugs commonly prescribed in the intensive care unit and surgical settings. Our study suggests that anesthetics may influence infectious disease phenotypes and merits further investigation.

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Critical Care-6 Novel Machine Learning Model to Predict Intensive Care Unit Readmission or Mortality After Cardiothoracic Surgery

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Introduction: Patients readmitted to the intensive care unit (ICU) after transfer to a lower acuity care unit demonstrate increased mortality, length of stay, and healthcare expenditures compared to those never readmitted.(1,2) In high acuity specialized units, such as the cardiothoracic ICU (CTICU), identifying patients at highest risk of readmission and subsequent complications is challenging. Traditional rule-based risk tools overpredict complications, illustrating the need for dynamic means of prediction.(3) Machine learning models have demonstrated improved success at identifying patients at risk for ICU readmission.(4) However, these models use datasets from a variety of different ICU types (e.g. surgical vs. medical), which limits specificity. We hypothesized that machine learning-based models will accurately discriminate cardiothoracic surgical patients at high risk for CTICU readmission or death within two weeks of discharge.

Methods: A dataset was curated to include 5559 encounters of patients between August 2015 and October 2018 who underwent cardiothoracic surgery then survived to initial CTICU discharge. Input features included both patient derived data such as past hospitalizations, and laboratory values along with provider actions such as orders and procedures performed (Table 1). The primary outcome was a composite of ICU readmission or mortality within 14 days of initial discharge from the CTICU (Figure 1). The model was trained using LightGBM (a gradient boosting method using tree-based learning algorithms) and compared to a logistic regression (LR) using sk-learn. Model performance was evaluated using 500 iterations of bootstrapping on a test split of 30% to calculate a 95% CI, and compared across three metrics: area under the receiver-operating characteristic curve (AUC), area under the precision-recall operating curve (AUPRC), and positive predictive value (PPV) at a fixed sensitivity of 20%.

Results: Of the 5559 encounters, 564 (10%) demonstrated decompensation or death within 14-days of discharge from the CTICU. The LightGBM model performed best compared to logistic regression (LR) across precision-recall and positive predictive value performance measures. AUCs were 0.834 ± 0.001 for LightGBM and 0.851 ± 0.001 for LR. The AUPRC was 0.400 ± 0.004 for LightGBM and 0.360 ± 0.003 for LR. Finally, the PPV at a fixed sensitivity of 20% was 0.568 ± 0.007 for LightGBM, compared to 0.405 ± 0.003 for LR.

Conclusion: A novel machine learning model achieves good discrimination in identifying post-cardiothoracic surgical patients at risk of ICU readmission or mortality. Compared to methods using only snapshot measurements, this model strengthens its predictions by integrating grouped trends data from multiple source domains - both related to patient-specific disease processes along with interventions (medication profiles, treatments, actions and orders) performed by the clinical team. Accurate prediction of unplanned readmission could be used in decision support tools to inform ICU discharge readiness and target resources for step-down unit care (increased patient surveillance), especially for high-risk patients requiring complex discharge planning.

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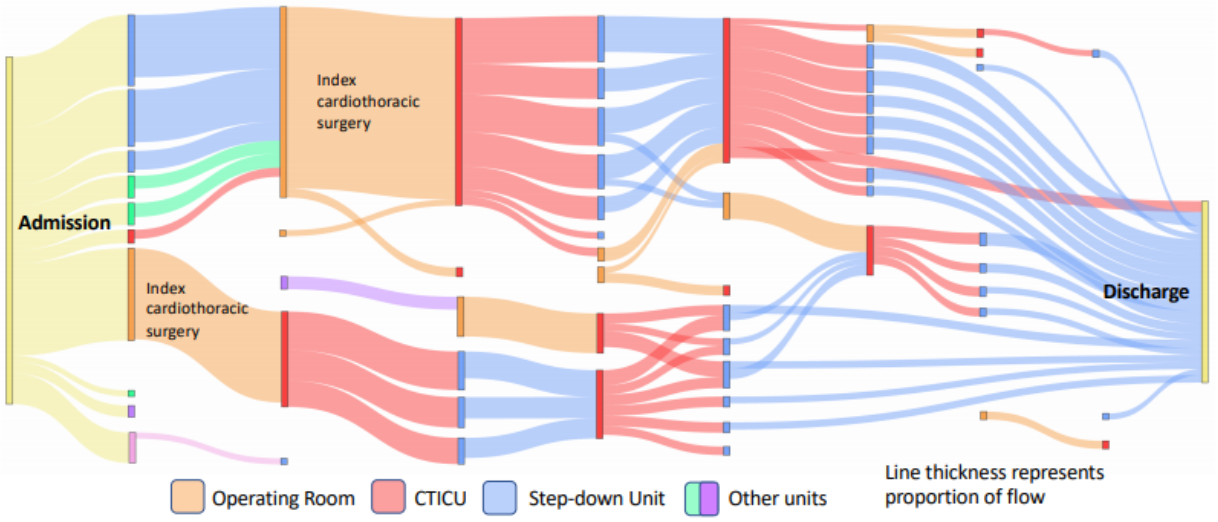

Figure 1. CTICU readmission phenotype: flow of encounters readmitted to the CTICU during index hospitalization. Readmission to the CTICU complicates hospital stay and often results in several transitions of care between the CTICU (red) and step-down units (blue). Avoiding these cycles through the identification of patients at risk (both by refining ICU discharge readiness and increase surveillance in step-down unit) could reduce the length of stay, complications, and improve patient mortality and failure to rescue rates.

Table 1. Multiple domain input features for ML model of patient decompensation (CTICU readmission or mortality)

Features (number of data elements)	**Variables**
I. Patient-specific disease processes, grouped trends	
Demographics (2)	Age, Gender
Encounter Info (10)	(12 and 3 month) Count of General Admissions, ED Visits and CTICU Admissions; Length of Stay in CTICU and/or Hospital Admission
Comorbidities (282)	Clinical Classification Software of ICD-10 Codes*
Laboratory Values† (25)	Albumin, ALT, Ammonia, Anion Gap, Arterial Bicarbonate, Arterial PCO_2, Arterial pH, AST, Bands, BUN, Creatinine, CRP, ESR, Fibrinogen, Glucose, Hematocrit, Hemoglobin A1c, INR, Lactate, LDH, Magnesium, OR Arterial PO_2, Platelets, Potassium, Sodium, Venous PCO_2
Physiologic Measures† (11)	Blood Pressure, BMI, Cardiac Index, Cardiac Output, Height, Level of Consciousness, Pulse, Pulse Oximetry, Respiratory Rate, Urine Output, Weight
Patient status‡ (4)	Delirium, Dyspnea, Hypothermia, Length of Stay, Stroke Work-up
II. Clinical interventions (medication profiles, treatments, actions and orders), grouped trends	
End Organ Support‡ (9)	Bilevel Positive Airway Pressure, Continuous Positive Airway Pressure, Continuous Renal Replacement Therapy, Extracorporeal Membrane Oxygenation, Impella, Intra-aortic Balloon Pump, Mechanical Ventilation, Ventricular Assist Device (VAD) (durable), VAD (temporary)
Orders for labs‡ (8)	Arterial Blood Gas, Blood Typing, Coagulation Panel, Cytomegalovirus, Human Papilloma Virus, JC virus, PT, INR, Toxoplasmosis, Sputum Culture
Orders of procedures/status changes‡ (12)	Arterial Line Insertion, Arterial line Removal, Chest Tube Placement, Intubation, NPO, Peripherally Inserted Central Catheter (PICC) insertion, PICC Removal, Stroke Workup, Tracheostomy Placement, Transfusion (Fresh frozen plasma/Platelet/RBC/Cryoprecipitate), VAD Placement, Wound Care
Orders for imaging/monitoring‡ (6)	Chest Radiograph, ECG, Echocardiogram, Kidneys Urine Bladder Radiograph, Telemetry, Ultrasound (any)

*-Classification categories listed at:
https://www.hcup-us.ahrq.gov/toolssoftware/ccs10/CCSCategoryNames(FullLabels).pdf

†-numeric data summarized over encounter using: max, min, mean, standard deviation, 1st quartile, 3rd quartile number of entries, time of first order, time of last order

‡-boolean event data summarized over encounter using: any event occurred, number of events, time of first event, time of last event

Critical Care-7 Echocardiographic Assessment Using Subcostal-Only View in Advanced Life Support (EASy-ALS): Feasibility of and Obstacles to Implementation in the In-Hospital Setting

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Introduction: Traditionally, echocardiography is performed by a technician and later interpreted by a cardiologist. Focused cardiac ultrasound (FOCUS) is different because it allows physicians in fields including anesthesiology to immediately assess and manage critically-ill patients [1]. High-quality cardiopulmonary resuscitation (CPR) is the backbone of resuscitation, but the American Heart Association [2] suggests FOCUS can be used to identify potentially reversible causes of cardiac arrest in patients with pulseless electrical activity (PEA). In the out-of-hospital setting, application of FOCUS to ALS was found effective in distinguishing true PEA (without wall motion) from pseudo-PEA (with wall motion); it also allowed identification of treatable conditions such as hypovolemia and pericardial effusion [3]. We applied ALS-compliant FOCUS to the in-hospital setting as echocardiographic assessment using subcostal-only view in ALS (EASy-ALS). We trained anesthesiology attendings and residents in FOCUS and EASy-ALS with a modified previously-described curriculum [4-6], allowing us to integrate FOCUS into peri-resuscitative management while exploring the feasibility of its performance after limited training and identifying obstacles to its routine implementation.

Methods: We explored the feasibility of anesthesiology attendings and residents performing FOCUS and EASy-ALS. A total of 29 patients were examined from December 2016 to December 2019. Patients were evaluated in the peri-resuscitative period, defined as a period of profound hypotension, cardiac arrest, or return of spontaneous circulation (ROSC). Patients for whom FOCUS could not be safely performed were excluded. Providers performed EASy-ALS exams after completion of a course consisting of didactics, hands-on practice, and simulation. EASy-ALS protocol is as follows. A provider is contacted by call from the primary service or overhead Code Blue page. On arrival, the provider places the ultrasound probe on the chest without obstructing chest compressions. The exam is performed during the pulse/rhythm check, never exceeding 10 seconds. After resumption of chest compressions, the provider interprets images and relays findings. Afterwards, the provider completes a report documenting indication for exam, initial cardiac rhythm, FOCUS findings, and immediate patient outcome. Descriptive statistics were used to summarize EASy-ALS exam findings. Cases in which diagnostic quality images were obtained, as determined by a FOCUS-credentialed attending anesthesiologist, were presented as a proportion.

Results: Data were collected for 29 patients. Indications for EASy-ALS included PEA (48%), post-ROSC (24%), pre-arrest (14%), asystole (7%), and pulseless ventricular tachycardia (7%). Image quality was good in 72% of cases and adequate in the rest. Major findings included absence of cardiac causes of event (45%), right ventricular syndrome (17%), severe hypovolemia (17%), cardiac standstill (7%), dilated left ventricle (3%), biventricular dysfunction (3%), pericardial effusion (3%), and systolic anterior motion of the mitral valve (3%). Pleural effusion was an additional finding in 2 cases. Of the 18 patients evaluated during cardiac arrest, 12 achieved ROSC.

Conclusion: It is feasible for trained providers to perform EASy-ALS in the in-hospital peri-resuscitation period, expanding the role of anesthesiologists in acute patient care. Providers consistently obtained diagnostic images and identified cardiac motion and causes of instability. Several system-wide obstacles, including a limited number of trained providers and a lack of readily-available ultrasound machines, hinder regular use of EASy-ALS. Use of handheld ultrasound devices and expanding training can help address these issues and allow routine implementation of EASy-ALS.

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1. Curr Opin Crit Care. 2010 Jun;16(3):211-5.

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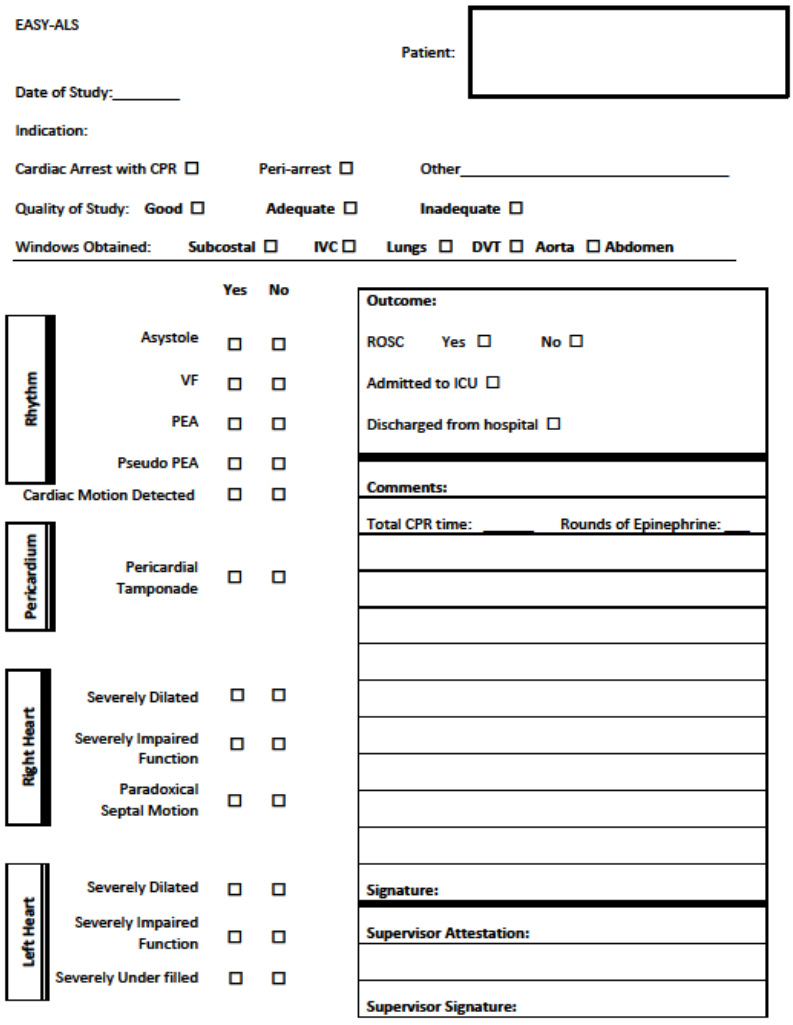
Table 1: Protocol for echocardiographic assessment using subcostal-only view in advanced life support (EASy-ALS Protocol)

Timing	Tasks
Prior to pulse/rhythm check	1. Wait until 2 minutes of chest compressions have been completed. 2. Remove barriers to ultrasound such as clothing or surgical dressing. 3. Place probe on patient to prepare to obtain subcostal 4-chamber view.
During pulse/rhythm check	4. Perform subcostal 4-chamber view and record images. • Do NOT delay resumption of chest compressions • Wipe ultrasound gel from skin
After pulse/rhythm check	5. Interpret recorded images. 6. Communicate findings to code leader. 7. Determine if patient would benefit from further FOCUS or lung ultrasound during subsequent pulse/ rhythm checks.

Figure 1: Standardized report completed after echocardiographic assessment using subcostal-only view in advanced life support (EASy-ALS) exam.



EASY-ALS

Patient:

Date of Study:_____

Indication:

Cardiac Arrest with CPR ☐ Peri-arrest ☐ Other_____

Quality of Study: Good ☐ Adequate ☐ Inadequate ☐

Windows Obtained: Subcostal ☐ IVC ☐ Lungs ☐ DVT ☐ Aorta ☐ Abdomen

		Yes	No
Rhythm	Asystole	☐	☐
	VF	☐	☐
	PEA	☐	☐
	Pseudo PEA	☐	☐
	Cardiac Motion Detected	☐	☐
Pericardium	Pericardial Tamponade	☐	☐
Right Heart	Severely Dilated	☐	☐
	Severely Impaired Function	☐	☐
	Paradoxical Septal Motion	☐	☐
Left Heart	Severely Dilated	☐	☐
	Severely Impaired Function	☐	☐
	Severely Under filled	☐	☐

Outcome:

ROSC Yes ☐ No ☐

Admitted to ICU ☐

Discharged from hospital ☐

Comments:

Total CPR time: _____ Rounds of Epinephrine: ___

Signature:

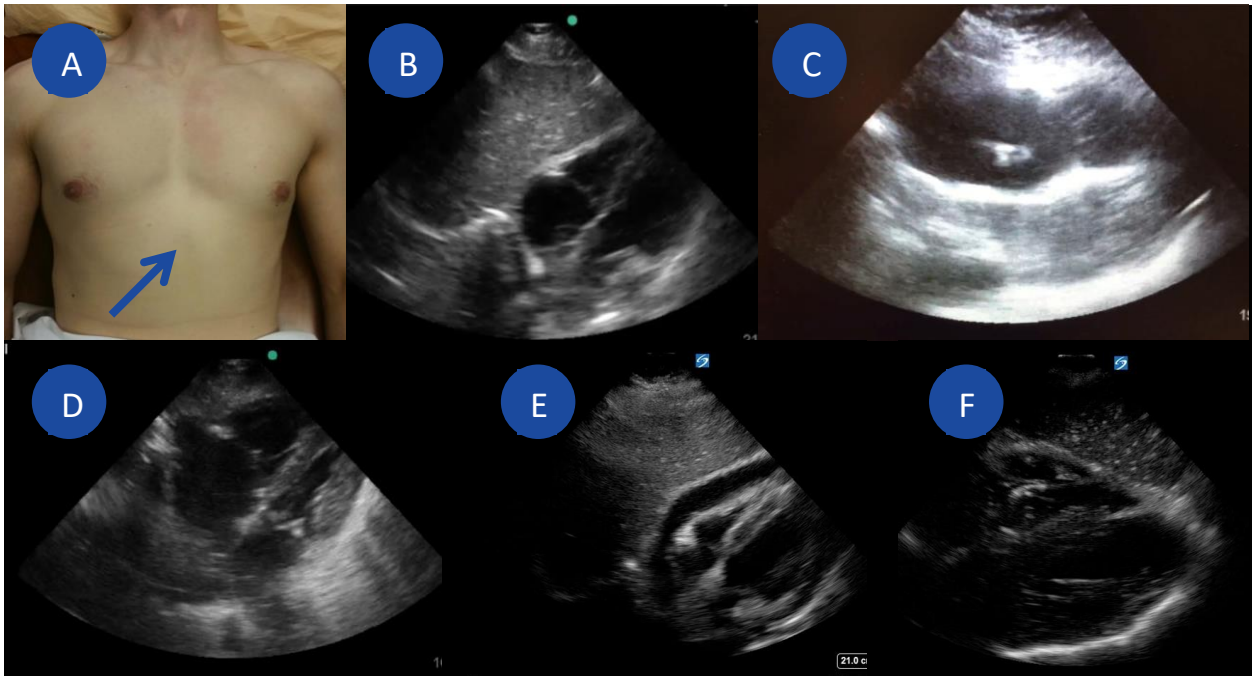
Supervisor Attestation:

Supervisor Signature:

Table 2: Results of focused cardiac ultrasound (FOCUS) evaluations

Case Number	Indication	Image Quality	Cardiac Motion	Assessment	ROSC Achieved
1	PEA	Adequate	Yes	Hypovolemia, pleural effusion	Yes
2	PEA	Adequate	Yes	Ruled-out cardiac causes of event	Yes
3	PEA	Good	Yes	Ruled-out cardiac causes of event	Yes
4	Asystole	Good	No	Cardiac standstill	No
5	Post-ROSC	Good	Yes	Ruled-out cardiac causes of event	Yes
6	Post-ROSC	Adequate	Yes	Biventricular dysfunction	Yes
7	Post-ROSC	Adequate	Yes	Ruled-out cardiac causes of event	Yes
8	Post-ROSC	Good	Yes	RV syndrome, pleural effusion	Yes
9	Asystole	Good	Yes	Hypovolemia	Yes
10	PEA	Good	Yes	Ruled-out cardiac causes of event	Yes
11	PEA	Good	Yes	Ruled-out cardiac causes of event	No
12	PEA	Good	Yes	Hypovolemia	Yes
13	Post-ROSC	Good	Yes	Pericardial effusion	Yes
14	Post-ROSC	Adequate	Yes	Ruled-out cardiac causes of event	Yes
15	Post-ROSC	Good	Yes	Ruled-out cardiac causes of event	Yes
16	PEA	Good	No	Cardiac standstill	No
17	Pre-Arrest	Good	Yes	RV syndrome	Not Applicable
18	PEA	Good	Yes	RV syndrome	Yes
19	Pre-Arrest	Good	Yes	SAM	Not Applicable
20	Pulseless ventricular tachycardia	Good	Yes	LV dysfunction	Yes
21	Pre-Arrest	Adequate	Yes	Ruled-out cardiac causes of event	Not Applicable
22	PEA	Good	Yes	Ruled-out cardiac causes of event	Yes
23	Pulseless ventricular tachycardia	Adequate	Yes	Ruled-out cardiac causes of event	No
24	PEA	Good	Yes	Ruled-out cardiac causes of event	No
25	Pre-Arrest	Good	Yes	Ruled-out cardiac causes of event	Not Applicable
26	PEA	Adequate	Yes	RV syndrome	Yes
27	PEA	Good	Yes	Hypovolemia	Yes
28	PEA	Good	Yes	RV syndrome	No
29	PEA	Good	Yes	Hypovolemia, ASD	Yes

Figure 2: Selection of resident-obtained subcostal echocardiogram images; (A) probe location (arrow), (B) normal heart, (C) clot in right atrium, (D) right ventricular syndrome, (E) pericardial effusion, (F) left ventricular failure



Critical Care-8 Limited English proficiency is not associated with sedation practices in intubated, critically ill patients

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Introduction: Limited English proficiency (LEP) is associated with disparities in health care, ranging from poor access to primary care, to increased adverse maternal health outcomes(1,2,3). In critical care, however, English proficiency is associated with a decrease in mortality independent of race(4). It is unclear, though, what effect communication and language may have on sedation. We performed a single-institution retrospective study of ICU propofol sedation dose in mechanically ventilated patients with respect to English proficiency at a tertiary academic medical center, hypothesizing that due to language barriers, and possibly through cultural barriers, non- or limited-English speakers receive less sedation than English speakers despite the non-verbal nature of intubation.

Methods: We included 1648 adults (18 and older) who were intubated (first episode during hospitalization) and mechanically ventilated at our center between June 1, 2015 and June 1, 2018, after exclusions for neurologic deficits/diagnoses (n=465), DNR/DNI status (n=190), and administration of dexmedetomidine (n=343), neuromuscular blockade (n=309), high-dose benzodiazepines (n=14), and high-dose opioids (n=30). The primary predictor was English language proficiency, as documented in our electronic medical record (EMR) by language preference. The primary outcome was propofol dosage (mean mcg/kg/min for each day of ventilation) for up to 7 days after initial intubation. We modeled propofol dose using linear mixed effects regression adjusting for sex, race, age, relationship status, SOFA score, insurance status, BMI, and oral morphine equivalents (OMEs), including participant-level random slopes and intercepts.

Results: 13.45% (222/1652) were identified as LEP. There was no impact of LEP on average hourly propofol dosage (-0.052 mcg/kg/min, 95% confidence interval, -6.419 to 6.315, P=0.987). There also was no significant interaction between race and LEP on propofol dosage. Propofol dosage was significantly affected by opioid dose (0.104 mcg/kg/min per additional OME, 95% confidence interval, 0.047 to 0.161, P=0.000).

Conclusion: We found no significant association between propofol dosage and LEP status at our institution. Our analysis was limited by inclusion of a medically heterogeneous cohort and inability to account for spontaneous awakening trials; however, the effect size estimate was relatively narrow, and large differences in propofol administration based on English proficiency are unlikely. Generalizability of this finding is unclear, as our hospital employs a large number of bilingual providers and may not be representative of national care practices. EMR-based data analysis may be a viable avenue by which medical centers can assess for disparities in care provided.

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Critical Care-9 Association of Skeletal Muscle Mass and Quality with Long-Term Functional Outcomes in Survivors of Critical Illness

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Introduction: Low muscle mass and density prior to hospitalization are associated with higher morbidity and mortality during critical illness. (1,2) Their association with long-term disability and physical function, however, is unclear. We hypothesized that lower pre-critical illness muscle mass and density would be associated with worse disability and physical function at 3 and 12 months after discharge.

Methods: We conducted a nested study within the BRAIN-ICU prospective cohort study of patients admitted to the medical or surgical intensive care unit (ICU) for respiratory failure and/or shock. We included only those patients who had abdominal CT imaging in the 6 months prior to admission and who survived and participated in follow-up assessments. We quantified the cross-sectional area of all skeletal muscle present in axial images at the L3 vertebrae using an automated version of Slice-O-Matic software (TomoVision, Magog, Quebec) and indexed this value by dividing by height (m2) to give the skeletal muscle mass index (SMI). We assessed muscle density based on Houndsfield units. At 3 and 12 months after hospital discharge, we assessed for functional disability in Basic Activities of Daily Living (BADLs) using the Katz ADL and Instrumental Activities of Daily Living (IADLs) using the Functional Activities Questionnaire (FAQ). We used multivariable regression to describe the association between skeletal muscle mass and density and functional outcomes, adjusting for baseline and in-hospital covariates including age, sex, baseline functional disability, and severity of illness.

Results: We included 133 patients who had abdominal CT imaging available for analysis and who participated in follow-up assessments. Patients were a median [IQR] of 56 [47-64] years old, 63 (47%) were female, median BMI was 29 [25-35], and 121 (91%) required mechanical ventilation. The SMI prior to ICU admission was 51.9 [42.3-64.9]. Using predetermined sex-specific cutoffs (3), 54 (40%) of patients met criteria for low muscle mass (Figure 1). At 3 and 12 months, baseline SMI was not associated with greater odds of new or worsened disability in BADLs (OR 1.0 [0.9-1.0] and 1.0 [0.9-1.0], respectively) or IADLs (OR 1.0 [0.9-1.0] and 1.0 [0.9-1.0], respectively). Similarly, muscle density was not associated with disability in BADLs (OR 1.0 [0.9-1.0] and 1.0 [0.9-1.1], respectively) or IADLs (OR 1.0 [0.9-1.0] and 1.0 [0.9-1.0], respectively).

Conclusion: In this nested cohort of survivors of critical illness, low skeletal muscle mass was present in 40% of patients despite 95% of the cohort presenting with a normal BMI. We did not find an association between skeletal muscle mass or density and long-term disability or physical function. Larger cohort studies are needed to better characterize the role of skeletal muscle in long-term recovery after critical illness.

Reference(s):

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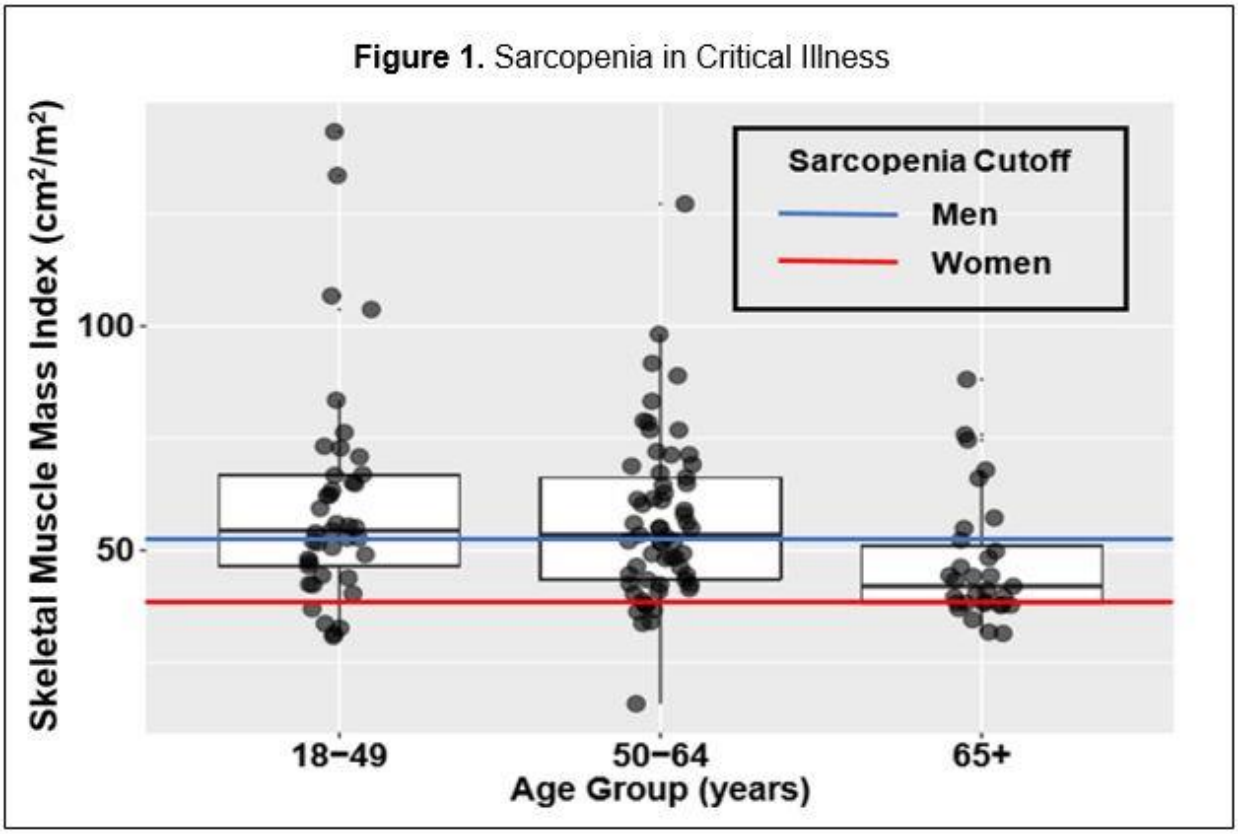
Figure 1. Sarcopenia in Critical Illness



Critical Care-10 Risk Factors and Complications associated with Post-lung Transplantation Vocal Cord Paralysis

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Introduction: Lung transplantation (LTx) has improved the quality of life and longevity of patients with end-stage lung diseases, including cystic fibrosis, interstitial lung disease, and pulmonary hypertension. These patients are particularly vulnerable to increased morbidity and mortality due to complications such as vocal cord paralysis (VCP), a result of recurrent laryngeal nerve injury. Although often overlooked postoperatively, VCP may present clinically as hoarseness of voice or impaired cough reflexes, often leading to aspiration pneumonia.[1] Despite a doubling of LTx in the past 15 years,[2] the risk factors associated with VCP in the setting of LTx are understudied. In this study, we assessed the risk factors and complications associated with VCP in unilateral and bilateral LTx recipients who developed dysphonia.

Methods: A retrospective chart review was conducted on patients who underwent unilateral or bilateral LTx between May 2013 and June 2018. Participants were identified as adult patients (≥18 years old) who presented to the ICU and subsequently developed hoarseness of voice post-LTx. Patients with a history of stroke, paralysis, and current state of coma were excluded from the study. Patients who met criteria and presented with dysphonia were referred to speech pathology for assessment of voice quality, impaired cough reflex, and VCP. Outcome variables measured included aspiration pneumonia, pneumonia, incidence of reintubation, length of intubation, incidence of arrhythmias (atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, and ventricular fibrillation), vocal cord paralysis, and incidence of vocal cord injections. Values are frequency (%) or mean (SD) and compared between groups using the chi-squared test or t-test.

Results: We screened 142 patients that underwent a unilateral or bilateral LTx, of which 141 were included for analysis. Of those patients, 87 (62%) were diagnosed with VCP. Bilateral LTx had VCP incidence of 65.7%, left LTx 56.0%, and right LTx of 47.1% ($p<0.281$) (Table 1). Outcomes comparing VCP vs. no VCP found that those with VCP had an increased incidence of aspiration pneumonia (11.5% vs 3.7%; $p<0.107$) and pneumonia (33.3% vs 20.4%; $p<0.097$). Patients without VCP had a higher reintubation rate vs those with VCP (16.7% vs 8.0%; $p<0.117$). Incidence of arrhythmias (Afib, SVT, Vtach, and Vfib) were higher in the VCP group vs no-VCP (32.2% vs 22.2%; $p<0.202$). Subgroup analysis found no statistical significance between VCP and atrial fibrillation. However, when comparing bilateral vs left vs right LTx patients separately, we found a statistically significant reduction of atrial fibrillation (18.2% vs 44.0% vs 47.1%; $p<0.004$). In sum, our results demonstrate trends in adverse outcomes in our patients who developed VCP after LTx, despite not reaching statistical significance.

Conclusion: Preliminary data analysis shows an increased incidence of VCP in bilateral vs unilateral LTx recipients. Such a higher rate may be expected, as surgical manipulation within bilateral thoracic compartments predisposes the patient to mechanical recurrent laryngeal injury. The increased diameter of a double-lumen tube, utilized for LTx, can be a significant risk factor contributing to laryngeal nerve injury as a result of compressive trauma. Additionally, our data demonstrates a higher incidence of VCP in left vs right LTx patients. While not certain, a possible reason for this finding is most likely due to a higher probability of mechanical injury from surgical manipulation given the long thoracic course of the left recurrent laryngeal nerve. Patients with VCP were at higher risk of aspiration pneumonia, which may in part be due to isolated VCP or a combination of VCP and impaired reflexes. Despite the fact that the exact mechanism is unknown, we found a significant reduction in atrial fibrillation in bilateral vs. unilateral lung transplant patients. Although there were no significant differences in outcomes in patients with vs without VCP, the lack of significance can, in part, be attributed to a limited sample size. VCP in patients undergoing LTx is associated with increased morbidity and mortality. Routine and comprehensive postoperative evaluation of VCP, especially in the presence of associated clinical symptoms such as dysphonia, may allow for timely treatment and decreased perioperative morbidity.

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2. National Data - OPTN. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#. Accessed December 18, 2019.

Table 1: Incidence of Vocal Cord Paralysis by Lung Transplantation Type

Right (n= 17)	**Left** (n= 25)	**Bilateral** (n= 99)
8 (47.1%)	14 (56.0%)	65 (65.7%)

Critical Care-11 GLIM Directed Malnutrition Predicts Morbidity and Mortality Following Emergent GI Surgery

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Introduction: Despite modern advances in food production and distribution, malnutrition remains a prevalent public health issue in the US. According to the USDA, as of 2017, up to 40 million Americans lived in food-insecure households. In 2016, the Global Leadership Initiative on Malnutrition (GLIM) was convened and proposed a set of consensus criteria for the diagnosis of malnutrition. Our project seeks to study the effects of GLIM positive malnutrition on the outcomes for patients undergoing emergent bowel surgery. We hypothesize that meeting GLIM criteria predicts increased length of stay (LOS), morbidity, and mortality for our study population.

Methods: Adapting NSQIP data, GLIM criteria are (1) BMI of ≤20 for age ≤70 and BMI ≤22 for age ≥71, (2) admission albumin ≤3.5, and (3) weight loss >10% within the past 6 months. All patients undergoing emergent small bowel, colon, and rectal procedures were extracted from the NSQIP database and included in the study. Multivariate linear and logistic regression models controlling for relevant covariates were developed to evaluate GLIM criteria on LOS, mortality, and overall complication rates.

Results: Review of small bowel, colon, and rectal cases in the NSQIP database between January 1, 2005 and December 31, 2010 revealed a total of 22,896 patients who underwent emergent abdominal surgeries. Overall demographics were 53.8% female (n=12,323), 11.2% (n=2,578) African American, 0.8% (n=191) Native American, 2.0% (n=448) Asian, 73.8% (n=16,893) Caucasian, and 4.5% (n=1,031) Hispanic. In total, 1,755 patients were excluded from analysis due to missing data. Overall, 3.0% (n=691) of the cohort qualified as malnourished as per modified GLIM criteria, with proportions varying by race and ethnicity with the lowest rates observed in Native Americans at 2.6% and the highest rates observed in Asians at 4.2%. Overall, case composition was split between 64.2% colon operations (n=14,692), 35.4% small bowel operations (n=8,112), and 0.4% rectal operations (n=92). Multivariate logistic regression model controlling for covariates demonstrated that GLIM criteria positive malnutrition was associated with a significantly higher mortality for both emergent colon (p=0.008, CI 1.1 | 1.8) and small bowel (p=0.000, CI 1.5 | 3.0) procedures. Controlling for covariates, multivariate linear regression analysis demonstrated that patients with GLIM criteria positive malnutrition had significantly longer LOS for emergent small bowel operations (p=0.002, CI 1.7 | 7.9), but the same association was not observed for emergent colon cases (p=0.104, CI -0.4 | 4.2). GLIM positive malnutrition was not significantly associated with an increase in post-operative complications for both emergent colon (p=0.593, CI 0.8 | 1.4) and small bowel (p=0.327, CI 0.6 | 1.2) procedures. Analysis of GLIM-criteria malnourished patients who underwent emergent colon surgery (n=207) found that African American patients were significantly more likely to have longer LOS than patients of any other ethnicity (p=0.04, CI 0.4 | 13.4). The only other covariates that significantly impacted LOS in this model were history of angina (p<0.001, CI 18 | 58), history of COPD (p=0.02, CI 1.7 | 15.3), and alcohol abuse (p=0.044, CI 0.2 | 18.6).

Conclusion: This analysis shows that a modified GLIM criteria can be used to predict poor outcomes in patients undergoing emergent general abdominal surgery. Patients who meet the newly standardized GLIM criteria for malnutrition were at increased risk for negative outcomes. The ability to predict risk and employ earlier nutrition interventions to improve outcomes will be a great asset to patient care across the board for all general surgeons and critical care physicians.

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Critical Care-12 The Role of Extracorporeal Membrane Oxygenation in Lung Transplantation: a Single Institution Retrospective Review

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Introduction: Extracorporeal membrane oxygenation (ECMO) is a closed circuit that provides days to weeks of cardiopulmonary and/or pulmonary support in critically ill patients with severe respiratory and/or cardiac failure (unresponsive to conventional treatment). (1) Based on the UNOS database from 2005 to 2011, prior to lung transplantation roughly 1% of critically ill patients required ECMO support as a bridge to lung transplantation. (2) The numbers have continued to grow since then as an increasing number of single-center studies have demonstrated the utility and successful outcomes associated with ECMO as a bridging strategy to lung transplantation. (3) However, few studies have examined the indications, impact, and related outcomes of ECMO pre-lung transplant, during lung transplant, and post-lung transplant. (3,4,5)

Methods: We performed a retrospective chart review of 43 patients who received ECMO support prior to lung transplant, during or after lung transplant, or as a bridge to lung transplantation and deceased. Patients were selected over 7 years (from 2013 to 2019) at Loyola University Medical Center and were divided into 4 groups: ECMO prior to lung transplantation, ECMO within 24 hours of lung transplantation, ECMO more than 24 hours after lung transplantation, and ECMO as a bridge to lung transplantation (with no lung transplantation) and support withdrawn. Exclusion criteria included patients who receive ECMO cannulation, but without an indication for a lung transplant. Patient age ranged from 15 to 70 years. Outcome variables examined in the retrospective review for all groups included patient demographics, medical history, co-morbidities, mortality rate, type of ECMO, whether conversion from VV to VA ECMO was performed, the duration of ECMO, and whether the patient was extubated on ECMO. In patients who received ECMO cannulation prior to lung transplantation, we looked at the number of days on ECMO prior to lung transplantation. In patients who received a lung transplant, we looked at 30 day survival, indications for the lung transplant, single versus bilateral lung transplant, whether intraoperative cardiopulmonary bypass was used (planned versus unanticipated), ventilation requirements prior to lung transplant, and ECMO complications. In patients who received ECMO cannulation as a bridge to lung transplantation and then had support withdrawn, we looked at the number of days on ECMO prior to patient deceased. Statistical analysis of our data was performed using the software of research data capture (REDCap).

Results: Of the 43 patients in our study population, 33% (14 of 43 patients) received ECMO prior to lung transplantation, 23% (10 of 43 patients) had ECMO cannulation during or within 24 hours of lung transplant, 19% (8 of 43 patients) received ECMO more than 24 hours after lung transplantation, and 26% (11 of 43 patients) received ECMO and then support was withdrawn with no lung transplantation (Chart 1). The combined mortality rate for the 43 patients studied was 49% (21/43). Of the total 21 deceased patients, 52% (11/21) were on ECMO as bridge to transplant and never received transplant, 33% (7/21) received ECMO cannulation more than 24 hours after lung transplantation, 14% (3/21) received ECMO cannulation during or within 24 hours of lung transplantation, and no patients were deceased in the population that received ECMO prior to lung transplantation (Chart 2). In addition, the mortality rate from all groups decreased from the year 2014 (100%) to the year 2019 (42%).

Conclusion: Preliminary analysis of our data reveals that ECMO cannulation prior to lung transplantion leads to the lowest post-transplant mortality rate in our study population. Survival rates in patients, who receive ECMO cannulation during or within the first 24 hours after a lung transplantation, are much higher than in patients who undergo ECMO cannulation more than 24 hours after a lung transplant. The overall decrease in mortality rate from 2013 to 2019 may be correlated to the increase in the number of ECMO cannulations pre-lung transplantation, improvements in critical care team experience, or surgeon experience in managing ECMO patients. While our preliminary data reveals key findings from a retrospective review at one institution, further statistical analysis must be completed to confirm the significance of variables examined as predictors of adverse outcomes and survival in potential and/or known lung transplant recipients undergoing ECMO cannulation.

Reference(s):

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2. George TJ, Beaty CA, Kilic A, et al. Outcomes and temporal trends among high-risk patients after lung transplantation in the United States. J Heart Lung Transplant 2012;31:1182-91.

3. Gulack BC, Hirji SA, Hartwig MG. Bridge to lung transplantation and rescue post-transplant: the expanding role of extracorporeal membrane oxygenation. J Thorac Dis. 2014;6(8):1070-9.

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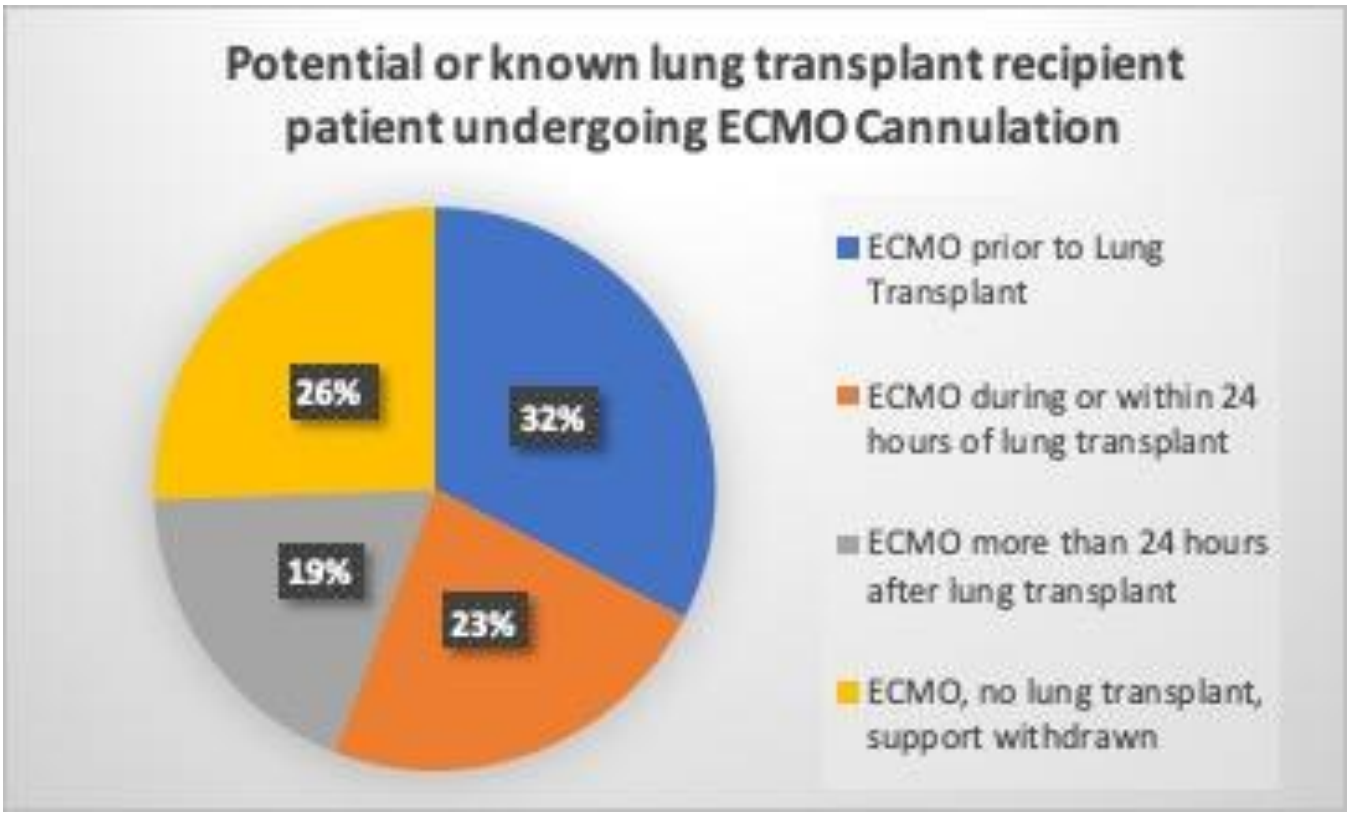
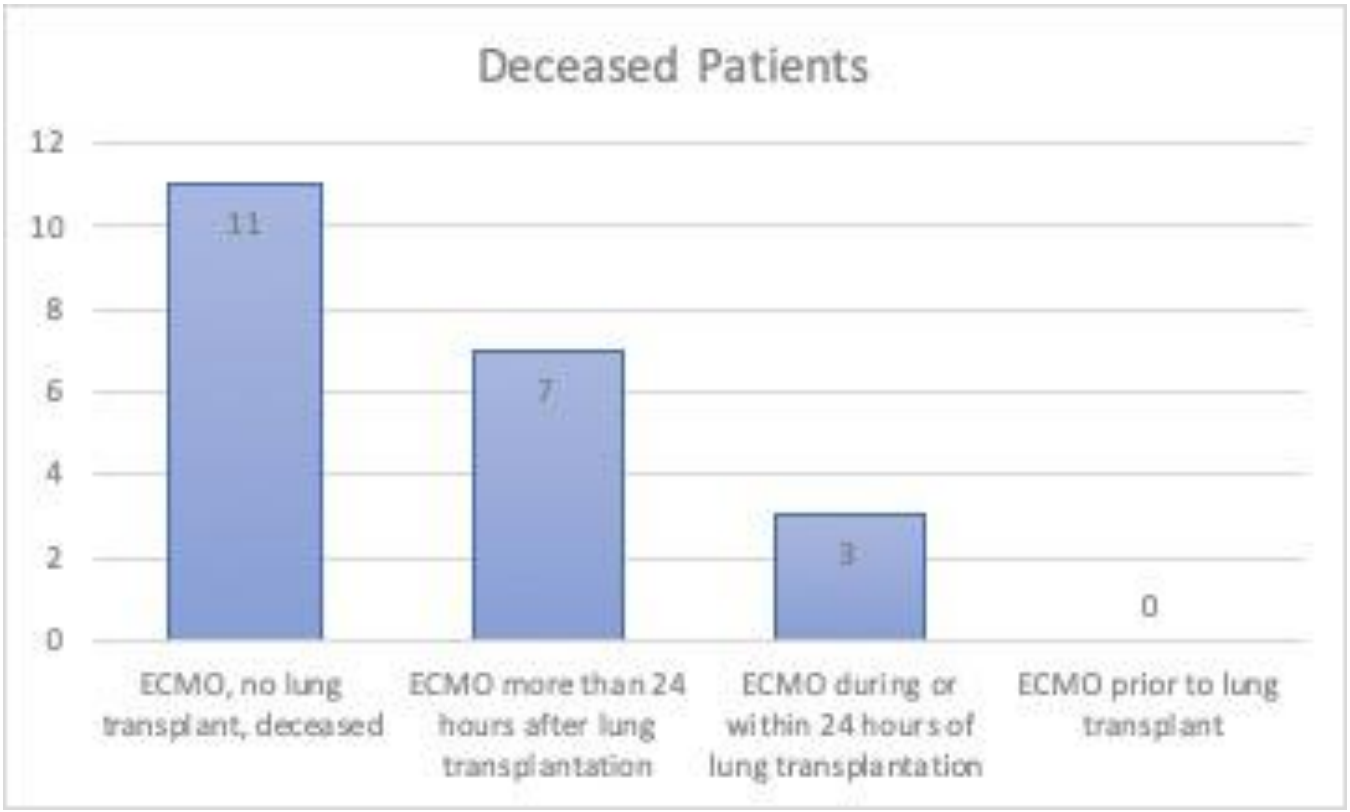
5. Mulvihill, Michael S., et al. “Extracorporeal Membrane Oxygenation Following Lung Transplantation: Indications and Survival.” The Journal of Heart and Lung Transplantation, vol. 37, no. 2, 2018, pp. 259-267


Potential or known lung transplant recipient patient undergoing ECMO Cannulation
26%
32%
19%
23%
ECMO prior to Lung Transplant
ECMO during or within 24 hours of lung transplant
ECMO more than 24 hours after lung transplant
ECMO, no lung transplant, support withdrawn


Deceased Patients
12
10
8
6
4
2
0
11
7
3
0
ECMO, no lung transplant, deceased
ECMO more than 24 hours after lung transplantation
ECMO during or within 24 hours of lung transplantation
ECMO prior to lung transplant

Critical Care-13 When intensivists pay heed to patient wills: impact on mortality and economics

Hendrik Booke[1], Rolf D Nordmeier[2]

[1]Kliniken des MTK, Frankfurt, Germany, [2]Main Taunus Kliniken GmbH Bad Soden, Bad Soden, Hessen

Introduction: More and more patients have a written patient's decree to make sure that doctors follow their end-of-life decisions even in cases of unconsciousness or inability to enforce their final will personally. We investigated, why patients died on an 18-bed Intensive Care Unit (ICU) in a teaching hospital of the Johann Wolfgang Goethe University of Frankfurt.

Methods: We included all patients admitted to the ICU in 2018. The patients were then divided into two groups depending on whether they stayed on the ICU for more than 24 hours or less than 24 hours.

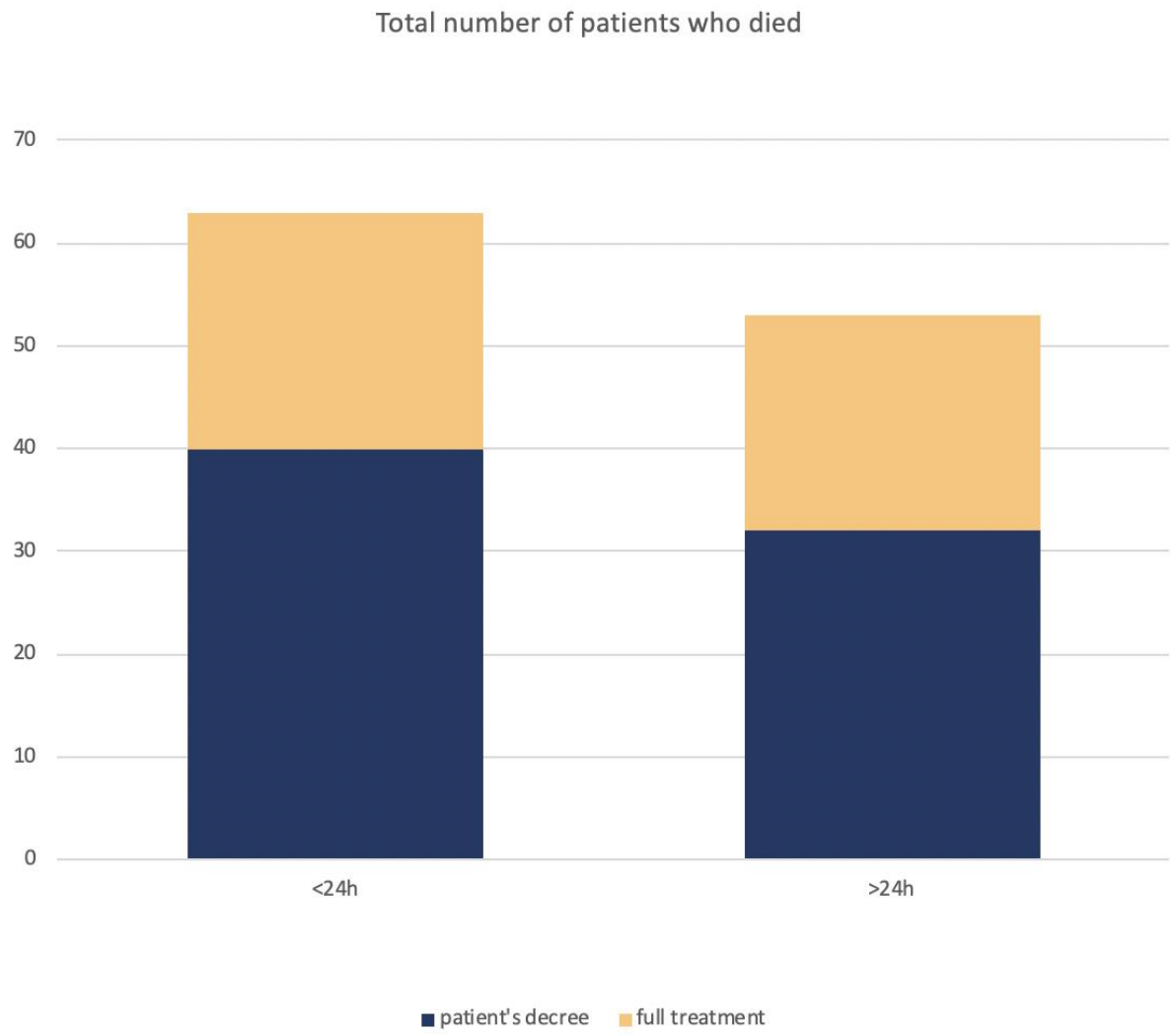
Results: A total of 801 patients were admitted to the ICU, from whom 116 died (mortality rate 14,5 %). Out of these 116 patients, 72 died based upon a patient's decree or when relatives assumed that full treatment was not wished by the patient. 44 patients died despite full treatment (mortality rate 5,5 %). Out of 63 patients who deceased within 24 hours after being admitted to the ICU, in 63,5% (40 out of 63 patients, Fig. 1) therapy was withheld because of a written patient's decree. 53 of those 116 patients who have died, had been on the ICU for more than 24h. In 60,3% of these patients therapy was terminated because of a patient's decree. They passed away after an average of 8,2 days on ICU.

Conclusion: Our overall mortality rate of 14,5% is in line with the mortality rate reported by Galloways Meta-Analysis published in 2018: 18,2% of 902,551 patients (1). Just a decade ago, mortality on ICU was primarily associated with the degree and severity of (multi) organ failure and the quality of the consecutive therapeutic regimen. Nowadays, more and more patients or their relatives present written patient's wills, limiting doctors in their ability to treat the underlying disease. As a result, more than two thirds of our patients died based upon a patient's decree, which, according to German law, is mandatory to be heeded by. Consecutively, the mortality rate is on the increase (14,5% versus 5,5%). Our data, showing that nearly two thirds of our ICU-patients refuse (ongoing) therapy, support the idea of the Improving Palliative Care in the ICU (IPAL-ICU) Advisory Board to increase the involvement of palliative care specialists for critically ill patients on ICU (2). Further, while ICU beds are rare, this resource is wasted when costly treatment is initiated in patients, who in the end refuse to be treated. ICU-beds are one of the most expensive resource in every hospital, especially on the day of admission (day 1), when new therapies are initiated in emergency cases. Reimbursement of cases staying only one or two days on ICU is inadequate, since the high costs are not adequately refunded. Subsequently, patients admitted to ICU despite an existing patient's decree, which is not on file right away, is an economic and ethical burden. We therefore suggest, that case managers have the patient's decree scanned before a patient is admitted to ICU or the Medical Emergency Team is called for. This would help to utilize our costly staff, equipment and knowledge for patients who really need it and want to be treated, leading to a significant improvement of ICU-efficiency and ICU-economics.

Reference(s):

1. The effect of ICU out-of-hours admission on mortality: a systematic review and Meta-Analysis. Crit Care Med 2018, 46: 290-299

2. Choosing and using screening criteria for palliative care consultation in the ICU: a report from the Improving Palliative Cae in the ICU (IPAL-ICU) Advisory Board. Crit Care Med 2013, 41: 2318-2327


Total number of patients who died
70
60
50
40
30
20
10
0
<24h
>24h
patient's decree
full treatment

Critical Care-14 Risk Factors for Increased Opioid Use in the Intensive Care Unit after Surgery

Lauriane Guichard[1], Stephanie Moser[2], Milo Engoren[2], Matthew Sigakis[2], Chad M Brummett[3], Daniel Clauw[2], Vijay Krishnamoorthy[1]

[1]Duke University, Durham, NC, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan Health System, Ann Arbor, Michigan

Introduction: With improved survival from the intensive care unit (ICU) (1), many patients are being discharged with impaired quality of life, and 30% have chronic pain attributed to the ICU stay (2). However, no studies to our knowledge have identified risk factors for increased opioid use during the ICU course. The purpose of this study is to describe the use of opioids during an ICU course after surgery and identify risk factors of increased opioid use.

Methods: Data for this single center prospective observational cohort was collected between 2012 and 2017 for the Michigan Genomics Initiative (MGI). Inclusion criteria were: 1) Adults (age > 18 years), 2) Had a procedure done at a University of Michigan site, 3) Experienced an ICU admission within 24 hours after surgery. Exclusion criteria were: 1) Language barrier, 2) Cognitive impairment, 3) Current pregnancy, or 4) Death during the ICU course. The database included baseline sociodemographic, pain, mental and physical health characteristics from a questionnaire completed prior to surgery. Moderate anxiety and depression were defined as scores ≥8 on PROMIS and HADS questionnaires. Preoperative opioid use and oral morphine equivalents (OME) administered in the ICU were collected from the electronic medical record. The primary outcome variable was average daily OME use in the ICU. Univariable and multivariable linear regressions were performed to examine associations of baseline risk factors with average daily OME in the ICU. Statistical analysis was conducted with SPSS.

Results: A total of 2135 participants were included. Mean (SD) age was 56 (15.2) years, 1097 (51%) were male, and 1023 (48%) were ASA Class III. The mean (SD) ICU length of stay was 2.5 (3.6) days. The most common type of surgery was neurosurgical followed by cardiac and abdominal surgery. Preoperative opioid use was noted in 25% of patients, and 26% and 47% had preoperative depression and anxiety, respectively. During the ICU stay, average OME use per day was 56 mg, and 66% of participants received opioids each ICU day (Graph 1). Some of the strongest univariate predictors of increased opioid use in the ICU were pre-surgery self-reported current tobacco use (B=29.6, 95% CI 18.1-41.1, p<0.001), current/past alcohol use (B=14.1, 95% CI 2.7-25.4, p=0.015), and current/past illicit drug use (B=29.5, 95% CI 12.6-46.5, p=0.001). Other significant univariate associations with increased ICU opioid use were preoperative opioid use, major surgery, lower age, increased anesthesia duration, depression, low life satisfaction, overall pain, and centralized pain (Table 1). By multivariable linear regression, preoperative opioid use, major surgery, age, and anesthesia duration remained significantly associated with opioid use in the ICU (Table 2).

Conclusion: Patient factors such as pre-existing tobacco use, substance use, opioid use, and depression could help predict, in addition to surgical factors, those who will be most at risk for increased opioid use in the intensive care unit.

Reference(s):

1. Zimmerman JE, Kramer AA, Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. Critical care. Apr 27 2013;17(2):R81.

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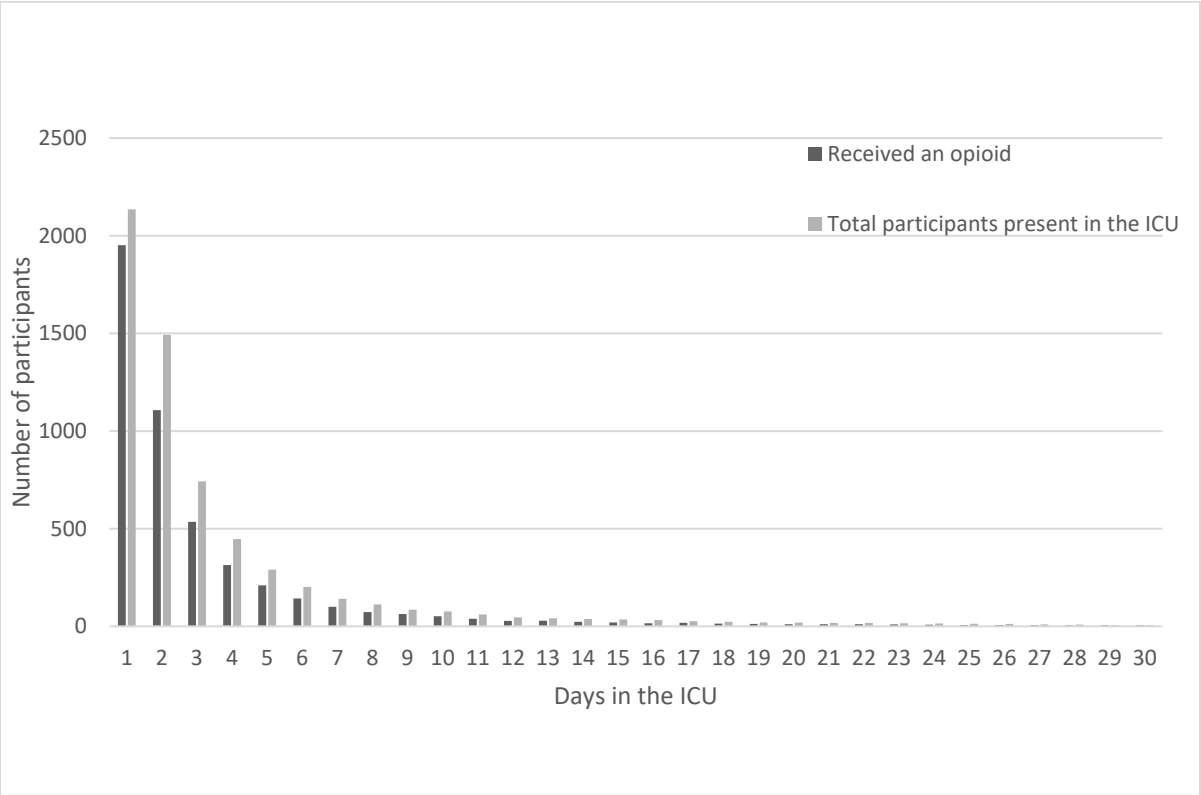
	n (%) unless otherwise noted N=2135	Coefficient	p-value	95% Confidence Interval		R^2
Male sex	1097 (51.4)	1.46	0.74	-7.18	10.10	0.007
Age in years (standard deviation)	56.44 (15.22)	-0.99	**<0.001**	-1.27	-0.71	-0.15
Race						
Caucasian *(reference)*	1966 (92.1)					
African American	98 (4.6)	0.001	1.00	-20.64	20.65	0.001
Other	71 (3.3)	-18.42	0.13	-42.51	5.68	-0.03
Insurance						
Medicaid / Medicare *(reference)*	740 (34.7)					
Private or other	948 (44.4)	1.41	0.78	-8.37	11.19	-0.01
Uninsured or unknown	740 (34.7)	11.00	0.07	-0.94	22.94	0.04
WHO Obesity Class*						
Class 1 BMI <18.5 (*reference)*	27 (1.3)					
Class 2 BMI 18.5-24.9	413 (19.3)	-31.60	0.14	-73.42	10.22	-0.03
Class 3 BMI 25.0-29.9	591 (27.7)	-20.30	0.34	-61.73	21.14	0.03
Class 4 BMI 30.0-34.9	441 (20.7)	-29.40	0.17	-71.14	12.34	-0.02
Class 5 BMI 35.0-39.9	213 (10.0)	-22.04	0.32	-55.05	20.97	0.01
Class 6 BMI >40.0	175 (8.2)	-28.55	-0.20	-72.08	14.98	-0.009
ASA Classification*						
ASA I *(reference)*	23 (1.1)					
ASA II	525 (24.6)	-5.71	0.80	-50.15	38.73	0.07
ASA III	1023 (47.9)	-19.45	0.39	-63.44	24.53	-0.03
ASA IV	324 (15.2)	-28.51	0.21	-73.52	16.51	-0.05
Major Surgery*	1602 (75.04)	26.84	**<0.001**	13.74	39.94	0.09
Surgical Service*						
Neurosurgical *(reference)*	616 (28.85)					
Cardiac surgery	349 (16.35)	-7.00	0.31	-20.42	6.41	-0.07
Abdominal/Colorectal	262 (12.27)	-9.42	0.21	-24.19	5.35	-0.07
Otolaryngology/Oral Maxillofacial	214 (10.02)	41.84	**<0.001**	25.95	57.73	0.11
Spine Surgery	175 (8.20)	91.88	**<0.001**	74.73	109.03	0.25
Plastic surgery	73 (3.42)	-9.80	0.44	-34.58	14.99	-0.04
Thoracic	47 (2.20)	3.23	0.83	-27.07	33.54	-0.008
Other	165 (7.73)	-16.34	0.07	-33.90	1.21	-0.07
ICU length of stay in days (Standard deviation)	2.51 (3.63)	1.11	0.07	-0.08	2.30	0.04
Anesthesia Duration in minutes (Standard deviation)	432.72 (180.93)	0.09	**<0.001**	0.06	0.11	0.14
Tobacco						
Never *(reference)*	863 (40.4)					
Current	463 (21.7)	29.60	**<0.001**	18.14	41.06	0.12
Former	789 (37.0)	0.04	0.99	-9.76	9.840	-0.05
Current or past Alcohol use¥	1234 (57.8)	14.07	**0.015**	2.73	25.40	0.06
Current or past Illicit Drug Use	147 (6.9)	29.53	**0.001**	12.59	46.46	0.08
Preoperative opioid use	537 (25.2)	55.35	**<0.001**	45.25	65.44	0.24

Preoperative Survey questionnaire						
Moderate Anxiety[¥]	790 (37.0)	9.62	0.067	-0.66	19.89	0.05
Moderate Depression[¥]	427 (20.0)	25.84	**<0.001**	14.09	37.58	0.11
Life Satisfaction Scale[¥] (0 least to 10 most satisfied)	6.64 (2.68)	-2.98	**0.002**	-4.86	-1.11	-0.08
Fibromayalgia Survey Score[¥] (range 0-28)	6.04 (4.76)	2.81	**<0.001**	1.75	3.88	0.13
Brief Pain Inventory[§] (average of two overall body pain items, 0 no pain to 10 worst pain)	3.02 (2.96)	8.31	**<0.001**	6.70	9.92	0.23
Pain Detect Neuropathic Pain Scale[¤] (range -1 to 34)	6.50 (7.50)	1.75	**<0.001**	1.24	2.26	0.20

Bold test denotes statistical significance of at least p < 0.05
**10-15% of data missing*
[§]15-20% of data missing
[¥] 20-25% of data missing
[¤]45-50% of data missing

Table 1: Univariate associations of sociodemographic and surgical factors with increased average daily oral morphine equivalent use in the intensive care unit. The r-squared for each predictor is also displayed.



Graph 1: Opioid administration over time in the ICU. Dark grey bars indicate number of participants who received an opioid. Light grey bars indicate the total number of participants in the ICU.

	Coefficient	p-value	95.0% Confidence		R^2
Age	-0.412	**0.030**	-0.78	-0.04	-0.08
Major Surgery*	18.94	**0.014**	3.90	33.98	0.15
Current smoker (vs never)	13.77	0.064	-0.80	28.34	0.15
Former smoker (vs never)	7.02	0.28	-5.69	19.72	-0.05
Alcohol use¥	4.63	0.46	-7.62	16.875	0.06
History of Illicit drug use	2.01	0.85	-19.14	23.15	0.06
Anesthesia Duration	0.043	**0.006**	0.013	0.074	0.17
Preoperative opioid use	20.17	**0.005**	6.12	34.22	0.19
Moderate Depression¥	5.03	0.50	-9.63	19.70	0.12
Moderate Anxiety¥	4.31	0.49	-7.90	16.52	0.10
Life Satisfaction Scale¥	-0.55	0.62	-2.76	1.65	-0.10
Fibromayalgia Survey Score¥	-0.78	0.37	-2.48	0.92	0.10
Brief Pain Inventory§	2.46	0.077	-2.534	5.18	0.15
Pain Detect Neuropathic Pain Scale¤	0.004	0.99	-0.97	0.97	0.12

Bold test denotes statistical significance of at least p < 0.05
**10-15% of data missing*
§15-20% of data missing
¥ 20-25% of data missing
¤45-50% of data missing

Table 2: Multivariate associations of sociodemographic and surgical factors with increased average daily oral morphine equivalent use in the intensive care unit. The r-squared for each predictor is also displayed.

Critical Care-15 Effect of Crystalloid: Additive Combinations on Packed Red Blood Cells Stored Integrity

Kristine Yarnoff[1], Jeffrey Dodd-o[2]

[1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins Hospital, Baltimore, MD

Introduction: Literature is beginning to challenge the belief that it is unsafe to coinfuse packed red blood cells (PRBC) with other solutions. We recently showed that additive-free PRBC tolerated co-incubation with plasmalyte or catecholamines dissolved in NS, though 5% dextrose in water (D5W) promoted hemolysis. Herein we evaluate the effect of co-incubating crystalloids on additive-preserved PRBC hemolysis, aggregation and membrane deformability.

Methods: PRBCs were co-incubated 5 minutes with plasma, normal saline (NS), plasmalyte, lactated ringers (LR) or D5W. Samples were then assessed for hemolysis (free hemoglobin), aggregation (critical shear stress [mPa]), and membrane deformability (elongation index, E.I.). Significance ($P < 0.05$) by t-test or ANOVA with post-hoc Tukey-Kramer test.

Results: Additive-prepared PRBC co-incubated with crystalloid instead of plasma demonstrated: 1) no increase, but in some cases a decrease, in hemolysis as indicated by plasma-free hemoglobin levels; 2) no increase, but in some cases a decrease, in aggregation as indicated by critical shear stress; 3) no deterioration in deformability except when the crystalloid D5W was used with the additive AS-1. In this case, deformability returned to normal when the crystalloid was subsequently diluted out with plasma.

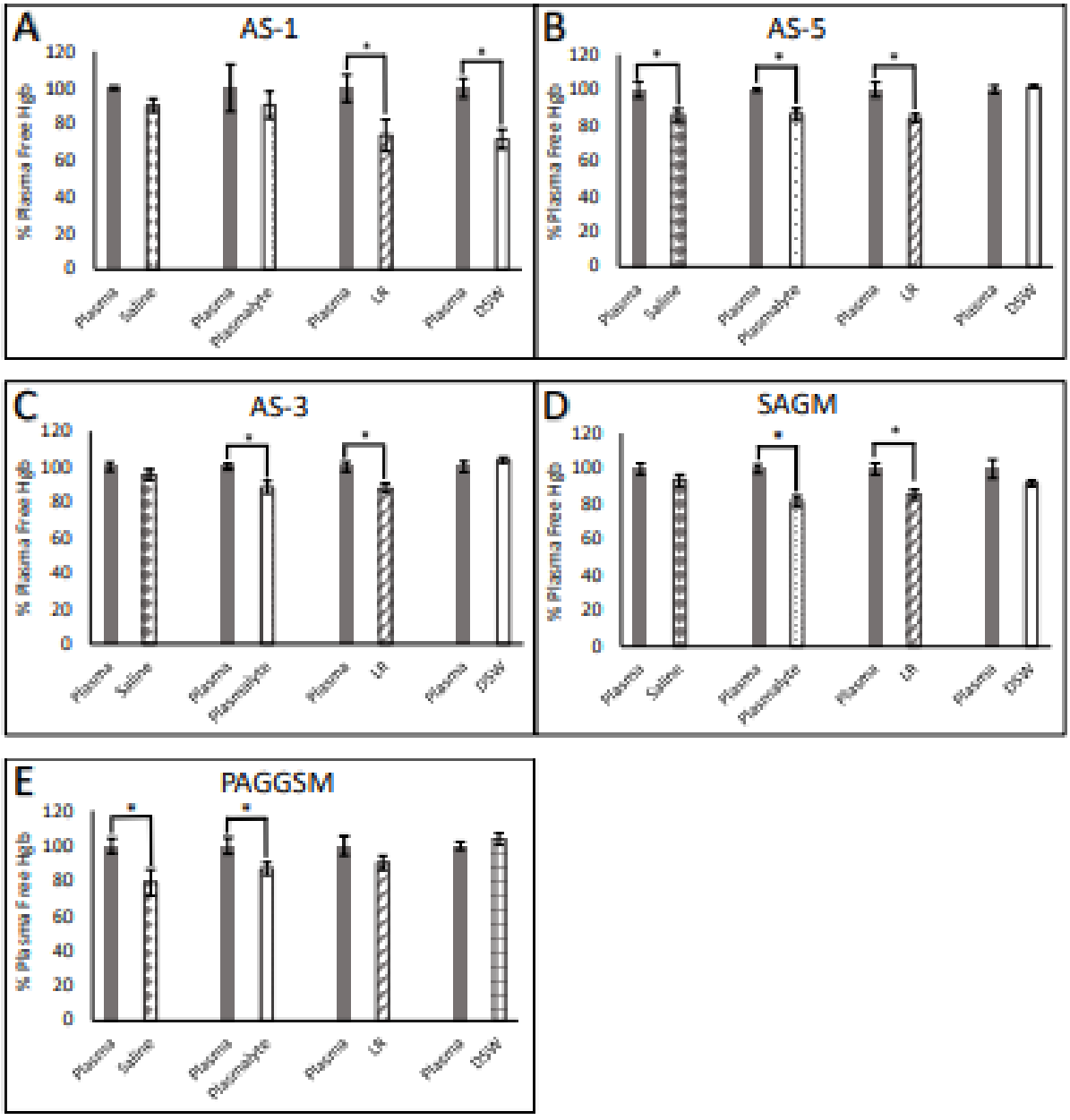
Conclusion: Our data suggest that, with one exception, additive-prepared PRBC co-incubated for 5 min with any of 4 common crystalloids demonstrate no increased lysis, increased aggregation, or deformability. The decreased deformability of AS-1-prepared PRBC co-incubated for 5 min with D5W normalizes within 5 min of dilution with plasma.

Reference(s):

1. Banks, A.o.A.B., Recommendations from AABB's Clinical Transfusion Medicine Committee on Sterile Saline Shortage (0.9% NaCl Solution). 2018.

2. Effect of incubation with crystalloid solutions or medications on packed red blood cells. Transfusion, 2019. 59(8): p. 2643-2651.

Figure 1:


A
AS-1
B
AS-5
C
AS-3
D
SAGM
E
PAGGSM
% Plasma Free Hgb
120
100
80
60
40
20
0
*
Plasma
Saline
Plasma
Plasmalyte
Plasma
LR
Plasma
D5W

Critical Care-16 Conceptualizing 'Central Line Free Days': Peripheral Vasopressors in the MSICU, a Quality Improvement Initiative

Adjoa Boateng[1], Jai Madhok[1], Javier Lorenzo[2]

[1]Stanford Health Care, Palo Alto, CA, [2]Stanford University Medical School, Palo Alto, CA

Introduction: Central venous catheters (CVCs) became mass produced in the 1950s with expanded knowledge of cardiac physiology and the ability to augment such physiology with direct medication administration. Nonetheless, their primary use in intensive care units and emergency departments is the administration of vasopressor agents for treatment of shock states. Concerns regarding tissue ischemic injury from local extravasation have propelled use of CVCs over peripheral intravenous lines. However, current literature questions if such concerns may have been overstated. This query is further muddied by the variability and disagreement between providers on threshold doses of vasoactive infusions via peripheral intravenous catheters (PIV). Extravasation of vasoactive drugs from a PIV into tissues may lead to serious morbidity and possibly mortality. Additionally, the risk for extravasation may be cited as a concern toward escalation of vasoactive drug infusion (VDI) doses through a PIV. Hesitancy to initiate a VDI via a PIV may lead patients to receive premature placement of a CVC and the associated risks of CVC placement. Oppositely, providers who are willing to administer higher doses of a VDI through a patient's PIV may raise the risks associated with extravasation and delay timely placement of a CVC. As such, our quality improvement initiative seeks to identify provider comfort and willingness to administer PIV VDI, creation and dissemination of a PIV VDI protocol, and a comprehensive extravasation management plan.

Methods: Prior to patient observation, a survey was created to examine providers' knowledge and comfort with peripheral administration of vasoactive medications as well as management of extravasation events. The initiative is still underway with our proposed protocol reviewed and vetted by the Continuous Quality Improvement Committee for the intensive care units. The protocol will then be disseminated to key members of the Stanford medical surgical ICU including: residents, fellows, attendings, RNs, and pharmacists. Following this, in a prospective manner, patients admitted to the medical surgical ICU who are being administered VDIs will be identified and categorized according to the: type, dose, duration and route of vasoactive drug administration for a period of 2 months. These patients will be followed to determine the incidence of extravasation events if any as well as any conversion from peripheral to central administration of the VDI. If an extravasation event occurs, any interventions for treatment, both pharmacologic and supportive will be identified and tracked. Finally, a post-protocol survey will be conducted. Measurable outcomes include: survey results examining provider knowledge and comfort with PIV VDI, the number of patients in the ICU that received peripheral infusions of vasoactive drugs, duration and maximum dose of peripheral VDI used, practice variation, number of potential central lines that were avoided, and any extravasation events that occurred.

Results: The developed protocol will outline the following (Table 1): Preliminary data on the incidence and indication of VDI as well as dosing, duration and complication rate reveal the following (Table 2).

Conclusion: Heterogeneity in VDI dose thresholds via different access routes often leads to practice variability and confusion resulting in the potential for delays and undue risks associated with a particular vascular access route. This is of further importance given complication rates among use of CVCs for the administration of VDIs, are estimated at 5- 20%. Complications generally type into three categories: mechanical (hematoma, arterial puncture, pneumothorax, hemothorax, catheter misplacement, and stenosis), infectious (insertion site infection, blood stream infection, CVC colonization and thrombotic (deep vein thrombosis) stratifying into rates ranging: 5%–19%, 5%–26% and 2%–26% of patients, respectively. As such, in the same manner in which the ABCDEF (Awakening and Breathing Coordination, Delirium monitoring/management, and Early exercise/mobility, Family engagement and empowerment) bundle has been popularized and promoted to help mitigate both the short and long term sequelae of critical illness, we posit that initiatives such as ours can contribute to a paradigm shift in the administration of vasoactive infusions ultimately to report 'central line free' days, thus addressing the potential aforementioned morbidity associated with CVCs.

Reference(s):

1. Cardenas-Garcia, J.,(2015) Safety of peripheral intravenous administration of vasoactive medication. J Hosp Med, 10(9), 581-585

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4. Lewis, T., (2019). Safety of the Peripheral Administration of Vasopressor Agents. J Intensive Care Med, 34(1), 26-33.

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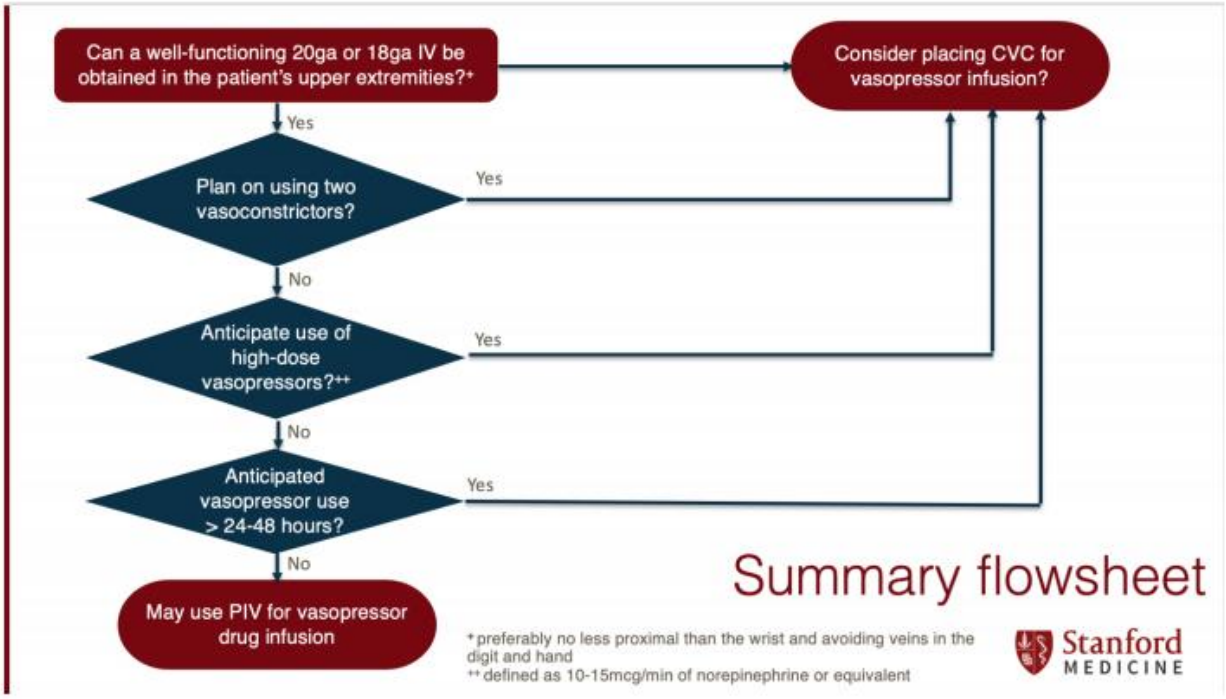

Stanford MSICU Vasopressor Distribution

Pressor Indication	Peripheral vs. Central	Vasopressor Agent	Maximum Dose	Duration	Extravasation/ Complication?
Septic shock	PICC	Phenylephrine, Norepi	40 (Phe), 5 (NE)	48hrs	No
S/p ECIC	14G, 20G pIV	Phenylephrine	55 (Phe)	12hrs	No
Septic shock	TLC	Epi, Norepi, Vaso	0.1 (Epi), 12 (NE), 0.04 (Vaso)	5 days	No
Septic, cardiogenic shock	PICC	Phenylephrine, Norepi, Vaso	20 (NE), 60 (Phe), 0.04 (Vaso)	10 days	No
S/p ECIC	14G, 20G pIV	Phenylephrine	20 (NE)	4hrs	No
Cardogenic shock	pIV, TLC, Trialysis	Dopa, Epi, Norepi, Vaso	3 (Dopa), 0.07 (Epi), 5 (NE), 0.04 (Vaso)	24 days	No
CVA	20G pIV	Norepi	1 (NE)	2hrs	No
Septic shock	TLC	Norepi, Vaso	10 (NE), 0.04 Vaso	6 days	No
Septic shock	TLC	Norepi, Vaso	11 (NE), 0.04 Vaso	17 days	No
Septic shock	TLC	Norepi, Vaso	8 (NE), 0.04 Vaso	8 days	No
Septic shock	TLC	Norepi, Vaso	5 (NE), 0.04 Vaso	5 days	No

Critical Care-17 Early mechanical circulatory support improves outcomes in idiopathic myocarditis

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Introduction: Idiopathic myocarditis (IM) is an inflammatory heart disease that has been attributed to both infectious and autoimmune etiologies. While the specific pathogenesis is incompletely understood, viral destruction of cardiac myocytes, endothelial injury with concomitant T-cell mediated autoimmune injury, and ischemic sequelae may play a mechanistic role. .1 Diagnosis is based on histopathological criteria and is often one of exclusion.2,3 Treatment is largely supportive and inlcudes immunosuppression, antiviral therapy, mechanical circulatory support (MCS) devices and transplantation.4 The outcome of mechanical circulatory device support in patients with IM, however, is poorly understood. 1,4 To better understand the epidemiology and outcomes of MCS use in IM patients, we reviewed the National Inpatient Sample from 2005-2014. We hypothesized that early implementation of MCS would mortality in adult patients with idiopathic myocarditis.

Methods: We conducted a retrospective cohort analysis using the 2005-2014 National Inpatient Sample database. Initial NIS data was extracted using ICD9 coding for IM (ICD9 422.91), and included all patient > 18 yrs with a diagnosis code for IM. Our primary outcome was to compare the incidence, outcomes, and comorbidities of IM in patients with early and late MCS utilization. The secondary outcome was to evaluate the mortality benefit of MCS in IM. We defined early MCS as <6 days from the start of hospitalization after a preliminary analysis of the dataset identified XXX as an average length of hospitalization prior to MCS initiation.

Results: We identified 25701 hospitalizations of patients with IM from 2005-2014. Adults with IM age 45-64 were significantly more likely to undergo late MCS than early MCS (p=0.026). Diagnoses significantly associated with IM included: fluid and electrolyte disorders, coagulopathy, hypertension, and congestive heart failure (Table 2). In-hospital mortality was significantly higher in patients with late MCS utilization (53.16%) compared to early MCS (3.34%) (p<0.0000) (Table 3). Early utilization of MCS in patients with IM varied over the course of the study, with a 4.94% incidence in 2005, 10.58% incidence in 2013, and 9.89% incidence in 2014. In comparison, late MCS has increased from an initial incidence of 0% in 2005 to 16.53% in 2013 and was 13.77% in 2014 (Figure 4). Early initiation of MCS reduced mortality when compared to late intervention (OR 0.04, CI 0.02-0.08) (Table 5).

Conclusion: In this retrospective nationwide analysis of IM, we observed that patients with IM have associated diagnoses that may complicate care their hospital course. We also found that early MCS intervention provided a significant mortality benefit in the management of IM.

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Table 1: Demographics of IM patients requiring MCS

Variables	Early MCS (%)	Late MCS (%)	P value
Age			
18-44	13785 (55.37%)	51 (28.65%)	
45-64	7717 (31.10 %)	87 (49.24%)	0.0258
65-84	2981 (12.01%)	39 (22.11%)	0.5000
>85	330 (1.33%)	0 (0%)	0.9443
Race			
White	14602 (67.89%)	108 (71.31%)	
Black	3216 (14.85%)	24 (16.19%)	0.2106
Hispanic	2216 (10.3%)	X	0.4636
Asian or Pacific Islander	527 (2.45%)	X	0.1081
Native American	138 (0.64%)	0 (0%)	X
Other	835 (3.88%)	X	0.2229
Region of hospital			
Northeast	6214 (24.35%)	50 (22.19%)	
Midwest	5542 (21.72%)	39 (21.58%)	0.9654
South	8387 (32.87%)	67 (36.91%)	0.6781
West	5377 (21.07%)	35 (19.32%)	1.0000
Primary expected Payer			
Medicare	4106 (16.13%)	54 (29.80%)	
Medicaid	3236 (12.71%)	30 (16.74%)	0.1804
Private insurance	14232 (55.92%)	97 (53.47%)	0.7517
Self-pay	2696 (10.59%)	0 (0%)	0.1463
No charge	269 (1.06%)	0 (0%)	0.1381
Other	912 (3.58%)	0 (0%)	0.9585

Table 2: Associated diagnoses in IM patients requiring MCS

Variables	Early MCS (%)	Late MCS (%)	P value
Fluid and electrolyte disorders	6885 (27.17%)	119 (65.41%)	0.0000
Coagulopathy	1828 (7.21%)	74 (40.53%)	0.0000
Hypertension	7529 (29.71%)	44 (24.44%)	0.007
CHF	4183 (16.51%)	39 (21.56%)	0.0091
Renal failure	1545 (6.10%)	39 (21.22%)	0.1509
Deficiency anemias	3025 (11.94%)	34 (18.93%)	0.0605
Obesity	2909 (11.48%)	29 (16.05%)	0.1155
Weight loss	913 (3.60%)	25 (13.77%)	0.0751
Chronic pulmonary disease	3615 (14.27%)	20 (11.07%)	0.9247
Valvular Disease	1254 (4.95%)	15 (8.5%)	0.5186
Peripheral vascular disorders	408 (1.61%)	15 (8.50%)	0.9490
Hypothyroidism	1673 (6.60%)	15 (8.35%)	0.9357
Depression	1667 (6.58%)	15 (8.26%)	0.1774
Diabetes, uncomplicated	2473 (9.76%)	14 (7.67%)	0.2574

Table 3: IM MCS subgroup mortality

Variables	Early MCS (%)	Late MCS (%)	P value
Died during hospitalization	853 (3.34%)	94 (53.16%)	0.0000

Figure 4: Percentage of total early and late MCS utilization in IM Per Year (2005-2014) (age > 18)

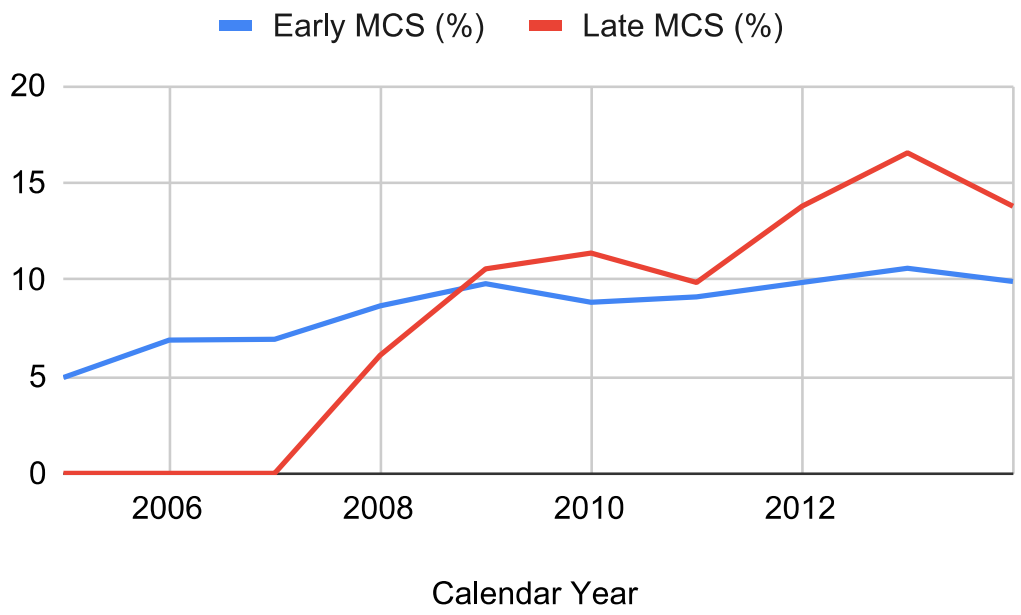

Table 5: Odds ratio of mortality in IM patients with early vs late MCS

Variables	Odds Ratio Mortality (95% CI)	Marginal Risk Ratio (95% CI)
Early versus late MCS	0.04 (0.02-0.08)	12.71 (9.22-17.52)

Critical Care-18 Echocardiogram Utilization Patterns and Association with Mortality Following Severe Traumatic Brain Injury: A Retrospective Cohort Study

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Introduction: 1.7 million traumatic brain injuries (TBI) occur annually in the US, resulting in 275,000 hospitalizations and 52,000 deaths(1). Initial traumatic injury in TBI is hypothesized to activate multiple catecholamine release pathways (2), which can result in left ventricular (LV) dysfunction, ECG changes, arrhythmia (3), as well as potential secondary brain injuries (4). One of the most common and readily available procedures to evaluate cardiovascular function is an echocardiogram, which can help diagnose early cardiac dysfunction resulting from severe TBI (5,6). While utilization of echocardiogram in the care of severe TBI patients may theoretically help clinicians prevent secondary brain injuries, there is a gap in the literature regarding utilization characteristics of echocardiogram in such patients. To address this gap, we examined the National Trauma Data Bank (NTDB) to describe utilization patterns of echocardiogram following severe TBI, as well as to examine the association of echocardiogram with in-hospital mortality following isolated severe TBI.

Methods: A retrospective cohort study was conducted using a large administrative trauma registry maintained by the National Trauma Databank (7) from 2007 to 2014. De-identified administrative data from the NTDB includes data about trauma patients and facility characteristics (7). Patients aged 18 to 65 with isolated severe traumatic brain injury (Glasgow Coma Scale [GCS] < 8 and Head Abbreviated Injury Scale [AIS] > 4) without concurrent severe polytrauma (non-head AIS >2) were included in the study. We examined the demographic, clinical, and facility factors associated with echocardiogram utilization, as well as variation, using multilevel, mixed effects, logistic regression. Additionally, we examined the association of exposure to echocardiogram and in-hospital mortality, using multivariable logistic regression.

Results: Among 47,808 patients, echocardiogram was utilized as part of clinical care in 2,548 (5.3%) patients. Clinical factors including vascular comorbidities and hemodynamic instability were associated with increased use of echocardiograms. Nearly half (46.0%, 95% CI 40.3% - 51.7%) of the variation in echocardiogram utilization was explained at the hospital level, above and beyond patient and injury factors. Exposure to echocardiogram was associated with decreased odds of in-hospital mortality following severe TBI (adjusted OR 0.77 (95% CI 0.69 - 0.87, p<0.001).

Conclusion: Echocardiogram utilization following severe TBI is relatively low, with wide variation in use at the hospital level. Exposure to echocardiogram was associated with decreased odds of mortality following isolated severe TBI. Further studies are needed to confirm these findings, as well to understand whether echocardiogram can contribute to enhanced hemodynamic management following severe TBI.

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Critical Care-19 Association between Hyperoxia, Supplemental Oxygen, and Mortality in Critically Injured Patients

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Introduction: Oxygen therapy has undisputed importance in combat casualty care to treat and prevent morbidity associated with hypoxia.1,2 However, generous supplemental oxygen is routine, and often results in hyperoxia.3 Emerging evidence indicates that even modest hyperoxia may increase morbidity and mortality,4-13 but limited evidence exists specifically for trauma patients.14-16 In addition, oxygen is a limited resource that is challenging to obtain in austere settings - requiring substantial resources, space, weight and logistics to procure.1,17,18 In this study, we evaluated the association between hyperoxia and supplemental oxygen delivery with in-hospital mortality in critically injured patients.

Methods: We conducted a multicenter, retrospective observational cohort study at one Level I and two Level II trauma centers in Colorado. Critically injured patients were those with an ICD-10 code for injury/trauma and requiring admission to the ICU. The primary predictor was oxygen saturation (SpO2) during the first 7 days of hospitalization. This was defined as hyperoxia (97-100%), normoxia (90-96%), mild hypoxia (88-89%), hypoxia (<88%). The primary outcome was in-hospital mortality.

Results: 3,464 visits met our inclusion criteria: mean age 53 years, 65% male, 68% white. The primary outcome occurred in 264 patients (7.6%), with 41% of all cases requiring mechanical ventilation. Of the 226,057 patient-hours recorded, 186,902 (46%) had hyperoxia, 212,360 (52%) had normoxia, 2,499 (1%) had mild hypoxia, and 3,921 (1%) had hypoxia (Figures 1A and 1B). During hyperoxia, the adjusted risk of mortality was higher for higher fraction of inspired oxygen (FiO2): at SpO2 of 100%, the adjusted hazard ratios for FiO2 at 100%, 80%, 60%, 30% and 21% were 7.0 (95%CI 3.8-12.9), 5.6 (95%CI 3.6-9.0), 2.7 (95%CI 1.8-4.2), 0.35 (95%CI, 0.26-0.45) and 0.15 (95%CI 0.10-0.22) respectively (Figure 2). Critically injured patients who died spent a greater amount of their time with hyperoxia (66%) than those who lived (48%) (Figure 3).

Conclusion: In this large multicenter cohort of critically injured civilian patients, hyperoxia was present during nearly half of the time during the first 7 days of hospitalization. During hyperoxia, higher oxygen administration was associated with a greater risk of mortality, while lower oxygen administration was associated with a lower risk of mortality. Previous studies which found an association between hyperoxia and increased mortality in trauma patients14,16,17,19 and critically ill medical patients3-5,18,20-30 recorded either the highest PaO2 within the first 24 hours or a mean PaO2. To our knowledge, this is the first study to investigate oxygenation continuously for the entire duration of exposure - an individual admission - instead of discrete measurements. Prospective interventional studies are required to determine the causal association between hyperoxia and clinical outcomes and optimal target oxygen concentrations in critically injured patients.

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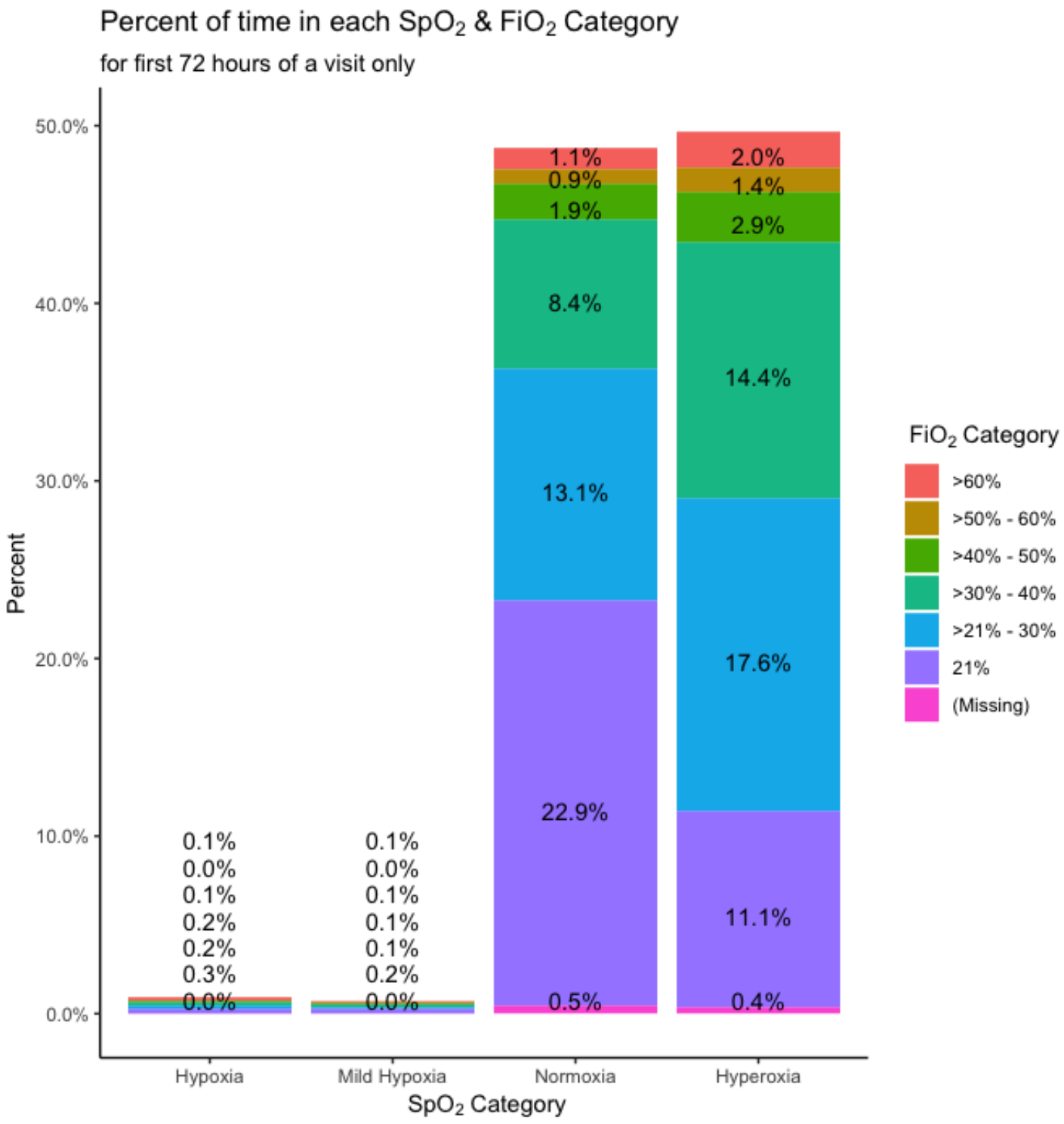
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for first 72 hours of a visit only
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20.0%
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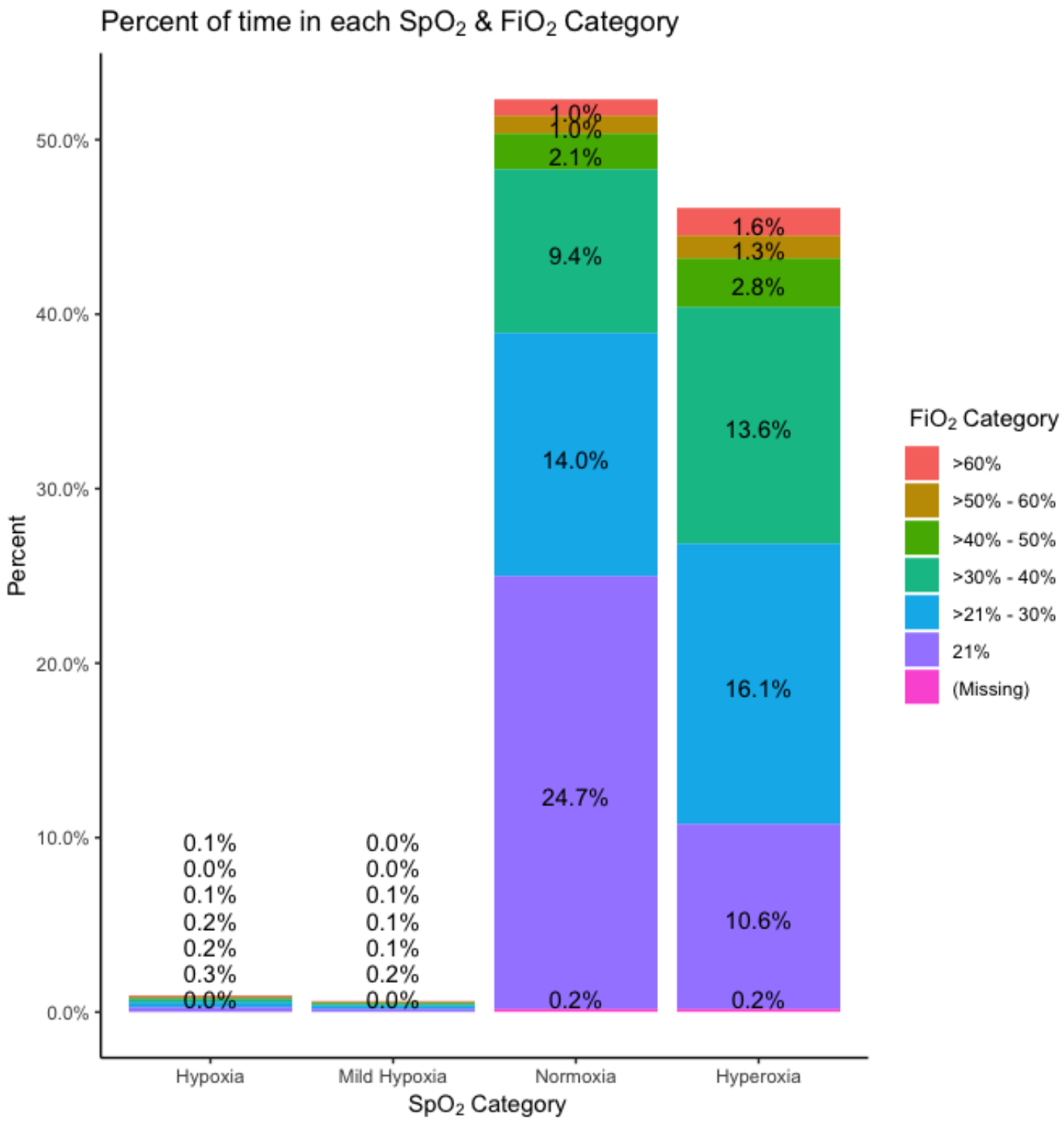
Percent of time in each SpO2 & FiO2 Category
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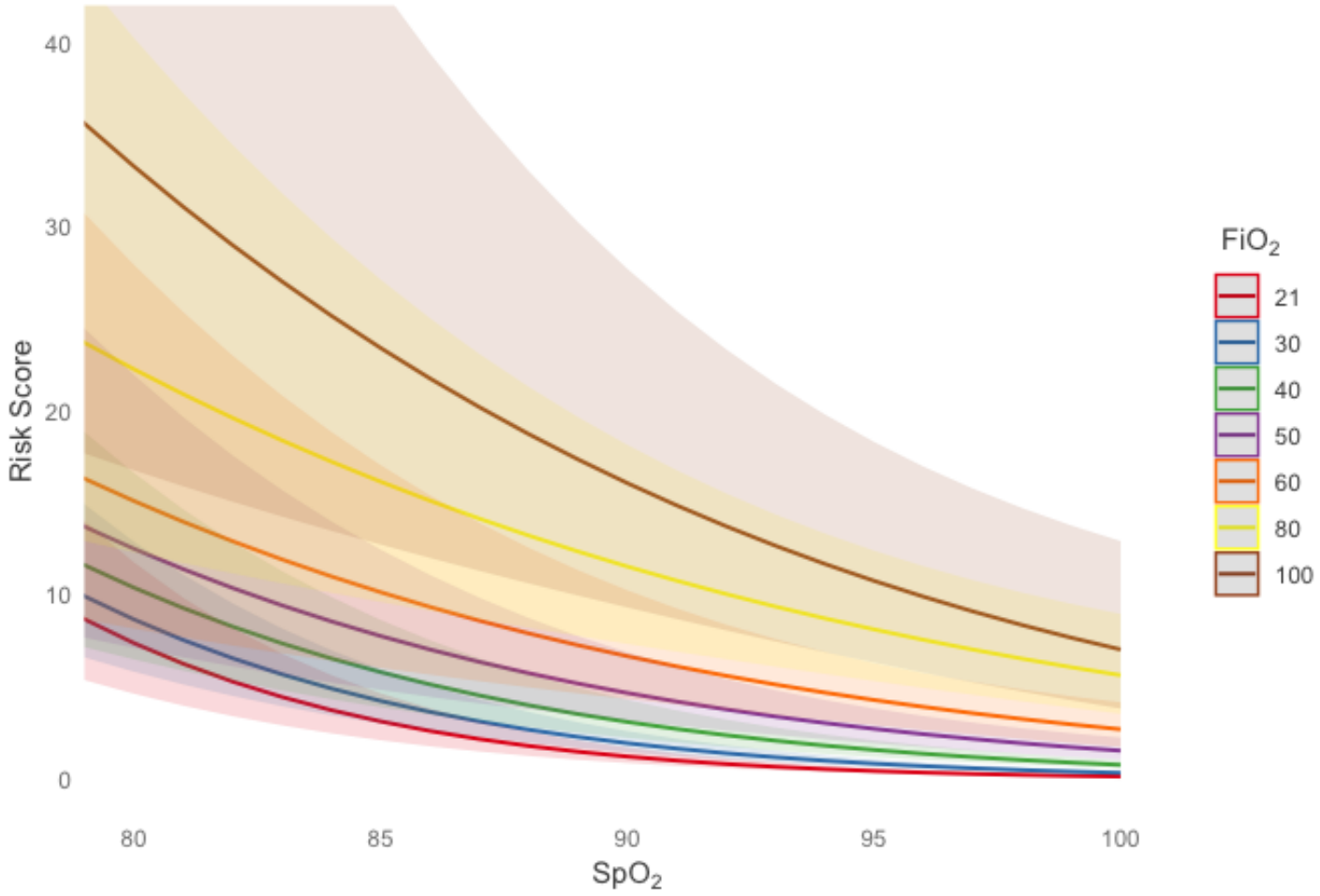

Figure 2. Adjusted risk score for mortality at each FiO2 and SpO2 category.

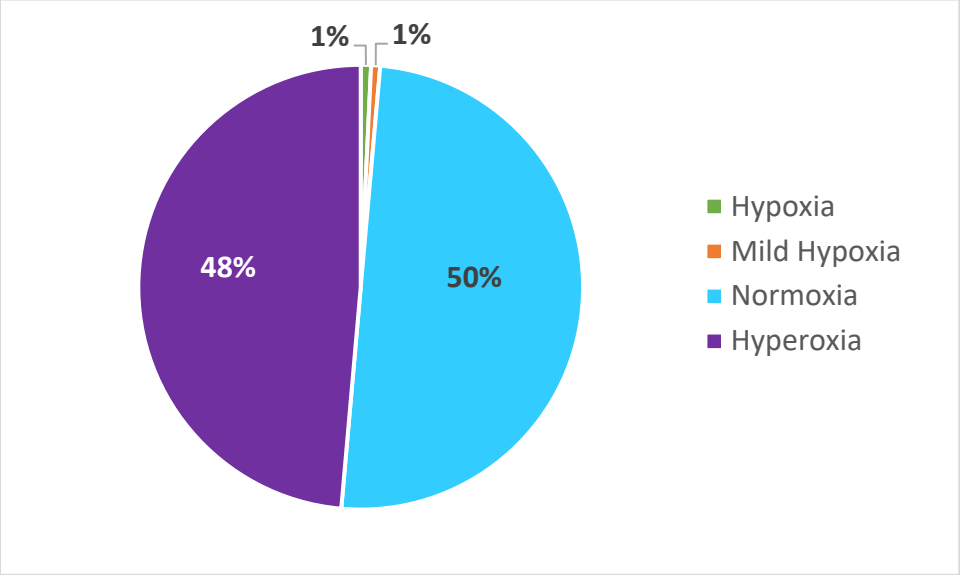

Figure 3A. Percentage of time spent at each SpO2 level for patients who lived. Hypoxia (SpO2<88%), Mild Hypoxia (SpO2 88-89%), Normoxia (SpO2 90-96%), Hyperoxia (SpO2>96%)

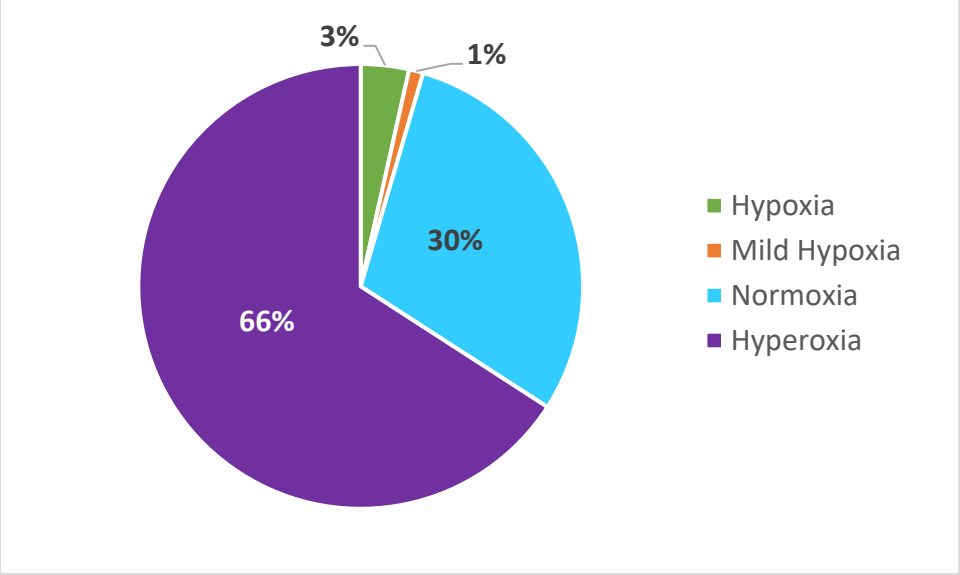

Figure 3B. Percentage of time spent at each SpO2 level for patients who died. Hypoxia (SpO2<88%), Mild Hypoxia (SpO2 88-89%), Normoxia (SpO2 90-96%), Hyperoxia (SpO2>96%)

Critical Care-20 Continuous Renal Replacement Therapy Leads to Severe Micronutrient Deficiencies in Critically Ill Patients: A Retrospective Study

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Introduction: Continuous renal replacement therapy (CRRT) is essential to the management of acute renal failure (ARF) in critical illness. Unfortunately, significant quantities of micronutrients are lost in CRRT effluent.1,2 Thus, we hypothesize that substantial, clinically-relevant, deficiencies in key micronutrients and vitamins are developing even with short-term CRRT creating a new, previously unrecognized category of 'nutrition risk.' These deficiencies are known to be associated with serious complications such as pancytopenia (copper), encephalopathy (Vit. B6), and severe muscle weakness which can be irreversible (copper). The aim of this study was to investigate incidence of micronutrient deficiencies in ICU patients on CRRT and a high malnutrition risk group of non-CRRT ICU patients and examine outcomes between groups.

Methods: Retrospective chart review was conducted at Duke University Hospital using the electronic medical record (Epic). Study group consisted of patients requiring ICU admission from 01/01/2017-12/31/2018 with one or more serum micronutrient level checked. All adult ICUs at Duke were included (Surgical, Medical, Cardiac, Cardiothoracic, and Neurocritical). Data collected included age, sex, primary diagnosis, whether CRRT was required, patient outcome, and serum micronutrient levels (Table 1). We describe patient outcomes of hospitalization, including in-hospital mortality and discharge destination.

Results: 131 ICU patients met inclusion criteria (including no known genetic metabolic disease) with one or more micronutrient level checked. A majority of ICU admissions were for postoperative management (37%) or due to sepsis or septic shock (19%), and over half required invasive mechanical ventilation or vasoactive infusions (Table 1). Overall, 36.6% of patients had ARF requiring CRRT. Among the CRRT patients, 89.6% developed one or more deficiencies in trace minerals or water-soluble vitamins, while only 44.5% of the high malnutrition risk patients developed such deficiencies (Table 2). This retrospective cohort study revealed a significant correlation between CRRT and development of trace mineral and water-soluble vitamin deficiencies in ICU patients ($p<0.00001$) versus other high nutrition risk ICU patients (Table 2). Regardless of whether patient required CRRT, data identified a significant association between micronutrient deficiency and mortality versus patients who did not develop deficiencies (Table 3)(OR=2.42, p=0.03).

Conclusion: Our data shows ~90% of patients on CRRT developed one or more trace mineral or vitamin deficiencies. A number of copper-deficient patients demonstrated severe pancytopenia, and encephalopathy was observed in association with Vitamin B6 deficiency, all of which corrected with simple supplementation. Due to limitations of retrospective cohort studies, conclusions are limited regarding the direct role of micronutrient deficiencies and clinical outcomes. Further prospective, randomized-controlled trials are needed to explore this new category of nutrition risk and develop simple supplementation strategies to prevent these clinically relevant deficiencies. We hope this data alerts clinicians to this new risk for nutrient deficiency from CRRT and leads to improved monitoring and correction of these key micronutrients.

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Table 1: Baseline Patient Characteristics

		ARF Patients on CRRT (n=48)	Nutritionally at-risk Patients (n=83)	All Patients (n=131)
Age		57.5 (13.5)	59.7 (15.0)	58.9 (14.6)
Sex				
	Male	33 (69%)	44 (53%)	77 (59%)
	Female	15 (31%)	39 (47%)	54 (41%)
ICU				
	Medical	3 (6%)	16 (19%)	19 (15%)
	Surgical	9 (19%)	28 (34%)	37 (28%)
	Cardiothoracic	35 (73%)	11 (13%)	46 (35%)
	Cardiac	1 (2%)	2 (2%)	3 (2%)
	Neurocritical	0 (0%)	26 (31%)	26 (20%)
ICU Admission Diagnosis				
	Acute Respiratory Failure	3 (6%)	8 (10%)	11 (8%)
	Sepsis / Septic shock	4 (8%)	21 (25%)	25 (19%)
	Cardiogenic shock	6 (13%)	3 (4%)	9 (7%)
	Hypovolemic shock	1 (2%)	1 (1%)	2 (2%)
	Trauma	3 (6%)	2 (2%)	5 (4%)
	Postsurgical, cardiothoracic surgery	8 (17%)	3 (4%)	11 (8%)
	Postsurgical, non-CT surgery	1 (2%)	10 (12%)	11 (8%)
	Postsurgical, abdominal/solid organ transplant	2 (4%)	3 (4%)	5 (4%)
	Postsurgical, heart or lung transplant	19 (40%)	3 (4%)	22 (17%)
	Altered Mental Status	0 (0%)	6 (7%)	6 (5%)
	Seizure/stroke/acute neurologic disorder	0 (0%)	17 (20%)	17 (13%)
	Miscellaneous	1 (2%)	6 (7%)	7 (5%)
Acute Care Interventions				
	Mechanical Ventilation	44 (92%)	46 (55%)	90 (69%)
	Vasopressors/Inotropes/Vasoactive Meds	48 (100%)	42 (51%)	90 (69%)
	ECMO (VA or VV)	17 (35%)	3 (4%)	20 (15%)
	LVAD/RVAD/IABP	15 (31%)	6 (7%)	21 (25%)
	Enteral Nutrition	43 (90%)	42 (51%)	85 (65%)
	Parenteral Nutrition	6 (13%)	21 (25%)	27 (21%)

Data are n (%) or mean (SD). VA or VV ECMO = veno-arterial or veno-venous extracorporeal membrane oxygenation, LVAD = left ventricular assist device, RVAD = right ventricular assist device, IABP = intra-aortic balloon pump

Table 2: Serum Micronutrient Deficiencies in ICU Patients

a. ARF Patients on CRRT

	Carnitine	Copper	Zinc	Selenium	Vitamin A	Thiamine	Folate	Vitamin B6	Vitamin B12	Vitamin C
CT ICU	11 (44%)	25 (71%)	7 (23%)	10 (36%)	0 (0%)	0 (0%)	2 (7%)	12 (63%)	0 (0%)	10 (43%)
SICU	1 (17%)	6 (67%)	2 (25%)	3 (50%)	0 (0%)	0 (0%)	2 (29%)	5 (83%)	0 (0%)	2 (40%)
MICU	1 (33%)	3 (100%)	0 (0%)	3 (100%)	1 (100%)	1 (50%)	2 (67%)	3 (100%)	0 (0%)	1 (50%)
CCU	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
All ICUs	13 (38%)	34 (71%)	9 (21%)	16 (43%)	1 (50%)	1 (4%)	6 (16%)	20 (71%)	0 (0%)	13 (43%)

b. Nutritionally at-risk Patients

	Carnitine	Copper	Zinc	Selenium	Vitamin A	Thiamine	Folate	Vitamin B6	Vitamin B12	Vitamin C
CT ICU	0 (0%)	1 (9%)	2 (25%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (67%)	0 (0%)	1 (33%)
SICU	0 (0%)	5 (19%)	13 (57%)	5 (31%)	2 (50%)	1 (20%)	2 (11%)	3 (38%)	1 (6%)	0 (0%)
MICU	0 (0%)	3 (19%)	3 (75%)	0 (0%)	0 (0%)	0 (0%)	1 (13%)	1 (100%)	0 (0%)	0 (0%)
CCU	0 (0%)	1 (50%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Neuro ICU	0 (0%)	2 (8%)	3 (43%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)
All ICUs	0 (0%)	12 (15%)	22 (51%)	7 (29%)	2 (33%)	1 (5%)	3 (6%)	6 (40%)	2 (3%)	1 (20%)

c. All Patients

	Carnitine	Copper	Zinc	Selenium	Vitamin A	Thiamine	Folate	Vitamin B6	Vitamin B12	Vitamin C
CT ICU	11 (35%)	26 (57%)	9 (23%)	11 (33%)	0 (0%)	0 (0%)	2 (6%)	14 (64%)	0 (0%)	11 (42%)
SICU	1 (6%)	11 (31%)	15 (48%)	8 (36%)	2 (40%)	1 (11%)	4 (16%)	8 (57%)	1 (4%)	2 (33%)
MICU	1 (2%)	6 (32%)	3 (43%)	3 (60%)	1 (50%)	1 (25%)	3 (27%)	4 (100%)	0 (0%)	1 (33%)
CCU	0 (0%)	1 (33%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Neuro ICU	0 (0%)	2 (8%)	3 (43%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)
All ICUs	13 (24%)	46 (35%)	31 (36%)	23 (38%)	3 (37%)	2 (4%)	9 (10%)	26 (60%)	2 (2%)	14 (40%)

Data are n (%). Deficiency defined as any measured serum level below the Duke laboratory reference range.

Table 3: Outcomes of Hospitalization

		Discharge to Home	Discharge to Outside Care Facility	ICU Mortality
ARF Patients on CRRT		9 (19%)	13 (27%)	26 (54%)
Nutritionally at-risk Patients		39 (47%)	28 (34%)	16 (19%)
Carnitine (n=54)		14 (26%)	16 (30%)	24 (44%)
ARF on CRRT (n=34)		4 (12%)	9 (26%)	21 (62%)
	Deficiency	1 (8%)	1 (8%)	11 (84%)
	No Deficiency	3 (14%)	8 (38%)	10 (48%)
Nutritionally at Risk (n=20)		10 (50%)	7 (35%)	3 (15%)
	Deficiency	0 (0%)	0 (0%)	0 (0%)
	No Deficiency	10 (50%)	7 (35%)	3 (15%)
Copper (n=130)		48 (37%)	40 (31%)	42 (32%)
ARF on CRRT (n=48)		9 (19%)	13 (27%)	26 (54%)
	Deficiency	6 (18%)	8 (24%)	20 (59%)
	No Deficiency	3 (21%)	5 (36%)	6 (43%)
Nutritionally at Risk (n=82)		39 (48%)	27 (33%)	16 (19%)
	Deficiency	6 (43%)	3 (21%)	5 (36%)
	No Deficiency	33 (49%)	24 (35%)	11 (16%)
Vitamin B6 (n=43)		17 (40%)	7 (16%)	19 (44%)
ARF on CRRT (n=28)		7 (25%)	5 (18%)	16 (57%)
	Deficiency	5 (25%)	4 (20%)	11 (55%)
	No Deficiency	2 (25%)	1 (13%)	5 (62%)
Nutritionally at Risk (n=15)		10 (67%)	2 (13%)	3 (20%)
	Deficiency	2 (33%)	1 (17%)	3 (50%)
	No Deficiency	8 (89%)	1 (11%)	0 (0%)
All Micronutrients (n=131)		48 (37%)	41 (31%)	42 (32%)
ARF on CRRT (n=48)		9 (19%)	13 (27%)	26 (54%)
	Deficiency	9 (21%)	10 (23%)	24 (56%)
	No Deficiency	0 (0%)	3 (60%)	2 (40%)
Nutritionally at Risk (n=83)		39 (47%)	28 (34%)	16 (19%)
	Deficiency	19 (51%)	10 (27%)	8 (22%)
	No Deficiency	20 (44%)	18 (39%)	8 (17%)

Data are n (%). Deficiency defined as any measured serum level below the Duke laboratory reference range.

Critical Care-21 Caskin2 is a Novel Regulator of Vascular Homeostasis.

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Introduction: Loss of vascular homeostasis is a hallmark of cardiovascular disease and pro-inflammatory states such as sepsis and acute lung injury. Under normal conditions, quiescent endothelial cells (ECs) actively maintain vascular homeostasis through signals that promote endothelial barrier stability and orderly blood flow, and downregulate inflammation and angiogenesis(1). The receptor tyrosine kinases Tie2 and Tie1 are major regulators of EC signaling, with Tie2 activity promoting EC quiescence and Tie1 leading to EC activation(2). Caskin2 is a novel cytoskeletal protein poorly described in the literature that our lab identified as a Tie1 interactor. We will present data strongly supporting a role for Caskin2 as a significant regulator of vascular homeostasis.

Methods: Recombinant adenoviral vectors were used to overexpress HA-tagged Caskin2 or GFP. Human umbilical vein endothelial cells (HUVECs) were grown under standard conditions except as otherwise indicated. Primary mouse lung ECs were isolated from 3 week-old Caskin2-KO mouse pups or wild type littermates by intratracheal injection of collagenase I/DNAse I, followed by excision of whole lungs and collagenase/DNAse digestion. ECs were then enriched by incubating the resulting cell suspension with anti-CD31-coated magnetic beads and plated onto tissue culture flasks coated with 2% gelatin. Western blots and Co-IP were carried out under standard conditions with lysates from indicated cell types. Caskin2-KO mice with replacement of the entire Caskin2 gene with LacZ were obtained from the Knockout Mouse Project (Project ID: VG10745; Allele identifier: Caskin2[sup]tm1(KOMP)Vlcg[/sup]; University of California-San Diego) on a C57BL/6 background, which was later backcrossed to the CD1 outbred strain. The effect of Caskin2 overexpression on HUVEC proliferation after serum treatment or survival following serum starvation and hypoxia was assessed by trypan blue staining and cell counts using an automated cell counter. Proliferation of Caskin2-WT or KO mouse lung ECs was assessed after serum treatment by EdU incorporation using the Click-iT EdU Cell Proliferation Kit (ThermoFisher). Cell migration was assessed using wound healing assays and transwell migration assays as described previously (3,4). For ex vivo aortic angiogenesis experiments, 1mm thoracic aorta segments were harvested from euthanized mice, embedded into Matrigel (BD Biosciences), cultured in growth medium for 6 days, then analyzed using the ImageJ Angiogenesis Analyzer macro (5). Oxygen-induced ischemic retinopathy was induced in neonatal Caskin2-KO mice (mixed CD1/BL6 background) as described previously (6,7). Total retinal area and total vascular area were analyzed using ImageJ by an investigator blinded to genotype. Avascular area was calculated as total vascular area subtracted from total retinal area. In vivo endothelial cell permeability (Miles assay) was assessed by measuring intradermal Evans Blue dye extravasation after histamine injection (8). All animal studies were conducted according to Duke IACUC-approved protocols. All reported results are based on a minimum of 3 biological replicates, and statistics were conducted with either Student's t-test or ANOVA.

Results: Caskin2 binds Tie1, and overexpression of Caskin2 downregulates Tie1 levels (Fig. 1). Caskin2 is primarily expressed in mature vasculature and multiple EC lines (Fig. 2). Caskin2 overexpression in HUVECs leads to a quiescent phenotype demonstrated by decreased cell proliferation, improved survival following nutrient deprivation/hypoxia, and decreased cell migration (Fig. 3). Conversely, lung ECs isolated from Caskin2-KO mice showed increased proliferation rates in vitro (Fig. 3C), and Caskin2-KO mice showed increased angiogenesis in aortic tissue explants and in the neonatal oxygen-induced retinopathy model (Fig. 4). Also, Caskin2-KO mice displayed decreased EC barrier stability in response to intradermal histamine injection (Fig. 4D).

Conclusion: Our data demonstrate that Caskin2 is an important modulator of EC quiescence and vascular homeostasis. Caskin2 overexpression leads to decreased EC proliferation and migration but improved survival after hypoxia/nutrient deprivation, whereas knockout of Caskin2 increases EC proliferation in vitro and increases angiogenesis and endothelial barrier permeability in vivo. Caskin2's mechanisms of action are still under investigation but may rely on its ability to modulate Tie1 signaling.

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Figure 1

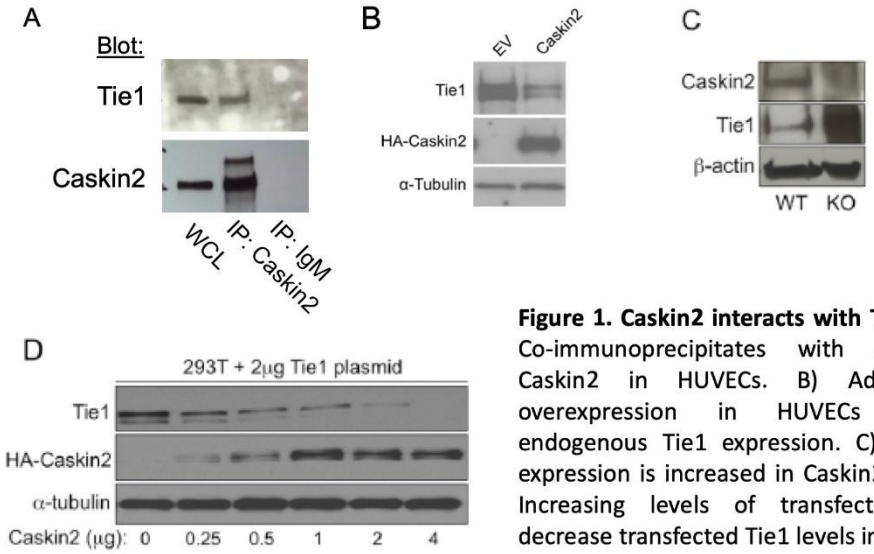


Figure 1. Caskin2 interacts with Tie1. A) Tie1 Co-immunoprecipitates with endogenous Caskin2 in HUVECs. B) Adeno-Caskin2 overexpression in HUVECs decreases endogenous Tie1 expression. C) Basal Tie1 expression is increased in Caskin2-KO ECs. D) Increasing levels of transfected Caskin2 decrease transfected Tie1 levels in 293 cells.

Figure 2

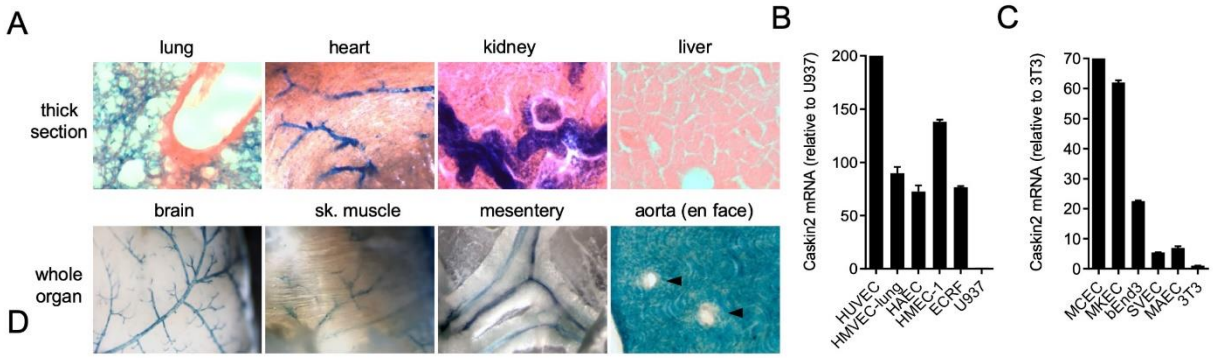


Figure 2. Caskin2 is expressed mature vasculature and endothelial cell lines. A) X-gal staining of tissue from Caskin2$^{LacZ/+}$ mice shows expression almost exclusively in vasculature. B) qRT-PCR shows Caskin2 mRNA is highly expressed in multiple human (B) and mouse (C) endothelial cell lines relative to either human U937 monocyte or mouse fibroblast 3T3 cells.

Figure 3

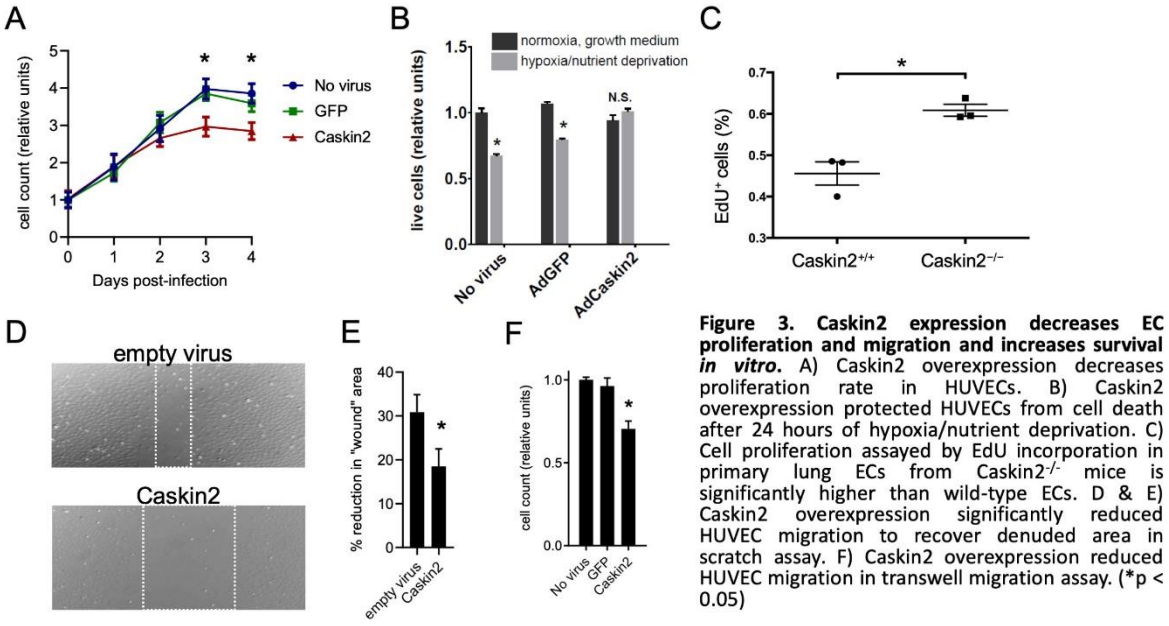
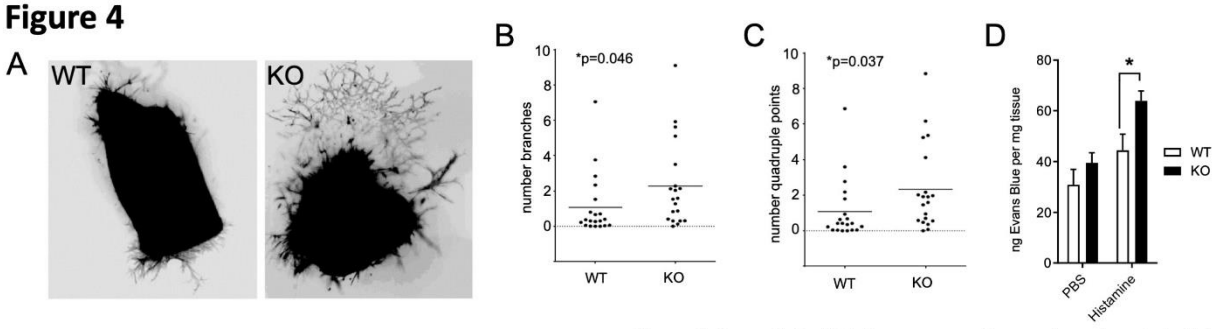


Figure 3. Caskin2 expression decreases EC proliferation and migration and increases survival *in vitro*. A) Caskin2 overexpression decreases proliferation rate in HUVECs. B) Caskin2 overexpression protected HUVECs from cell death after 24 hours of hypoxia/nutrient deprivation. C) Cell proliferation assayed by EdU incorporation in primary lung ECs from Caskin2$^{-/-}$ mice is significantly higher than wild-type ECs. D & E) Caskin2 overexpression significantly reduced HUVEC migration to recover denuded area in scratch assay. F) Caskin2 overexpression reduced HUVEC migration in transwell migration assay. (*p < 0.05)

Figure 4



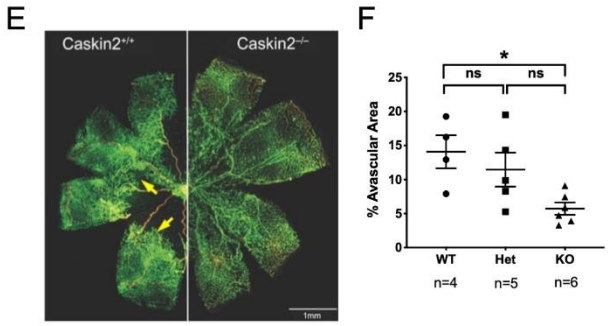


Figure 4. Loss of Caskin2 increases angiogenesis and endothelial permeability *in vivo*. A) Thoracic aorta segments were explanted from mice and grown in Matrigel for 6 days. B&C) Quantification of angiogenic branching from explants using ImageJ Angiogenesis Analyzer. D) Caskin2-KO mice had significantly more endothelial barrier permeability after intradermal histamine injection compared to WT littermates, as measured by Evans Blue extravasation at 30 minutes, *p < 0.05. No difference was observed between genotypes at sites injected with PBS. E) Neonatal mouse retinas were stained for isolectin-GS-IB$_4$ (green) and SMA (red) after oxygen-induced retinopathy. Yellow arrows indicate border of avascular area. P7 mice were subject to 75% oxygen for 5 days, then allowed to recover for 5 days prior to retinal harvest on P17. F) Quantification of avascular area from previous panel shows significant reduction in avascular area in Caskin2-KO vs WT, *p < 0.05. No differences in avascular area were present immediately after injury on P12 (data not shown).

Critical Care-22 Impact of Intensivists on Postoperative Outcomes for new Left Ventricular Assist Device (LVAD) implantations in the Cardiac Surgery Intensive Care Unit (CSICU)

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Introduction: High-intensity intensivist presence has a positive effect on patient outcomes in medical and surgical intensive care units (ICUs). Data for patients in cardiac surgery ICUs are more limited, but suggest similar improvements in outcomes. The aim of this study was to compare mechanical ventilation (MV) and length of stay (LOS) outcomes before and after high-intensity intensivist staffing in newly implanted LVAD patients in a CSICU.

Methods: After Institutional Review Board (IRB) approval, a single-center, retrospective analysis of new postoperative LVAD patients admitted to the CSICU between May 2013 and December 2018 was conducted. High-intensity intensivist staffing began on June 1, 2014. Data was obtained from the Society of Thoracic Surgeons (STS) Intermacs database and medical records. Outcomes examined were reintubation rates, duration of mechanical ventilation, and post-operative hospital LOS. Continuous variables are expressed as mean and standard deviation (SD), and skewed variables are expressed as median and interquartile range (IQR). For reintubation rates, Fisher's exact test was used. For MV and LOS analysis, the log-rank test was used.

Results: Of the 212 patients reviewed, 39 were treated prior to high-intensity intensivist staffing (pre) and 173 were treated after (post). Pre and post, 76.9% and 82.7% were male, with mean ages 55.8 (SD 13.7) and 57.1 (SD 11.5), respectively. The proportion of patients requiring reintubation was decreased after implementation of full-time intensivists (10.3% pre v. 5.8% post, $p = 0.01$). The median duration of MV prior to intensivists was 29.3 h (IQR 17.8-104.3 h) v. 21.4 h (IQR 13.6-35.9 h) post ($p = 0.27$). Median postoperative hospital LOS was similar pre- and post-intensivists (16 d [IQR 14-24 d] v. 18 d [IQR 14-24 d] respectively, $p = 0.49$).

Conclusion: High-intensity intensivist presence in the CSICU is associated with a decreased risk of extubation failure, but no changes in duration of MV or postoperative hospital LOS.

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3. Does the full-time presence of an intensivist lead to better outcomes in the cardiac surgical intensive care unit? (In press) J Thorac Cardiovasc Surg. 2019;

Critical Care-23 Machine learning in the septic surgical patient: a systematic review of postoperative sepsis diagnosis and prediction machine learning algorithms

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[2]Massachusetts General Hospital, Charlestown, MA

Introduction: Sepsis is one of the leading causes of morbidity and mortality in surgical patients with estimated mortality rates for sepsis and septic shock of 5.4% and 33.7%, respectively. Early diagnosis and treatment of sepsis with appropriate antibiotic coverage and source control is critical to improving outcomes and reducing end-organ damage. Unfortunately, sepsis has a wide range of clinical presentations and nonspecific signs and symptoms, making the early diagnosis of sepsis and detection of sepsis progression challenging. SIRS (systemic inflammatory response syndrome) and qSOFA (quick sepsis-related organ failure assessment) scores have poor sensitivity for diagnosing organ dysfunction, ranging 39-88% and 10-54%, respectively, in a 2018 review (Serafilm, Chest 2018). Early evidence suggests that machine learning can improve perioperative medicine and management of high-risk surgical patients through development of algorithms capable of identifying septic surgical patients prior to clinical decompensation. The aim of this systematic review is to evaluate the performance of machine learning models for perioperative sepsis, severe sepsis and septic shock.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for Diagnostic Test Accuracy Studies extension statement (McInnes, JAMA 2018). PubMed, MEDLINE and Embase databases were broadly searched for English-language literature until October 1, 2019. Studies meeting all eligibility criteria were included in the qualitative and quantitative data analyses. Data extracted from eligible studies included study population, sample size, sepsis definition, predicted outcomes (sepsis, severe sepsis or septic shock), machine learning model type, validation method, input features and model performance (AUROC, sensitivity, specificity, accuracy and contingency tables).

Results: A total of 57 studies were identified by the combined search queries following removal of 19 duplicates (Fig. 1). After title and abstract screening, 41 irrelevant studies were excluded and 16 full-text studies were assessed for inclusion. Nine studies met the inclusion criteria for data extraction (Fig. 2). Eligible studies evaluated machine learning algorithms for prediction of sepsis (n=6), severe sepsis (n=3) and septic shock (n=2) in surgical and mixed medical-surgical patient populations. Studies evaluated patients that underwent any inpatient surgical procedure (n=3), adult critical care (n=2), pediatric critical care (n=1), exploratory laparotomy (n=1), labor and delivery (n=1) and hepaticopancreatic and colorectal surgery (n=1). Input features of the studied algorithms included age, sex, socioeconomic factors, BMI, coexisting diseases, medications, ASA status, functional status, surgical history, prior ICU admissions and length of admissions, laboratory results, surgical procedures, anesthetic types, vital signs and other patient variables (Fig. 3). All studies evaluated predictive model accuracy using AUROC (area under the receiver operating characteristic curve). AUROC for each individual machine learning model ranged from 0.66 to 0.95. Mean AUROC for studies grouped by machine learning methodology (Fig. 4a) and severity of sepsis (Fig. 4b) were calculated and no statistically significant differences were found. However, mean AUROC for prediction of septic shock was 0.13 (15.6%) greater than the mean AUROC for prediction of sepsis, and this finding approached significance (p=0.037). As only two studies evaluated machine learning algorithms for prediction of septic shock, additional studies are needed to assess performance.

Conclusion: In this systematic review, machine learning algorithms appeared to outperform historical SIRS and qSOFA scores in the prediction of postoperative sepsis, severe sepsis and septic shock with all except one studied algorithm having acceptable discrimination, as defined by AUROC greater than 0.7. The accuracy of machine learning algorithms in predicting sepsis was consistent across all surgical populations, machine learning methodologies and illness severities, except for the study by Betts et al of an XGBoost algorithm for the prediction of postpartum sepsis.

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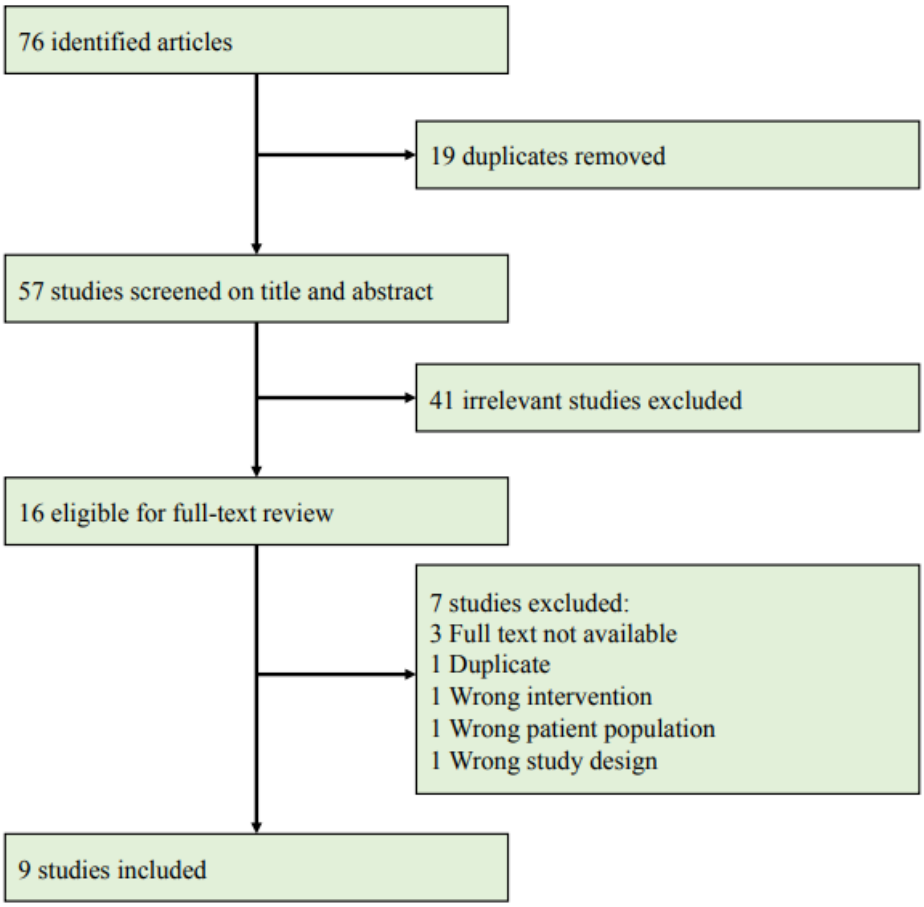
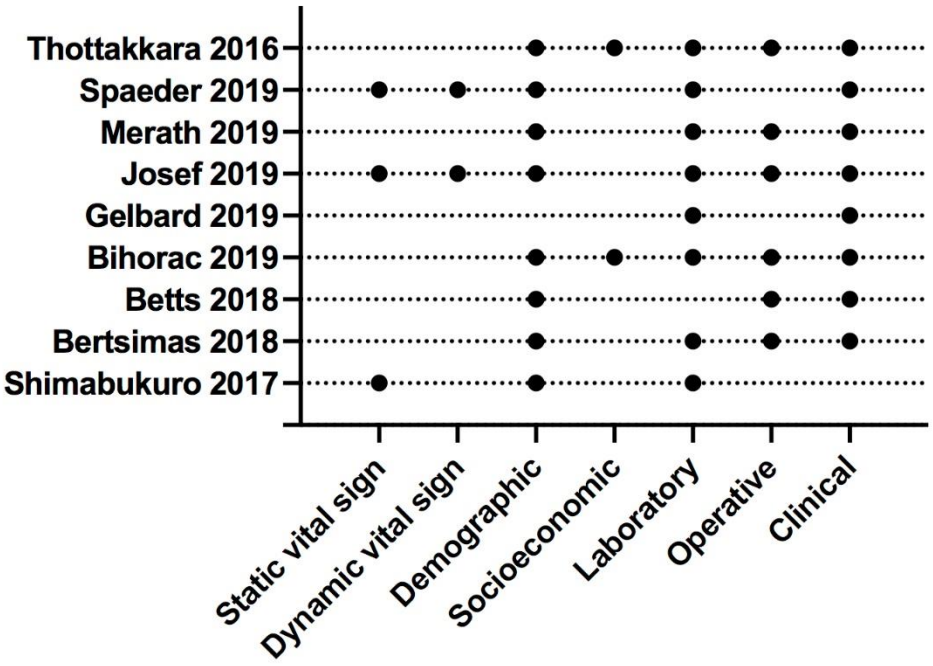


Study	Study type	Test population	Training Population	Operation type	Relevant Output(s)	Machine Learning Model	Training Set Size	Validation Method	Performance (AUROC/Sens/Spec)
Shimabukuro et al, 2017	Single center RCT of existing model	Medical-surgical intensive care units	MIMIC II (MICU)	n/a	Severe Sepsis	Proprietary (Insight)	1394	4-FCV	0.952/0.9/0.9
Bertsimas et al, 2018	Retrospective	ACS-NSQIP (2014)	ACS-NSQIP (2007-2013)	all surgical procedures	1) Sepsis 2) Septic Shock	OCT, Optimal Impute	382,960	Bootstrapping	1) 0.844 2) 0.92
Betts et al, 2018	Retrospective	PDC/QHAPDC (n=61177)	PDC/QHAPDC (n=361332)	cesarean section, vaginal delivery	Sepsis	XGBOOST	361332	5-FCV	0.66
Bihorac et al, 2019	Retrospective	Single site EHR (n=10291)	Single site EHR (n=41166)	all inpatient surgical procedures requiring at least 24 hour hospital stay	Sepsis	GAM, SVM	41166	5-FCV on 50 bootstrap samples	0.91/0.82/0.86
Gelbard et al, 2019	Retrospective	Single site EHR (n=15)	Single site EHR (n=117)	exploratory laparotomy for abdominal trauma	Severe Sepsis	RF	117	LOOCV	0.798/0.797/0.74
Josef et al, 2019* (abstract only)	Retrospective	Multi-site EHR (ICUs)	Multisite EHR (ICUs)	SICU (all surgical patients)	Sepsis	Proprietary (AISE)	15223	10-FCV (80%/20%)	0.853/0.85/0.683
Merath et al, 2019	Retrospective	ACS-NSQIP (2014-2016)	ACS-NSQIP (2014-2016)	Hepatic, pancreatic and colorectal surgery	1) Sepsis 2) Septic Shock	Decision Tree	15657	Bootstrapping (50%)	1) 0.79 2) 0.87
Spaeder et al, 2019	Retrospective	Single site EHR (PICU)	Single site EHR (PICU)	Mixed medical-surgical PICU (pediatric surgeries)	Sepsis (24h prior)	RF	1425	LOOCV	0.762
Thottakkara et al, 2016	Retrospective	Single site EHR	Single site EHR	all inpatient surgical procedures requiring at least 24 hour hospital stay	Severe Sepsis	1) GAMs 2) SVM 3) Naive Bayes	50318	CV (70%/30%)	1) 0.852 2) 0.762 3) 0.83


Thottakkara 2016
Spaeder 2019
Merath 2019
Josef 2019
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Betts 2018
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Shimabukuro 2017
Static vital sign
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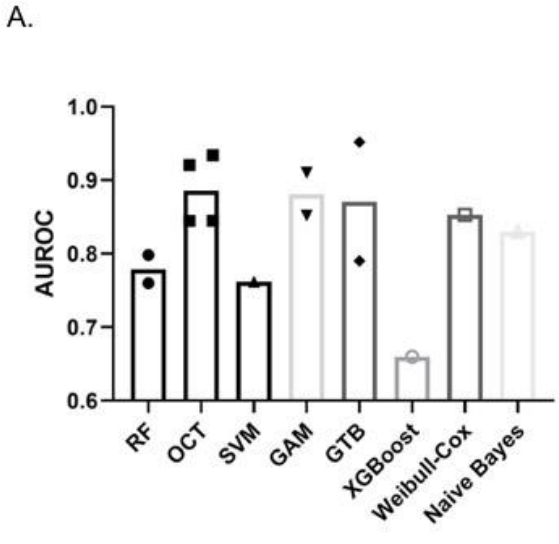
Socioeconomic
Laboratory
Operative
Clinical


A.
AUROC
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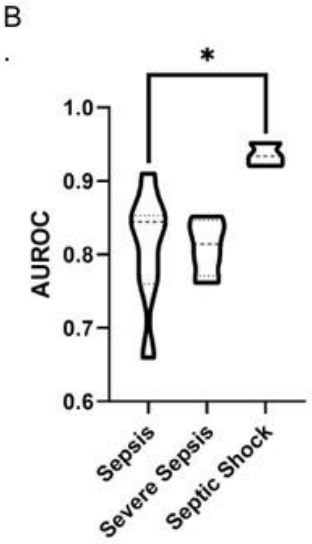
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Critical Care-24 USE OF EXTRACORPOREAL CARDIOPULMONARY RESUSCITATION FOR INTRAOPERATIVE CARDIAC ARREST AT AN ACADEMIC MEDICAL CENTER

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Introduction: Intraoperative cardiac arrest has distinctive characteristics that differentiate it from other in-hospital and out-of-hospital cardiac arrest. It occurs in a highly monitored and controlled environment and it is typically managed by surgeons, nurses, and anesthesiologists using advanced cardiac life support techniques. Extracorporeal Cardiopulmonary Resuscitation (ECPR) in patients with refractory cardiac arrest represents a unique approach in the intraoperative setting. The ultimate aim of this study is to determine patient and procedural barriers to ECPR as well ECPR utilization rates during cardiac and non-cardiac surgery. Our hypothesis is that decision-making regarding ECPR is a complex process integrating multiple procedural factors. ECPR may not be utilized in some instances because of an overall lack of familiarity with the process and eligibility criteria. We aim to compare rates of ECPR in cardiac and non-cardiac surgery and to identify barriers to deployment of ECPR that could serve as opportunities for education.

Methods: We queried the department of anesthesiology quality improvement and patient safety database at Duke University Hospital (from July 2013 until November 2018) for intraoperative cardiac arrest and other similar events. The search yield 297 patients suspected to have suffered intraoperative cardiac arrest. After retrospective chart review, we confirmed 112 intraoperative cardiac arrest events. Of those patients, 83 arrested during non-cardiac surgery and 29 had cardiothoracic surgical procedures. Confirmed cardiac arrests were then crosschecked with our ECMO database by using name and medical record number. We determined the rate of intraoperative ECPR utilization and also compared patient and procedural characteristics.

Results: During the study period, 112 patients had confirmed intraoperative cardiac arrest in all operating rooms. The overall rate of ECPR utilization was 12.5% (14 total, 8 non-cardiac). Cardiac patients suffered 25.9% of all arrest events. Of the 29 cardiac surgical patients with intraoperative cardiac arrest, 6 received ECPR (20.7%). In 5 out of 6 cardiac surgery ECPR patients, it was VF/VT cardiac arrest occurring during or shortly after induction and PEA arrest in 1 patient secondary to hypoxemia during lung transplantation. In the non-cardiac patients ECPR was used for 9.6% of cardiac arrests. For these patients the etiology was unexpected surgical complications in 3, hemorrhage/hypovolemia in 2, amniotic fluid embolism in 1, and VF/VT arrest in 1 patient.

Conclusion: At our institution, ECPR utilization is higher in cardiac surgery patients. It is possible that familiarity with ECPR initiation techniques play a role. We plan to identify discrete knowledge gaps that may exist preventing appropriate utilization of ECPR outside of the cardiac OR. We hope that with further education this potentially lifesaving technique could be employed in a higher percentage of appropriate patients.

Reference(s): Anesth Analg 2015;120(2):364-70 J Cardiothorac Vasc Anesth 2016;30(2):338-344

Critical Care-25 Intraoperative Dexmedetomidine Use and Atrial Fibrillation following Cardiac Surgery

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Introduction: Atrial fibrillation affects between 17-45% of patients following cardiac surgery and is an independent predictor of increased ICU and hospital length of stay, cost of care, and mortality. Evidence continues to emerge that post-operative atrial fibrillation may be linked to inflammation and oxidative stress. Dexmedetomidine is an alpha-2 adrenergic agonist with known anti-inflammatory effects, and some anesthesiologists have been administering dexmedetomidine infusions to cardiac surgery patients in the perioperative period. We hypothesized that perioperative dexmedetomidine use is associated with a decreased incidence of post-operative atrial fibrillation.

Methods: We analyzed data from cardiac surgery patients at Vanderbilt University Medical Center who underwent surgery from 11/2/2017 to 7/12/2019. Cardiac surgery was defined as surgery on the heart or aorta that required sternotomy or thoracotomy. Repeat procedures (e.g. re-exploration) were excluded. Perioperative dexmedetomidine use was defined as the initiation of a dexmedetomidine infusion at any point during the intraoperative period. At our institution, dexmedetomidine infusion is typically continued post-operatively until patient extubation. Post-operative atrial fibrillation was defined as atrial fibrillation for any duration of time from ICU admission to hospital discharge. Post-operative atrial fibrillation data were obtained by querying nursing flow sheets, medication administration records, and cardioversion procedure notes. We compared post-operative atrial fibrillation to dexmedetomidine administration using Chi-square and logistic regression and performed sub-group analyses in patients with and without a history of atrial fibrillation.

Results: One thousand eight hundred ninety-six patients underwent cardiac surgery (44.7% CABG, 30.2% valves, 6.3% aorta, 4.3% LVAD, 7.5% transplant, 7.0% other) during the study period with a median patient age of 66 (Range 17-87). Thirty-one percent of patients were female, and 28.6% of patients had a history of atrial fibrillation prior to surgery. Six hundred ninety-nine patients (36.9%) developed post-operative atrial fibrillation, and 710 patients (37.4%) received perioperative dexmedetomidine. Of patients who received dexmedetomidine, 257 (36.2%) developed post-operative atrial fibrillation, while 442 (37.3%) of patients who did not receive dexmedetomidine developed post-operative atrial fibrillation (p=0.64). Among patients with a history of atrial fibrillation, 137 (67.8%) of those who received dexmedetomidine developed post-operative atrial fibrillation, and 216 (63.5%) of those who did not receive dexmedetomidine developed post-operative atrial fibrillation (p=0.31). Among patients with no history of atrial fibrillation, 120 (23.6%) of those who received dexmedetomidine developed post-operative atrial fibrillation, and 226 (26.7%) of those who did not receive dexmedetomidine developed post-operative atrial fibrillation (p=0.21). Adjusted for the impact of age, sex, and procedure type, perioperative dexmedetomidine use was not associated with post-operative atrial fibrillation in the total cohort (OR: 0.94; 95% CI 0.76-1.17; p=0.58), in patients with a history of atrial fibrillation (OR: 1.10; 95% CI 0.74-1.63; p=0.64), or in patients with no history of atrial fibrillation (OR: 0.86; 95% CI 0.65-1.12; p=0.26).

Conclusion: Perioperative dexmedetomidine infusion was not associated with post-operative atrial fibrillation. Further study is necessary to elucidate whether specific patient populations may benefit from perioperative dexmedetomidine use during cardiac surgery. Clinical trials will better characterize the effect of perioperative dexmedetomidine on post-operative atrial fibrillation as well as other outcomes associated with perioperative inflammation such as delirium, acute kidney injury, and acute lung injury.

Reference(s): Arsenault KA, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. Cochrane Database of systematic reviews. Issue 1, Art No. CD003611. 2013. M. Zakkar, et al. Inflammation, oxidative stress and postoperative atrial fibrillation in cardiac surgery. Pharmacology & Therapeutics, Volume 154, Pages 13-20, 2015.

Critical Care-26 Baseline serum albumin concentration is associated with length of stay and 90-day mortality in patients after transcatheter aortic valve replacement

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Introduction: Transcatheter aortic valve replacement (TAVR) is an increasingly popular intervention for high-risk patients with severe aortic stenosis. Although it is considered minimally invasive, in-hospital costs of TAVR are comparable to surgical aortic valve replacement. TAVR candidates have significantly greater comorbidities compared to their surgical counterparts and 90-day mortality ranges from 6-13%. Given that it is an expensive therapy, with relatively high mortality, patient selection may help to improve outcomes. Emerging data suggests that frailty plays an important role in recovery after TAVR. However, to data there is no universally accepted scoring system or biomarker to assess frailty in TAVR patients. Serum albumin concentrations have been used to assess for frailty in various disease states; preliminary data suggest that it may be useful for short (30-day) or long-term (1-year) risk-stratification in TAVR patients. Our goal was to investigate whether baseline serum albumin concentrations are associated with outcomes within a clinically meaningful period (90-days) after TAVR.

Methods: We conducted a retrospective analysis of data from patients who presented for TAVR at the Tufts Medical Center (Boston, MA). We only included patients who had serum albumin concentrations measured between one and four weeks before TAVR. We also excluded all patients who had been hospitalized within 4 weeks before the procedure. We constructed a locally weighted scatterplot smoothing (LOWESS) curve to graphically represent the relationship between serum albumin concentration and 90-day mortality. Kaplan-Meir curves were constructed and compared using long-rank tests for intensive care unit (ICU) as well as hospital length of stay (LOS), stratified by albumin concentration. A Cox Proportional-Hazards model was used to investigate the relationship between albumin concentration and ICU as well as hospital LOS, controlling for potential confounders. Logistic regression, adjusting for potential confounders, was used to investigate the association of albumin concentration with 90-day mortality.

Results: 245 patients comprised the analytic cohort and 90-day mortality was 8%. Characteristics of the cohort are shown in Table 1. LOWESS curve (Figure 1) analysis demonstrated a notable flattening of the risk between albumin concentrations of 3 g/dL and 4 g/dL. As such, we assumed that the 'normal' population serum albumin concentration threshold of 3.5 g/dL may be applicable to TAVR patients as well. Kaplan-Meir curves comparing TAVR patients with baseline serum albumin concentrations of <3.5 g/dL to those with concentration >3.5 g/dL, and who survived to hospital discharge, demonstrated a significant difference between groups for ICU (Figure 2) as well as hospital LOS (Figure 3). Cox-proportional hazards analysis demonstrated that when controlling for Society of Thoracic Surgeons (STS) score and New York Heart Association (NYHA) classification, patients with albumin concentrations <3.5 g/dL were 70% more likely to have prolonged ICU LOS compared to their counterparts with albumin concentrations >3.5 g/dL (HR 1.70;95%CI 1.04-2.46, p=0.03). Similarly, when controlling for ICU LOS and NYHA classification, patients with albumin concentrations <3.5 g/dL were greater than 50% more likely to have prolonged hospital LOS compared to their counterparts with albumin concentrations >3.5 g/dL (1.56; 95%CI 1.01-2.42, p=0.04). Logistic regression analysis, controlling for STS score and NYHA classification, demonstrated that patients with albumin concentrations <3.5 g/dL were almost 4 times more likely to not survive to 90-days post-TAVR compared to their counterparts with albumin concentrations >3.5 g/dL (OR 3.79; 1.13-12.64, p=0.03).

Conclusion: Our data suggests that TAVR patients with low baseline serum albumin concentrations are at an increased risk for prolonged hospitalization and have a greater likelihood of not surviving to 90-days post-procedure when compared to their counterparts with 'normal' albumin concentrations. Further studies are needed to validate our findings and to determine whether baseline serum albumin concentrations can be used as a biomarker of frailty to better risk-stratify and improve patient selection for TAVR.

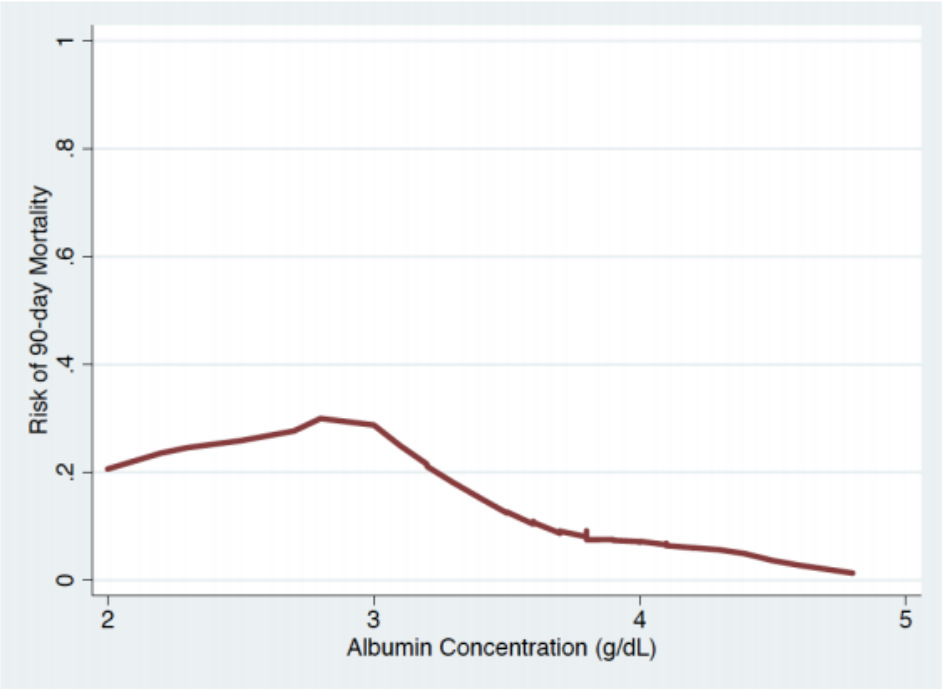
Reference(s): Comparison of U.S. Hospital Costs Between Transcatheter Aortic Valve Replacement (TAVR) and Surgical Aortic Valve Replacement (SAVR) 20(9), A579-A580 (2017,) Utility of 90-day mortality vs 30-day mortality as a quality metric for transcatheter and surgical aortic valve replacement outcomes (2019,) Habitual Physical Activity in Older Adults Undergoing TAVR Insights From the FRAILTY-AVR Study 12(8), 781-789 (2019,) Albumin Is Predictive of 1-YearMortality After Transcatheter AorticValve Replacement 106(5), 1302-1307 (2018)

Table 1. Characteristics of the study cohort (n=245).

	90-days - Deceased (n=19)	**90-days - Alive (n=226)**	**P-value**
Age (years)	81 ± 7	80 ± 9	0.57
Sex (%)			0.78
Female	53	51	
Male	47	49	
BMI (kg/m^2)	26 ± 5	28 ± 6	0.12
BSA (m^2)	1.8 ± 0.2	1.8 ± 0.3	-
Major comorbidities	3 ± 1	3 ± 1	-
STS Risk Score	3 ± 1	10 ± 8	**<0.001**
6-minute walk test (%)			**0.03**
No	47	32	
Yes	53	68	
KCCQ12	51 ± 24	92 ± 18	**<0.001**
NYHA Classification (%)			**0.02**
Class I	0	3	
Class II	16	13	
Class III	53	70	
Class IV	0	1	
Class V	32	13	
Class VI	0	0	
LVEF (%)	48 ± 17	53 ± 13	0.23
AVA (cm^2)	0.71 ± 0.18	0.74 ± 0.20	0.50
AMG (mmHg)	44 ± 14	39 ± 15	0.15
Albumin (g/dL)	3.7 ± 0.5	4.0 ± 0.4	**0.02**
ICU LOS (hours)	74 (55-135)	46 (27-75)	**0.04**
Hospital LOS (days)	5 (2-8)	4 (3-6)	**0.01**

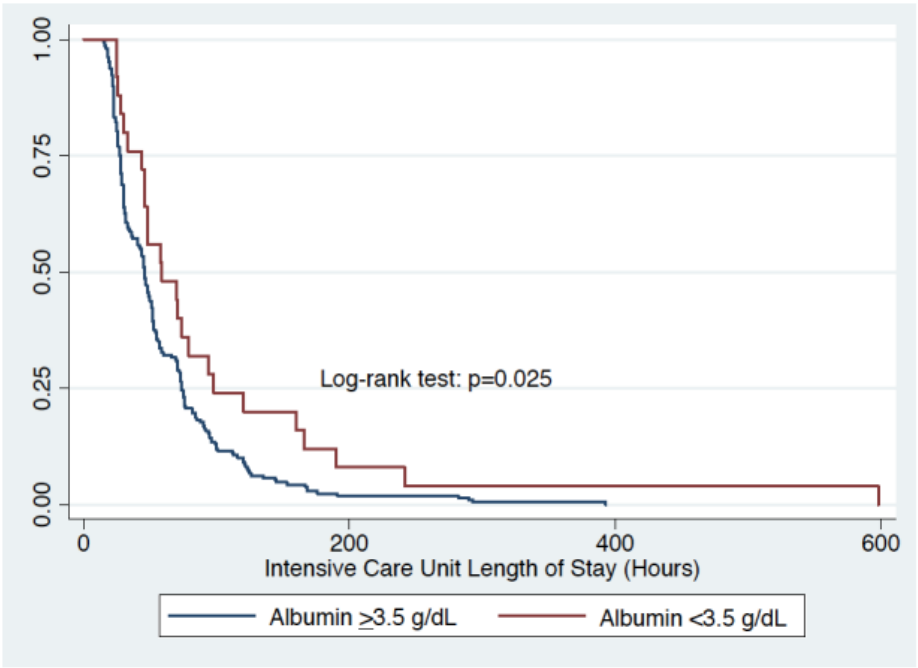
Data are shown as mean ± standard deviation, medial (interquartile range), or proportions and compared using t-tests, log-rank tests, and chi-square tests, respectively. Statistically significant p-values are shown in bold. BMI = body mass index; BSA = body surface area; STS = Society of Thoracic Surgeons; KCCQ12 = Kansas City Cardiomyopathy Questionnaire; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; AVA = aortic valve area; AMG = aortic valve mean gradient; ICU = intensive care unit; LOS = length of stay.

Figure 1. Graphical representation of the relationship between baseline serum albumin concentration and risk of 90-day mortality (n=245).



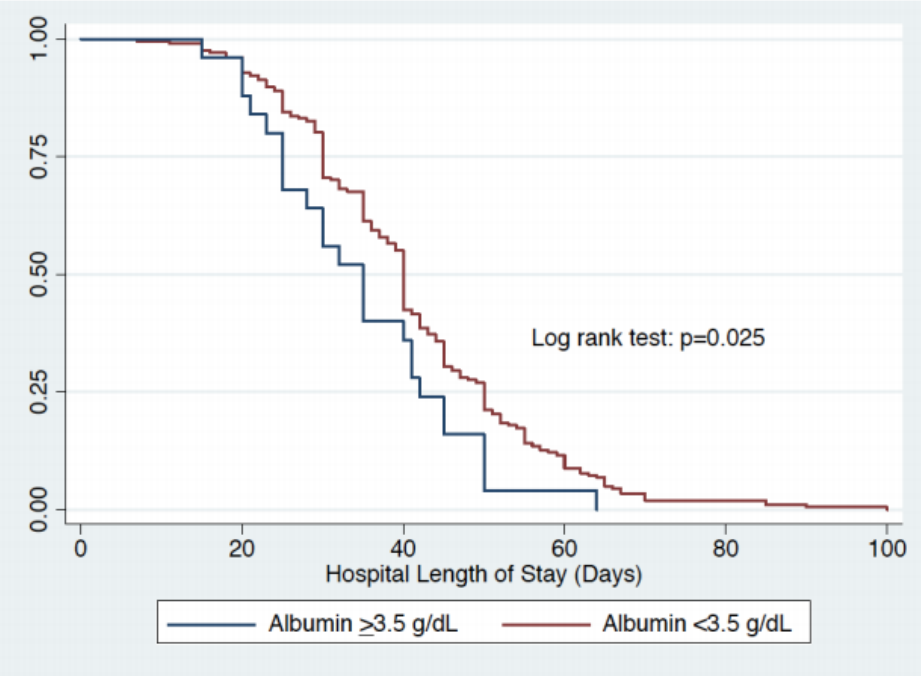
Locally weighted scatterplot smoothing demonstrates significant flattening of the risk curve between albumin concentrations of 3 d/dL and 4 g/dL.

Figure 2. Intensive care unit length of stay stratified by albumin concentration (n=238).



Kaplan-Meir curves demonstrate that intensive care unit length of stay (in hours) is significantly longer in patients with albumin concentration <3.5 g/dL compared to patients with concentrations ≥3.5 g/dL. All patients survived to hospital discharge.

Figure 3. Hospital length of stay stratified by albumin concentration (n=238).



Kaplan-Meir curves demonstrate that hospital length of stay (in days) is significantly longer in patients with albumin concentration <3.5 g/dL compared to patients with concentrations ≥3.5 g/dL. All patients survived to hospital discharge.

Critical Care-27 Immune Profile of Sepsis-Related Myocardial Injury

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Introduction: Sepsis is characterized by multisystem organ dysfunction. The heart is frequently affected in sepsis, with many individuals suffering from conditions such as worsened diastolic function and myocardial injury. Despite the high prevalence and negative impact on patients, the mechanisms that produce sepsis-related cardiac dysfunction are not completely understood. Sepsis-related myocardial injury represents an important critical care issue given its high prevalence and association with worse outcomes. This study examined the relationship between a panel of immune cytokines and myocardial injury in sepsis. We hypothesized that troponin elevations often seen in myocardial injuries would be associated with alterations in cytokine concentrations.

Methods: Subjects were selected from a biorepository of adult patients admitted to an intensive care unit at a single institution. Individuals meeting the current definition of sepsis were included. Those who had undergone a recent cardiac procedure, with limitations on their care, or with renal failure were excluded. Cardiac troponin levels were measured with a high-sensitivity electrochemiluminescence assay and cytokine levels were measured using a bead-based multiplex assay. The false discovery rate was used to identify cytokines that were associated with cardiac troponin concentrations. These were then entered individually into a multivariable linear regression to adjust for subject characteristics, renal function, and severity of illness.

Results: Ninety-four subjects were included. The study population had a mean age of 58 years, sequential organ failure assessment score of 7, and Charlson Comorbidity Index of 5. Screening of 19 inflammatory cytokines revealed that interleukin (IL)-4, IL-5, IL-13, IL-23, and macrophage inflammatory protein 1β were associated with cardiac troponin levels after adjusting for multiple comparisons. When adjusting for age, sex, severity of illness, renal function, and comorbidities, IL-4 ($\beta=3.4$, $p<0001$), IL-5 ($\beta=40.0$, $p<0.0001$), IL-13 ($\beta=5.7$, $p<0.0001$), and IL-23 ($\beta=0.4$, $p<0.0001$) remained associated with sepsis-related myocardial injury.

Conclusion: Sepsis-related myocardial injury is associated with increased levels of cytokines produced by Th2 T-helper cells. These findings support future research to determine whether this type-2 immune response is a cause of, or response to, myocardial injury in sepsis.

Reference(s): Frangogiannis, N. G. (2014). The inflammatory response in myocardial injury, repair, and remodelling. Nature Reviews Cardiology, 11(5), 255–265. doi: 10.1038/nrcardio.2014.28 Hussain, N. (2013). Elevated Cardiac Troponins in Setting of Systemic Inflammatory Response Syndrome, Sepsis, and Septic Shock. ISRN Cardiology, 2013, 1–7. doi: 10.1155/2013/723435 Xu, J.-Y., Xiong, Y.-Y., Lu, X.-T., & Yang, Y.-J. (2019). Regulation of Type 2 Immunity in Myocardial Infarction. Frontiers in Immunology, 10. doi: 10.3389/fimmu.2019.00062

Critical Care-28 Does Use of Near-Infrared Spectroscopy Impact Rate of Limb Complications or Mortality in Patients on VA-ECMO?

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[1]NYU Langone Health, New York City, NY

Introduction: Acute limb ischemia is a known complication of peripheral VA-ECMO. The femoral arterial cannula increases the risk of devastating complications ranging from limb ischemia potentially leading to limb loss or even death. Currently acute limb ischemia remains a clinical diagnosis without one test to serve as a diagnostic standard1,3. Literature review shows that Near-infrared Spectroscopy (NIRS) and direct intracompartmental pressure measurement with Stryker device to be the most reliable and methods to help support the diagnosis1,2. NIRS allows continuous noninvasive monitoring of hemoglobin oxygenation and thus tissue oxygenation, providing numerical data that can be trended and correlated to clinical exam. Purpose: NYU Langone Health started offering V-A ECMO in 2014 Since then use has expanded from eCPR to also include supporting patients undergoing lung transplant, bridge to heart transplant, bridge to VAD, and even catastrophic pulmonary embolus. Recently, use of NIRS monitoring to help detect at-risk limbs has begun to be implemented on all V-A ECMO patients We sought to compare the rate of limb ischemia events before and after institution of the NIRS monitoring device. We hypothesized that the NIRS monitor would be more aid in detection of limb ischemia and would correspond with lower rates of ischemic complications.

Methods: All cases using ECMO from 12/1/2014 to 9/1/2019 were identified (n=126). Patients who had VV-ECMO or central cannulation were excluded, leaving 86 patients on peripheral V-A ECMO to be analyzed. Indications for ECMO were codified and limb complications of any type were identified. Number of limb complications were compared before and after 4/1/2018, which is when use of NIRS for detection of limb ischemia became codified part of treatment and nursing protocol for patient monitoring. Outcomes of ECMO cannulations at time of discharge also compared (Figure 1).

Results: After characterization of indications for patients who received ECMO at NYU Langone (Table 1) and exclusion criteria were applied (Figure 1), a total of 86 patients with peripheral V-A ECMO cannulas were identified. Next, the total number of patients that had limb complications, as well as their condition at discharge (alive vs. expired) was compared with regard to 4/1/18, when NIRS monitoring became institution standard (Table 2). There was no difference in either the rate of limb complication or rate of mortality at discharge.

Conclusion: At our institution, we did not detect a change in incidence of limb ischemia after implementing the routine use of NIRS monitors in 4/2018. This could mean that NIRS is not helpful in early identification of at-risk-limbs or that our study was simply not able to detect a true difference. Limitations of small sample size, lack of actual NIRS data (instead of analyzing the binary presence/absence of monitor) could be investigated. Additionally, outcomes could be correlated to presence or absence of distal reperfusion catheters.

Reference(s): Moretensen, S.,Vora, M., Mohamadi, A., Wright, C., Hanna, P., Lechtig, A., Egan, J., Williamson, P., Wixtend, J., Rutkove, S., Nazarian, A. (2019). Diagnostic Modalities for Acute Compartment Syndrome of the Extremities: A Systematic Review. JAMA surgery https://dxdoi.irg/10/1001/jamasurg.2019.1050 Lamb, K., DiMuzio, P., Johnson, A., Batista, P., oudgill, N., McCullough, M., Eisenberg, J., Hirose, H., Cavarocchi, N. (2017). Arterial protocol including prophylactic distal perfusion catheter decreases limb ischemia complications in patients undergoing extracorporeal membrane oxygenation. Journal of Vascular Surgery (65(4), 1074-1079. https://dx/doi.org/10/1016/j.jvs Fellahi, J. Butin, G., Zamparini, G., Fischer, M. Gerard, J., Hanouz, J. (2014) Lower limbperipheral NIRS parameters during a vascular occlusion test: An experimental study in healthy volunteers. Annales Francaises d'Anesthesie et de Reanimation 33(1), e9-e14. https:dx.doi.org/10.1016/j.ejcts.2008.08.027

Table 1: Indications for VA-ECMO	
Diagnosis	**Number of Patients**
Advanced Heart Failure	7
Cardiogenic Shock	23
eCPR	30
Liver Transplant	1
OHT, Graft Dysfunction	1
Peri-Lung Transplant	24
Post Cardiotomy	39
Asc. Aorta Tear Req. Emergent Repair	1

Example of NIRS Monitor

Figure 1: Study Design

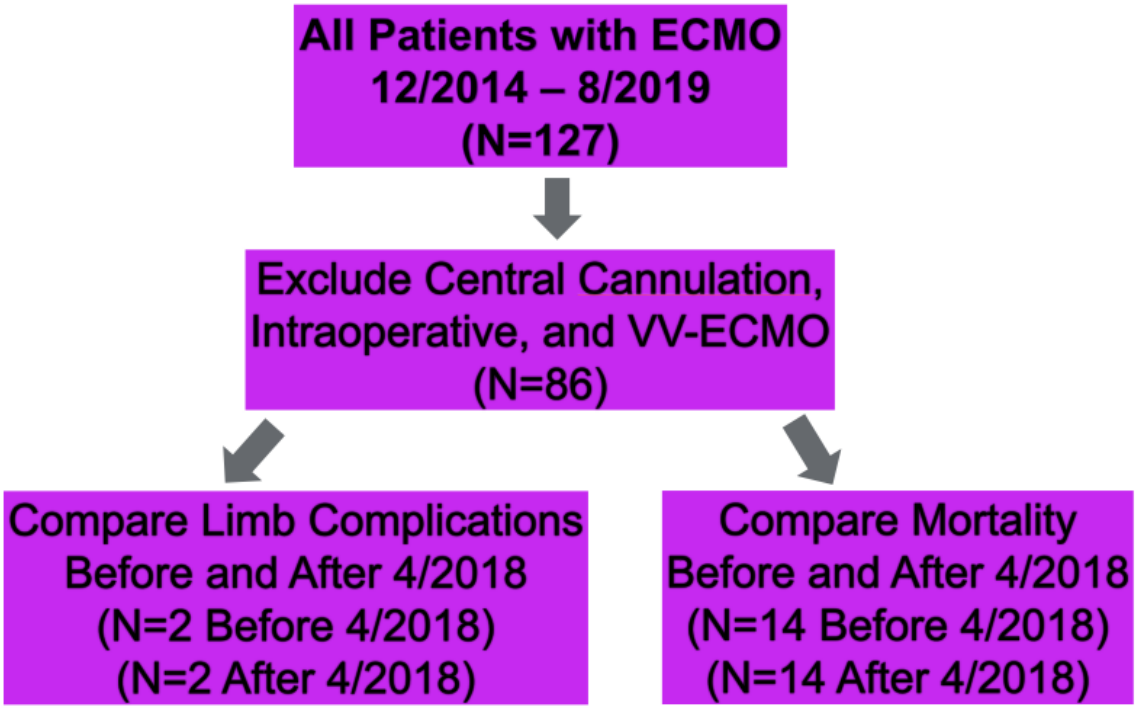


Table 2: Complication Rates After NIRS Monitors Used on VA-ECMO Patients

	Before NIRS Monitoring: 12/1/2014 - 4/1/2018	After NIRS Monitoring: 4/1/2018 - 9/1/2019
Limb Complication	N=2, 5.4%	N=2, 4.08%
In-Hospital Mortality	N=14, 37.83%	N=14, 28.5%

Critical Care-29 Two Decades after the Original ARDS Network Study : Adherence to ≤ 8 milliliters Tidal Volume per Ideal Body Weight in Mechanically Ventilated Patients

Andrew S Goodrich[1], Albert P Nguyen[2], Ulrich Schmidt[2]

[1]University of California, San Diego, CA, [2]University of California, San Diego, La Jolla, CA

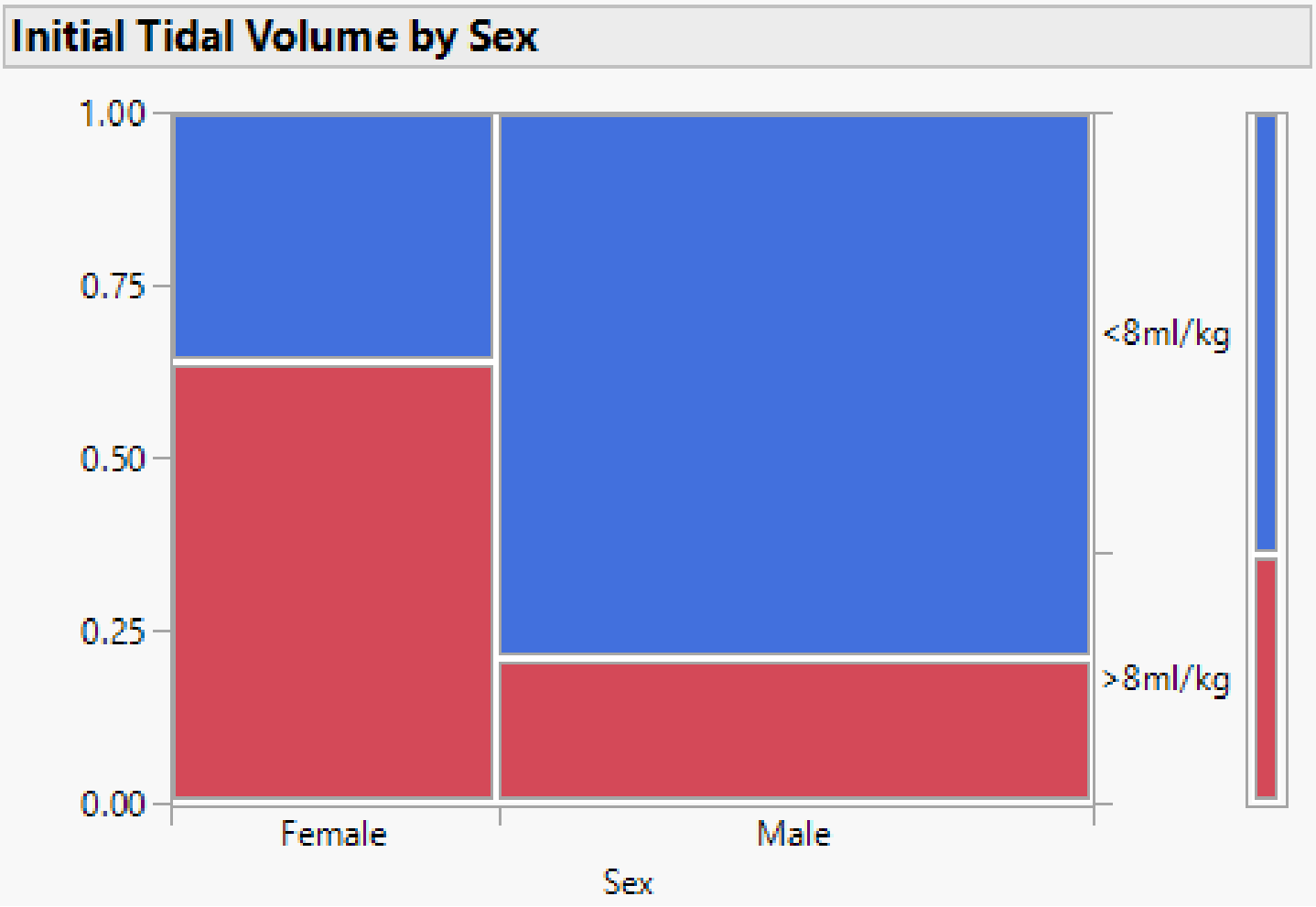
Introduction: The ARDSnet protocol, published in 2000, has been a guiding principal for mechanical ventilation, particularly in those with acute respiratory distress syndrome (ARDS)1. This lung protective ventilation strategy using tidal volumes between 6-8cc/kg of ideal body weight has become the standard of care to reduce ventilator-induced lung injury2–5,Although lung-protective ventilation has become a standard recommendation with an established 20 year history, the adherence to this guideline in major academic centers is not known. We hypothesized that there is good adherence (> 80%) to use initial tidal volumes lower then 8cc/kg ideal body weight at admission to the ICU.

Methods: This was a retrospective chart review of all patients admitted to ICU's at a major academic center from 2017 to 2019. Pediatric and burn patients were excluded. Patient demographics were recorded, and ideal body weight (IBW) and tidal volumes were calculated. The first recorded tidal volume was compared to an ideal tidal volume of less than 8ml/kg IBW, and adherence to this recommendation was examined with respect to gender and individual ICU

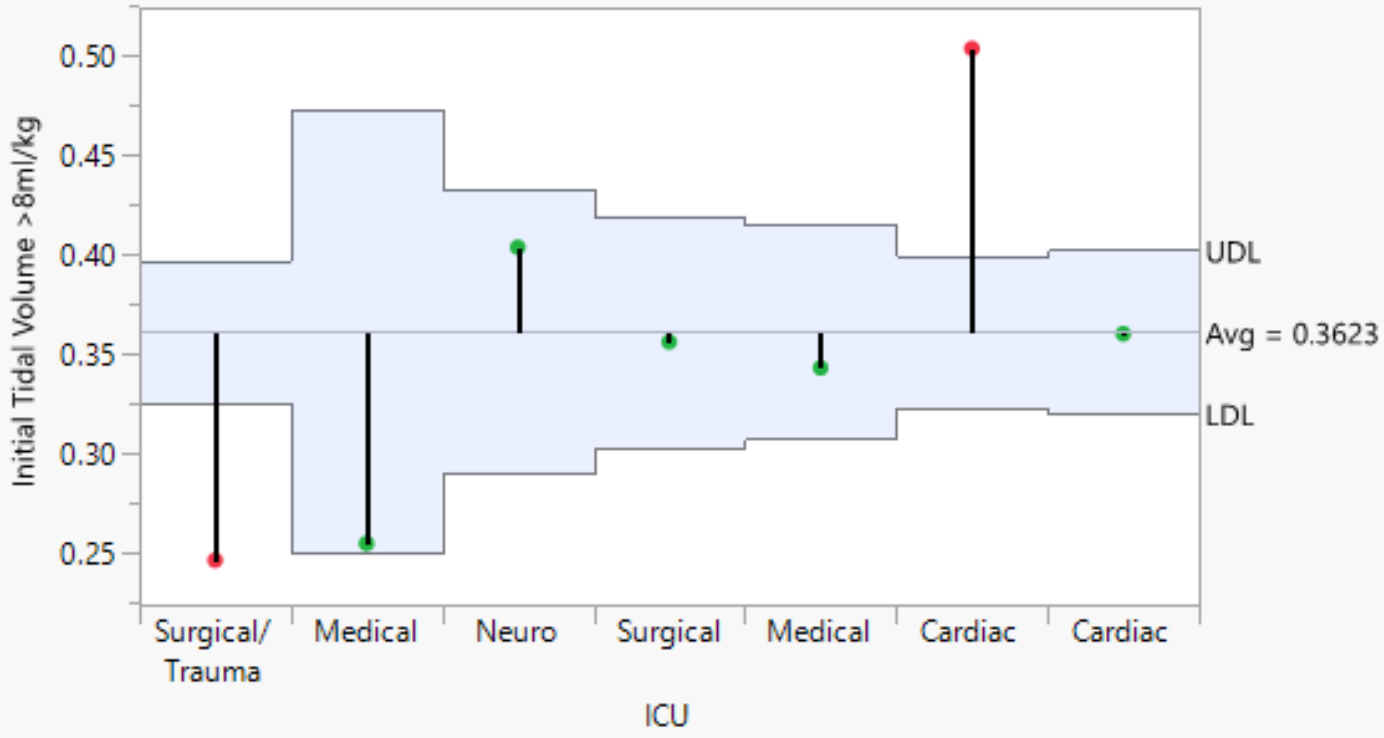
Results: 4071 ICU admissions were included, and 71 were excluded due to lack of height data. The average age was 56.5 (± 16.8) years, average height was 67.1 inches (± 4.2), and 64.4% of the patients were male. Overall 63.8% of patients had initial tidal volumes below 8ml/kg IBW, and there was a significant difference between males (79.0%) and females (36.2%) ($p<0.0001$). Amongst ICU's, a cardiac ICU had a lower compliance and a surgical/trauma ICU had higher compliance, as compared to remaining ICU's ($p<0.05$ for analysis of means for proportions).

Conclusion: Adherence to initial lung-protective ventilation was only 63.8% for all ICU patients during this 2-year period. While male patient almost reached our set target of good compliance, adherence for female patients was much lower. A cardiac ICU had a lower compliance rate while a surgical/trauma ICU had an increased compliance rate, as compared to other ICU's. The reasons for this low compliance rate, potential strategies to improve performance as well as outcomes are currently studied.

Reference(s): N Engl J Med. 2000 May 4;342(18):1301-8, Am J Respir Crit Care Med. 2017 Feb 15;195(4):438–42, Ann Emerg Med. 2017 Sep;70(3):406-418.e4, Ann Emerg Med. 2016 Nov;68(5):614–7, N Engl J Med. 2013 Nov 28;369(22):2126–36


Initial Tidal Volume by Sex
1.00
0.75
0.50
0.25
0.00
Female
Male
Sex
<8ml/kg
>8ml/kg

Analysis of Means for Proportions - Initial Tidal Volume by ICU



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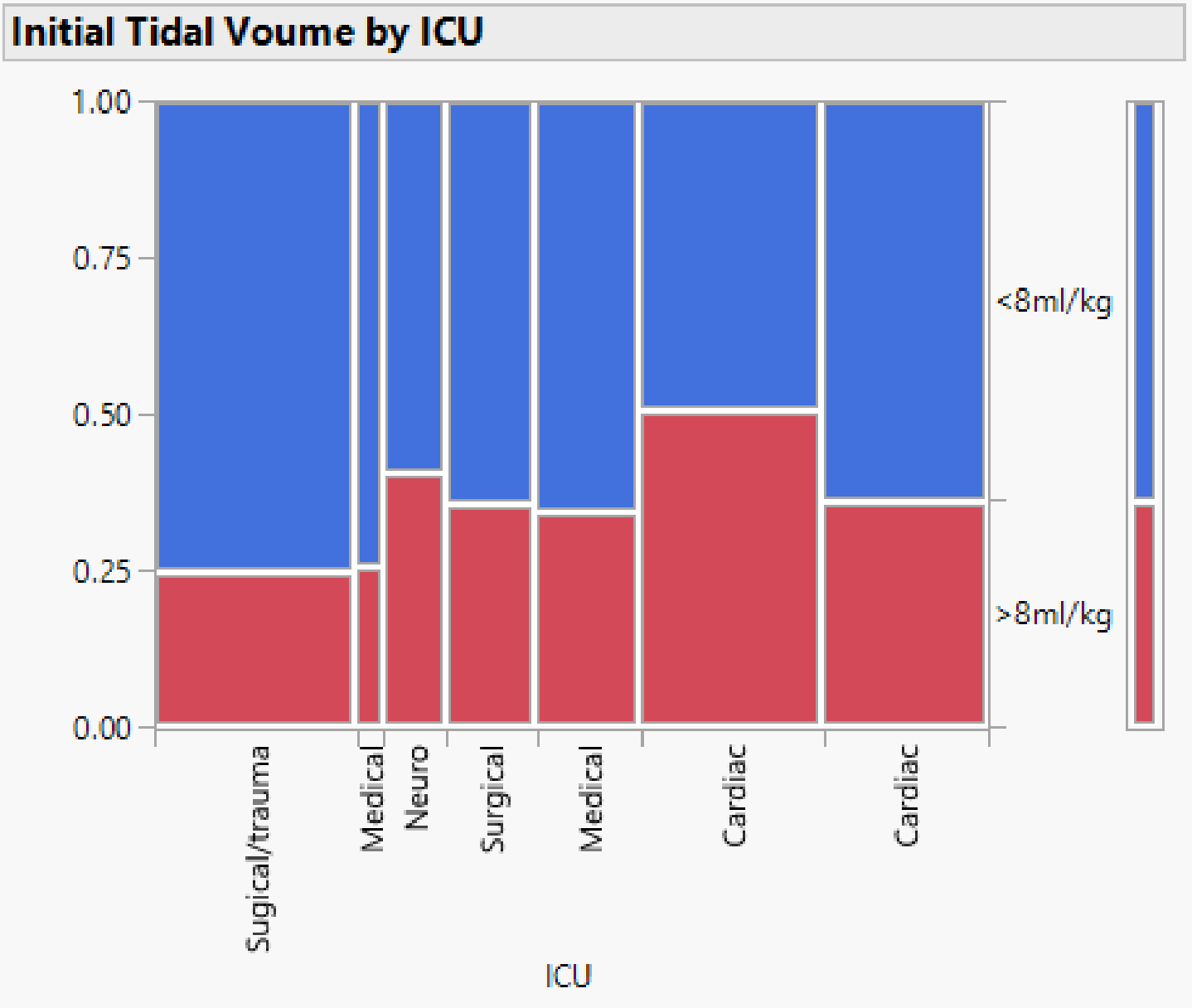
Initial Tidal Voume by ICU
1.00
0.75
0.50
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Medical
Neuro
Surgical
Medical
Cardiac
Cardiac
ICU

Critical Care-30 Incidence and Outcomes Associated with Acute Kidney Injury Following Severe Traumatic Brain Injury

David Luu[1], Jordan M Komisarow[2], Vijay Krishnamoorthy[1]

[1]Duke University, Durham, NC, [2]Duke University, Durham, United States of America

Introduction: Severe traumatic brain injury (TBI) is a leading cause of morbidity and mortality in the United States that can lead to a tremendous economic burden to the patient and their family. Recent advances in the understanding of TBI pathophysiology have revealed that severe TBI can cause multi-organ dysfunction in the setting of critical illness, including acute kidney injury (AKI). While AKI is a common occurrence in many intensive care settings, the impact of severe AKI on outcomes following severe TBI is poorly understood. The purpose of this study is to evaluate the incidence of severe AKI and its impact on clinical outcomes, among adult patients who suffered from an isolated severe TBI.

Methods: The National Trauma Data Bank (NTDB) dataset were used to identify adult patients who suffered isolated severe traumatic brain injury, and did not have kidney disease prior to hospitalization. The diagnosis of severe acute kidney injury was defined according to Acute Kidney Injury Network (AKIN) as Stage 3 or greater. The primary outcome was In-hospital mortality and secondary outcomes included markers of healthcare utilization (need for dialysis, placement of a tracheostomy, placement percutaneous endoscopic gastrostomy tube and hospital length of stay). Multivariable logistic and linear regression models were used to analyze the association of severe AKI development with clinical outcomes.

Results: Overall 37,861 patients experienced isolated severe TBI during the study period, with 27,800 (73.5%) being male and had a mean age (SD) of 49.5 (20.5). Further demographic and clinical characteristics of the cohort are described in Table 1. The incidence of severe AKI following isolated severe TBI patients was 2.1% (95% CI 1.9% - 2.2%) and 12.5% of these patients required dialysis in the hospital. The development of severe AKI in the hospital was independently associated with mortality (OR 2.03, 95% CI 1.64 - 2.52) and need for tracheostomy (OR 2.10, 95% CI 1.52 - 2.89) and PEG tube (OR 1.88, 95% CI 1.45 - 2.45). These patients also have a prolonged hospitalization stay (mean difference 12.4 days, 95% CI 9.9 - 15.0).

Conclusion: Severe AKI following isolated severe TBI occurs in approximately 2% of patients who did not have kidney disease prior to injury, and it is associated with increased mortality and utilization of healthcare resources. Further research is necessary to understand how to identify patients at high-risk for developing severe AKI and strategies for prevention.

Reference(s): Neurocritical Care, (14)377-381, 2011 Critical Care, issue 16, 1-7, Dec 2012

Table 1		AKI	
		Absent (%)	Present (%)
Age		49.5±20	55.8±20
Gender			
Male		27,172 (73.3)	628 (79.9)
Female		9,875 (26.7)	158 (20.1)
Mechanism of Injury			
Motorcycle		10,197 (27.5)	183 (23.3)
Fall		16,446 (44.4)	413 (52.5)
Firearm		1,810 (4.9)	35 (4.5)
Pedal Cyclist		2,498 (6.7)	45 (5.7)
Assault		3,144 (8.5)	44 (5.6)
Other		2,969 (8.0)	67 (8.4)
ED GCS Score		4.2±1.8	4.1±1.7
Injury Severity Score		4.1±0.4	4.2±0.4
Head AIS Score		20.3±5.1	21.3±6.0
Admission Sys. BP (mmHg)		146±33	147±39
Admission HR (bpm)		92±25	93±27
Dialysis Catheter*	yes		98. (12.5)
	no		689 (87.5)
Tracheostomy**	yes	6,704 (24.7)	169 (42.0)
	no	20,435 (75.3)	233 (58.0)
PEG placement**	yes	6,691 (24.6)	162 (40.3)
	no	20,448 (75.4)	240 (59.7)
LOS (days)**		15.8±16.6	23.8±23.6
Mortality	yes	9,925 (26.8)	385 (48.9)
	no	27,139 (73.2)	402 (51.1)

*only in patients who developed AKI

**survivors only

Critical Care-31 Hemoadsorption of cytokines in multiorgan failure from septic shock: A retrospective analysis of 70 critically ill patients

Dietrich Henzler[1], Philipp Schultz[2], Elke Schwier[2], Thomas Koehler[2]

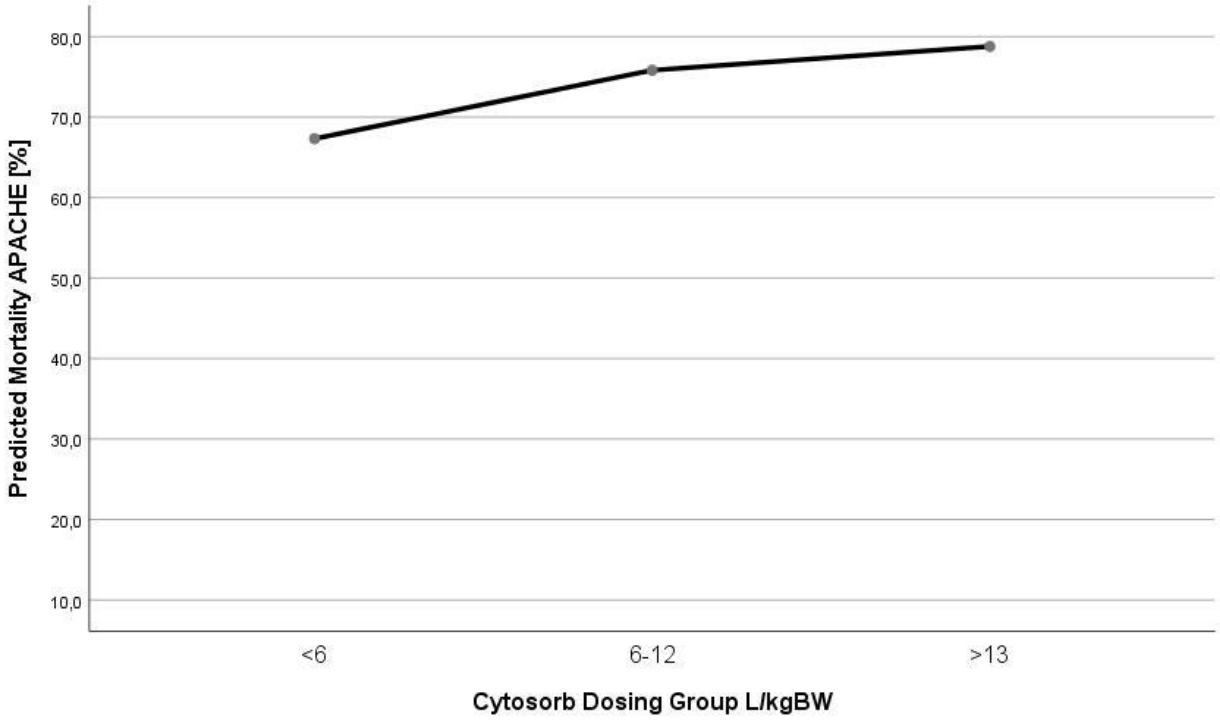
[1]Ruhr University Bochum, Herford, NRW, [2]Ruhr-University Bochum, Herford, Germany

Introduction: Septic shock is a life-threatening disease with persistent high mortality. Haemoadsorption by extracorporeal cytokine adsorption offers a new therapeutic approach, but has been discussed controversially with regard to reduction of mortality. Indications, timing, dosing and duration of treatment have not yet been determined.

Methods: In a retrospective study 70 patients were analyzed who were treated with cytokine hemoadsorption by a polymer-beads adsorber in addition to standard therapy in a university hospital in Germany between May 2016 and December 2018. The treatment was initiated according to the institution's clinical standard if septic shock of any cause including acute renal failure had developed. Data on physiologic parameters, vasopressors, IL6 and lactate concentrations were routinely collected 1h before and 4, 8, 24, 48, 72 and 96h after the start of the hemoadsorption treatment and extracted from the electronic patient record. The predicted mortality was calculated based on the APACHE II and SOFA scores and compared with actual 28-day survival.

Results: A total of 70 episodes with a mean treatment of 95±55 h with haemoadsorption were analyzed. Septic shock was caused by abdominal (n=39), pulmonary (n=22) or other focus (n=7) or non-infectious SIRS (n=12). 43 patients were male, the mean age was 70±14 years. All but 2 patients were mechanically ventilated, all were receiving CRRT and were on norepinephrine support (mean dose 0.42 mcg/kg/min). The mean plasma IL6-concentration was 7,841±13,253 pg/l. The mean predicted mortality rate based on a SOFA score of 13.9 was 63%, based on an APACHE2 score of 30.3 it was 74%, while the observed mortality rate was 50% ($p<0.05$). Survival was independently associated with lower IL6 levels and norepinephrine dosage, faster lactate clearance and reduction in positive fluid balance. IL6 decreased rapidly by a mean of 29% within 4h and 68% within 24h, but an increase in IL6 after 48h was predictive of poor outcome. The treatment duration and amount of purified blood was higher in survivors (8.4± 4.4 vs. 6.1±3.6 l/kg BW, $p=0.017$), with a linear dose-response relation between blood purification volume and survival.

Conclusion: The use of cytokine hemoadsorption appears safe and effective for various etiologies of septic shock, although the optimal duration and dosing remain unclear. The time course of IL6 levels and vasopressor dosage within the first 48h after the start of the treatment were comparable between survivors and non-survivors, such that a prediction of response can be estimated at this time point the earliest. An increase in IL6 after 48h was prognostically unfavorable. In a cohort of severely ill septic patients the observed mortality rate was 24% lower than predicted and decreased linearly with blood purification volumes > 6 l/kg BW. Dose-finding studies and RCT's are necessary to assess, whether hemoadsorption is causative for this improvement in outcome.


80,0
70,0
60,0
50,0
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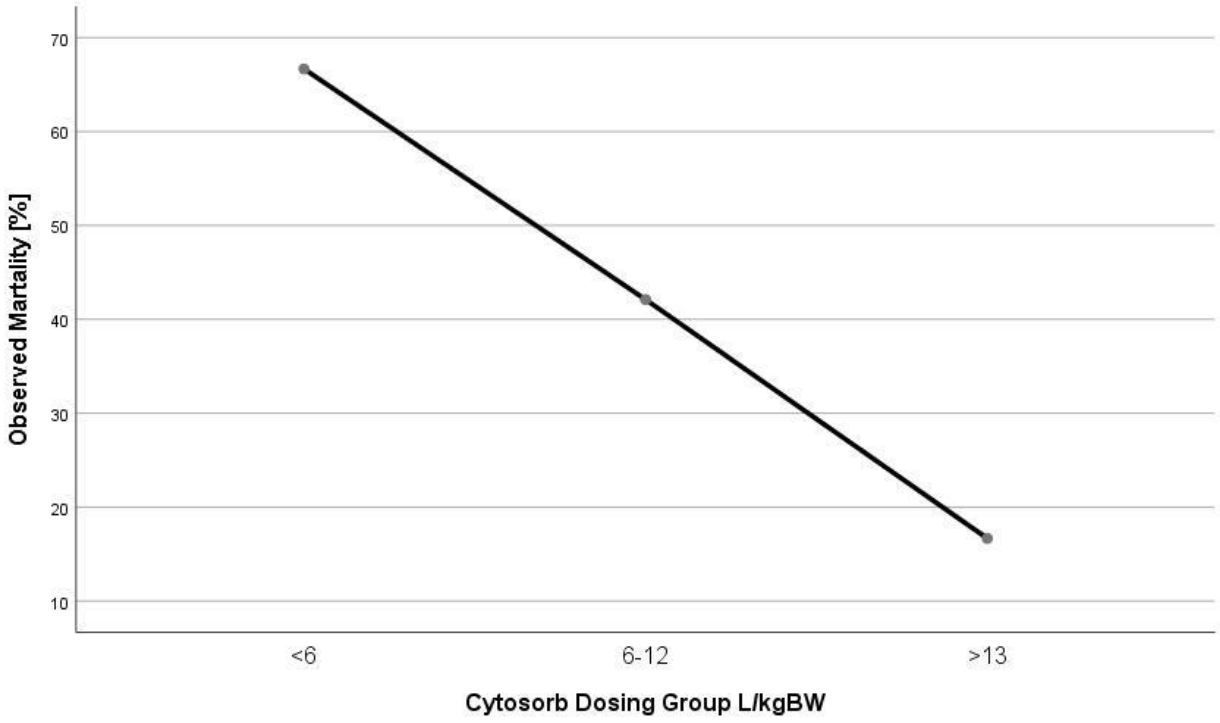
30,0
20,0
10,0
Predicted Mortality APACHE [%]
<6
6-12
>13
Cytosorb Dosing Group L/kgBW


70
60
50
40
30
20
10
Observed Martality [%]
<6
6-12
>13
Cytosorb Dosing Group L/kgBW

Critical Care-32 Intraoperative Narcotic Use and Its Effect on Extubation Time After Cardiac Surgery

Philip Sommer[1], Greta Piper[1], Samir Kendale[2]

[1]NYU Langone Health, New York, NY, [2]NYU Langone Health, New York City, NY

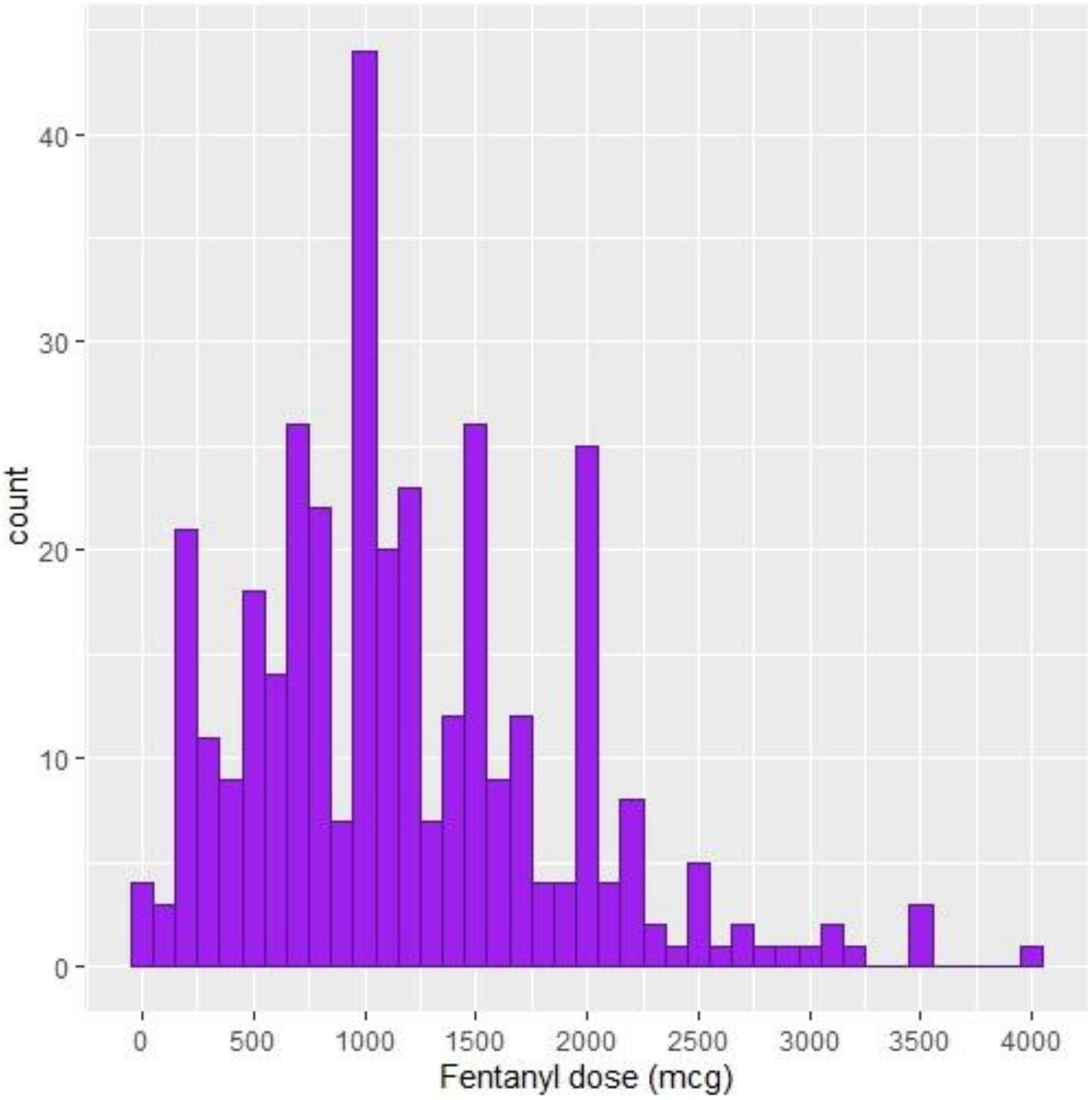
Introduction: The Society of Thoracic Surgeons (STS) has been promoting the use of early extubation after cardiac surgery, as defined by extubation within 6 hours, as a quality of care benchmark[1]. Institutions are implementing fast-track cardiac recovery programs that try and focus on decreasing costs, reducing length of stay in the hospital and intensive care unit (ICU), and improving clinical outcomes for patients[2]. One initiative has been to promote the use of a 'balanced anesthetic' to reduce the amount of narcotics and benzodiazepines that could contribute to increased time on the ventilator[3]. With this study, we looked to see if there was a correlation in our anesthesia practices with the amount of narcotic given in the operating room (OR) and the time to extubation in the ICU. Our hypothesis was that the more narcotic given in the OR, the longer the patients remained intubated in the ICU and missed the 6 hour extubation mark. The goal of this study is to try and change clinical practice in the operating room and create a fast track program that identifies patients who could be optimized prior to ICU admission to decrease ICU LOS.

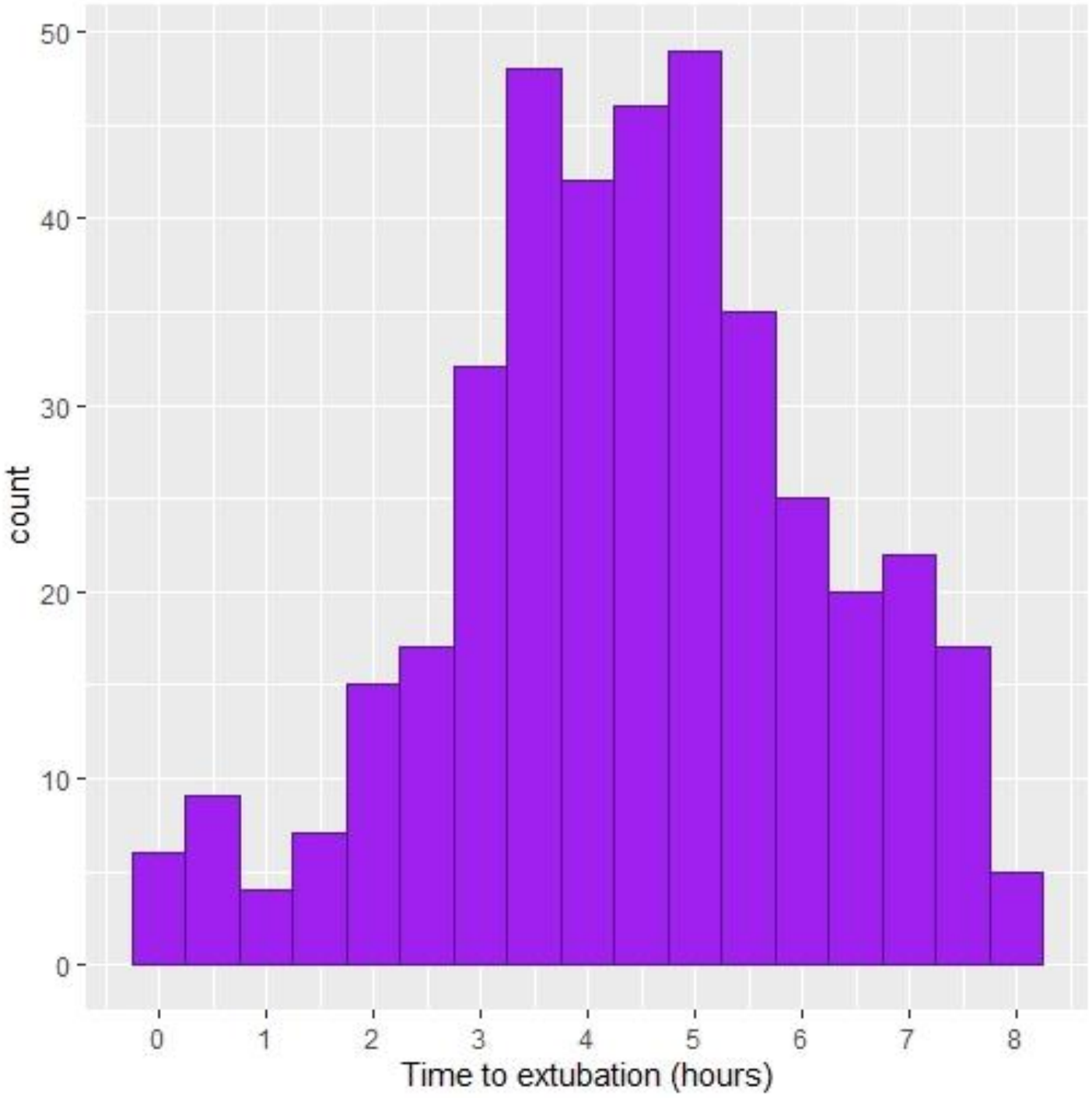
Methods: This study was a retrospective chart review looking at cardiac cases done between November 1, 2018 and October 31, 2019. Data was gathered from electronic health records with patients age, ASA status, type or surgery, surgery time, and time of extubation. The total dose of fentanyl was gathered from the intraoperative record as fentanyl is the sole narcotic used in the cardiac ORs. The data was compared and validated against the STS data that is collected in the hospital. A cutoff of 8 hours from the time frame to extubation was used as those who were intubated longer than 8 hours had more significant clinical confounders relating to prolonged intubation. We plotted the data comparing the dose of fentanyl with extubation times controlling for length of operation, the type of procedure, and the ASA score.

Results: Using an 8 hour extubation as a cut off, there were a total of 398 patients included in the analysis. All patients undergoing cardiac surgery were included in the study except patients who were take backs to the OR as indicated by two procedures in the same day. When controlling for length of case, type of surgery, and ASA score, beta value being 0.00031 and the p-value was 0.075.

Conclusion: In this study, we attempted to show a correlation between the amount of intraoperative fentanyl being used and the effect it has on the time to extubation in the ICU. When controlling for the length of the case, type of surgery, and ASA score, a trend that was not statistically significant was seen with increased fentanyl dose. While not statistically significant, this information will help guide our anesthesia teams to adopt a more balanced anesthetic approach to pain control in the operating room by using other adjuncts that do not affect extubation times. Using this data will be one part of a more comprehensive fast track cardiac surgery program that will be implemented with the aim to decrease ICU and hospital LOS.

Reference(s): STS Quality Webinar Series: Prolonged Ventilation. Available at: https://www.sts.org/sites/default/files/documents/pdf/ProlongedVentilarWebinarSlides_120414.pdf Pro: Early Extubation after cardiac surgery decreased intensive care unit stay and cost. J Cardiothoracic Vasc Anesth 1995;9:460-4 Current evidence on fast track cardiac recovery management. Eur Heart J Suppl 2017;19;A3-7


count
40
30
20
10
0
0
500
1000
1500
2000
2500
3000
3500
4000
Fentanyl dose (mcg)


50
40
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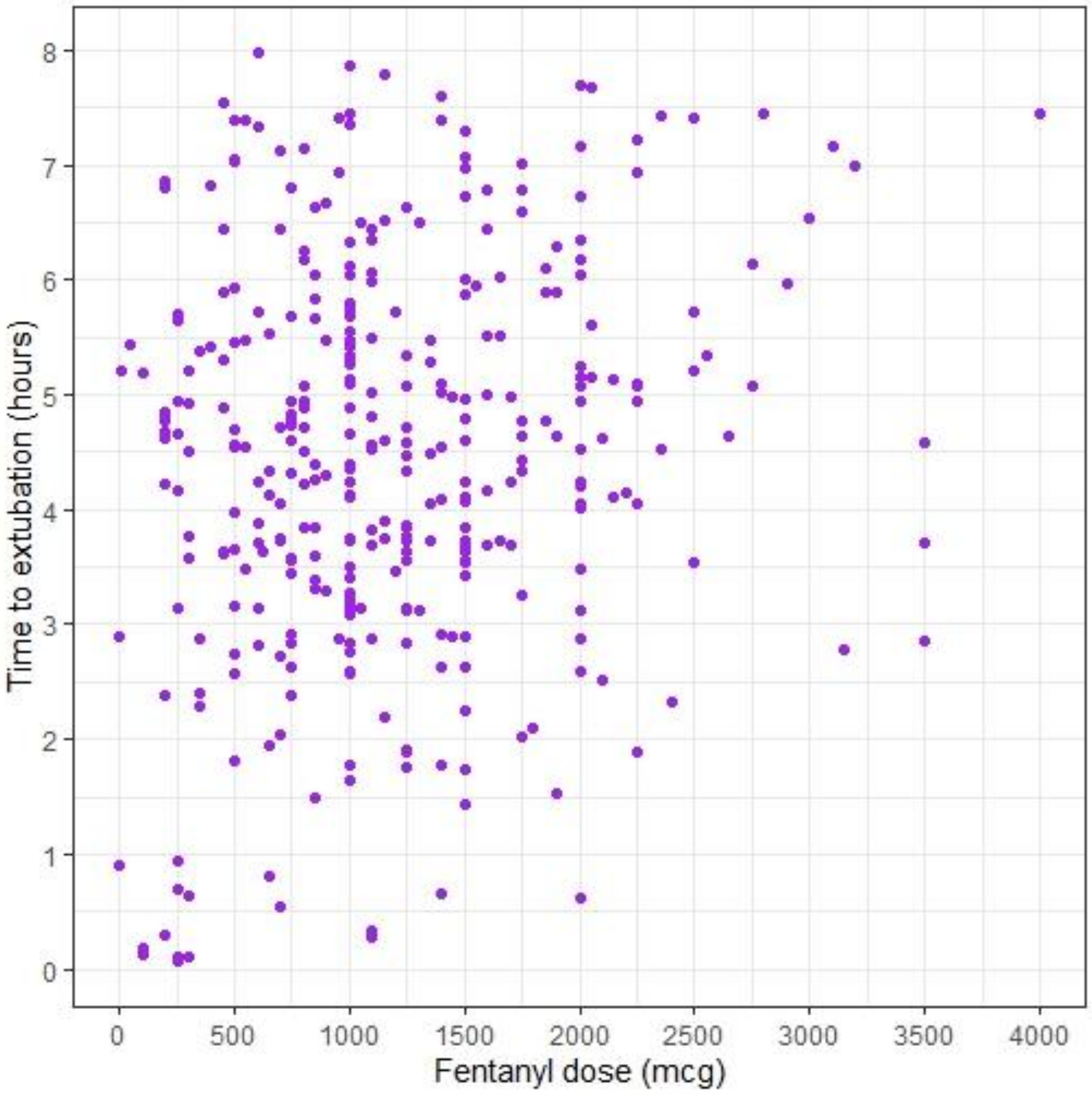
count
0
1
2
3
4
5
6
7
8
Time to extubation (hours)


Time to extubation (hours)
0
1
2
3
4
5
6
7
8
0
500
1000
1500
2000
2500
3000
3500
4000
Fentanyl dose (mcg)

Critical Care-33 Trigger Medicine and Palliative Care Consults

James McAvoy[1], Rebecca A Aslakson[2], Hannah Bechtold[3], Tara Ramaswamy[3], Angela X Ji[4], Diana Hylton[5]

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Introduction: A systematic review was conducted to evaluate the effect of palliative care (PC) consultations for patients admitted to an intensive care unit (ICU).

Methods: This systematic review extends a 2014 systematic review (with articles through 08/13/2012) to the present. We systematically searched MEDLINE, Embase, ProQuest and CINAHL from inception until December 31, 2019. Eligible articles were published in English, involved adult patients (age over 18 years), admitted to an intensive care unit, with palliative care consultant, delivered by a palliative care-trained specialists/consultants, initiated by a positive screen (i.e. 'trigger').

Results: The earlier systematic review yielded nine articles published through 8/13/2012. For articles from 8/13/2012 through 12/31/2019. The focus of this study is the screening criteria in the form of 'triggers'. After de-duplication, we screened 2,156 citations by title/abstract screen yielding 76 articles for full review and 8 studies for final inclusion. In total, 20 studies met our full inclusion criteria. As the original search revealed much variation in form of screening the majority of the studies incorporated 'trigger' criteria; thus, the focus of this review. The majority of these studies involved palliative care consults for ICU patients that were triggered through specific screening criteria that varied by study. There is a trend for decreased ICU and hospital length-of-stay, however final analysis is underway.

Conclusion: There is a growing evidence supporting the feasibility, safety, and potential benefit of integrating screening criteria in the form of 'triggers' into the daily workflow of ICUs to engender an 'opt-out' culture of palliative care consultations. Screening tools that triggered the palliative care consult varied from a daily checklist performed by provider on admit, RN initiated document, or electronic health record alerts.

Critical Care-34 A Physiology-Driven Machine Learning Model for Post-Cardiac Arrest Outcome Prediction Using a Large Multi-Center Database

Robert D Stevens[1], Han Kim[2]

[1]The Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD

Introduction: Cardiac arrest (CA) poses a significant risk of neurological disability, however there remains a large unmet need for accurate and reliable methods to predict post-CA neurological outcomes and mortality. The aim of this study is to build novel machine learning models to predict post-CA outcome by leveraging high-dimensional data available early after admission to the intensive care unit (ICU). Additionally, we hypothesize that model performance could be enhanced by integrating physiological time series (PTS) data obtained from ICU bedside monitoring devices.

Methods: We utilized the critical care Philips eICU database, which spans 208 hospitals and 200,859 ICU admissions. Our pipeline incorporated data of CA patients within 24 hours of ICU admission. We first exhaustively extracted statistical PTS and electronic health record (EHR) features and performed feature selection using nested Random Forest. We then combined various machine learning algorithms (GLM, Random Forest, Gradient Boosting, Neural Networks) and optimization techniques (hyperparameter tuning, model stacking, and transfer learning) to maximize the prediction of mortality and neurological outcome.

Results: We built a neurological outcome prediction model combining EHR and PTS features. Our best-performing neurological outcome prediction model achieved a higher sensitivity (0.78), specificity (0.88), and AUC (0.87±0.01) compared to the APACHE III baseline model (AUC: 0.74±0.01, sensitivity: 0.77, specificity: 0.63). Additionally, our highest performing mortality prediction model (AUC: 0.85±0.01, sensitivity: 0.80, specificity: 0.75) also significantly outperforms the APACHE III baseline model (AUC: 0.75±0.01, sensitivity: 0.86, specificity: 0.56). The incorporation of PTS was observed to increase mean AUC by 3.7% for neurological outcome and 4.5% for mortality.

Conclusion: Results attest to the effectiveness of machine learning models for post-CA predictive modeling, and suggest that PTS recorded in very early phase after resuscitation encode short-term outcome probabilities following CA.

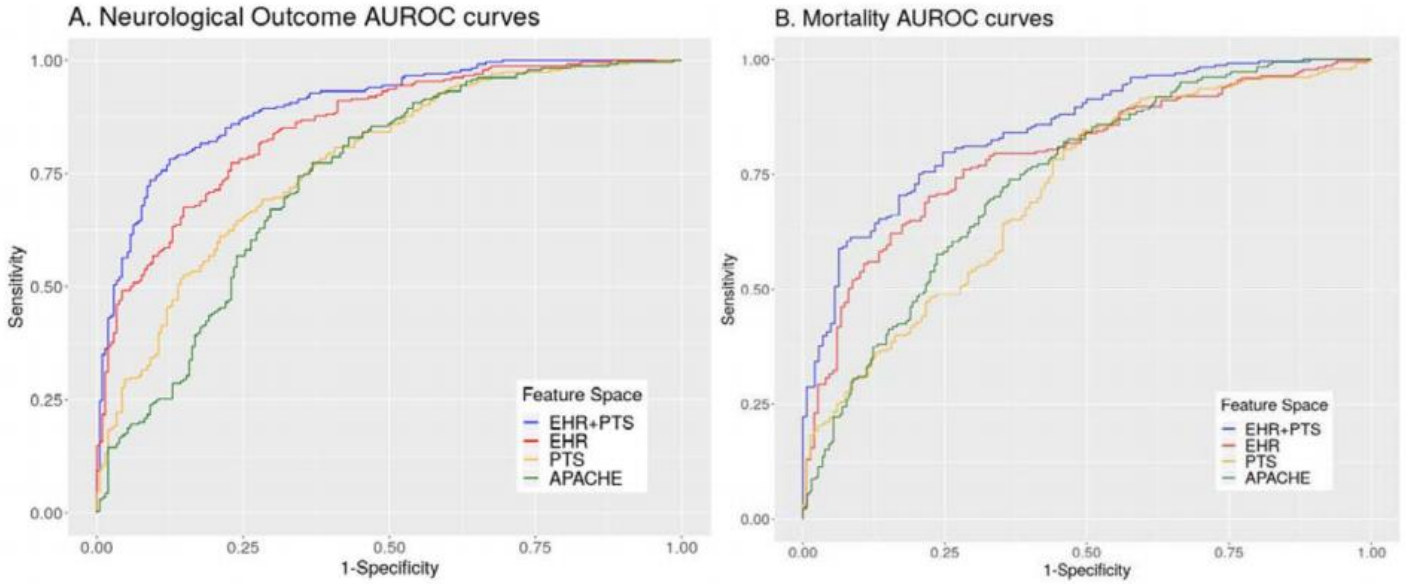


Fig.1. Median receiver operating curves of the best performing model using different feature subsets

Critical Care-35 Postoperative delirium in veterans undergoing cardiac surgery: an analysis of predisposing and precipitating factors

Carolyn Pinkerton[1], Matthew D Russell[1], Katherine Sherman[2], Thomas Ebert[1], Paul Pagel[3]

[1]Medical College of Wisconsin, Milwaukee, WI, [2]Clement J Zablocki VA Medical Center, Milwaukee, WI, [3]Zablocki Veterans Affairs Medical Center, -, United States of America

Introduction: Patients treated at Veterans Affairs (VA) facilities are in poorer health, suffer from more medical and psychiatric conditions, and make greater use of medical resources than patients in the general population. We examined our recent experience at a large VA Medical Center to determine the incidence and risk factors associated with the development of postoperative delirium (POD) in VA patients after cardiac surgery and hypothesized that the risk factors for POD after cardiac surgery are different between VA and non-VA patients.

Methods: After IRB approval, 250 consecutive patients undergoing cardiac surgery from July 2014 to March 2016 were retrospectively studied. Patients undergoing deep hypothermic circulatory arrest were excluded. Demographics, coexisting diseases, medications, the type and duration of the procedure, and the duration of bypass were recorded from the medical record. Intraoperative crystalloid, colloid, cell saver, and blood product volumes were compiled. Progress notes and ICM-10 codes were searched for documentation of POD. A stepwise logistic regression analysis was performed to determine the association between predisposing and precipitating factors and POD. Descriptive and univariate statistics were performed, and odds ratios were computed.

Results: Thirty-eight patients (15.2%) developed POD. Congestive heart failure (2.223 [1.046-4.722]; odds ratio [95% confidence interval], P=0.0377), preexisting cognitive impairment (5.147 [1.994-13.28], P=0.0007) and the presence of a neuropsychiatric disorder (2.015 [1.004-4.043], P=0.0487) were predisposing factors associated with higher odds of POD. The duration of surgery (1.236 [1.003-1.524], P=0.0469), transfusion of blood products (1.190 [1.038-1.364], P=0.0125), the durations of mechanical ventilation (1.254 [1.109-1.419], P=0.0003) and conscious sedation (e.g., propofol: 1.736 [1.301-2.317], P=0.0002), and the length of intensive care unit (ICU) stay (1.649 [1.368-1.988], P<0.0001) were precipitating factors associated with higher odds of POD.

Conclusion: Congestive heart failure, preexisting cognitive impairment, and the presence of a neuropsychiatric disorder are predisposing risk factors for POD after cardiac surgery in VA patients, whereas the duration of surgery, transfusion of blood products, the durations of mechanical ventilation and conscious sedation, and the length of ICU stay were precipitating factors for POD. These findings in VA patients are generally similar to those observed in the civilian population despite the well-known differences between these cohorts.

Critical Care-36 Timing and Etiology of Post-Operative Rapid Response Team Activation

Sameer Lakha[1], Jeremy P Walco[1], Dorothee Mueller[1], Liza M Weavind[1], Jacob C Clifton[1], Robert Freundlich[1]

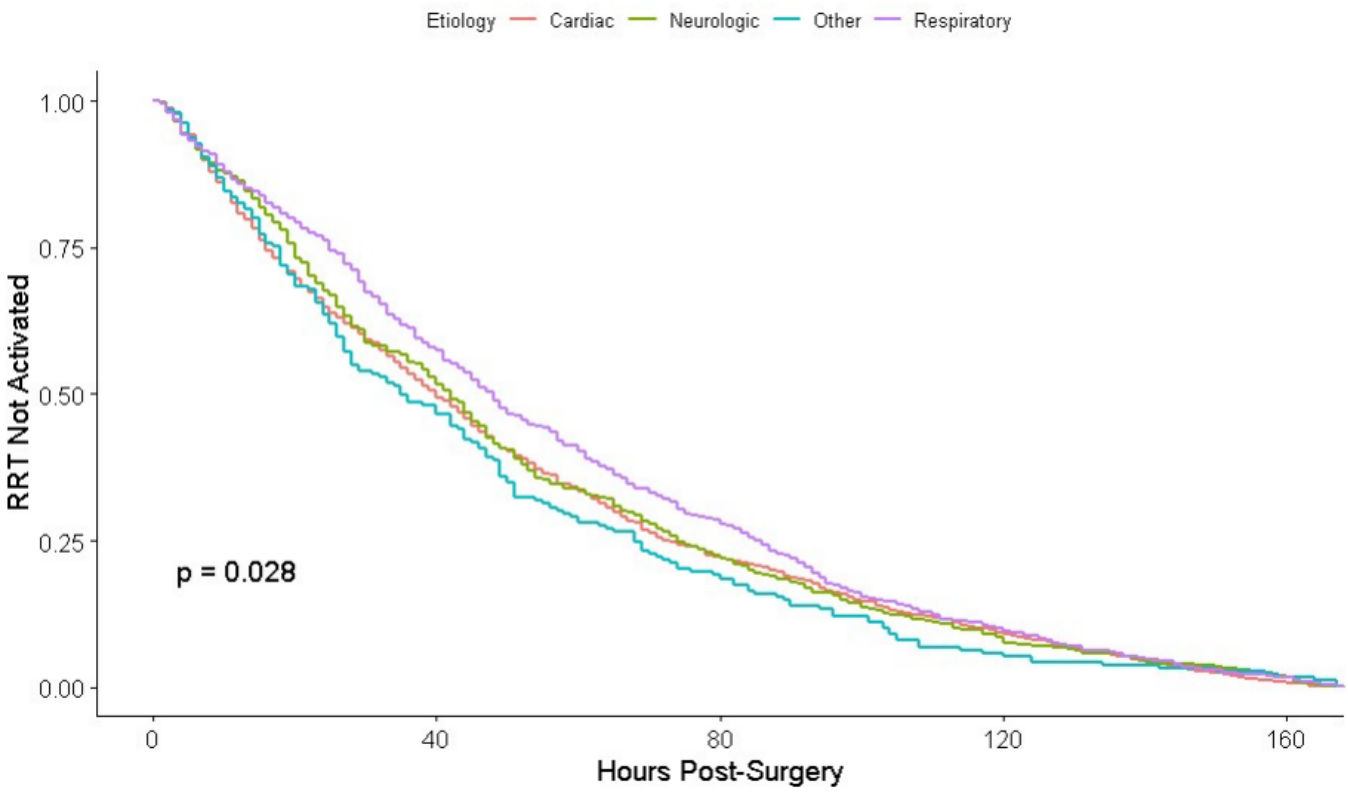
[1]Vanderbilt University Medical Center, Nashville, TN

Introduction: Hospital rapid response teams (RRTs) aim to reduce preventable morbidity and mortality by intervening upon patients at risk for potentially catastrophic clinical deterioration. A growing evidence base suggests that the etiology of clinical deterioration is associated with its timing within the hospitalization, and with downstream outcomes. Better understanding of the likely time course of different organ system manifestations of clinical deterioration may help to refine triage and monitoring of patients at high risk for complications. We evaluated the association between etiology and timing of post-operative RRT activation in a population of surgical inpatients, and will evaluate the association of etiology and timing with downstream outcomes.

Methods: We prospectively gathered data on post-operative RRT activations on adult inpatients at our institution from 2010 to 2016. The principal etiology of clinical deterioration was recorded by a responding RRT clinician, which we manually categorized as 'cardiac', 'respiratory', 'neurologic', or 'other.' Our Perioperative Data Warehouse indicated the number of hours post-operatively at which the RRT was called. Univariate analysis of the association between RRT etiology and timing was performed using the Kaplan-Meier method. We have collected and are presently cleaning data on patient demographics, inpatient laboratory tests, comorbidities, and intra-operative fluid resuscitation and blood loss for planned multivariable analyses of associations of RRT etiology and timing with in-hospital mortality, ICU-free days, and ventilator-free days.

Results: We identified 2,399 post-operative RRT activations in the study period. Cardiac etiologies of deterioration were cited in 1,243 activations; respiratory etiologies were implicated in 566 activations; neurologic causes in 399; and other causes ('general nursing concern') in 191. The time course of post-operative RRT activation is shown in Figure 1. The median post-operative time to RRT activation was 40 hours for cardiac etiologies, 48 hours for respiratory causes, 42 hours for neurologic etiologies, and 35 hours for all other causes.

Conclusion: The timing of post-operative clinical deterioration varies by the etiology of decompensation. Cardiac causes of deterioration manifest earlier in the post-operative course than respiratory or neurologic causes. Once the relevant data are cleaned, we will perform multivariable analyses of these associations, as well as associations with hospital mortality, ICU-free days, and ventilator-free days. These results add to our understanding of the time course of unexpected post-operative clinical deterioration, and may inform triage and monitoring strategies for high-risk patients.


Etiology
Cardiac
Neurologic
Other
Respiratory
1.00
0.75
0.50
0.25
0.00
RRT Not Activated
p = 0.028
0
40
80
120
160
Hours Post-Surgery

Economics, Education and Policy

Economics, Education and Policy-1

Operating Room Efficiency: Addressing Issues in an Academic Institution GI Suite

Marcus A Lehman[1], Santhanam Suresh[2]

[1]University of Cincinnati, Cincinnati, OH, [2]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

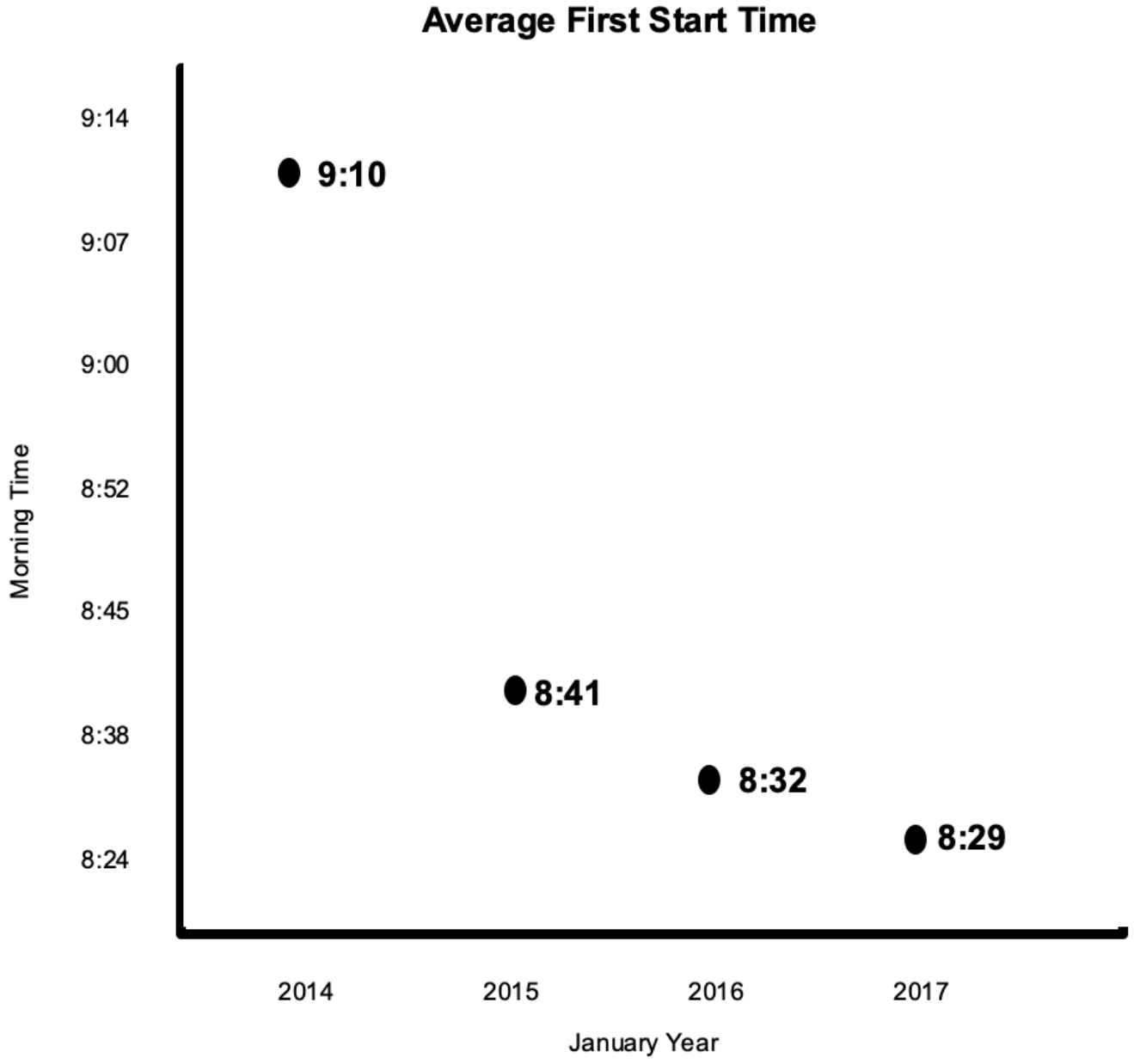
Introduction: The Digestive Disease Center (DDC) at the University of Cincinnati is part of a large, Academic hospital complex. It serves acute and specialized patients that other satellite locations cannot; it must also participate in the larger peri-operative service system of the Hospital, provides a catch-all for indigent care, serves a central teaching function for GI, and has many process 'traditions.' So intertwined, the DDC has been a known source of frustration for providers and patients alike, and a source of concern for the system, particularly in the setting of increasing demand and budgetary limitations[1]. Many working there cited failed reform attempts because of the academic setting noted above[2], or things like time-and-motion studies are too advanced to begin with in a complex setting[3]. Our process improvement strategy focused on problems that, oftentimes, all staff 'know' about but no one has addressed. We hypothesized that fixing 'known' things would have a practical impact, such as by creating an earlier first procedure start time.

Methods: Our 'known' intervention strategy started at the end of 2014 and ran through the end of 2016, and included the following components: 1. We made a team including nursing, GI, Anesthesia, and Support Staff that met weekly and spent time on the 'front lines' i.e. actually working in the DDC. 2. We interviewed providers and support staff such as cleaning and transportation. 3. We noted issues from our own regular work experiences there. 4. We gathered data from the EMR to corroborate information. We took the information gathered, expressed the 'known' issues, and then addressed them: 1. Addressed tardiness directly using data with staff and their leadership. 2. Aligned all staff to report for duty at the same time each day. 3. Removed excess equipment, fixed broken/faulty equipment, supplied missing equipment. 4. Renumbered bed spaces to reduce confusion. 5. Recruited recovery nurses help with intake before the first start. 6. Made sure each computer had EMR access. We used Student's T-Test to compare the independent means of the first start times before and after our intervention.

Results: Because first start time impacts the rest of the day, patient/provider experience, and costs, we hoped to find that our first start times improved in comparison to before our interventions began. We compared January 2014 to the first month our interventions were complete (January 2017). Holding the month the same reduced fluctuations due to time of year, provider skillset, etc. We included only rooms using nursing, GI, and anesthesia staff, which are the most complex to start from a staffing, equipment, and patient care standpoint. Average first start time was 9:10am (95%CI: 8:56 to 9:24) in January 2014 for 105 first cases, while by 2017 it had improved to 8:29am (95%CI: 8:18-8:40) in the 95 first start cases (p=0.0000109). Assuming an 8:56am start time for 2014, and the 8:40 start time for 2017, the DDC starts a minimum of 16 minutes earlier per room, per day.

Conclusion: There are many ways to address issues in a system, but often they can seem, or get, very complicated--and as a result, have little impact. After just addressing the 'known' issues staff experience daily we start on average 41 minutes earlier, and at least 16 minutes earlier--enough time at minimum to do an additional EGD. This additional efficiency can create even more process improvement, reduce costs further based on procedural room costs4, or just get patients and staff home on time for the day for once and improve their experience! Impactful system improvement does not have to be overwhelming; it can be achieved just creating a team to express and address what staff members 'know' need to be done.

Reference(s): “Endoscopy Unit Efficiency: Quality Redefined” Clinical Gastroenterology and Hepatology 11:1046–1049; 201
“PTU-081”…Enhancing efficiency in endoscopy unit using the ”˜time and motion’ model.” Gut 68: A231-A232; 2019.
“Efficiency of an endoscopy suite in a teaching hospital: delays, prolonged procedures, and hospital waiting times.“ Gastrointestinal Endoscopy 64: 760–764; 2006.
“Understanding Costs of Care in the Operating Room.” JAMA Surg 153(4):e176233; 2018.


Average First Start Time
9:14
9:07
9:00
8:52
8:45
8:38
8:24
Morning Time
9:10
8:41
8:32
8:29
2014
2015
2016
2017
January Year

Economics, Education and Policy-2

Regional Disparities in Orthotopic Heart Transplantation

Imaobong Chinedozi[1], Andrea Tsai[1], Sadeq Quraishi[1]

[1]Tufts Medical Center, Boston, MA

Introduction: Heart failure is a widely prevalent disease with known racial and geographic variations in care, morbidity and mortality [1–3]. Studies have shown that heart failure disproportionately affects blacks [4], and that healthcare disparities have regional variability [2]. Orthotopic heart transplant (OHT) remains one of the final common pathways for the treatment of advanced heart failure. Here we aim to determine whether racial disparities exist in access to and receipt of OHT in the US, and whether there is regional variability in these disparities.

Methods: This is a retrospective cohort analysis of OHT candidates and recipients from July 1, 2018 through June 30, 2019. OHT demographic waitlist and recipient data were obtained from the publicly available Scientific Registry of Transplant Recipients (SRTR), and population demographic data were obtained from the US Census Bureau databases. Outcomes analyzed were incidence of new OHT wait listing and incidence of OHT per respective racial demographic population for each Organ Procurement and Transplantation Network (OPTN) region in the US. Proportions of patients wait listed and transplanted were analyzed using chi square analysis.

Results: In the US from July 1, 2018 through June 30, 2019, 4,673 patients were newly wait listed for OHT (60.8% white, 23.7% black), with 3,525 OHT performed during this same period (62.5% white, 21.7% black). Across OPTN regions, incidence of new wait listing ranged from 0.99 per 100,000 to 1.81 per 100,000 among whites versus 1.86 per 100,000 to 5.16 per 100,000 among blacks. Across OPTN regions, incidence of OHT ranged from 0.75 per 100,000 to 1.66 per 100,000 among whites versus 1.17 per 100,000 to 3.22 per 100,000 among blacks. Odds of OHT / new wait listing ranged from 0.69 to 0.92 for whites versus 0.61 to 1.18 for blacks with OR for blacks vs. whites ranging from 0.75 (95% confidence interval [CI] 0.68-0.80) in OPTN Region 6 to 1.29 (95% CI 1.18-1.40) in OPTN Region 1. Compared to whites, blacks had decreased odds of OHT / new wait listing in all OPTN Regions except for Region 1 (OR = 1.29, 95% CI 1.18-1.40) and Region 9 (OR = 1.07, 95% CI 0.98-1.17).

Conclusion: Although blacks had an increased incidence of new wait listing and OHT compared with whites, their odds of OHT / new wait listing was generally lower than whites. This suggests that the rate of OHT for blacks is not commensurate with their rate of new wait listing, as compared with whites. Racial disparities may exist in progressing towards transplantation from the wait list and warrant further investigation.

Reference(s):

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3. Circulation. 2019;139: e56–e528.

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Economics, Education and Policy-3 CVC Coaching, a Multimodal Approach to Central Venous Catheter Training

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Introduction: Research evaluating central venous catheter (CVC) adverse events, has revealed statistically significant increases in patient morbidity, mortality, and cost to American healthcare1. This consequently negatively impacts the profession of all health care workers and, most importantly the health of our patients. Quality improvement (QI) initiatives through education have been shown to decrease CVC complication rates2. Previous studies have concluded that medical professionals learn more effectively if material was taught using a combination of visual, auditory, and kinesthetic instruction3 (VAK). These studies suggested revising medical curriculum to incorporate a combination of VAK resources for more efficacious teaching. To address CVC complication rates and this instruction gap, we developed a multimodal curriculum based on these aforementioned educational principles. This was done in order to provide a more effective CVC curriculum for medical students, residents, and attendings. During this first phase of our program, we aim to show that CVC placement knowledge and confidence is improved with the VAK based training program we developed.

Methods: 23 subjects consisting of University of Texas Medical Branch Anesthesiology residents consented and participated in our multi-stage approach. Participants first watched our online video. Instructors then lectured and demonstrated these skills, in person, on a CVC training mannequin. Subsequently, subjects practiced what they had been taught on the CVC training mannequin (figure 1). Our instructional videos and training via our CVC mannequin were supplemented by checklists. Our approach also used principles based on Mayer's cognitive theory of multimedia learning. Aspects of this theory include teaching using two modes of representation rather than only using one. By design, our approach to CVC instruction targeted the three aspects of VAK learning. Our CVC curriculum incorporated online training videos, checklists, in-person instructor training, participant kinesthetic practice with CVC mannequins, and assessments. Another principle of Mayer's cognitive theory emphasizes explaining a principle while the corresponding material is illustrated. For example, lecturing on central line placement while illustrating the procedure at the same time.

Results: Pre and post-training questionnaire data was compared using paired t-tests, with significance set to $\alpha = .05$. This revealed a statistically significant mean increase in objective CVC knowledge and confidence post-training. This increase was found in all parameters described in figure 2.

Conclusion: Our CVC curriculum incorporated online training videos, checklists, hands-on training with CVC mannequins, and assessments. By design, it targeted all three aspects of VAK learning. We attribute the effectiveness of the program to this multimodal approach. We are currently using this preliminary data and participant feedback to further improve our program. We are working on an affordable CVC trainer prototype of our own design to make the visual/kinesthetic aspect of our initiative more affordable and ubiquitously available to medical professionals. We hope to expand our comprehensive CVC training program, state and nationwide. The statistically significant results are most likely due, in part, to this multimodal approach with applied Mayer's cognitive theory of multimedia learning.

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2. Department of Anesthesiology and Intensive Care, Amar Hospital Patiala, Punjab, India Corresponding author: Dr. Sukhminder Jit Singh Bajwa, House No-27-A, Ratan Nagar, Tripuri, Patiala - 147 001, Punjab, India.

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Economics, Education and Policy-4

Publication Trends and Levels of Evidence in Anesthesiology Literature

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Introduction: The purpose of publication of scholarly articles in any peer-reviewed journal is to present quality research which contributes to the scientific community. However, in the field of anesthesiology, research production in the United States has been on a decline sharply since the 1980s (Pagel and Hudetz, 2012). Previous studies have shed light on this trend but on a rather superficial level. This study was designed to assess the study design and quality of literature published in major anesthesiology journals in order to provide insight as to whether there has been improvement over the past two decades.

Methods: We performed a literature search through three anesthesiology journals: Anesthesiology: Journal of the American Society of Anesthesiologists (ASA), British Journal of Anaesthesia (BJA), and Anesthesia & Analgesia (A&A). We identified all original research articles from the month of January for over a twenty-year period in three-year increments and analyzed them for measures of quality and article type. Two different reviewers who were blinded to each other's assessments performed the data collection. The assessments were then analyzed for concordance using kappa which signifies agreement beyond chance.

Results: A total of 552 original research articles were assessed for publication trends and levels of evidence. Since 1997, there has been a 52%, 32%, and 29% decrease in publication quantity across the three journals ASA, BJA, and A&A, respectively. The proportion of studies that are randomized has stayed consistent over the past 20 years, as have the proportions of controlled and blinded studies. Investigations utilizing multi-center collaborations have increased (0% to 19.61%), but the proportion of research that is prospective has decreased considerably (92.5% to 58.82%). Studies addressing questions of therapy/prevention composed the largest portion, followed by etiology/harm, until 2012. Since 1997, the proportion of level I articles has remained fairly stagnate. However, the proportion of level II articles has decreased while the proportion of level IV articles has drastically increased. Within therapy/prevention, there is a higher proportion of high levels (I and II) compared to low levels (III and IV), and when comparing the three journals, ASA appears to publish greater proportions of high levels of evidence whereas BJA appears to have an indistinct spread. When analyzed, there is a larger proportion of publications with high levels of evidence in ASA (72.7%) compared to A&A (65.4%) and BJA (69.9%).

Conclusion: The results of this study may serve clinicians and researchers in understanding the climate of anesthesiology research. We recommend for investigators to assess the metrics of experimental design and rigor in order to produce studies of high levels of evidence; these studies can contribute to the adherence to EBM standards so that the gap in translation of academia to clinic is better bridged.

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Economics, Education and Policy-5

Correlations of Faculty Evaluations to ACGME Milestone Assessments in Anesthesia Critical Care Fellows

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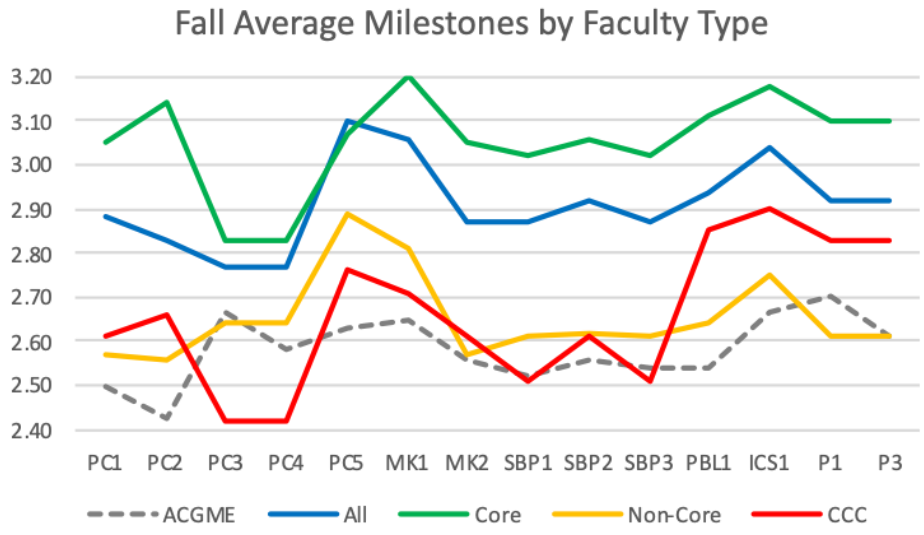
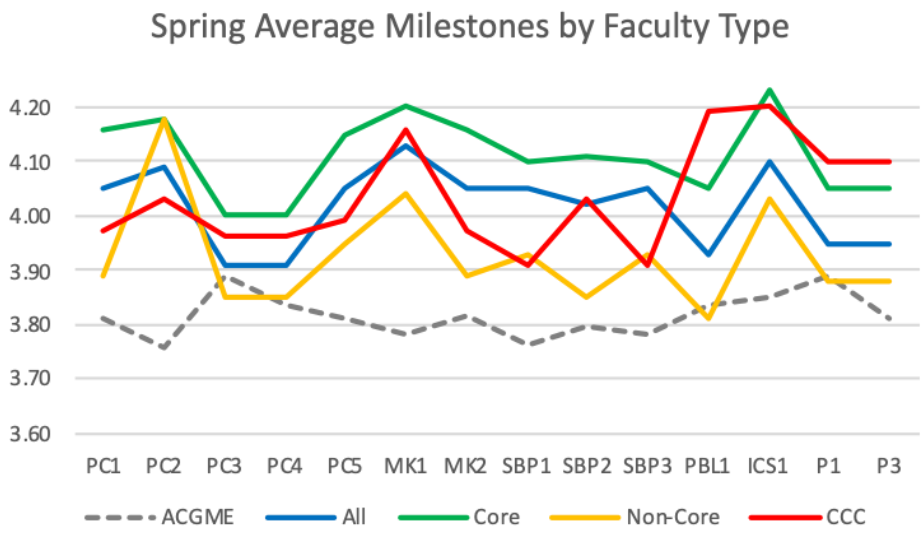
Introduction: Evaluation of fellow competency remains challenging due to its subjective nature and the 1-year duration of fellowships. The ACGME Milestone Project standardized competence evaluation of trainees and provided a framework for longitudinal evaluation. Program leadership and Clinical Competency Committees (CCC), however, rely on faculty evaluations to inform achievement of milestones. The correlation between CCC consensus milestone scoring and faculty evaluations in our institution has not yet been examined. We developed a system whereby questions on faculty clinical evaluations, including rotation-specific clinical performance, were mapped to relevant milestones. Using this system, we hypothesized that milestone mapping linked to rotation-based faculty evaluations correlates positively with the CCC-assigned milestone evaluation of Critical Care Fellows. We also hypothesized that individual CCC faculty evaluation scores would correlate most with CCC milestone scoring, followed by core teaching faculty, with non-core teaching faculty scores correlating least with CCC milestone scoring.

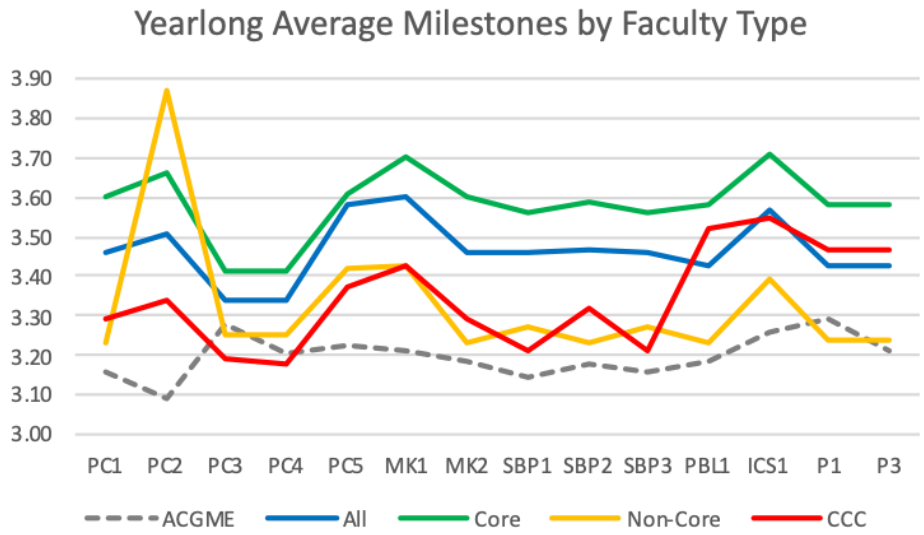
Methods: A retrospective cohort study was performed with all Anesthesiology Critical Care Medicine fellows from the preceding three years included (n=25). Faculty evaluations and CCC Milestone assignments, as reported to the ACGME, were deidentified by participant, rotation, and evaluator, and blinded milestone mapping was generated. Faculty attendings were classified as core education faculty (which included CCC members), non-core faculty, and CCC faculty members. Descriptive data and direct correlation analyses were performed to illustrate milestone scoring determined by milestone mapping and by the CCC, as well as for the faculty evaluation scores based on faculty type.

Results: Overall, faculty evaluations were, when averaged, generally within 0.5 points of the CCC determined ACGME reported milestones (Figure 1). Across all milestones, core teaching faculty reported the highest average milestone for fellows. In contrast, CCC members and non-core faculty evaluation-based milestones were most similar to the CCC reported milestones, with the all faculty average still higher than the CCC reported milestones. There was wider spread in reported milestones across faculty types in the fall than in the spring. The non-core faculty scores correlated most with ACGME reported milestones, followed by CCC faculty scores. The core faculty scores correlated least with ACGME reported milestones.

Conclusion: While often overestimating the ACGME reported milestones, there was positive correlation between milestone mapping linked to faculty evaluations with all faculty types. Because of this, milestone assignments can become more automated and objective by leveraging the milestone mapping system with faculty evaluations. Similarly, increased confidence can be placed on the quality of the evaluation questions and faculty understanding of milestones, including non-core teaching faculty. Thus, in our institution, we believe that all faculty should continue to evaluate fellows. Our study is limited by a lack of randomization and the use of only descriptive data and is unable to identify causes for the differences in evaluation scores between faculty types.


Fall Average Milestones by Faculty Type
3.20
3.10
3.00
2.90
2.80
2.70
2.60
2.50
2.40
PC1 PC2 PC3 PC4 PC5 MK1 MK2 SBP1 SBP2 SBP3 PBL1 ICS1 P1 P3
ACGME
All
Core
Non-Core
CCC


Spring Average Milestones by Faculty Type
4.20
4.10
4.00
3.90
3.80
3.70
3.60
PC1 PC2 PC3 PC4 PC5 MK1 MK2 SBP1 SBP2 SBP3 PBL1 ICS1 P1 P3
ACGME
All
Core
Non-Core
CCC


Yearlong Average Milestones by Faculty Type
3.90
3.80
3.70
3.60
3.50
3.40
3.30
3.20
3.10
3.00
PC1 PC2 PC3 PC4 PC5 MK1 MK2 SBP1 SBP2 SBP3 PBL1 ICS1 P1 P3
ACGME
All
Core
Non-Core
CCC

Geriatric Anesthesia

Geriatric Anesthesia-1 Association between the 5-HT3 receptor antagonists and postoperative delirium in elderly patients undergoing orthopedic lower limb surgery: A retrospective study

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Introduction: Delirium is a major postoperative complication. We investigated the association between the selective 5-hydroxytryptamine (serotonin, 5-HT) receptor, 5-HT3, antagonists and the occurrence of postoperative delirium (POD).

Methods: We retrospectively reviewed the electronic medical records of patients (> 65 years) who underwent orthopedic lower limb surgeries at a single tertiary academic hospital between July 2012 and September 2015. POD incidence and patient-, surgery-, and anesthesia-related factors were evaluated. Multivariable logistic regression analysis was conducted to investigate an association between 5-HT3 receptor antagonists and the occurrence of POD.

Results: In total, 855 patients were included, and 710 (83%) were associated with 5-HT3 receptor antagonists use. POD was confirmed for 46 (5.4%) patients. In multivariable logistic regression analysis, 5-HT3 receptor antagonists reduced the POD incidence by 63% (odds ratio [OR] 0.37, 95% confidence interval [CI] 0.15”’0.94, P = 0.036). Moreover, the POD incidence was decreased by 72% (OR 0.28, 95% CI 0.10”’0.77, P = 0.014), when palonosetron was administered. Other identified risk factors of POD were older age, lower body mass index, emergency surgery, hip surgery, and intraoperative propofol sedation.

Conclusion: 5-HT3 receptor antagonists may be associated with a significantly lower risk of POD in elderly patients undergoing orthopedic lower limb surgeries; palonosetron was a more effective 5-HT3 receptor antagonist for POD prevention.

Global Health

Global Health-1 Using Peer and Near-Peer Assisted Learning (PAL) in Point of Care Ultrasound (POCUS): Piloting a Resident-Driven Training Program for Global Anesthetic Capacity Building

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Introduction: Surgical conditions comprise approximately one third of the global burden of disease. Yet still, access to quality surgical, obstetric, and anesthetic care in low- and middle-income countries (LMICs) is a harrowing global health disparity. Five billion people are unable to reach surgical services that are timely, safe, and affordable.1 To that end, Point of Care Ultrasound (POCUS) is a useful tool in clinical evaluation and management of patients in low resources settings. Short-stent training interventions are common global health initiatives that quickly enrich ultrasound skill and result in long-term skill retention.2-4 In centers across the US, POCUS is becoming increasingly utilized in preoperative regional anesthesia procedures, vascular access, diagnosis, and resuscitation5-6. Nonetheless, overstretched bandwidth for experienced clinical faculty is a near universal challenge in clinical academia, which restricts time for teaching.8-9 To fill that need, peer or near-peer assisted learning (PAL) is commonplace throughout residency training. Moreover, it is an evidence supported, effective instructional modality for focused knowledge and skill transfer with comparable outcomes for milestone progression to faculty lead teaching.9-13 In this abstract, we describe our institution's development of a collaborative, resident-driven Global Anesthesia Program between our institution and an anesthesiology residency program in Toluca, Mexico. Through international resident exchanges and reciprocal peer/near-peer assisted learning (PAL), our program aims to structure a short-stent, resident lead POCUS training program as a global anesthetic capacity building tool.

Methods: Our program is structured as a bi-directional, two to four week resident rotation for US residents to travel to Mexico and vice versa for Mexican residents to travel to the USA. The US based curriculum centers on a flipped classroom model for POCUS with online modules covering transthoracic and transesophageal echo, lung, airway, FAST, gastric, regional, vascular access, and foundations of ultrasound physics. Residents engage in peer/near-peer assisted experiential learning with task trainers, needle work phantoms, standardized patient simulations, and bedside scanning for patients in ambulatory, perioperative, critical care, and PACU settings. The Mexican curriculum continues and reinforces learned ultrasound knowledge and skill foundations through core content review and repetition, as well as augments POCUS training by incorporating pediatric and obstetric scanning for neuraxial anesthetics.

Results: Data will be gathered by near-peer instructor pre-series/post-series self-assessments that use Likert scales, Objective Structured Teaching Evaluations that use a checklist, and Likert scale learner satisfaction surveys along with learner Objective Structured Clinical Examinations that uses a checklist. Datasets will be gathered in both the US and at the clinical sites in Toluca, Mexico to examine validity and inter-rater reliability in different clinical environments/low resource settings.

Conclusion: Launched in 2018, our Anesthesia Global Health Outreach Program is a collaboration between our Department of Anesthesiology and an Obstetric Hospital in Mexico to provide medical education and training, working towards developing sustainable surgical systems. Our main objectives in this collaboration were to develop knowledge, skills, behaviors essential for effective anesthesia practice in less developed, international healthcare settings; broaden awareness of cultural diversity and international healthcare delivery systems; and teach and exchange knowledge and clinical skills regarding perioperative management and Point-of-Care Ultrasound. We hope to use our initial project as a pathway to enrich our international collaborations. Likewise, we believe a compact, Train-the-Trainer educational delivery framework is amenable to an array of clinical anesthesia content beyond our starting point of PoCUS. This specific project, if successful, and its underlying framework similarly could be transferrable to other international sites as a cornerstone of the larger vision for global, sustainable anesthetic and surgical capacity building.

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Global Health-2 Development, Implementation and Evaluation of a Rapid Response Program at a Nigerian Teaching Hospital, a Novel Idea in Sub-Saharan Africa

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Introduction: The primary goal of this study was to assess the feasibility of implementing a functional rapid response team at a Nigerian teaching hospital. In addition, we did a controlled before and after study of mortality within the same hospital.

Methods: An academic partnership was established with hospital leaders at Lagos University Teaching Hospital (LUTH), a 761-bed tertiary hospital in Nigeria. In collaboration with LUTH, we developed and implemented a rapid response program (RRP) as our intervention. Our prospective cohort study included one male and one female medical unit, each with a 30-bed capacity, in the intervention cohort and one male and one female medical unit in the control cohort. The project started in April 2018 and was implemented in multiple phases over the course of 16 months including development, education, and implementation of the RRP. We compiled baseline historic data from July 2017 through July 2018 from hospital logbooks and death certificates. Implementation of the RRP took place between January and July 2019. Recent graduates from LUTH medical school were hired as research assistants to collect data. They would make daily rounds through the four wards to update patient records. This included demographic data, diagnosis, disposition and rapid response outcomes.

Results: Data compiled from Hospital logbooks and death certificates, from July 2017 through July 2018, were evaluated to assess baseline mortality and compare the characteristic of patients between intervention and control wards (Table 1). During this period, hospital records documented a total of 1,838 admissions and 334 deaths for a mortality rate of 18.2%. Intervention (E5 and A3) wards had a mortality rate of 17.5% and control wards (A2 and A4) had a mortality rate of 18.9%. During the implementation phase, a total of 1248 patients were admitted to the four wards with 675 patients in the intervention wards and 573 patients in the control wards. Mortality was 14.2% in the study wards and 14.6% in the control wards (Table 2). Most patients who passed away were in the young adult range (36.6%), and neoplasm was the most common cause of death (34.3%), followed by infections (20.9%) (Table 3). There was a total of 95 RRT events. There were 11 RRT calls where no RRT members responded (11.6%), and none of the RRT events had all four team members present together (Fig. 2). Of the 55 first time RRT calls, 42 (76%) survived the RRT. However, 35 (77.7%) of those patients that survived ultimately passed away during their hospital course. The need for increased level of care in an Intensive Care Unit (ICU) was noted several times, however ICU beds were either unavailable or patients refused due to financial constraints. In these cases, the patients were managed in the temporary ICU beds set up in the intervention wards.

Conclusion: This study was not designed to detect a mortality difference between the intervention wards and the control wards, but there were several limitations and factors that may have contributed to small differences of mortality between the two groups. Two hospital-wide resident strikes took place during our short study period where the hospital stopped accepting new patients. As the main teaching hospital in this region, patients are likely of much higher acuity. Neoplasm was consistently the most common cause of death suggesting many patients may have had terminal illnesses. Additionally, most patients live in poverty and are unable to afford lifesaving care resulting in inappropriate disposition despite timely rapid response care. . Many challenges exist to implementing a rapid response program in a low-resource setting with wide variability in hospital infrastructure, resources, and capacity to care for acutely ill patients. To our knowledge, this is the first study to assess the feasibility of implementing a rapid response system (RRS) in this setting. We demonstrate that implementing an RRS is not only feasible but necessary in a setting where mortality rates are as high as 18%. The plan going forward is to expand the rapid response team to all medical and surgical wards at the LUTH hospital. We implemented a 'train the trainers' model to identify nurse champions who are engaged in teaching and educating the new nursing staff and are willing to teach staff in other units. We hope to make this a model that can be shared with other hospitals within and outside of Lagos.

Liver

Liver-1 A Long-Term Follow Up: Liver Transplantation Outcome in Patients with Angiographically Proven Coronary Artery Disease

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[2]Ronald Reagan UCLA Medical Center, Los Angeles, CA

Introduction: The prevalence of coronary artery disease (CAD) in orthotopic liver transplant (LT) has been increasing over the last two decades, yet few studies have characterized the effect of CAD severity and treatment on post-LT outcomes. With the increasing age of LT recipients and limited organ resources, coronary angiography has been increasingly employed for the definitive assessment of CAD in LT recipients. This study aims to evaluate the long-term outcomes of LT patients with CAD diagnosed by coronary angiography at a single institution.

Methods: Following IRB approval, we performed a retrospective cohort study of adult patients at a tertiary academic center who underwent primary LT over a 12-year period ending in December 2010 whose pretransplant evaluation included coronary angiography. All patients underwent standard perioperative surgical and anesthetic management. Patients were selected for preoperative angiography based on established institutional screening criteria. Catheterization results were categorized as CAD positive (50% stenosis of one or more vessels), the CAD (+) group, or negative (<50% stenosis), the CAD(−) group. Positive angiography results were further stratified based on the degree of stenosis as severe CAD (>70% stenosis), the CADsev group, or moderate CAD (50–70% stenosis), the CADmod group. In the case of multiple coronary arteries, the angiography prior to the LT was used in the analysis, except in those patients that underwent coronary interventions in which case the angiography performed prior to the intervention was used. The primary outcome was post-LT survival measured by time between LT and time of death or last date of follow-up.

Results: A total of 243 patients were included in this study. Of these patients that underwent preoperative angiography followed by LT, we identified 34 CAD(+) patients and 209 CAD(-) patients. The CAD(+) patients were further stratified into the CADsev (n=16) and CADmod (n=18) groups. Demographic characteristics and recipient and donor organ covariates were compared between the CAD(-), CADmod, and CAD sev groups; these did not differ significantly except for gender (Table 1) Median follow-up (or time to death) in all patients was 79.6 months (11.1, 115.4). There were 114 deaths (46.9%) in the entire cohort, 19 deaths (56%) in CAD(+) group and 95 deaths (45%) in CAD(-) group. There was no difference in survival between CAD(+) and CAD(-) groups and amongst those with different severities of CAD (Table 2, Figures 1-2).

Conclusion: Among 243 patients, we found that long-term survival after liver transplantation is similar in patients with and without obstructive CAD as proven by pretransplant angiography. Although there was a trend toward worse long-term survival in the CAD(+) group, it was not statistically significant. In addition, similar survival was demonstrated between patients with varying degrees of CAD severity and those without angiographic evidence of CAD. Our results suggest that obstructive CAD should not preclude transplantation in candidates that are otherwise deemed acceptable, and that the use of donor organs in patients with obstructive CAD is warranted.

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Table 1. Descriptive Statistics by CAD Group

	CAD (-) n= 209	**CAD moderate n = 18**	**CAD severe n= 16**
MELD	31.6 (7.2)	31.1 (7.1)	29.2 (8.0)
Recipient age in years (SD)	59.4 (7.8)	62.8 (4.9)	59.4 (5.7)
Recipient Gender (%)			
Recipient Male	**134 (64.1%)***	14 (77.8%)	**14 (87.5%)****
Recipient Female	**75 (35.9%)***	4 (22.2%)	**2 (1.25%)****
Donor COD (%)			
Trauma	74 (35.4%)	6 (33.3%)	5 (31.3%)
Anoxia	38 (18.2%)	3 (16.7%)	5 (31.3%)
CVA	87 41.6%)	8 (44.4%)	6 (37.5%)
Other	10 (4.8%)	1 (5.6%)	0 (0%)
Living Donor	0 (0%)	0 (0%)	0 (0%)
Liver Etiology			
Hepatitis C	42 (20.1%)	4 (22.2%)	5 (31.3%)
Alcoholic Liver Disease	38 (18.2%)	2 (11.1%)	1 (6.3%)
Cholestatic Liver Disease	9 (4.3%)	0 (0%)	1 (6.3%)
Hepatocellular Carcinoma	50 (23.9%)	8 (44.4%)	5 (31.3%)
Other	70 (33.5%)	4 (22.2%)	4 (25.0%)

Data listed as mean +/- SD or n (%). CAD = coronary artery disease; MELD = model end-stage liver disease; COD = cause of death; CVA = cerebrovascular accident

* (0.0284), **0.0480

Table 2: Summary of Unadjusted Survival by CAD Group

	HR (95 CI)	**p-value**
CAD-negative	Ref	-
CAD-positive	1.47 (0.83, 2.43)	0.17
CAD-negative	Ref	-
CAD-moderate	1.37 (0.67, 2.51)	0.36
CAD-severe	1.42 (0.66, 2.65)	0.34
CAD-negative	Ref	-
CAD-no intervention	1.64 (0.73, 3.16)	0.21
CAD-intervention	1.26 (0.64, 2.25)	0.48

CAD = coronary artery disease; HR = hazards ratio; CI = confidence Interval; ref = reference group

Figure 1. Unadjusted survival CAD-positive and CAD-negative groups

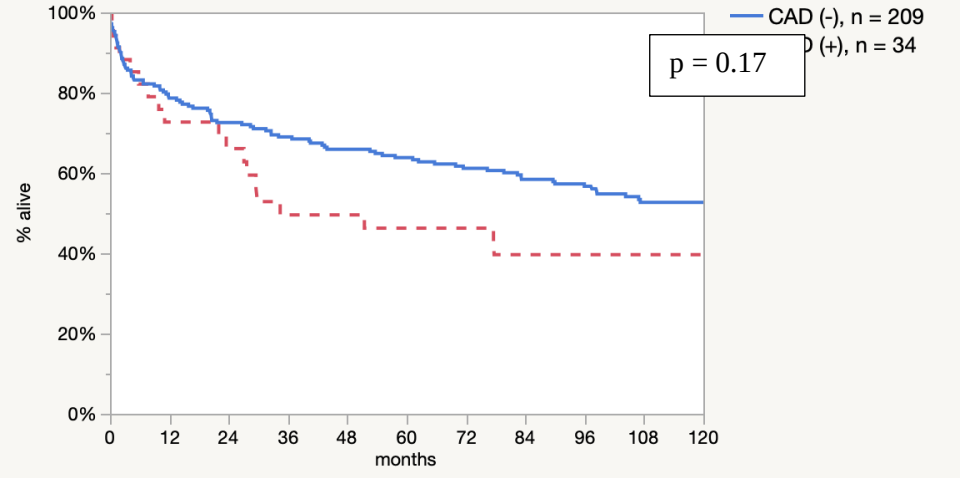
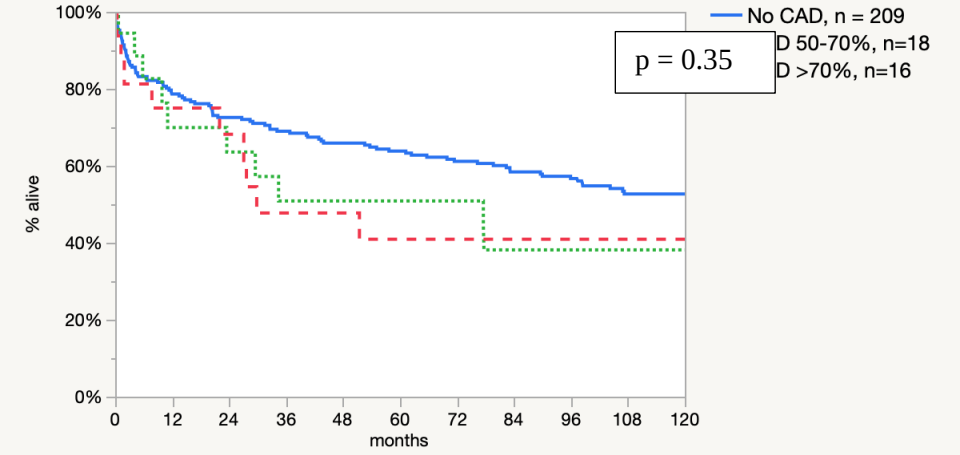


Figure 2. Unadjusted survival CAD-negative, moderate CAD and severe CAD groups



Neuroscience in Anesthesiology and Perioperative Medicine

Neuroscience in Anesthesiology and Perioperative Medicine-1 Neuroprotective effects of 1-O-hexyl-2,3,5-trimethylhydroquinone on ischemia/reperfusion-induced neuronal injury by activating the Nrf2/HO-1 pathway

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Introduction: With the acceleration of the aging population and formation of unhealthy living habits, the incidence of stroke is increasing in the world yearly. Notably, stroke remains the second leading cause of death worldwide, and the second most common cause of disability adjusted life-years, yet its diseases burden has been under-recognized[1]. Clinical data showed that ischemic strokes account for over 80% of all stroke cases[2]. Accumulating evidence indicates that oxidative stress plays a pivotal role in cerebral ischemic/reperfusion (I/R) injury. Under conditions of oxidative stress, Nuclear factor-E2-related factor 2 (Nrf2) binds to the antioxidant response element (ARE) sequences and promotes the expression of antioxidant enzymes, including haemoxygenase-1(HO-1)[3]. Data from numerous studies indicated that Nrf2 plays an important role in the protection of brain from I/R injury[4]. 1-O-Hexyl-2,3,5-trimethylhydroquinone (HTHQ), a lipophilic phenolic agent, has potent antioxidant activity and reactive oxygen species (ROS) scavenging properties[5]. The recent research indicated that HTHQ can ameliorate dopaminergic neuronal cell death induced by oxidative stress in vitro[6]. However, the role of HTHQ on cerebral I/R injury and the underlying mechanisms remain unclear. In the present study, we provide evidence that HTHQ significantly ameliorate cerebral I/R injury in vivo and protect PC12 cells against hypoxia and reperfusion (H/R) injury in vitro via Nrf2-mediated antioxidant pathway.

Methods: Focal cerebral ischemia was induced by MCAO in mice. The mice were randomly assigned into: Sham, MCAO, HTHQ 100 and 200 group. The sham and MCAO groups received an equivalent volume of tween 80. The HTHQ 100 and 200 groups were orally administered with HTHQ (100 or 200 mg/kg) for three consecutive days before MCAO. The operation was performed after 30min the last administration. The neurological deficits were assessed using a previously described neurologic scoring system[7]. TTC staining was used to detect the infarct volume. Brain water content was also calculated. SOD, CAT, GSH activities and MDA contents were measured by commercially available kits. The number and percentage of positive cells in the region were detected by staining with TUNEL kit and calculated to evaluate the extent of cell apoptosis. Protein expression were detected by Western blot. The intensity of the blots was normalized to that of β-actin. si-Nrf2 were designed and manufactured according to the previous literature to knockdown the genes. For hypoxic treatment, the PC12 cells were cultured in preconditioned hypoxic medium under 5% CO2 and 95% N2 in a humidified chamber for 6 h, and then re-oxygenation 18 h under normal growth conditions. Meanwhile, the cells were exposed to HTHQ for 3 h before H/R injury. The cell apoptosis was detected by Annexin V-APC/7-AAD apoptosis detection kit. Flow cytometer was used to detect the percentage of apoptotic cells. Data were analyzed by GraphPad Prism 6.0 by using Student's t-test or one-way ANOVA followed by Tukey's Post-Hoc test. Values were considered statistically significant when $P < 0.05$. Data are presented as the mean ± SD unless stated otherwise.

Results: HTHQ treatment significantly decreased the infarct volume ratio and neurologic scores dose dependently, and also significantly ameliorated brain water content; restored SOD, CAT and GSH activities and decreased MDA contents; decreased neuronal apoptosis following I/R; increased the expression of Nrf2 and HO-1; in addition, increased the expression levels of Nrf2 in the nucleus, while decreasing its expression in the cytoplasm compared with MCAO group; restored SOD, CAT, GSH activities and decreased MDA contents compared with H/R group; decreased neuronal cell death following H/R. PC12 cells were more vulnerable to H/R-induced oxidative stress after si-Nrf2 transfection. Meanwhile, the HTHQ mediated protection was lost in PC12 cells transfected with siNrf2. Knockdown of Nrf2 accordingly increased the apoptosis ratio after H/R, and HTHQ treatment did not affect neuronal apoptotic in PC12 cells transfected with siNrf2.

Conclusion: The present study indicates that HTHQ can significantly ameliorate cerebral I/R injury in vivo and protect PC12 cells against H/R injury in vitro via Nrf2/HO-1 pathway. These findings suggest that potential of HTHQ for prevention or treatment of stroke.

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Neuroscience in Anesthesiology and Perioperative Medicine-2 Soluble Epoxide Hydrolase Inhibition and Delayed Cerebral Ischemia after Subarachnoid Hemorrhage

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Introduction: Epoxyeicosatrienoic acids (EETs) are arachidonic acid metabolites with multiple neurovascular actions, including suppression of endothelial inflammation and promotion of smooth muscle vasodilation.[1] Inhibition or deletion of EETs metabolizing enzyme, soluble epoxide hydrolase (sEH), decreases infarct size and improves neurobehavioral performance after cerebral ischemia in animal models.[2] Human genetic polymorphisms linked to increased sEH activity and decreased EETs availability are associated with increased mortality and risk of stroke after subarachnoid hemorrhage (SAH).[3] A novel pharmacological inhibitor of sEH, GSK2256294, has recently been demonstrated as safe and effective in healthy volunteers.[4, 5] We sought to evaluate the safety and pharmacodynamic effects of GSK2256294 in patients after aneurysmal SAH.

Methods: We conducted a phase 1b double-blind, placebo-controlled randomized trial of GSK2256294 in 20 patients admitted to the neuroscience ICU at a comprehensive stroke center with a diagnosis of aneurysmal SAH. Patients receive GSK2256294 or placebo daily for 10 days. Patients were monitored for adverse events during drug administration. At baseline, days 7 and 10, blood and cerebrospinal fluid (CSF) samples were collected and analyzed for eicosanoid levels, and a battery of inflammatory cytokines and endothelial injury biomarkers. Clinical outcomes were assessed at hospital discharge, and after 90 days. The primary study endpoint was the evaluation of safety based on the frequency of serious adverse events.

Results: 9 patients were enrolled in the placebo group and 10 in the GSK2256294 group. Patients in the GSK2256294 group tended to have higher GCS at admission. There were 5 serious adverse events in the GSK2256294 group and 5 serious adverse events in the placebo group, none of which were determined to be related to study drug administration. There was no difference between GSK2256294 and placebo in the 14,15 EET/DHET ratio measured in the CSF on day 7 or day 10, however, this ratio was significantly higher in the serum, comparing the GSK2256294 with the placebo group: absolute difference (95%CI): 0.18 (0.10; 0.26) at day 7 and 0.15 (0.09; 0.20) at day 10. Cytokines IFN-gamma, IL-1b, IL-8 and TNF-alpha were all lower at day 7 and day 10 in the GSK2256294 group compared to placebo, but none of the differences were statistically significant. There were no differences in the incidence of transcranial doppler or angiographic vasospasm or new stroke. There was a trend of shorter length of stay and better neurological and functional outcome at discharge and 90 day follow up in the GSK2256294 group vs placebo.

Conclusion: GSK2256294 is safe to administer in patients with SAH, and increases serum EETs levels compared to placebo. Pharmacologic sEH inhibition may reduce neuroinflammation after SAH and improve functional outcome as demonstrated by trends of decreased neuroinflammatory cytokines in the CSF following drug administration and favorable follow-up outcomes. A larger randomized trial is needed.

Reference(s):

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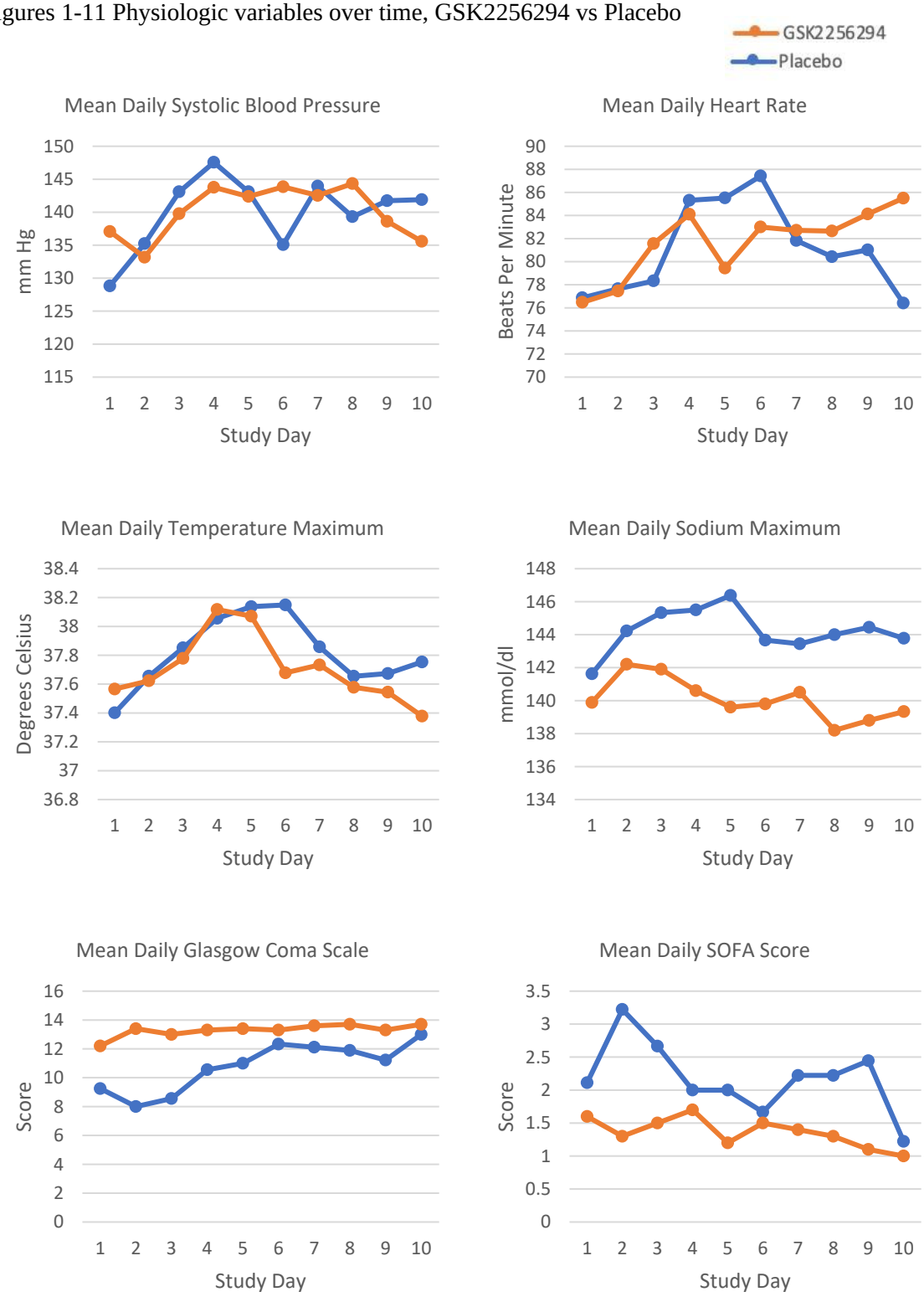
Table 1. Patient baseline characteristics. Data are expressed as mean ± SD unless otherwise specified.

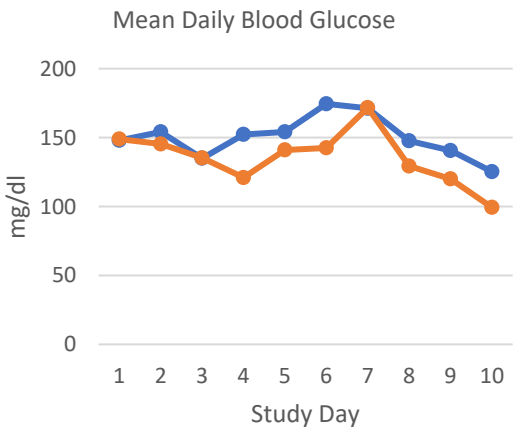
Characteristics	GSK2256294 (n=10)	Placebo (n=9)
Age, years	61.2 ± 11.2	60.4 ± 11.6
Female, n (%)	6 (60.0)	6 (66.7)
BMI (kg/m^2)	28.8 ± 6.6	27.7 ± 4.7
Race, n (%)		
White	8 (80.0)	8 (88.9)
Asian	2 (20.0)	0
Unknown	0	1(11.1)
Hispanic	0 (0)	2 (22.2)
Smoking		
Never/Passive Smoker	2 (20.0)	5(55.5)
Active	5 (50.0	3 (33.3)
Former	3 (30.0)	1 (11.1)
Substance Abuse, n (%)		
Charlson Comorbidity Score	2.4 ± 1.4	3 ± 2.3
Medical History, n (%)		
Hypertension	6 (60.0)	9 (100)
Seizure	0 (0)	0 (0)
Prior Brain Aneurysm	1 (10.0)	0 (0)
Medications, n (%)		
Anti-hypertensives	3 (30.0)	8 (88.9)
Anti-coagulants	0 (0)	2 (22.2)
Anti-platelets	2 (20.0)	2 (22.2)
Statins	1 (10.0)	1 (11.1)
Anti-diabetic agents	0 (0)	0 (0)
Hunt & Hess Scale	3 ± .94	3 ± 1
Modified Fisher Grade	3.9 ± .32	3.67 ± .71
GCS at Randomization	13.3 ± 2.7	10.7 ± 3.6
Location of Aneurysm, n (%)		
Anterior Cerebral	4 (40.0)	2 (22.2)
Artery/Branches	3 (30.0)	4 (44.4)
Middle Cerebral	1 (10.0)	0 (0.0)
Artery/Branches	2 (20.0	3 (33.3)
Posterior Cerebral		
Artery/Branches		
Vertebrobasilar System		
Treatment of Aneurysm, n (%)		
Craniotomy	4 (40.0)	2 (22.2)
Endovascular	6 (60.0)	6 (66.7)
Unsecured	0 (0)	1 (11.1)
Baseline Liver Function		
AST	22.7 ± 5.7	25.5 ± 11.8
ALT	27.5 ± 13.4	24.4 ± 15.7
Baseline QTc Interval (ms)	451.6 ± 24.3	456.4 ± 31.5
Admitted Intubated, n (%)	2 (20.0)	4 (44.4)

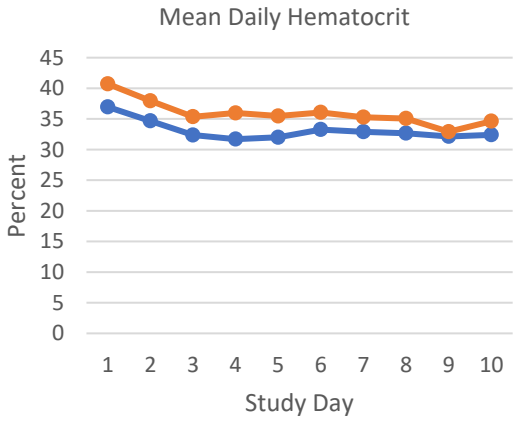
Table 2. Summary of Serious Adverse Events

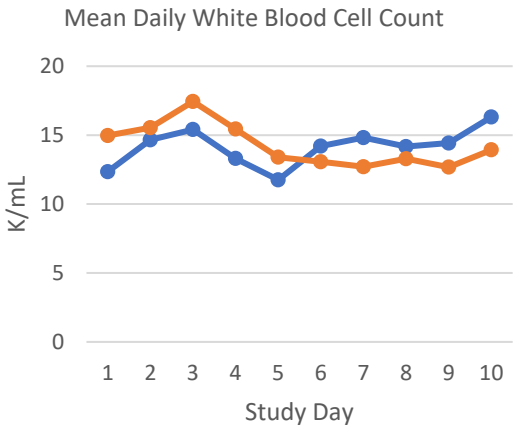
Study ID	Treatment	SAE Term	Fatal?	Expected?	Related?
OHSU-001	Placebo	Leukopenia	N	N	N
OHSU-004	Placebo	Aspiration pneumonia	N	Y	N
OHSU-004	Placebo	Rebleed of unsecured aneurysm	Y	Y	N
OHSU-008	GSK2256294	Femoral deep vein thrombosis	N	N	N
OHSU-038	Placebo	DCI with stroke event	N	Y	N
OHSU-039	GSK2256294	DCI, diffuse ACA/ MCA narrowing/ bifrontal infarctions	N	Y	N
OHSU-039	GSK2256294	Proximal LLE DVT	N	N	N
OHSU-046	GSK2256294	CLABSI	N	N	N
OHSU-046	GSK2256294	DCI	N	Y	N
OHSU-048	Placebo	ALI/ARDS	N	Y	N

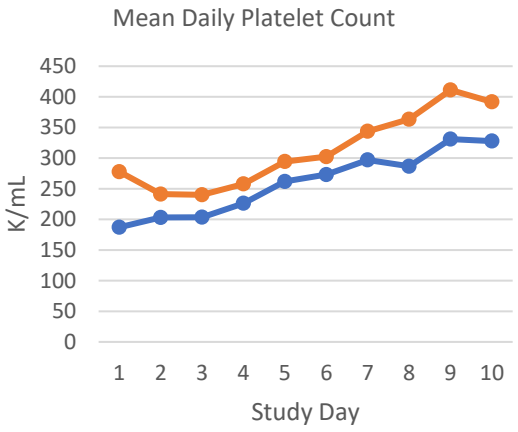
Figures 1-11 Physiologic variables over time, GSK2256294 vs Placebo




Mean Daily Blood Glucose
mg/dl
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10
Study Day


Mean Daily Hematocrit
Percent
45
40
35
30
25
20
15
10
5
0
1 2 3 4 5 6 7 8 9 10
Study Day


Mean Daily White Blood Cell Count
K/mL
20
15
10
5
0
1 2 3 4 5 6 7 8 9 10
Study Day


Mean Daily Platelet Count
K/mL
450
400
350
300
250
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10
Study Day

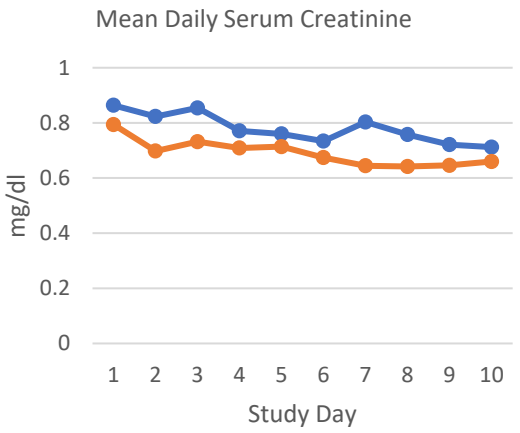

Mean Daily Serum Creatinine
mg/dl
1
0.8
0.6
0.4
0.2
0
1 2 3 4 5 6 7 8 9 10
Study Day

Table 3. Summary of safety and disease related events. Data are expressed as mean ± SD unless otherwise specified.

Characteristics	GSK2256294 (n=10)	Placebo (n=9)	Absolute difference or relative risk (95% CI)
Worst Headache Score	7.6 ± 2.7 (n=9)	6.5 ± 2.6 (n=4)	1.1 (-2.4 – 4.6)
Duration of EVD, days	11.6 ± 2.6	11.7 ± 3.9	-.10 (-4.1 – 3.9)
Required VP Shunt, n (%)	3 (30.0)	3 (33.3)	.90 (.24 – 3.38)
Cerebral salt wasting, n (%)	3 (30.0)	2 (22.2)	1.35 (.29 – 6.34)
Hypertonic saline used, n (%)	6 (60.0)	4 (44.4)	1.35 (.56 – 3.28)
NSTEMI/Cardiomyopathy, n (%)	0 (0)	0 (0)	
Thromboembolism, n (%)	2 (20.0)	0 (0)	
Seizure, n (%)	1 (10.0)	1 (11.1)	.9 (.07 – 12.38)
Day 7 Liver Function			
AST units	33.0 ± 7.7	39.8 ± 30.4	-6.8 (-30.5 – 17.0)
ALT units	51.4 ± 32.5	44.7 ± 35.7	6.7 (-26.3 – 39.7)
Change from baseline AST and ALT			
Any QTc >500ms, n (%)	0 (0)	0 (0)	
Any Infection, n (%)	4 (40.0)	6 (66.7)	.60 (.25 – 1.46)
UTI, n (%)	2 (20.0)	5 (55.6)	
Pneumonia, n (%)	1(10.0)	2 (22.2)	
Cellulitis, n (%)	1 (10.0)	0 (0)	
Bacteremia, n (%)	1 (10.0)	2 (22.2)	
Ventriculitis, n (%)	0 (0)	1 (11.1)	
Clostridium difficile, n (%)	0 (0)	1 (11.1)	
Shingles, n (%)	0 (0)	1 (11.1)	

Table 4 Clinical Outcomes. Data are expressed as mean ± SD unless otherwise specified.

Characteristics	GSK2256294 (n=10)	Placebo (n=9)	Absolute difference or relative risk (95% CI)
TCD MCA Vasospasm (LR>3)	4 (40.0)	5 (55.6)	P=.5
Maximum MCA Velocity	3.01 ± 1.36	3.37 ± 1.29	-.36 (-1.64 - .92)
Angiographic vasospasm	5 (50.0)	4 (44.4)	1.13 (.43 – 2.93)
New Stroke on imaging	1 (10.0)	1 (11.1)	.9 (.07 – 12.38)
ICU length of stay, days	12.9 ± 2.8	18.5 ± 7.9	-5.6 (-11.2 – -.04)
Hospital length of stay, days	16.9 ±3.3	28.8 ±19.8	-11.9 (-25.3 – 1.4)
Hospital Discharge			
mRS	3.4 ± 1.5	4.1 ± 1.4	-.71 (-2.1 - .7)
GCS	14.4 ± .97	12.6 ± 3.5	1.8 (-.6 – 4.3)
Discharged Home	7 (70.0)	2 (22.2)	3.2 (.9 – 11.4)
90 day follow up			
mRS	2.2 ± 1.6	3.3 ± 1.7	-1.1 (-2.7 - .5)
GOSE >4	4 (44.4)	2 (22.2)	1.8 (.4 – 7.6)
Living at Home	8 (80.0)	6 (66.7)	1.2 (.69 – 2.1)

Table 5. Serum Eicosanoid and Linoleic Acid Metabolite Ratios over Treatment Course

	GSK2256294 (n=10)	Placebo (n=9)	Absolute Difference (95% CI)
CSF			
14,15 EET/14,15 DHET			
Baseline	.08 ± .07	.08 ± .03	.001 (-.05 – .05)
Day 7	.17 ± .07	.19 ± .16	-.02 (-.14 – .09)
Day 10	.45 ±.78	.52 ± 1.04	-.07 (-1.1 – .95)
Serum			
14,15 EET			
Baseline	31.1 ± 11.3	24.0 ± 6.0	7.1 (-1.8 – 16.0)
Day 7	67.4 ± 31.0	21.8 ± 8.1	45.6 (23.1 – 68.1)
Day 10	55.8 ± 20.1	24.4 ± 11.3	31.3 (13.3 – 49.3)
14,15 EET/14,15 DHET			
Baseline	.14 ± .05	.13 ± .04	.016 (-.03 – .06)
Day 7	.30 ± .11	.12 ± .027	.18 (.10 – .26)
Day 10	.27 ± .065	.12 ± .016	.15 (.09 - .20)
9,10 EpOME / 9,10 DiHOME			
Baseline	.13 ± .07	.17 ±.12	-.37 (-.24 – .06)
Day 7	.37 ± .19	.15 ± .047	.23 (.09 – .37)
Day 10	.40 ± .21	.20 ± .14	.20 (.00 – .40)
12,13 EpOME / 12,13 DiHOME			
Baseline	1.02 ± .63	1.32 ± .95	-.31 (-1.1 – .47)
Day 7	6.0 ± 4.3	1.8 ± .92	4.2 (1.1 – 7.3)
Day 10	8.7 ± 7.1	1.7 ± .90	7.1 (1.3 – 12.8)

Table 6. Endothelial Injury and Inflammatory Biomarkers

	GSK2256294 (n=10)	Placebo (n=9)	Absolute Difference (95% CI)
Serum			
ICAM (ng/mL)			
Baseline	7.7	7.6	.07 (-3.6- 3.7)
Day 7	8.4	8.3	.12 (-6.8 – 7.1)
Day 10	17.8	6.7	11.1 (-11.3 – 33.5)
VCAM (ng/mL)			
Baseline	10.9	8.9	2.0 (-2.2 – 6.1)
Day 7	8.3	7.9	.37 (-2.1 – 2.8)
Day 10	8.9	7.9	1.0 (-1.7 – 3.8)
PECAM-1(ng/mL)			
Baseline	1.7	1.4	.28 (-.16 - .91)
Day 7	1.4	1.7	-.32 (-1.0 - .4)
Day 10	1.7	1.6	.13 (-.72 - .97)
E-Selectin (ng/mL)			
Baseline	53.8	44.5	9.3 (-15.5 – 34.1)
Day 7	46.6	48.0	-1.4 (-29.7 – 26.9)
Day 10	53.0	44.7	8.3 (-19.6 – 36.3)
P-Selectin (ng/mL)			
Baseline	1.8	1.3	.53(-.11 – 1.2)
Day 7	1.4	1.1	.33 (-.28 - .95)
Day 10	1.7	2.0	.31 (-2.0 – 1.3)
CSF			
IFN-g (pg/mL)			
Baseline	.81	.38	.43 (-.17 – 1.0)
Day 7	1.9	4.6	-2.6 (-7.2 – 1.9)
Day 10	1.5	5.8	-4.3 (-14.1 – 5.5)
IL-1b (pg/mL)			
Baseline	1.4	.48	.94 (0.81 – 2.7)
Day 7	1.6	5.0	-3.4 (-9.8 – 3.1)
Day 10	1.0	4.4	-3.4 (-10.4 – 3.5)
IL-6 (pg/mL)			
Baseline	1109.5	583.2	526 (-301.1 – 1353.9)
Day 7	2991.2	3417.9	-426.6 (-4185.1 – 3331.8)
Day 10	2089.4	2051.6	37.8 (-3764.8 – 3840.4)
IL-8 (pg/mL)			
Baseline	1074.2	1064.7	9.4 (-1538.0 – 1556.9)
Day 7	1652.4	3971.0	-2318.5 (-4745.2 – 108.2)
Day 10	1093.6	1485.8	-392.1 (-1384.2 – 599.9)
TNF-a (pg/mL)			
Baseline	5.9	3.0	2.8 (-4.4 – 10.0)
Day 7	7.8	13.1	-5.3 (-15.9 – 5.2)
Day 10	5.9	8.1	-2.3 (-10.7 – 5.5)

Neuroscience in Anesthesiology and Perioperative Medicine-3 Incidence of and Risk Factors for Emergence Delirium and Post-Operative Delirium in Neurosurgical Patients- A Prospective Cohort Study

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Introduction: Delirium after surgery is a spectrum of clinical syndrome constituting emergence delirium (ED) and/or post-operative delirium (POD). ED is a transient state (minutes to hours) of marked agitation or excessive sedation after the discontinuation of general anesthesia. POD is a fluctuating metal status commonly occurring between post operative day 1 to 3. The primary objective of this study was to evaluate the incidence of ED and POD in patients after neurosurgical procedures. The secondary objectives were: to examine the relationship between ED and POD and to identify peri- operative risk factors of ED and POD.

Methods: This is a prospective cohort study conducted at a tertiary referral neurosciences university hospital. After IEC approval ,we intended to study 200 neurosurgical patients undergoing cranial and spine surgeries from February 2018 onwards. Inclusion criteria were neurosurgical patients > 18 years with Glasgow coma scale (GCS) =15. Patients <18 years old and with GCS <15 are excluded.No preoperative sedation was administered to any patient prior to the completion of baseline delirium assessment. All study participants were assessed for pre-existing delirium using Confusion Assessment Method (CAM)[4]. Standard practices of anesthesia and postoperative care were provided for all patients. The attending anesthesiologists were free to select anesthetic drugs and techniques of their choice. Preoperative patient data and anesthetic details were retrieved from the electronic anesthesia record.Outcome measures included ED and POD. ED was assessed in the first hour of the postoperative period using sedation agitation score (SAS)[5] and highest score was considered for analysis. Patients with SAS of 4 were labelled as normal or having no ED. POD was evaluated using CAM (Supplements 1, 2) to identify presence of delirium at pre-determined time points- after 12 hours, 48 hours and 72 hours of surgery.

Results: A total of four hundred and sixty-five patients undergoing elective cranial and spinal neurosurgery were screened during the study period. Of these, two hundred and thirty-eight patients were found eligible based on our selection criteria and consented for participation into the study.Two hundred neurosurgical patients completed all the assessments of our study outcomes during the study period and data of these patients were analyzed. Of these, 157 underwent cranial surgery and 43 underwent spine surgery. The [mean ± SD] age in years was 44 ± 14 and 133 patients were males in this study. Eighty-two of the 200 neurosurgical patients (41%) developed ED 9table 1). Patients with ED manifested with self-removal of intravenous lines, urinary catheters, random spitting and delayed ability for neurological assessment. All patients required more than one healthcare worker to hold and restrain the patient to the bed and few of them required pharmacological intervention and urgent imaging to exclude post-surgical complication. The incidence of POD in all neurosurgical patients was 20% (N=40). Those patients who developed POD required physical restraints in bed and occurrence of POD resulted in delayed discharge from high dependency unit to the ward. Patients with POD needed intravenous haloperidol bolus or dexmedetomidine infusion to control agitation. The incidence of ED and POD occurring in the same patient as a delirium spectrum was 15% (N=30).Incidences of ED-POD spectrum were 7% after spine surgeries and 17 % after cranial surgeries.As per the multivariate model, patients undergoing spine surgeries were found to have 44% less risk of ED than cranial surgeries ($p = 0.032$). Males were associated with 2.5 times higher risk of POD than females ($p = 0.005$), and presence of ED was associated with 1.8 times higher risk of POD ($p < 0.001$) (Figure 2). None of the other factors were significantly associated with ED or POD.

Conclusion: Incidences of ED and POD after neurosurgery were higher than that reported after non-neurosurgical procedures previously. Also, incidences of ED and POD was higher after cranial neurosurgery than spine surgery. Neurosurgical patients with predisposing (male gender) and precipitating (presence of ED) risk factors are at high risk for development of POD.Demonstration of ED and POD co-existing as a continuum of delirium syndrome is a novel finding of this observational study. This study also confirms that ED is a strong predictor of POD after neurosurgery.

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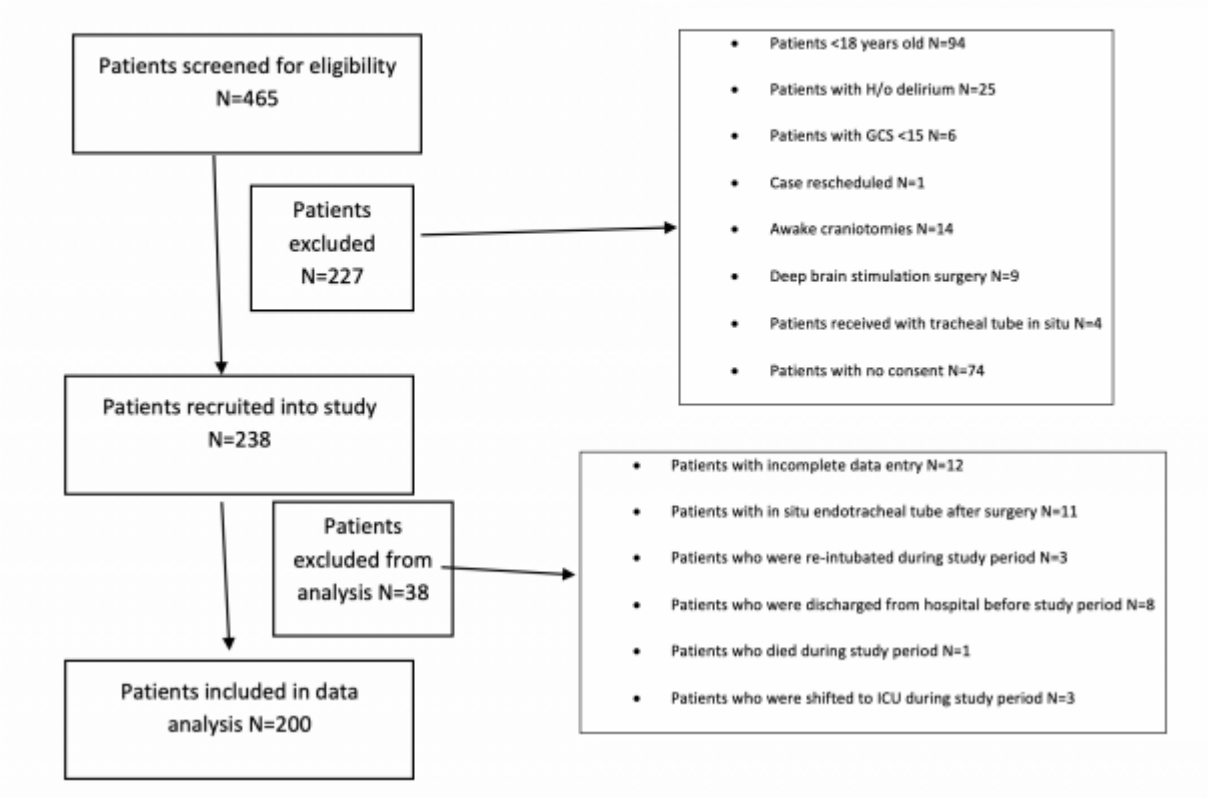
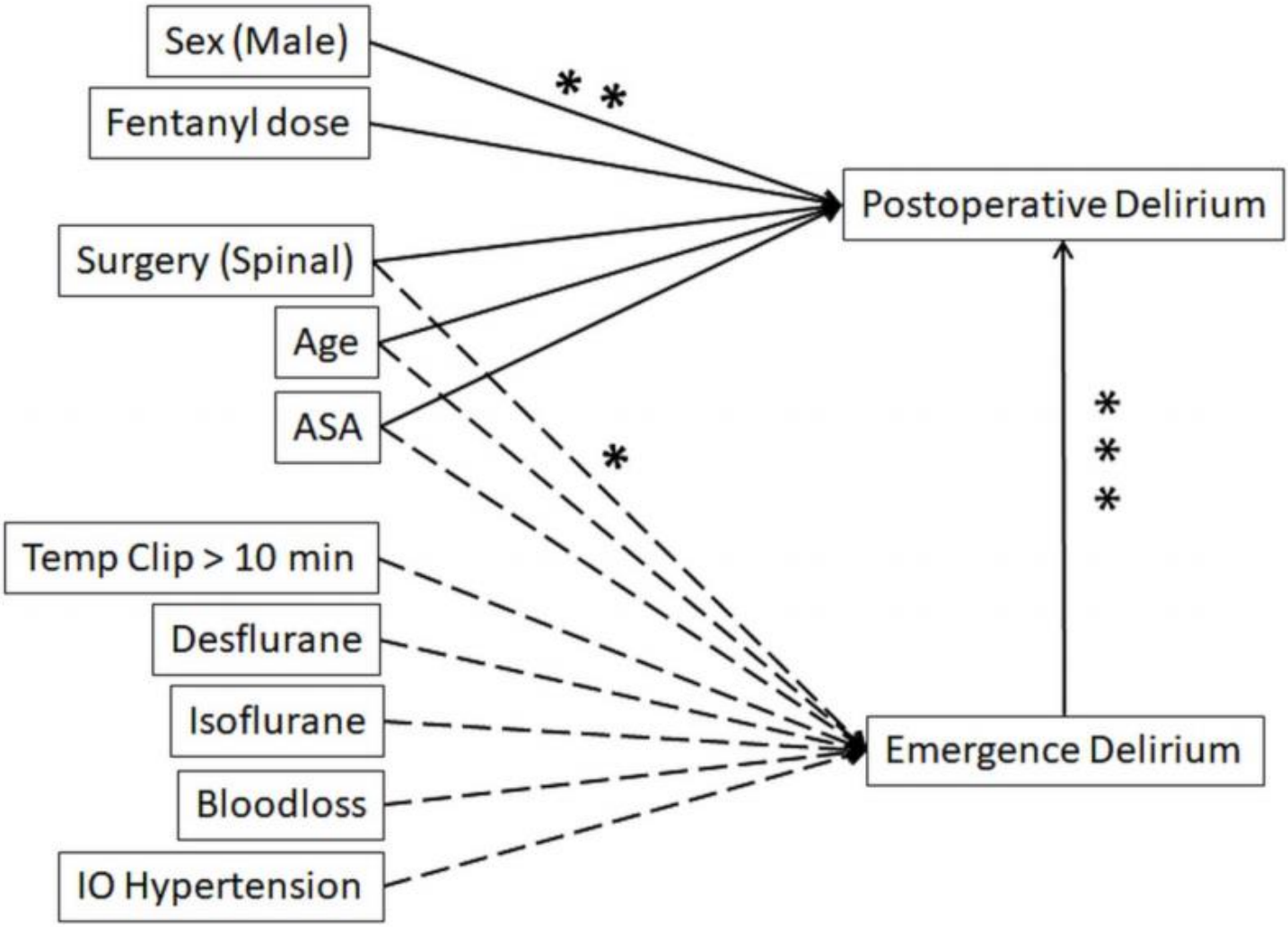
Table 1: Incidence of Emergence Delirium and Post-Operative Delirium

Surgical procedure (N)	Emergence delirium N (%)	Postoperative delirium N (%)
All Neurosurgical cases (200)	82 (41%)	40 (20%)
Spine surgery (43)	11 (26%)	4 (9%)
Cranial surgery (157)	70 (44%)	36 (23%)
a) Cerebrovascular surgery (Aneurysm + arterio-venous malformation) (18)	11 (61%)	4 (22%)
b) Surgery for supratentorial lesion (81)	33 (40%)	21 (26%)
c) Epilepsy surgery (4)	2 (50%)	1 (25%)
d) Endoscopic pituitary surgery (10)	5 (50%)	4 (40%)
e) Extradural surgery (18)	8 (44%)	2 (11%)
f) Infratentorial surgery (26)	11 (41%)	4 (14%)

Figure 1: Consort diagram depicting the flow of patients into the study




Sex (Male)
Fentanyl dose
Surgery (Spinal)
Age
ASA
Temp Clip > 10 min
Desflurane
Isoflurane
Bloodloss
IO Hypertension
Postoperative Delirium
Emergence Delirium
* *
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Supplement 1: Confusion Assessment Method (CAM)

Diagnosis of Delirium by CAM requires presence of both features A and B	
A. Acute onset and fluctuating course	Is there an evidence of an acute change in mental status from baseline?
	Does the abnormal behavior
	• come and go? • fluctuate during the day? • Increase/decrease in severity
B. Inattention	Does the patient:
	• Have difficulty focusing attention • Become easily distracted • Have difficulty keeping track of what is said?
And the presence of either feature C or D	
C. Disorganized thinking	Is the patient's thinking
	• disorganized • incoherent
	For example, does the patient have
	• Rambling speech/irrelevant conversation • Unpredictable switching of subjects • Unclear or illogical flow of ideas
D. Altered level of consciousness	Overall what is the patient's level of consciousness:
	• Alert (normal) • Vigilant (hyper-alert) • Lethargic (drowsy but easily roused) • Stuporous (difficult to rouse) • Comatose (unarousable)

Supplement 2: Riker's Sedation Agitation (SAS) score

7	Dangerous agitation	Pulling at tracheal tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side-to-side
6	Very agitated	Does not calm, despite frequent verbal reminding of limits; requires physical restraints, biting tracheal tube
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Non-agitated, Calm and cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands , may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

Neuroscience in Anesthesiology and Perioperative Medicine-4 Temporal trend of mechanical thrombectomy utilization in treatment of perioperative ischemic stroke following elective inpatient surgery in the United States

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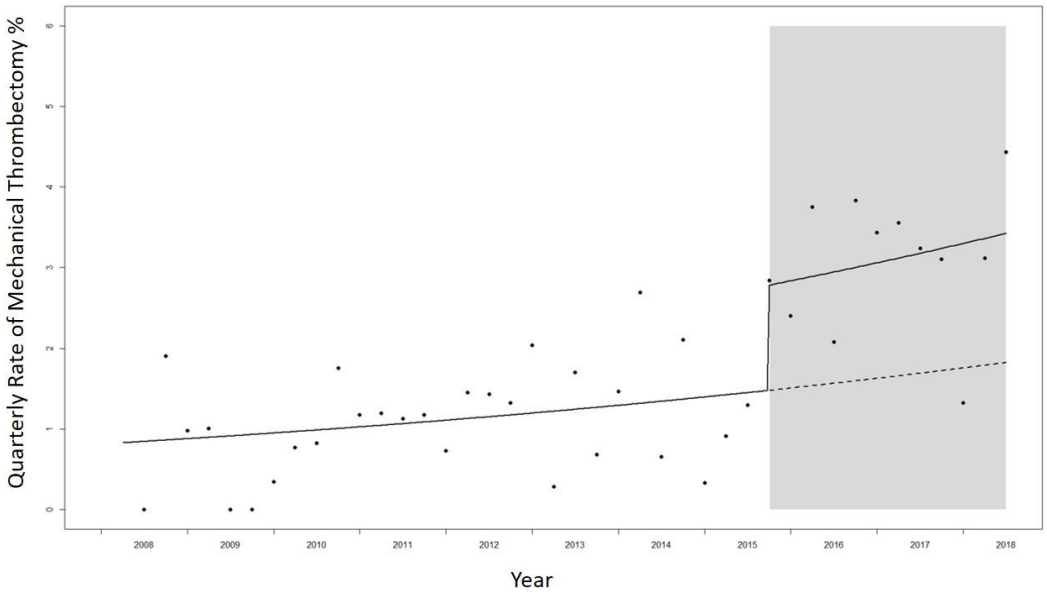
Introduction: Perioperative ischemic stroke significantly increases morbidity and mortality in patients undergoing elective surgery. Mechanical thrombectomy can improve outcomes of ischemic stroke caused by large vessel occlusion, but the frequency and trend of its utilization for treatment of perioperative ischemic stroke is not studied.

Methods: In this retrospective observational study using the Premier Healthcare Database, we identified adults who underwent elective inpatient surgery from 2008 to 2018. Patients with perioperative ischemic stroke were identified using the established International Classification of Diseases (ICD) ninth revision codes or equivalent ICD, tenth revision codes. Cases that underwent mechanical thrombectomy were further identified using established ICD9 and ICD10 procedure codes. Descriptive statistics were used to compare patient and center level characteristics between patients who received mechanical thrombectomy versus did not after perioperative ischemic stroke.

Results: Of 6,349,668 patients with elective inpatient surgery, 12,507 (0.2%) had perioperative ischemic stroke. The mean age (and standard deviation) of these patients was 69.5 (11.7) years, and 48.8% were female. Mechanical thrombectomy was used in 1.7% of all patients with perioperative ischemic stroke and its use increased from 0.0% in 3rd quarter, 2008 to 4.4% in 4th quarter, 2018. There was a significant increase in the use of mechanical thrombectomy after 3rd quarter, 2015 when mechanical thrombectomy use was incorporated in acute stroke treatment guideline (1.14% before 3rd quarter, 2015 versus 3.07% after; $p<0.0001$). Amongst patients with perioperative ischemic stroke, patients who received mechanical thrombectomy were more likely to have their surgery performed at a teaching institute (67.3% versus 53.9%).

Conclusion: Although there was a significant increase in rates of utilization of mechanical thrombectomy after guidelines were changed, rates of utilization remain low, especially in non-teaching hospitals. This highlights improvements in the management of perioperative ischemic strokes and further opportunities to improve outcomes.

Figure: Trend of patients treated with mechanical thrombectomy for perioperative ischemic stroke by quarter



Neuroscience in Anesthesiology and Perioperative Medicine-5 The SANDMAN Study: Sleep Apnea, Neuroinflammation, and Cognitive Dysfunction Manifesting After Non-cardiac surgery

Michael Devinney[1], Andrew R Spector[1], Jeffrey N Browndyke[1], Patrick J Smith[1], Jennifer Dominguez MD Asst Professor of Anesthesio M Dominguez[1], Mary Cooter[1], Sarada Eleswarpu[1], Thomas Bunning[1], Keith W VanDusen[2], Pallavi Avasarala[1], Victor Cai[1], Joseph P Mathew[1], Miles Berger[1]

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Introduction: Up to 40% of older patients will develop perioperative neurocognitive disorders, including delirium and neurocognitive disorder, postoperative. Neurocognitive disorder, postoperative includes subjective cognitive complaints as well as objective thinking/memory deficits that occur 1-12 months after surgery; these objective cognitive deficits alone have been referred to as postoperative cognitive dysfunction (POCD). POCD and other perioperative neurocognitive disorders have been associated with decreased quality of life, increased mortality, and further long-term cognitive decline. One possible POCD risk factor is obstructive sleep apnea (OSA), a frequently undiagnosed disorder characterized by repetitive breathing cessations (apneas and hypopneas) during sleep. OSA is highly prevalent in older surgical patients and can be diagnosed with home sleep apnea tests (HSAT), which measure the respiratory event index (REI, respiratory events per hour: an estimate of the apnea-hypopnea index). OSA has been associated with long-term cognitive decline, earlier dementia onset, and postoperative delirium. Yet, the role of OSA in POCD severity is unknown. POCD is thought to be caused partly by neuroinflammation. Increased neuroinflammation might occur in OSA patients, since OSA is associated with increased peripheral inflammation and magnetic resonance spectroscopy (MRS) markers of neural damage. In SANDMAN, we will determine the extent to which OSA is associated with POCD severity and neuroinflammation. In addition, we will obtain whole-brain MRS feasibility data.

Methods: SANDMAN is a sub-study of the INTUIT study, in which 200 patients age>60 undergoing major non-cardiac/non-neurologic surgery undergo blood and cerebrospinal fluid (CSF) sampling and cognitive testing before, 24hrs and 6 weeks after surgery. CSF inflammatory markers are measured with multiplex ELISA assays. In SANDMAN, 80-100 INTUIT patients will also complete preoperative HSAT to diagnose OSA and quantify its severity. Ten SANDMAN patients will also undergo pre- and postoperative MRS scans to measure markers of neural (N-Acetylaspartate) and white matter (choline) damage. The association of REI with postoperative cognition will be assessed via multivariate analysis adjusting for age, body mass index, preoperative cognition, and years of education. The relationship between REI and CSF cytokines will be assessed with univariate linear regression.

Results: As of 1/1/2020, 58 patients have enrolled in SANDMAN, with 55 patients successfully completing HSAT (Figure 1; mean REI 10.9, SD 14.4). The mean duration of HSAT evaluation per patient was 330 minutes (SD 104). The distribution of OSA severity shown in Figure 2; 56% of patients were diagnosed with OSA. Two patients have completed whole-brain MRS scans.

Conclusion: SANDMAN is assessing the relationship between OSA, neuroinflammation, and POCD. We hypothesize that OSA is associated with POCD severity and increased neuroinflammation. If true, this finding could lead to potential interventions, such as preoperative detection and treatment of OSA, to prevent POCD.

Figure 1: SANDMAN Consort Diagram:

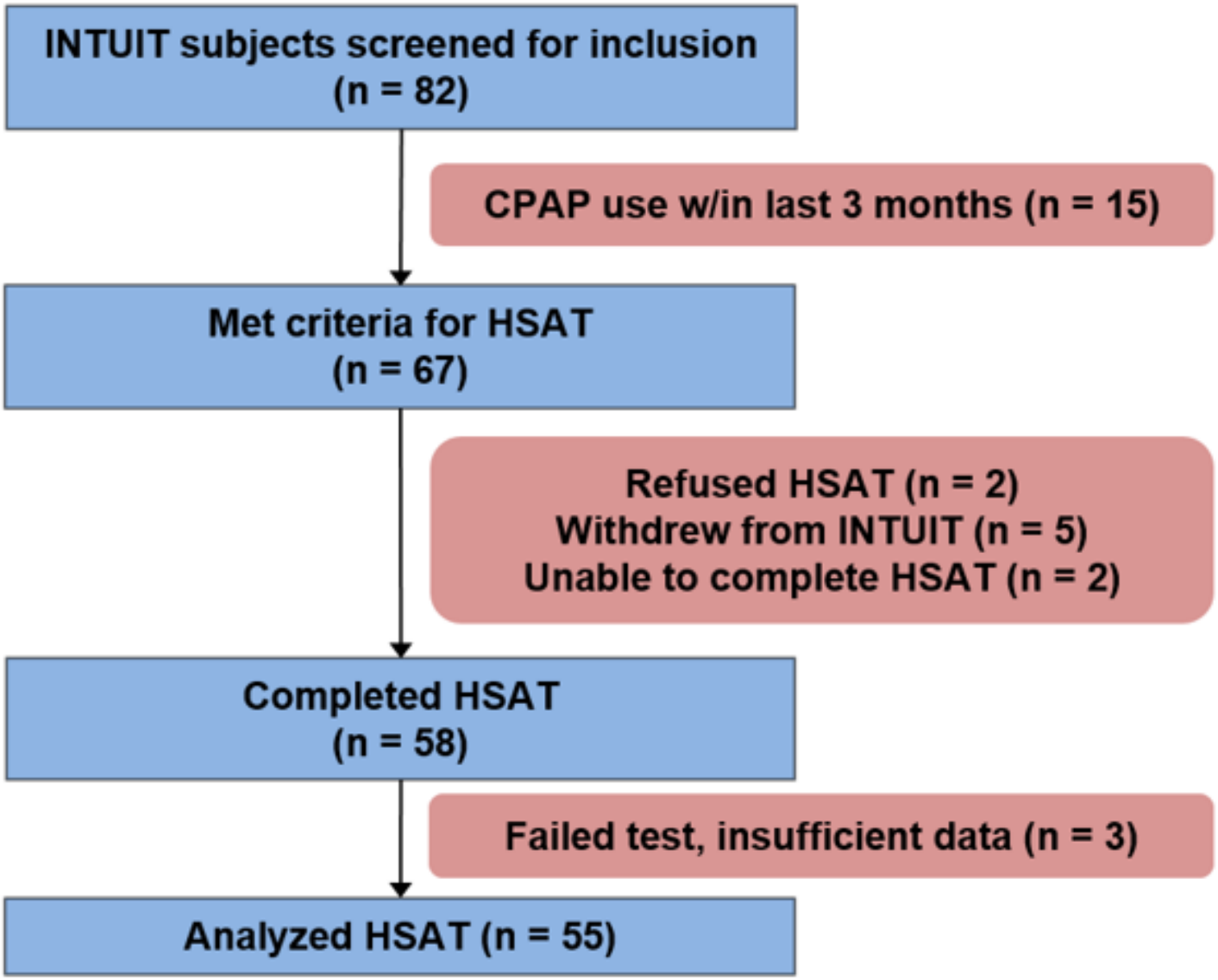

Figure 2: Obstructive Sleep Apnea Severity Distribution:

Negative for OSA (REI<5) n = 24, 44%	Mild OSA (REI 5-14.9) n = 15, 27%	Moderate OSA (REI 14.9-29.9) n = 10, 18%	Severe OSA (REI>29.9) n = 6, 11%

Neuroscience in Anesthesiology and Perioperative Medicine-6 Transcriptomic Analysis of Thoracic Spinal Cords in Experimental Pulmonary Hypertension Reveals Novel Therapeutic Targets

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Introduction: Pulmonary hypertension (PH) is an incurable disease characterized by pulmonary artery pressure overload, right ventricular (RV) hypertrophy, failure, and death. PH is associated with sympathetic activation, however the involvement of spinal cord-lung-heart axis is yet to be investigated. Here, we performed the first ever transcriptome analysis of thoracic spinal cords in two pre-clinical rat models of PH using bioinformatics approach.

Methods: Male Sprague Dawley rats (~300g) received either Monocrotaline (MCT, 60mg/kg, s.c., n=8) and were followed for 30 days or Sugen (Su/Hx group, 20mg/kg, s.c., n=9) and kept in hypoxia (10% O2) for 3-wks followed by 2-wks of normoxia. Saline treated rats served as controls (CTRL, n=10). Echo and RV catheterization were performed terminally. Hearts, lungs and spinal cords were harvested and lung histology was assessed by Trichrome staining. RNASeq was performed on thoracic spinal cords. Differential expression analysis was conducted using R-program. RT-qPCR was performed for gene validation. Values are mean±SEM and $p<0.05$ is considered significant.

Results: Severe PH was confirmed by increased RV systolic pressure (RVSP, mmHg) in MCT (97.6±6.6) and Su/Hx (85.26±15.6) compared to CTRL (37.1±1.3; $p<0.05$). RV hypertrophy index (RV/LV+IVS) was significantly increased in MCT (0.82±0.07) and Su/Hx (0.61±0.1) compared to CTRL (0.27±0.01; $p<0.05$). MCT and Su/Hx rats demonstrated increased pulmonary vascular remodeling. RNASeq demonstrated differential expression of multiple pathways and genes in thoracic spinal cords of both models. Gene Set Enrichment Analysis revealed 14 significantly upregulated pathways in both MCT and Su/Hx among which 12 were overlapping. From these overlapping pathways 162 leading edge genes had significantly increased expression in MCT, 171 genes in Su/Hx and 168 overlapping genes in both models. Conversely, 9 pathways were significantly downregulated in MCT, among which 8 were overlapping in both models. From these overlapping pathways 77 leading edge genes had significantly decreased expression in MCT, 93 leading edge genes in Su/Hx and 360 overlapping genes in both. Both MCT and Su/Hx revealed similar significant up-regulation of hedgehog signaling, IL6 JAK STAT3 signaling, KRAS signaling, epithelial mesenchymal transition, apical junction and apical surface pathways and down-regulation of E2F target, DNA repair and fatty acid oxidation pathways. RNASeq data were validated with PCR by selecting several key dysregulated genes from hedgehog signaling (SLIT1), IL6 JAK STAT3 signaling and KRAS signaling (CNTFR), epithelial mesenchymal transition (TGFβ1), apical junction (VWF), apical surface (CX3CL1), E2F target (SMC4), DNA repair (RALA), and fatty acid metabolism (IDI1).

Conclusion: Severe PH in rats demonstrates characteristic transcriptome signature of thoracic spinal cords. Targeting these specific pathways and genes may yield novel therapeutic strategies for this incurable disease.

Obesity

Obesity-1 “Kiss of Death' - Elevated BMI, “Kissing Carotid Arteries' Incidence, and Clinical Significance in Anesthesiology

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Introduction: Retropharyngeal extracranial common (eCCA) or internal carotid artery (eICA) approaching or 'kissing' at midline may have critical anesthesiology complications including hemorrhage from traumatic intubation, sleep apnea, stroke, laceration, and inadvertent anesthetic injection. Although described in early nineteenth century otolaryngology literature1, limited research about increasing incidence and relevance in anesthesiology is available. This research compared 13 cross-sectional images of retropharyngeal eCCAs or eICAs to age- and sex-matched images with normal vessel course.

Methods: After IRB approval, 13 cases of cross-sectional retropharyngeal carotid arteries on contrast computed axial tomography (CT) were compared to age- and sex-matched controls with normal vessel course, comparing distances between right and left arteries, Body Mass Index (BMI), and subcutaneous adipose tissue at the eICA origin.

Results: Total n=13 retropharyngeal eCCA or eICAs, n = 6 eICA, n=5 eCCA, n=2 both eCCA and eICA, 9 females, 4 males, mean age 61.8 years, distance between right and left ICA = 0.5 - 4 mm, BMI = 29.8 - 58.8 with mean 40.6 (kg/m2), subcutaneous adipose measured 15-76 mm, mean of 31.8 mm. The age- and sex-matched normal controls had mean age 64.3 years, distance between right and left ICA = 40.98- 58.9 mm, BMI = 22.5 - 40.5, mean of 27.5 (kg/m2), and subcutaneous adipose tissue measuring 6.17- 33.8 mm, mean 13.3 mm.

Conclusion: Embryonically eICAs arise from 3rd aortic arch and dorsal aorta. During 8th week of fetal life, dorsal aortic root descends in thorax straightening eICA. Etiologic theories of retropharyngeal vessels include incomplete straightening as dorsal aortic root descends, aging physiologic effects, and elevated BMI affecting tortuosity4. A retrospective review of 'kissing' retropharyngeal eCCAs and eICAs demonstrated significantly elevated BMIs compared to normal controls. Conclusion: Retropharyngeal eCCA or eICAs 'kissing' near midline had increased mean BMIs of 40.6 and increased subcutaneous adipose tissue compared to normal controls mean BMI of 27.52. Excess adipose tissue may displace vessels medially, the increasing incidence of retropharyngeal eCCAs and eICAs may reflect obesity prevalence. Because retropharyngeal eCCA or eICA may lead to catastrophic anesthetic complications including massive hemorrhage from traumatic intubation, anesthesiology awareness is necessary to reduce unwanted morbidity

Reference(s):

1. Kelly A: Tortuosity of internal carotid in relation to the pharynx. J Laryng Otol 1925; 40:15–23

2. Rojas R, et al: Anomalous course of cervical carotid arteries. Ear Nose Throat J 2002; 81:377–8

3. Marcucci C, et al. Retropharyngeal carotid artery: an important anatomic variation for the anesthesiologist. Anesthesiology. 2009 Aug;111(2):454-5.

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Obesity-2 Opioid-free Anesthesia in Bariatric Surgery: A Retrospective Cohort Study

Masha Zeltsman[1], Oonagh Dowling[1], Madina Gerasimov[2], Greg Palleschi[2], Judith Aronsohn[2]

[1]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, NY, [2]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY

Introduction: Enhanced recovery after surgery (ERAS) pathways utilize intraoperative opioid sparing techniques in concert with multimodal pain management strategies to minimize opioid-related adverse effects. While opioid-free anesthesia (OFA) has been studied in a variety of surgical populations, its efficacy in the bariatric surgery population is still unclear. The purpose of this study was to determine whether combining our institution's enhanced recovery pathway with intraoperative OFA reduces postoperative opioid requirements, enhancing patient recovery.

Methods: Data from 128 morbidly obese patients who underwent laparoscopic vertical sleeve gastrectomy from December 2018 to September 2019 was analyzed. All patients were managed within our institutional ERAS pathway utilizing general anesthesia with fentanyl or non-opioid adjuncts (non-OFA versus OFA) according to anesthesiologist preference. Data collected included patient demographics (Table 1), pain scores (visual analog scale), early postoperative opioid use (oral morphine equivalents; OME) and postoperative nausea and vomiting (PONV). Descriptive statistics consisting of means (95% confidence intervals), medians (interquartile ranges for continuous data) and percentages (with frequencies for categorical data) were performed. Comparison between groups was carried out using student's t-test for parametric continuous data or non-parametric tests. Chi square test was used for categorical data comparisons. Multivariate regression was performed to control for baseline characteristics with bivariate $p<0.2$. A p-value of ≤ 0.05 was considered significant.

Results: No significant differences between groups with respect to postoperative pain scores at timed intervals were observed (Table 2). Similarly, no differences were observed with respect to postoperative OME requirements in the first 6 hours (10.6 versus 10.0, p=0.50 for OFA versus non-OFA groups, respectively).The incidence of PONV in the immediate postoperative period was 82.14% in OFA group versus 83.33% in non-OFA group (p=0.86). After adjustment for age, gender, ASA physical status and presence of obstructive sleep apnea, no statistically significant association among OFA and postoperative OME use in the first 6 hours (p=0.08) or PONV (p=0.99) was observed.

Conclusion: This study found no differences between OFA and non-OFA groups with respect to immediate postoperative recovery characteristics including postoperative pain, opioid use and PONV. Prospective, randomized clinical trials are needed to confirm these findings and define the benefits of OFA on other important outcome metrics in bariatric surgery patients.

Reference(s): Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. 2003 Oct;13(5):676-83. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. 2009;5:263–276 Non-opioid analgesia improves pain relief and decreases sedation after gastric bypass surgery. 2003 Apr;50(4):336-41

Table 1: Patient demographic data.

Demographic Variable	OFA (n=56)	non-OFA (n=72)	P-Value
Age (years)	46.44 (42.89-50.00)	41.74 (39.18-44.29)	0.03
Gender (% female)	83.93 (n=47)	84.72 (n=61)	0.90
Race (% African American)	44.64 (n=25)	38.89 (n=28)	0.51
BMI	43.39 (41.44-45.44)	43.01 (41.44-45.44)	0.77
OSA (% yes)	69.64 (n=39)	55.56 (n=40)	0.10
ASA Physical Status (% III)	80.36 (n=45)	69.44 (n=50)	0.15

Data presented as number of patients (percentage) or geometric mean
ASA – American Society of Anesthesiologists; BMI – Body Mass Index

Table 2: Postoperative pain scores, opioid consumption and incidence of PONV.

Recovery Variable	OFA (n=56)	non-OFA (n=72)	P-Value
Median Maximal Pain Score			
0-6 h	4.0 (0-7.0)	3.0 (0-6.0)	0.17
6-12 h	2.0 (0-3.5)	1.0 (0-4.0)	0.70
12-24 h	1.0 (0-3.0)	1.0 (0-3.5)	0.34
OME Opioid Consumption			
0-6 h	10.6 (6.1-12.5)	10.0 (0-15.0)	0.50
Opioid Rescue (%)			
0-6 h	80.36% (n=45)	66.67% (n=48)	0.09
PONV Rescue (%)	82.14% (n=46)	83.33% (n=60)	0.86

Data presented as geometric mean or median (interquartile ranges)
OME – Oral Morphine Equivalents; PONV – Postoperative Nausea and Vomiting

Obstetric Anesthesiology

Obstetric Anesthesiology-1 Epidural Replacement Rate and Cost of Care Following Labor Epidural Analgesia at a Single Tertiary Care Hospital

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Introduction: Epidural analgesia is commonly used in alleviating labor pain due its effectiveness and superiority when compared to other methods of analgesia in alleviating labor pain (1). Prior studies have shown an epidural catheter failure rate average of 12% and 13% (2, 3). However, few studies have evaluated the effects of these rates on cost of healthcare. In this study, we determine the incidence of epidural failure in a single tertiary care hospital and review the total cost difference of epidural replacements with and without complications.

Methods: We conducted a retrospective cohort study of patients who received an epidural for labor analgesia at the University of Texas Medical Branch. This project has been approved by the University of Texas Medical Branch Institutional Review Board. We collected data from electronic health records at UTMB to identify parturients aged between 18 and 50 who had epidural anesthesia for planned vaginal delivery between November 2015 and February 2019. The epidural anesthesia procedures were identified using current procedural terminology code 01967. For the cost analysis, we estimated the total cost for the hospital stay for delivery and readmission if any. We first categorized patients into two groups by the presence of epidural replacement. Within each group, we further categorized the patients into three groups: 1) no headache or epidural blood patch (EBP), 2) with headache but no EBP, and 3) with EBP. Patients who had multiple orders for epidural anesthesia during the hospitalization were considered to have epidural replacement. All costs were adjusted to the same time period, using the consumer price index for medical care.

Results: We included 4973parturients in this study. The parturient characteristics during the inpatient visit for delivery are presented in Table 1. The incidence of epidural replacement rate noted in our patient population was 9.35%. Among 4973 parturients 465 of had epidural replacement within 24 hours of initial epidural placement. The median cost of care for parturients who had epidural replacement without complication such as PDPH was found as 20457.53 USD (Table 2). The median cost of care for parturients who had no epidural replacement without complication was found as 16272.40.

Conclusion: In our single institution study, the vast majority of labor epidurals are placed by resident trainees. The incidence of epidural replacement rate noted in our patient population was 9.35%. We found the average cost for the majority of our parturients who received epidurals was approximately $17,500. We found that the mere replacement of an epidural with no further signs of dural puncture headache increased cost by about $5000 or 29%. Despite the increased average cost, the range of costs was also very significantly increased, perhaps reflecting on the myriad reasons underlying the requirement for epidural replacement. We found approximately a 2% risk of headache in our epidurals. Of those patients with headache, patients were more than twice as likely to require an epidural blood patch if they had previously required replacement of their epidural versus if they did not. The patients that required an EBP after epidural replacement on average had the highest cost, 48% higher than the cost of single epidural alone.

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Table 1. Paturient characteristics at the inpatient visit for delivery

Paturient characteristic	Mean ± SD	Median
Age	27.4 ± 5.7	26.7
BMI[#]	32.3 ± 6.5	31.3
Gravidity	2.7 ± 1.7	2.0
Parity	1.7 ± 1.3	1.0
	N	%
Race/ethnicity		
Asian	168	3.75
African American	506	11.29
Caucasian/White	1197	26.70
Hispanic or Latino	2591	57.80
Other	21	0.47
Gravidity		
0-1	1277	28.49
2-3	2048	45.68
3-4	792	17.67
> 5	312	6.96
Unknown	54	1.20

[#]319 records did not have info on BMI.

Table 2. Cost associated with epidural anesthesia for planned vaginal delivery

Epidural replacement	**Headache**	**EBP**	**N**	**Mean ± SD[#]**	**Median[§]**
No	No	No	3928	17414.53 ± 6335.22	**16272.40**
	Yes	No	66	19201.23 ± 13686.01	17026.01
		Yes	20	23772.33 ± 6856.11	21359.12
Yes	No	No	450	22452.14 ± 13038.52	**20457.53**
	Yes	No	8	24935.07 ± 5093.90	24212.93
		Yes	7	25700.02 ± 4157.85	25279.51

[#] Total cost for the hospital stay for spontaneous vaginal delivery and readmission.

[§]Median costs were used in the Cost-Effectiveness model.

EBP: Epidural Blood Patch.

Pain Mechanisms

Pain Mechanisms-1 The Effect of Deep Versus Moderate Neuromuscular Block on the Pain after Laparoscopic Colorectal Surgery: A Randomized Clinical Trial

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Introduction: Postoperative pain of laparoscopic surgery is less intense than laparotomy, but patients still suffer from considerable discomfort. Optimal pain control is an important part of enhanced recovery after surgery. Recent studies indicated that deep neuromuscular block (NMB) to laparoscopic surgery may result in less postoperative pain with a lower intra-abdominal pressure (IAP). The purpose of this study was to evaluate the effect of deep NMB on the postoperative pain of laparoscopic colorectal surgery.

Methods: Ninety-one patients finally completed the study. Patients were randomized to either deep (post-tetanic count 1 to 2, PTC=1-2, group D) or moderate (train-of-four 1 to 2, TOF=1-2, group M) NMB group. Postoperative pain at rest and on coughing was assessed using the numeric rating scale (NRS) with a range of 0 to 10 (0=no pain, 10=the worst possible pain) at 1, 6, 24, 48 hours after surgery. The primary outcome was the NRS scores at rest and on coughing during the first 48 hours after surgery. Second outcomes included bolus attempts and deliveries, rescue analgesics, the incidence of postoperative nausea and vomiting (PONV), IAP, the surgical rating scale, the time of first flatus and length of hospital stay.

Results: The postoperative NRS scores were significantly better in group D compared with group M both at rest ($P < .001$) and on coughing ($P < .001$) at 1, 6, 24, 48 hours after surgery. Patients in group D had a significant lower number (median [interquartile range]) of bolus attempts (4 [2-6] vs 9 [5-13], $P < .001$; median difference = -5 [95% CI, -7 to -3]) and deliveries (4 [2-6] vs 9 [5-12], $P < .001$; median difference = -5 [95% CI, -6 to -2]) on postoperative day (POD) 1. Deep NMB improved the surgical conditions ($P < .001$) with a lower IAP ($P < .001$). The number of patients who required additional rescue analgesics was less in group D than group M on POD 2 ($P = .005$). The frequency of PONV was lower in group D ($P = .023$).

Conclusion: Compared with moderate NMB, Deep NMB had better pain relief and lower opioid consumption after laparoscopic colorectal surgery. Deep NMB facilitated a lower IAP and better surgical condition in laparoscopic surgery.

Pain Medicine

Pain Medicine-1 More Sopor, Less Dolor: A Systematic Review and Meta-analysis on the Impact of Cannabinoids on Sleep Health and Pain in Patients with Chronic Neuropathic Pain

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Introduction: Neuropathic pain (NP) syndromes are debilitating conditions which can impact sleep health and overall quality of life significantly.[1] Pharmacological treatment with cannabinoids has not been evaluated for its impact on sleep health (sleep quality and daytime somnolence). The objectives of this systematic review and meta-analysis (SR-MA) were to determine the effect of cannabinoids on sleep quality, pain control, and patient impression of treatment efficacy.

Methods: We reviewed randomized controlled trials comparing synthetic and natural cannabinoids (CB) to placebo in patients with central and peripheral neuropathic pain syndromes. A systematic search of the standard literature databases from database conception to July 2019 was carried out with the help of an information specialist. Inclusion criteria were randomized controlled trials evaluating the pharmacological treatment of NP syndromes using cannabinoids, with an active treatment or a placebo as a comparator. Data on eleven-point (0-11) numerical rating scales for pain and sleep quality, incidence of daytime somnolence, nausea, and dizziness as adverse effects, and patient global impression of change (PGIC) scores were recorded. Meta-analysis using the random effects model was conducted where appropriate.

Results: Of the 3536 studies screened, a total of 8 randomized controlled trials including 1051 patients (placebo: 478 patients; CB: 573 patients) with neuropathic pain were included. Cannabinoids most commonly included in the studies were Sativex (GW-1000-02), Nabilone, and medical cannabis preparations with THC dose ranging from 1mg to 130mg per day. Pain scores were significantly reduced in the CB group (standardized mean difference, SMD = -0.50, 95% CI -0.79 to -0.22, p=0.001) compared to placebo (Figure 1). Significant improvement in sleep quality (Figure 2) was also observed in the CB group (SMD=0.39, 95% CI 0.18 to 0.60, p<.001). Additionally, patients in the CB group were more likely to report improvement in PGIC scores (OR=2.3, 95% CI 1.37 to 3.7, p=0.001) compared to patients treated with placebo (Figure 3). Notably, CB-treated patients were more likely to experience daytime somnolence (OR=2.2, 95% CI 1.3 to 3.9, p=0.004), nausea (OR=1.7, 95% CI 1.1 to 2.5, p=0.02), and dizziness (OR=3.8, 95% CI 2.6 to 5.7, p<.001).

Conclusion: Cannabinoids are useful agents for NP as evidenced by significant improvement in pain, sleep quality, and PGIC. However, these benefits were noted at the expense of several adverse events including daytime somnolence. With the advent of new agents and more refined cannabis derivatives, further research is needed to comprehensively explore treatment effectiveness. Moreover, future work should incorporate clinically validated measures of sleep health to better evaluate this outcome.

Reference(s):

1: Ferini-Strambi L. Neuropathic Pain and Sleep: A Review. Pain and therapy. 2017;6:19-23

Study name	Dose	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Berman 2004	129.6 mg THC / day	-0.490	0.208	0.043	-0.898	-0.081	-2.351	0.019
Berman 2004	129.6 mg THC + 120mg CBD / day	-0.489	0.209	0.044	-0.899	-0.079	-2.336	0.020
Nurmikko 2007	129.6 mg THC + 120mg CBD / day	-1.579	0.205	0.042	-1.981	-1.178	-7.707	0.000
Rog 2005	129.6 mg THC + 120mg CBD / day	-0.734	0.254	0.065	-1.232	-0.235	-2.884	0.004
Toth 2012	1-4mg nabilone /day	-0.677	0.403	0.163	-1.467	0.114	-1.678	0.093
Ware 2010	25mg of 2.5%, 3x/daily	-0.114	0.305	0.093	-0.712	0.485	-0.372	0.710
Ware 2010	25mg of 6%, 3x/daily	-0.028	0.309	0.095	-0.633	0.577	-0.091	0.928
Ware 2010	25mg of 9.4%, 3x/daily	-0.424	0.308	0.095	-1.028	0.181	-1.374	0.170
Langford 2013	32.4 mg THC + 30 mg CBD/day	-0.129	0.109	0.012	-0.342	0.084	-1.184	0.236
Serpell 2014	64.8 mg THC + 60 mg CBD/day	-0.189	0.128	0.016	-0.440	0.061	-1.481	0.139
Guido van Amerongen 2017	16mg THC	-0.803	0.424	0.180	-1.635	0.028	-1.893	0.058
		-0.503	0.146	0.021	-0.789	-0.217	-3.447	0.001

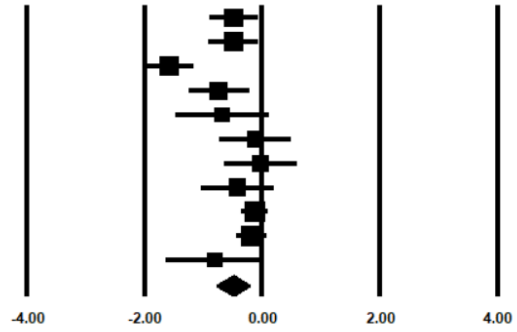

Figure 1. Forest plot evaluating changes in patient daily pain scores in CB and placebo groups

Study name	Dose	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Berman (1) 2004	129.6 mg THC + 120mg CBD	0.493	0.209	0.044	0.082	0.903	2.352	0.019
Berman (2) 2004	129.6 mg THC / day	0.697	0.211	0.045	0.283	1.112	3.299	0.001
Serpell 2014	64.8 mg THC + 60 mg CBD/day	0.347	0.129	0.017	0.095	0.599	2.700	0.007
Langford 2012	32.4 mg THC + 30 mg CBD/day	0.023	0.109	0.012	-0.190	0.236	0.211	0.833
Rog 2005	129.6 mg THC + 120mg CBD	0.772	0.255	0.065	0.271	1.272	3.022	0.003
Toth 2012	1-4mg nabilone /day	0.739	0.405	0.164	-0.055	1.534	1.824	0.068
Ware (1) 2010	25mg of 2.5%, 3x/daily	0.061	0.305	0.093	-0.538	0.659	0.198	0.843
Ware (2) 2010	25mg of 6%, 3x/daily	0.221	0.310	0.096	-0.386	0.828	0.714	0.476
Ware (3) 2010	25mg of 9.4%, 3x/daily	0.534	0.310	0.096	-0.075	1.142	1.720	0.085
		0.390	0.105	0.011	0.184	0.597	3.713	0.000

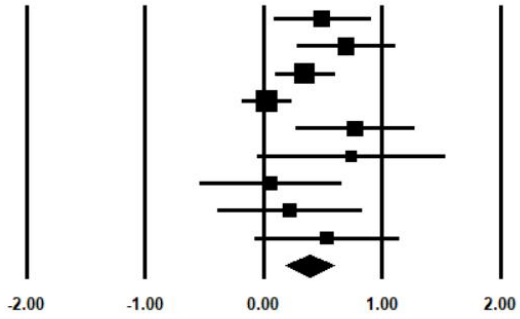

Figure 2. Forest plot evaluating changes in patient sleep quality in CB and placebo groups

Study name	Dose	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Rog 2005	129.6 mg THC + 120mg CBD / day	2.520	0.690	9.204	1.398	0.162
Toth 2012	1-4mg nabilone /day	10.286	1.018	103.948	1.975	0.048
Serpell 2014	64.8 mg THC + 60 mg CBD/day	1.762	1.080	2.875	2.267	0.023
Langford 2013	32.4 mg THC + 30 mg CBD/day	1.470	0.991	2.181	1.913	0.056
Nurmikko 2007	Blank	4.583	2.058	10.209	3.726	0.000
		2.250	1.373	3.688	3.216	0.001

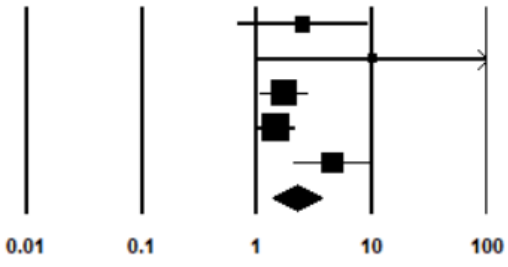

Figure 3. Forest plot evaluating changes in PGIC scores (odds ratios) in CB and placebo groups

Pain Medicine-2 Postoperative Pain in Pediatric Scoliosis Repair: Comparing Subjective and Objective Pain Scores

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Introduction: Scoliosis is a multidimensional deformity of the thoracolumbar spine, and can be categorized as idiopathic, congenital, or neuromuscular. Adolescent idiopathic scoliosis is the most common variant seen. Since severity of symptoms is associated with progression of this disease, surgical correction is undertaken based on a Cobb angle of >40 to 50 degrees. Patients undergoing this surgical correction experience severe pain in the postoperative period, and intraoperative and postoperative management of these patients varies. Postoperative management commonly includes the use of opioid-based patient-controlled analgesia (PCA) and adjuncts such as valium and ketorolac. We present here the initial results of prospective review of 122 cases including idiopathic, congenital, and neuromuscular scoliosis at a quaternary freestanding children's hospital that is a leading center for scoliosis repair.

Methods: We prospectively gathered data over a one year period. Data extracted included demographics, perioperative management, length of stay, and blood management techniques employed. Data relating to the intraoperative and postoperative care and hospital course was recorded using a RedCap database. Inclusion criteria were age between 5 and 18 years, and procedure of posterior spinal instrumentation and fusion or anterior spinal instrumentation and fusion. All personal health identifiable data were de-identified. Institutional review board approval was obtained prior to the start of data collection. Pain scores as recorded in the electronic medical record were reported. Both Numeric Rating Scale (NRS) patient reported data and nurse-reported Face, Legs, Activity, Cry, Consolability (FLACC) Scale data were recorded.

Results: Our preliminary data totals 122 records included for analysis. 91 patients had idiopathic scoliosis repair, 16 had congenital scoliosis repair, and 12 had neuromuscular scoliosis repair. Average age was 14.1 years (s.d. 2.24 years). Pain scores in the post-anesthesia recovery unit and on post-operative days 0, 1 and 2 were examined. Scores differed by scoliosis type, with significantly higher NRS scores reported by congenital scoliosis patients on post-operative days 0, 1 and 2 ($p<0.05$) and significantly higher FLACC scores reported on post-operative days 0 and 1. FLACC scores were significantly lower than NRS scores for all types of scoliosis throughout the hospital stay ($p<0.05$).

Conclusion: Though scoliosis is commonly considered to be one of the more painful pediatric surgeries, objective data on post-operative pain has been sparse. These data represent a unique opportunity to examine post-operative pain scores and how they differ by types of scoliosis in a large, single-center series. The results have implications for pain management, particularly given the discrepancies between the objective FLACC and subjective NRS scores in all types of scoliosis.

Reference(s): Altaf, F., et al., Adolescent idiopathic scoliosis. BMJ, 2013. 30(346). Yamada, K., et al., Etiology of idiopathic scoliosis. Clin Orthop Relat Res, 1984(184): p. 50-7. Machida, M., Cause of idiopathic scoliosis. Spine (Phila Pa 1976), 1999. 24(24): p. 2576-83. Giampietro, P.F., et al., Congenital and idiopathic scoliosis: clinical and genetic aspects. Clin Med Res, 2003. 1(2): p. 125-36.

Pain Medicine-3 Reducing postoperative opioids consumption with intraoperative methadone in long oral and maxillofacial surgeries

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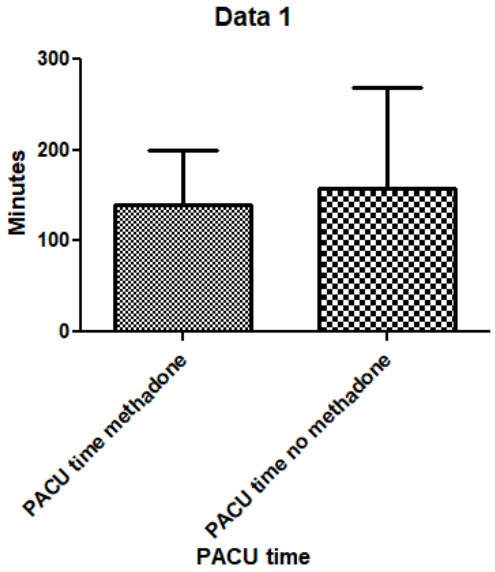
Introduction: This is a retrospective study that explored the effectiveness of intra-operative iv methadone used in reducing the post-operative opioids consumption in Oral and Maxillofacial (OMF) Surgeries of 4 hours or longer. Due to the clinical course of OMF surgeries, patient usually stays as inpatient for less than 48 hours and a portion of these patients will be discharged on post-op day 1. We compared the patient group with intra-op iv Methadone (10mg) to the regular management group where other opioids are administrated. Our result demonstrated that lower dose of methadone administration introperatively associated with significant clinical reduction in post-op opioids requirement. No side effects from medication observed in the methadone group. We recommend low dose Methadone as prefered opioids for these long OMF cases.

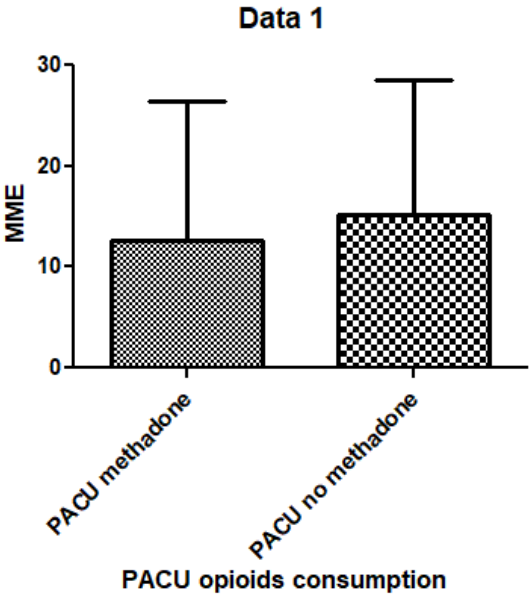
Methods: This is a retrospective cohort study. We reviewed OMF surgery cases which longer than 4 hours for surgical time in the lasts 10 years from 2009 to 2019. From the recent years, Methadone 10mg iv has been used for intra-op pain management. We studied inpatients only and excluded patients that were chronically on opioids medication, Methadone, or Suboxone treatment in both groups. The patient age is between 18-65 with no other major organ disease, no allergy to opioids. Group 1, 28 cases with intra-op Methadone administration (10mg iv) were selected as treatment group. Group 2, 28 cases without intra-op methadone administration were selected as control group. The control group is age/gender/surgery time matched to the treatment group.The post-operative pain management in both groups were kept identical which were managed by primary team. The pain medication in both groups includes: NSAIDs, Tylenol and Opioids. The pain scale of each patient was evaluated by the nursing team or primary team, and then the primary team decided which pain medication should be administrated for pain management. We compared the PACU stay time, opioid consumption in PACU time, opioid consumption in 24 hours after PACU, and opioid consumption in 24-48 hours after PACU between two groups with t test. All the opioids were converted to Morphine Milligram Equivalent (MME) using Stanford Opioid equivalent Dosing table.

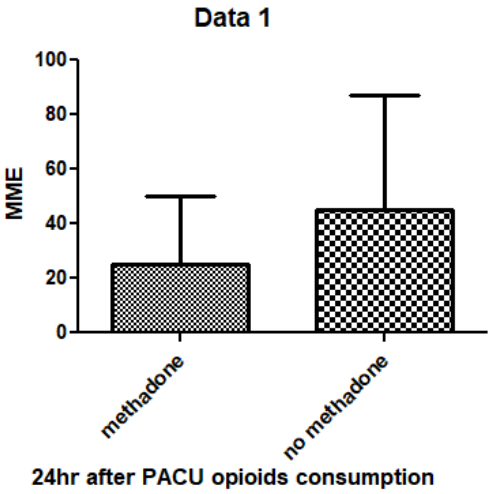
Results: Result is done using t test and showing as Mean ± SEM. There is NO significant difference in the PACU stay time between Methadone treatment group (139.8 ± 11.24 mins) and control group (157.9 ± 20.87 mins) (p=0.45. 95% confidence interval -65.66 to 29.44). There is NO significant difference in the PACU time opioid consumption between Methadone treatment group (12.57 ± 2.624 MME) and control group (15.18 ± 2.526 MME) (p=0.48, 95% confidence interval -9.915 to 4.701). There is significant difference in oipoid consumption in the 24 hours after PACU period. Methadone treatment group (24.93 ± 4.738 MME) vs. control group (45.29 ± 7.864 MME) (p=0.0308, 95% CI -38.78 to -1.937). Most patient were discharged within 48 hours. There are only 9 patients in the Methadone group and 11 patients in the control group remained inpatient by 48 hours after PACU. This makes the result of 24-48 hours post PACU less reliable. The result shows NO significant difference in oipoid consumption in the 48 hours after PACU period, Methadone treatment group (13.07 ± 4.298 MME) vs. control group (15.43 ± 5.516 MME) (p=0.73, 95% CI -16.39 to 11.67).

Conclusion: 1. Intra-op iv Methadone (10mg) can be used safely as primary analgesia medication for OMF surgeries longer than 4 hours. No side effect from Methadone was recorded. 2. Methadone takes longer to reach the full effect, it does not affect the over all PACU stay time comparing to other opioid medication. 3. Low dose of Methadone provided significant pain relief and reduced the opioid consumption significantly within 24 hours after patients left PACU, but does not reduce the opioid consumption in the PACU period. 4. There is no difference in the inpatient time observed from our limited cases using methadone comparing to other regular management. 5. Despite the long time to reach the full efficacy, methadone provides similar pain relief in the immediately post-op period comparing to other short/long acting opioids which was demonstrated as no difference in the PACU opioids consumption.

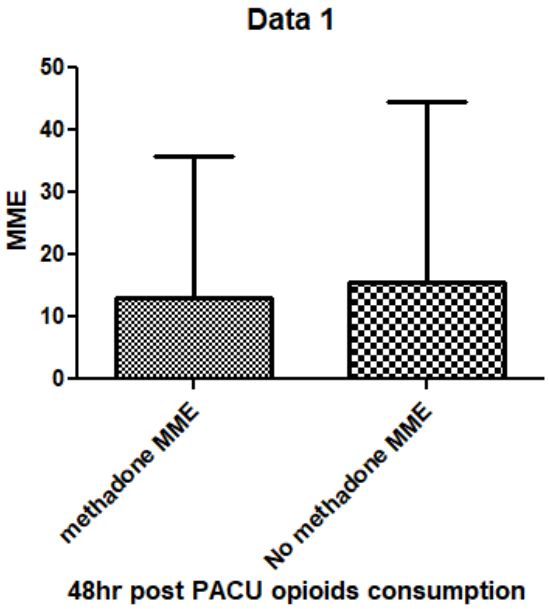
Reference(s): Intraoperative methadone improves postoperative pain control in patients undergoing complex spine surgery. Anesth Analg. 2011 Jan;112(1):218-23.
Intraoperative Methadone for the Prevention of Postoperative Pain: A Randomized, Double-blinded Clinical Trial in Cardiac Surgical Patients. Anesthesiology. 2015 May;122(5):1112-22.
Intraoperative methadone: rediscovery, reappraisal, and reinvigoration? Anesth Analg. 2011 Jan;112(1):13-6.
Treatment of postoperative pain in oral and maxillofacial surgery Br J Oral Maxillofac Surg. 2000 Dec;38(6):588-592.


Data 1
300
200
100
0
Minutes
PACU time methadone
PACU time no methadone
PACU time


Data 1
30
20
10
0
MME
PACU methadone
PACU no methadone
PACU opioids consumption



24hr after PACU opioids consumption



48hr post PACU opioids consumption

Pain Medicine-4 A Predictive Model for 2-Week Postoperative Opioid Use Following Ambulatory Joint Arthroscopy

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Introduction: Introduction: The number of joint arthroscopy procedures performed in the ambulatory surgery setting is steadily increasing. Management of perioperative pain in ambulatory surgery is challenging and necessitates communication between anesthesiologists, surgeons and patients, as well as early interventions to manage pain experienced after surgery. Unfortunately, there are very few studies that have examined risk factors for continued postoperative opioid use in the outpatient setting. We developed a predictive model to identify variables predictive of need to refill opioid prescription 2 weeks postoperatively.

Methods: A predictive model was developed using single institutional data from patients undergoing joint arthroscopy (knee arthroscopy, anterior cruciate ligament repair, hip arthroscopy, shoulder arthroscopy, or rotator cuff repair) from 2018-2019 using various demographic, comorbidity, intraoperative and recovery room data. The primary outcome was need to refill opioid prescription after 2 weeks. Variables were entered into a multivariable logistic regression model if they met a significant level of $p<0.05$ on univariate analysis. The final model was built using a combination of forward selection and backwards elimination based on the Akaike Information Criterion. Variables were allowed to stay in the model if significance level of $p<0.1$. The final model was then validated on bootstrapped samples (R=1,000) and the average area under the receiver operating characteristic curve (AUC) and Hosmer-Lemeshow (HL) p-value for discrimination and goodness-of-fit, respectively, were reported. The odds ratio (OR) and 95% confidence interval (CI) for each covariate was reported.

Results: There were a total of 406 patients included in the analysis. The rate of 2-week opioid use was 14.8% (n=60). The final model included: native English speaker (OR 0.23, 95% CI 0.07 - 0.82, p = 0.02), alcohol use (OR 4.33, 95% CI 1.77 - 10.62, p = 0.001), active smoker (OR 2.89, 95% CI 1.27 - 6.52, p = 0.01), hypertension (OR 2.19, 95% CI 0.99 - 4.85, p = 0.05), history of anxiety and/or depression (OR 1.76, 95% CI 0.92 - 3.38, p = 0.09), chronic pain (OR 3.40, 95% CI 1.46 - 7.88, p = 0.004), and total intravenous morphine equivalents use in the recovery room (OR 1.06, 95% CI 1.01 - 1.12, p = 0.01). The average AUC calculated from the bootstrapped samples was 0.748 (95% CI 0.675 - 0.821) and the average HL-test p-value was p = 0.86.

Conclusion: This predictive model revealed that in patients undergoing ambulatory joint arthroscopy, the need to refill opioid prescriptions 2 weeks after surgery were increased in those who were native English speakers, had alcohol use, active smoking, hypertension, history of anxiety and/or depression, chronic pain and total intravenous morphine equivalents use in the recovery room. We hope that with this information, we can better predict who is at risk for chronic opioid use and therefore improve patient education and intervene earlier to attempt to decrease long term postoperative opioid use.

Pain Medicine-5 ACETAMINOPHEN, UNDERUTILIZED IN OLDER ADULT TRAUMA PATIENTS

Justin G Vaughan[1], Matthew Fuller[2], Karthik Raghunathan[3], Vijay Krishnamoorthy[3], George Kasotakis[2], Suresh Agarwal[1], Krista L Haines[4]

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Introduction: Given the vulnerability of older patients and opioid associated morbidity, this study focused on pain medication escalation in the immediate post-operative setting. The purpose of this study was to determine the frequency of acetaminophen use in post-operative older adult trauma patients once able to tolerate oral medications.

Methods: From 2008-2014, 175,787 older adult trauma patients (≥65) suffered falls (E880-E888) resulting in hip fractures requiring femur or hip fixation (79.15,79.35,78.55,81.51,81.52) and were recorded in the Premier database. Patients were excluded if they were admitted to the ICU prior to surgery or on POD 1 or 2 had concurrent tibia/fibula procedures, or were above the 95th percentile for opioid use on their last hospital day. We examined patients to identify the frequency of opioid medication administration without prior acetaminophen exposure in the post-operative setting. To examine the use of opioids used the day before and day of discharge, a mixed effects linear regression model was fit with fixed effects for patient demographics, hospital characteristics, patient comorbidities, surgery type, and co-treatments, as well as a random intercept for each hospital to control for patient clustering. Main exposure was acetaminophen on DOS or postoperatively before receipt of opioid/acetaminophen combination drugs or oral opioids.

Results: In this analysis, 8%(15,428) of patients received opioid medications without first being administered acetaminophen, and only 19.8%(38080) of patients received acetaminophen prior to opioids. Of this cohort, 81.6% were Caucasian, 74% were female, average age was 82 years, and 26.4% (50801) of patients were given a combination acetaminophen/opioid pill before Tylenol or opioids. Tylenol first was associated with reduced opioids on day before and day of discharge (3.60 MME less [3.41, 3.79]; p<.0001).

Conclusion: There is clearly potential to improve delivery of non-opioid medications, including acetaminophen, prior the administration of opioid-based medications. According to this data 1/3rd (34%) of older adult patients would benefit from acetaminophen as first line analgesia, minimizing the exposure of older adult trauma patients to the side effects and addiction potential of opioids.

Pain Medicine-6 The Impact of Non-Steroidal Anti-Inflammatory Drugs on Older Adult Trauma Patients with Hip Fractures

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Introduction: Non-Steroidal Anti-Inflammatory Drugs (NSAID) are frequently incorporated into multimodal pain control treatment plans. A major goal of multimodal therapy is improved pain control while simultaneously reducing the amount opioids used. This reduction in opioid morbidity allows for improved patient outcomes. Falls are a frequent source of morbidity and mortality in trauma. This study focused on the impact NSAIDs have on hospital length of stay (LOS), perioperative bleeding, opioid consumption, and intensive care unit (ICU) admission rates in adult fall trauma patients undergoing hip surgery. Given the mechanism of injury and surgery type studied, this project focused on the older adult population.

Methods: Using the Premier database, a retrospective cohort study of 190,057 adult trauma patients over a 6-year period (2008-2014) was performed. Patients aged 65 or older undergoing hip repair surgeries (E codes 880-888) following fractures due to falls (ICD9 codes: 79.15,79.35,78.55,81.51,81.52) were analyzed to determine the impact of NSAIDs on LOS, ICU admissions, bleeding risk, and opioid requirements. Billing data from the database was used to determine the outcomes measured. A mixed effects logistic regression model with the receipt of NSAIDs on DOS as the outcome was utilized to explore the impact of NSAIDs on these patients. Fixed effects were included for patient and hospital characteristics, patient comorbidities, co-treatments, and surgery type. The type I error rate was set at 0.05 as the threshold for statistical significance. Analysis were performed using SAS version 9.4 (SAS Institute; Cary, NC).

Results: Provided the mechanism of injury and surgery studied the average age of the population studied was 83 years old. NSAIDs had a positive impact in reducing the hospital LOS 5.61 days vs. 5.96 days, 0.18 days shorter, 95% CI [-0.24, -0.12]; p < .0001) and decreasing ICU admissions (9.73% vs. 10.59%; OR: 0.91, 95% CI [0.86, 0.96]; p < .0001). Despite increased transfusion requirements on POD1 (OR: 1.15 [1.11, 1.20]; p<.0001), no overall increase in bleeding was noted throughout the hospital admission (40.83% vs. 43.18%; OR 1.02 [0.99, 1.05]; p<.0001). Overall NSAIDs did decrease the amount of opioids prescribed (12.01 MME vs. 11.43 MME β = -0.23 mg (or MME), 95% CI [0.41, -0.06]; p = .2625)

Conclusion: NSAID use on the day of surgery was associated with improved hospital LOS and decreased ICU admissions. Although NSAIDs were associated with an increase in bleeding on POD1, no overall increase in bleeding rates were identified over the entire admission. A decrease in opioid prescribing during these hospitalizations was found. To our knowledge, this is the first study focused linking NSAIDs to decreased ICU admission rate in older adult trauma patients after surgery.

Patient Safety

Patient Safety-1 A Prospective Randomized Trial of Durapore vs. Hy-Tape for Securing Endotracheal Tubes During Anesthesia

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[1]Tufts University School of Medicine, Boston, MA, [2]MetroWest Medical Center, Boston, United States of America, [3]Tufts Medical Center, Boston, United States of America, [4]Tufts Medical Center, Boston, MA

Introduction: While adhesive tape is commonly used to secure endotracheal tubes (ETT) during general anesthesia, its use is also associated with facial skin injuries. Although a variety of adhesive tapes are used in clinical practice, few studies have investigated the relative safety profiles and likelihood of adhesives in producing injury. The purpose of this study was to determine the effect of 3MDurapore (DP) and Hy-Tape (HT) on facial skin injury and patient satisfaction.

Methods: Between September, 2018 and October, 2019, a single-center, prospective, randomized trial of patients undergoing general endotracheal anesthesia (GETA) longer than 30 minutes was conducted. Patients were randomized in a blinded fashion to using DP on either the right or left side of the face to secure the ETT, with HT on the contralateral side. In this way, patients served as their own internal control. Photographs of the skin were taken immediately prior to tape application and immediately following tape removal. In the recovery area, patients rated satisfaction with the condition of their skin on each side of the face using a 5-point Likert scale. Skin photographs were evaluated by a blinded dermatologist to determine presence or absence of perioral erythema, scaling, edema, and tearing. Differences in skin injury and patient satisfaction were dichotomized into present vs. absent or 5 vs. <4, respectively, then compared using McNemar's test. Primary outcome was incidence of increased postoperative skin erythema.

Results: Among 112 patients, 33.0% were male with mean age 55.6 years (SD 15.9). Median surgical duration was 130 min (IQR 87-189 min). Use of DP versus HT did not produce significant differences in erythema (25.0% vs. 27.7%, p=0.66), scaling (13.4% vs. 10.7%, p=0.61), edema (1.8% vs. 0.9%, p>0.99), or tearing (1.8% vs. 2.7%, p>0.99). 77.9% of patients were satisfied (score 5/5) with their skin condition after use of DP versus 82.6% with HT (p=0.29).

Conclusion: No differences in skin injury and patient satisfaction were observed with use of DP versus HT for securing the ETT during GETA.

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Patient Safety-2 Decreasing Colon Surgical Site Infections through Multidisciplinary Engagement using a Practice Bundle

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Introduction: Despite an increased recognition of evidence-based interventions, surgical site infections (SSIs) remain a source of patient harm. Our 280 bed acute care hospital had an elevated colon SSI rate (18.6%) and SIR (3.81) which was higher than predicted. The purpose of this quality improvement project was to decrease colorectal surgery SSI through the implementation of a formal, measurable bundle of evidence-based actions.

Methods: Our hospital lacked specific actions for colon SSI prevention. We hypothesized that the SSI rate would be reduced by adherence to an evidence-based bundle. Consensus was developed to implement a 7 element prevention bundle involving all phases of perioperative care and a 'stop-the-line' culture to promote compliance. In December 2018 a 7 element bundle was implemented, standardization of the following items: 2 step surgical skin preparation, glucose management, active warming, preoperative antibiotics, wound protector use and bowel isolation technique was fully implemented in December 2018. Compliance was actively measured and reported to front-line stakeholders weekly. Full compliance took close to 4 months.

Results: There was a substantial reduction in colon SSI's between the periods T1 (April - December 2018) and T2 (January - September 2019). An SIR of 4.31 (95% Confidence Interval [2.50, 6.95], p-value: 0.00), with a statistical interpretation of higher than predicted, has been reduced to 0.87 (95% Confidence Interval [0.22, 2.38], p-value: 0.88), or no different than predicted. When comparing periods, an 80% reduction in colon SSI's (T1: 15 infections, T2: 3 infections) was observed. Fisher's Exact Test shows a statistically significant difference between T1 and T2 (p-value: 0.005).

Conclusion: The SSI rate was significantly reduced by the implementation of our 7 element bundle. Improved patient outcomes was sustained over an 8-month time-frame with over 95% compliance to each component. Successful implementation of the bundle required support from all levels of the organization and empowerment of front-line staff to 'stop-the-line' to achieve full bundle compliance.

Reference(s): J American College of Surgery, 216;1, p23-22, 2013ASHP Therapeutic Guidelines, p654-739, 2013CHOC Antibiotic prophylaxis for surgery guideline 2017Infection control and hospital epidemiology, 35:6, p605-627, 2014

Pediatric Anesthesiology

Pediatric Anesthesiology-1 Association Of Race and Ethnicity with Postoperative Analgesic Administration and Pain Scores in Pediatric Patients: A Single-Center Study of 29,614 Surgical Cases

Felipe D Perez[1], Beth De Souza[2], Ellen Wang[2], Julia M Rosenbloom[3], Thomas A Anderson[2]

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Introduction: Disparities in the medical and surgical care of adults of different races and ethnicities have detrimental health outcomes.1,2 However, few studies have been published regarding pediatric healthcare disparities, and particularly the perioperative care of children. We are investigating the association between race and ethnicity and pediatric postoperative analgesic administration, pain scores, and related adverse events at a tertiary care children's hospital.

Methods: The medical records of children ≤18 years old undergoing general anesthesia and surgery from May 2014 to August 2019 are included. The exposure is racial and ethnic groups: Asian, Black, Hispanic, Other, Pacific Islander, and White non-Hispanic (White-nH). The primary outcome is PACU weight-adjusted morphine equivalent dose (MED, mg kg-1). Secondary outcomes are: PACU mean pain score (0-10), PACU length of stay, and PACU anti-emetic administration (any vs none). The association of race or ethnicity with each outcome is modeled using linear or logistic regression as appropriate, adjusting for confounders and covariates.

Results: 29614 cases are included (39.0% Hispanic, 33.8% White-nH, 18.5% Asian, 2.0% Black, 1.3% Pacific Islander, 5.3% Other race or ethnicity. In the PACU, no race or ethnicity was associated with receipt of a higher or lower MED. Asian, Black, and Pacific Islander were associated with lower mean PACU pain scores, and Other race was associated with higher mean PACU pain scores, than White-nH. Compared to White-nH Pacific Islanders were estimated to be discharged sooner from the PACU. Asian, Hispanic, and Pacific Islander were associated with lower odds of receiving anti-emetic drugs than White-nH. See quantitative results in Table 1.

Conclusion: Given the adverse events associated with both too little and too much analgesic administration, poor pain control, and postoperative nausea and vomiting, investigations on differences in postoperative pain medication administration, pain scores, and associated adverse events in children of different races and ethnicities are important.3 The differences of the PACU pain scores of some races and ethnicities compared to White-nH found here, while statistically significant, are not clinically significant. The decreased PACU length of stay of Pacific Islander patients compared to White-nH patients (6.4 minutes) while statistically significant, is also not clinically significant. White-nH were found to be more likely to receive antiemetics than Asian, Hispanic, and Pacific Islander patients. The reason(s) for this difference are not apparent but may be a result of cultural differences in nursing assessment of nausea, patient expression of nausea, patient understanding of medication availability for nausea, and/or language differences between healthcare providers and patients and their caregivers. (Additional analyses of inpatient outcomes are pending but will be available before the AUA/IARS meeting in May 2020.)

Reference(s):

1. Institute of Medicine (US) Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. In: Smedley BD, Stith AY, Nelson AR, eds. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington, DC: National Academies Press; 2003.

2. National Center for Health Statistics (US). Health, United States, 2015: With Special Feature on Racial and Ethnic Health Disparities. Hyattsville, MD: National Center for Health Statistics (US), 2016.

3. Long DR, Lihn AL, Friedrich S, et al. Association between intraoperative opioid administration and 30-day readmission: a prespecified analysis of registry data from a healthcare network in New England. Br J Anaesth. 2018;120:1090–1102.

Association Of Race and Ethnicity with Postoperative Analgesic Administration and Pain Scores in Pediatric Patients: A Single-Center Study of 29,614 Surgical Cases

Table 1

PACU Opioid Dose mg/kg (weight-adjusted morphine equivalents)			
Race	Change in dose	(95% Conf. Interval)	p-value
Asian	-0.001	(-0.002, 0.0001)	0.094
Black	-0.002	(-0.005, 0.001)	0.304
Hispanic	-0.001	(-0.002, 0.0002)	0.119
Other	0.000	(-0.002, 0.001)	0.608
Pacific Islander	-0.003	(-0.007, 0.0003)	0.069
White-nH	Reference		

PACU Mean Pain Score (pain scale of 0-10)			
Race	Change in score	(95% Conf. Interval)	p-value
Asian	-0.134	(-0.179, -0.089)	**<0.001**
Black	-0.119	(-0.231, -0.007)	0.037
Hispanic	-0.019	(-0.055, 0.018)	0.314
Other	0.073	(0.001, 0.145)	**0.046**
Pacific Islander	-0.214	(-0.351, -0.077)	**0.002**
White-nH	Reference		

PACU Length of Stay (minutes)			
Race	Change in LoS	(95% Conf. Interval)	p-value
Asian	-0.65	(-2.056, 0.763)	0.368
Black	-1.04	(-4.578, 2.493)	0.563
Hispanic	-0.06	(-1.208, 1.081)	0.913
Other	-1.17	(-3.432, 1.101)	0.314
Pacific Islander	-6.35	(-10.642, -2.063)	**0.004**
White-nH	Reference		

PACU Anti-Emetic Medications (any vs none)			
Race	Odds Ratio	(95% Conf. Interval)	p-value
Asian	0.735	(0.613, 0.881)	**0.001**
Black	0.685	(0.436, 1.075)	0.100
Hispanic	0.738	(0.641, 0.849)	**<0.001**
Other	0.763	(0.568, 1.025)	0.073
Pacific Islander	0.402	(0.205, 0.786)	**0.008**
White-nH	Reference		

Pediatric Anesthesiology-2 Continuous infusion of Lidocaine for Erector Spinae Plane Blocks in Pediatric Cardiothoracic Surgery is Lidocaine Safe

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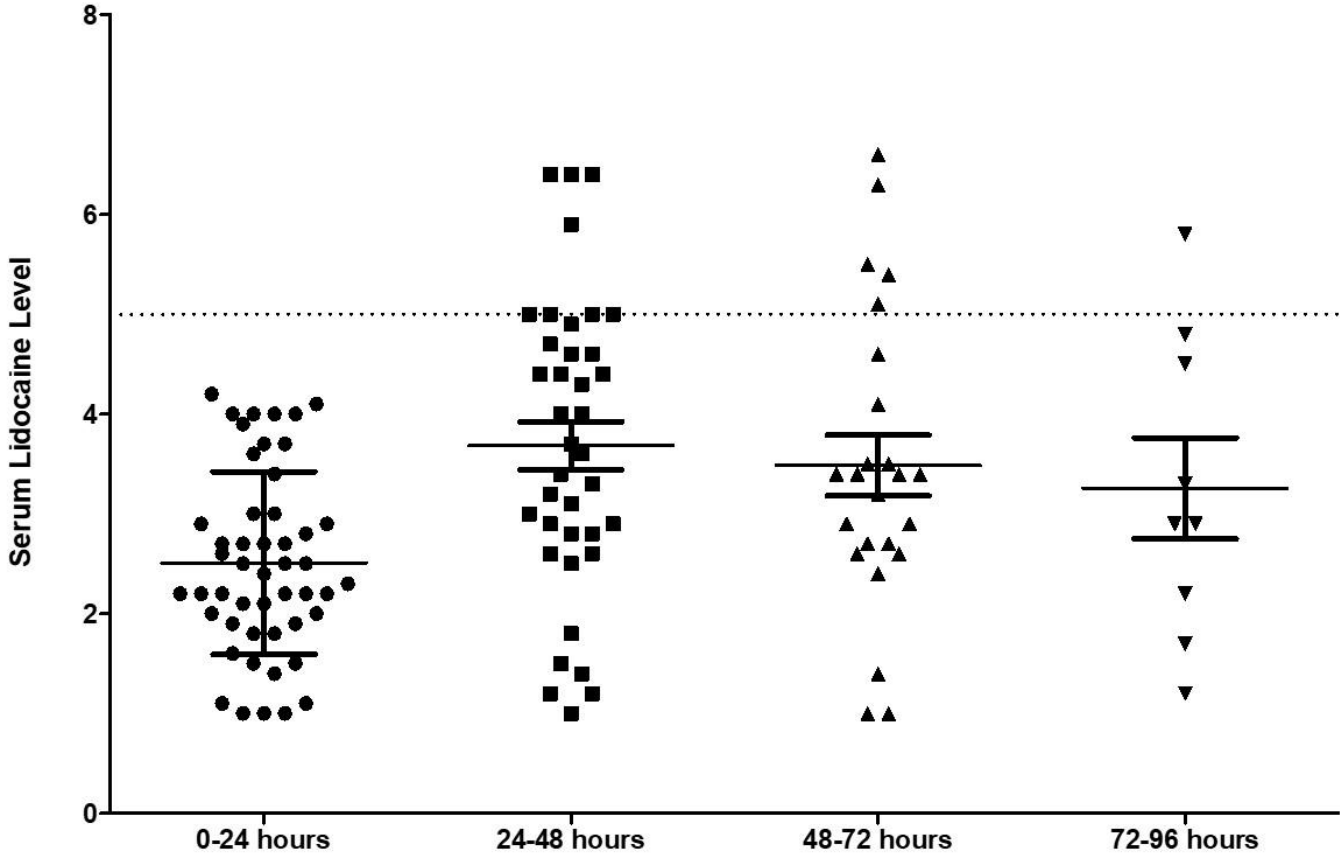
Introduction: Pain relief in Children undergoing cardiothoracic is surgery is a critical portion of their intraoperative and postoperative care. While there are many different approaches to achieving this goal regional analgesic techniques have become attractive as they provide analgesia without the complications associated with narcotics. The erector spinae plane block (ESPB) has been used at our institution for the past two years and has become the predominant mode of postoperative analgesia in these patients. The ESPB has been able to significantly reduce the need for postoperative narcotics. A concern in this population is the pharmacokinetics of local anesthetics in the ESPB. Intravenous infusions of lidocaine are frequently used in this population for control of arrhythmias. Intravenous lidocaine Infusion rates from 10-40 mcg/kg/min are used to maintain lidocaine in the therapeutic range. The purpose of this study was to determine the incidence of toxic levels of local anesthetic associated with the ESPB when lidocaine infusion levels were maintained in the range usually considered safe and effective for controlling ventricular arrhythmias.

Methods: This study approved by the WVU institutional review board for human subjects. Children 3 months to 18 years coming for cardiothoracic surgery were entered into the study if they received an ESPB for their cardiothoracic surgery, and had a continuous infusion of lidocaine in the postoperative period. Lidocaine infusion were maintained at rates less than 40 mcg/kg/min combined for all catheters the patient had placed. Lidocaine levels were obtained every 24 hours while ESPB catheters were infusing. Lidocaine levels greater than 5.0 mcg/ml were considered toxic.

Results: . Sixty-four patients have received lidocaine infusions for their ESPB. All lidocaine infusions were infused at rates less than or equal to 40 mcg/kg/min total regardless of the number of catheters in place. No patients had levels outside of the therapeutic range on post op day 1. On post op day two 4 patients had levels above 5 mcg/ml. Three of these patients were 1 year of less and one was 17 years. The highest lidocaine level in these 4 patients on day one was 3.7 mcg/ml. At 48-72 hours 5 patients had levels above 5 and only one of these had abnormal value at 48 hours. None of these patients had signs of local anesthetic toxicity.

Conclusion: Amide local anesthetics are widely used because of their duration of action, and their lack of allergic reactions. The uptake of these local anesthetics varies by location of the block. The uptake of local anesthetic placed in the erector spinae plane in children has not been well studied. Additionally, the impact of cardiothoracic surgery on the kinetics of this block has not been studied. This study documents that lidocaine levels exceeding therapeutic levels (5 mcg/ml) can be seen in pediatric patients with continuous ESPB despite maintaining the lidocaine infusion rates at accepted intravenous infusion rates. Lidocaine was chosen because of the ease in obtaining serum blood levels. Toxic levels with amide local anesthetics are more common in younger children because of immaturity of their metabolic systems and low concentrations of the alpha 1-acid glycoprotein. This along with the results of our study support the recommendation that 2-Chloroprocaine be the local anesthetic of choice for ESPB in children less than 6 months. Additionally bypass and hepatic congestion in some of these cardiac lesions may further depress metabolism. Some of the highest levels on Day 1 were observed in Fontan Patients. The fact that toxic concentrations were not observed on day 1 probably relates to the increased volume of distribution for the local anesthetics which becomes full as the continuous infusion of local anesthetics persisted. 3.7 mcg/ml was the highest level recorded on post op day 1 in those patients that developed toxic levels on post op day 2. Conclusion: Children undergoing cardiothoracic procedures with ESPB can develop toxic lidocaine levels on day 2 despite receiving lidocaine infusion rates generally considered safe. These patients had no outward signs of Lidocaine toxicity. Because of the elevated serum levels found in our study we recommend using lidocaine for ESPB in children undergoing cardiothoracic procedures, and obtaining daily lidocaine levels to avoid toxicity.


Serum Lidocaine Level
8
6
4
2
0
0-24 hours
24-48 hours
48-72 hours
72-96 hours

Perioperative Anesthesia

Perioperative Anesthesia-1 Factors and clinical outcomes associated with preoperative Do-Not-Resuscitate designation differ across surgical groups: an analysis of the National Surgical Quality Improvement Database

Julien Cobert[1], Reginald Lerebours[2], Vijay Krishnamoorthy[3], Karthik Raghunathan[3], Leila Mureebe[4]

[1]University of California, San Francisco, San Francisco, CA, [2]Duke University, Durham, NC, [3]Duke University School of Medicine, Durham, NC, [4]Duke University Medical Center, Durham, NC

Introduction: The role of do-not-resuscitate (DNR) orders pose a unique clinical challenge in the preoperative setting [1]. Patients with pre-existing DNR orders who undergo surgical procedures have been shown to have a higher risk of perioperative mortality [2] and increased length of stay and postoperative complications [3]. Still, there is limited research elucidating the patient factors associated with a DNR designation, as well as the factors associated with key outcomes for interest for individuals with a DNR designation. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database provides a cohort of patients with DNR information along with relevant procedural and demographic information. In addition, Clinical Classifications Software (CCS) classes can be leveraged to identify three broad disease/procedure groups of interest: colorectal, vascular, and orthopedics. We use the data from the NSQIP database to: a) identify factors associated with a pre-existing DNR designation in homogeneous cohorts of patients undergoing colorectal, vascular and orthopedic procedures; b) identify preoperative factors that are associated with 30-day mortality, death prior to discharge and length of stay in these patients; and c) identify unique phenotypes of patients with pre-existing DNR orders who develop various patient-centric outcomes.

Methods: Using data from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database, patients with a pre-existing DNR were queried. The most common procedures in the vascular, orthopedic and colorectal classes were included based on Current Procedural Terminology (CPT) codes. Demographic and baseline characteristics were summarized using mean with standard deviation, median with interquartile range or frequency with percentage where appropriate. To identify variables associated with pre-existing DNR, 30-day mortality, death at discharge, increased length of stay for each disease/procedure group, a pseudo machine learning algorithm using Least Absolute Shrinkage and Selection Operator (LASSO) was used. Adjusted logistic/linear regression models were also postulated.

Results: Between the years of 2010-2013, 2,001,405 unique observations were initially queried from the NSQIP database. Applying inclusion and exclusion criteria, 211,420 unique observations remained in the dataset. Of this cohort, patients with a 'yes' designation for DNR were included in this study, totaling 2755 unique observations of which 1,149 patients in the colorectal group, 736 patients in the orthopedics group and 870 patients in the vascular group. Baseline clinical and demographic information is shown in TABLE 1 and outcome information is shown in TABLE 2. Of patients with a pre-existing DNR on day of surgery, 30-day mortality for colorectal, orthopedic and vascular subsets was 27.2%, 15.4% and 19.5%, respectively. Death at discharge across groups were 10.3%, 4.9% and 6.1%, respectively. Length of hospital stay was highest in colorectal patients. LASSO analysis demonstrated unique odds ratios for a number of different parameters some of which were associated with increased or decreased association with the outcomes of interest, even across different surgical groups. Typically, parameters corresponding to increased comorbidities and baseline illness were associated with having a pre-existing DNR, increased 30-day mortality, risk of death at discharge and increased length of stay. Parameters showing discrepant risk (increased versus decreased) were noted across all surgical classes for each outcome. Some of these included a male gender, increased age, higher BMI and Hispanic descent. Additionally, odds ratios had dramatically different values for individual parameters across different surgical classes.

Conclusion: Using a machine learning methodology, we show that patients with pre-existing DNR at time of common colorectal, orthopedic or vascular procedures carry different risks for morbidity and mortality. This is important because it demonstrates that (1) there are distinct phenotypes of DNR patients in the preoperative setting that carry unique risk profiles for perioperative morbidity and mortality; (2) a personalized risk assessment prior to undergoing certain procedures in DNR patients can be performed for specific surgical subsets; and (3) patient-centered outcomes beyond mortality alone should be used when communicating risk to clinicians, patients and families.

Reference(s):

[1] JAMA 1991, 266(17):2407-2412

[2] Ann Surg 2012, 256(3):453-461.

[3] Arch Surg 2011, 146(8):922-928

Figure 1: CONSORT Diagram for Inclusion and Exclusions for Both Study Aims

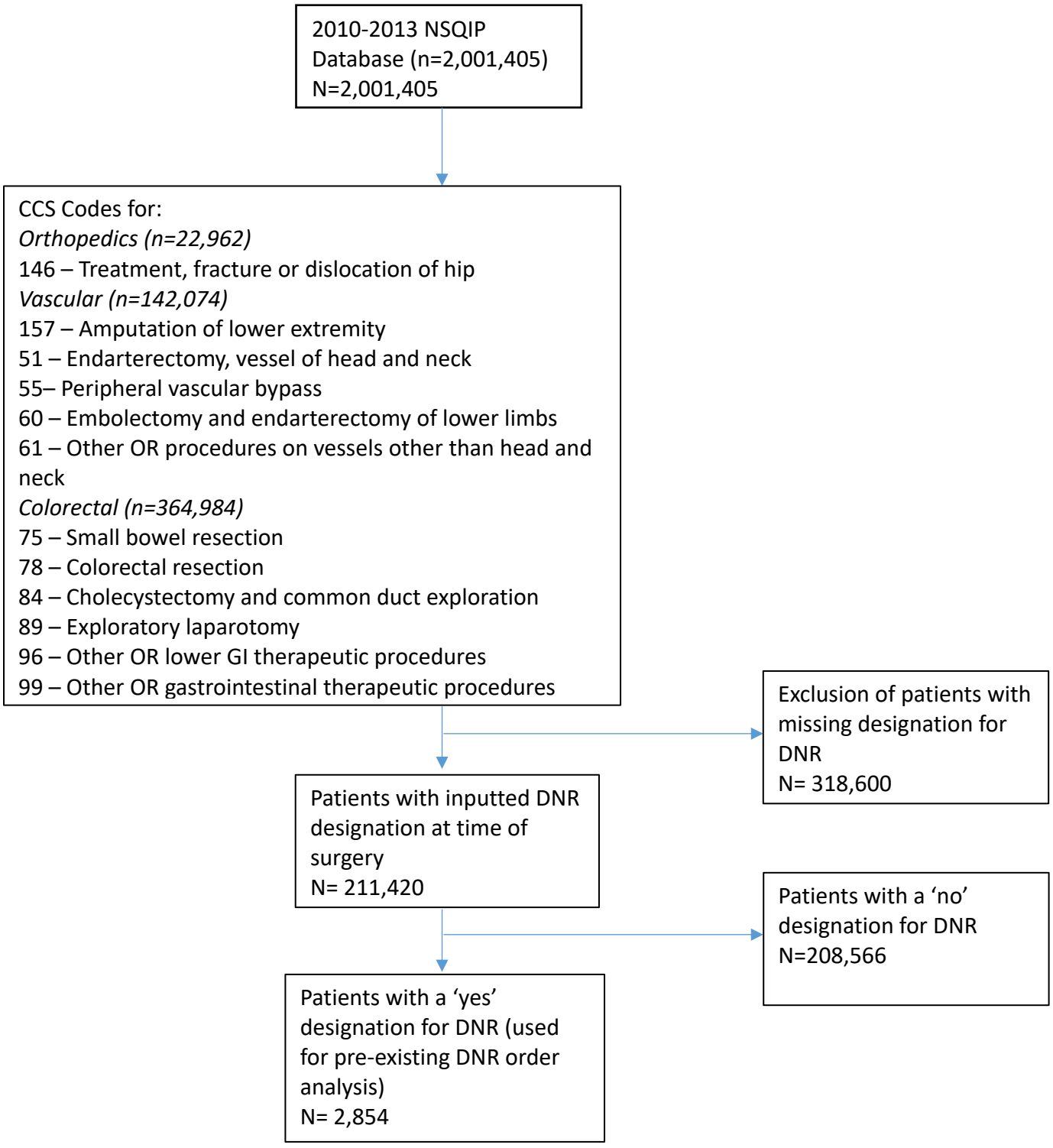


Figure 2: Adjusted Odds Ratios for Selected Predictors of a Pre-existing DNR Order (By Surgical Group)

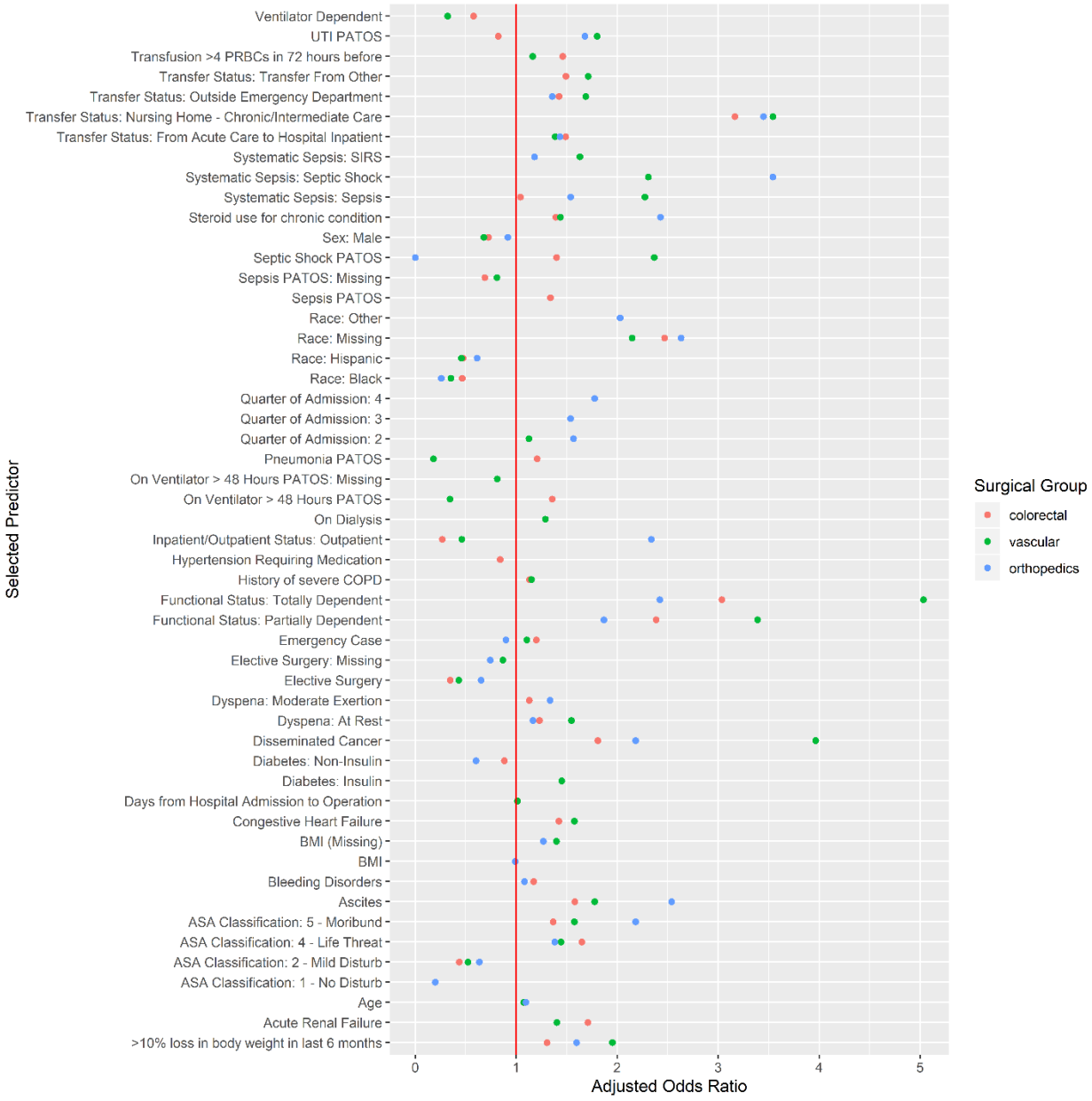


Figure 3: Adjusted Odds Ratios for Selected Predictors of 30-Day Mortality (By Surgical Group)
(Adjusted Odds Ratios > 5 are shown as 5 on this graph)

Figure 4: Adjusted Estimates for Selected Predictors of Total Hospital Length of Stay (By Surgical Group)

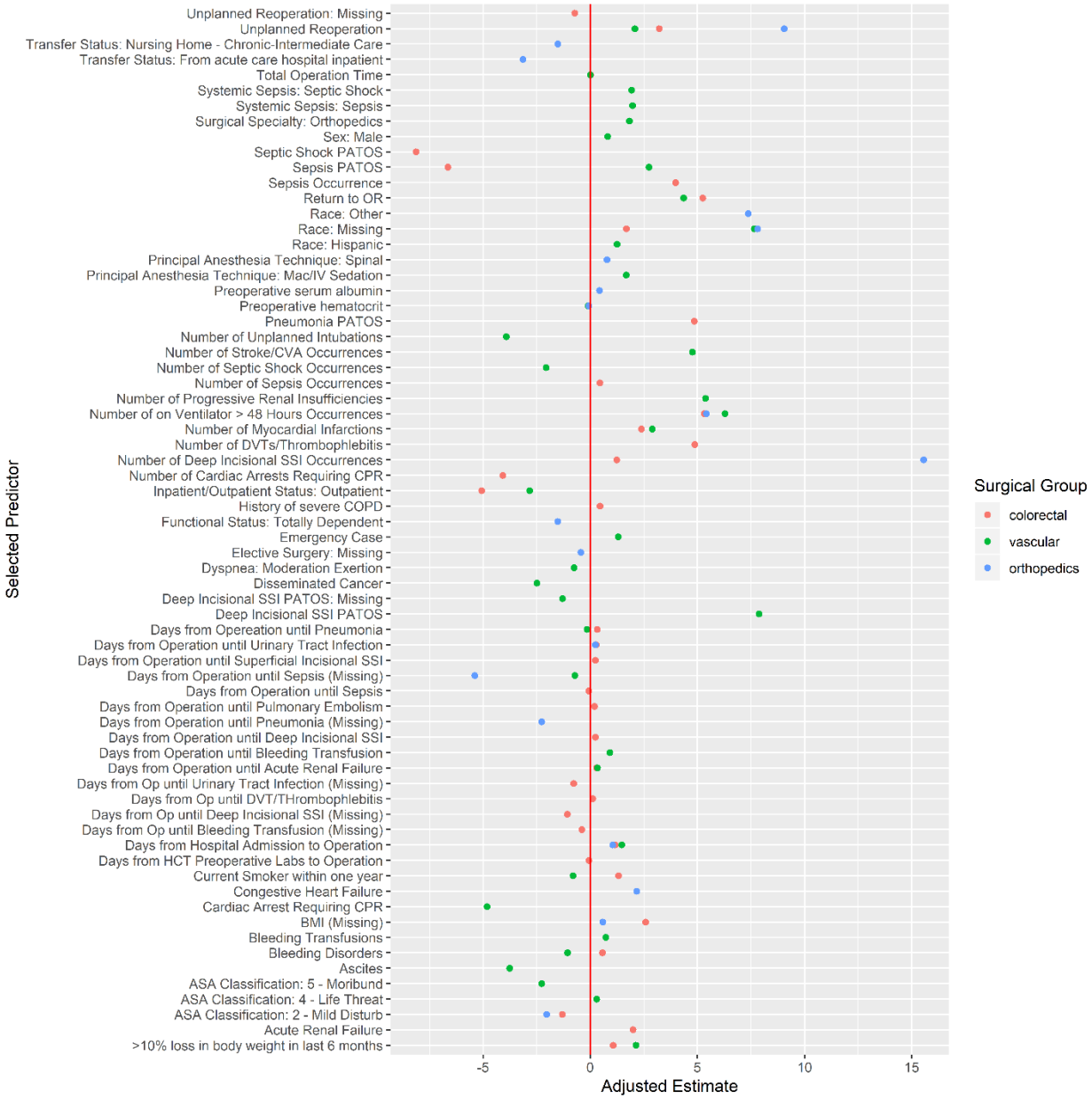
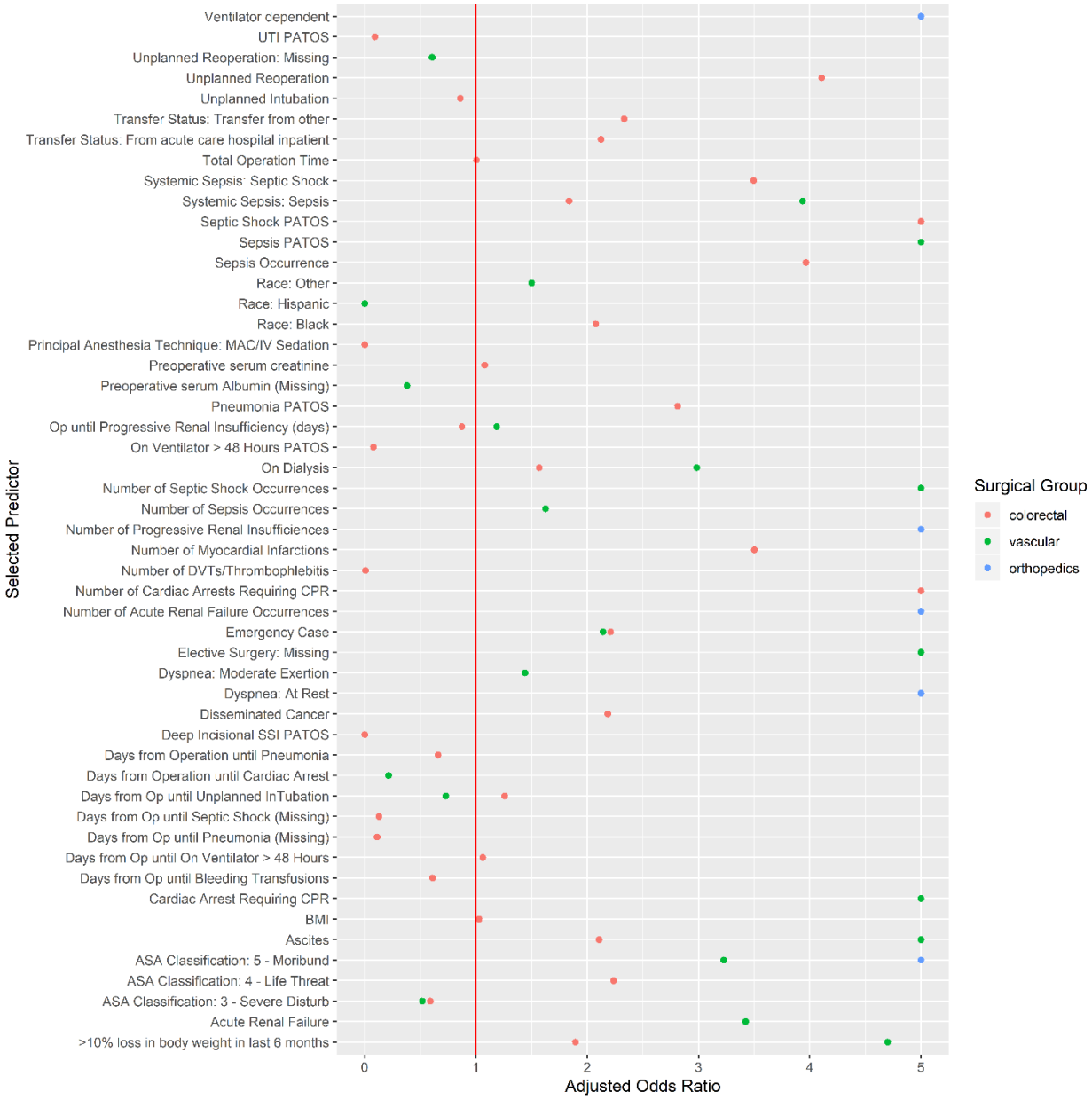


Figure 5: Adjusted Odds Ratios for Selected Predictors of Death During Hospitalization Surgical Group) (Adjusted Odds Ratios > 5 are shown as 5 on this graph)



Perioperative Anesthesia-2 A Multi-Center Randomized Controlled Trial of Perioperative Palliative care in Cancer Surgery (the PERIOP-PC trial) - Barriers and Opportunities for Palliative Care Trials in Surgical Settings

Rebecca A Aslakson[1], Elizabeth Rickerson[2], Fabian Johnston[3], Bridget N Fahy[4], Arden Morris[5], Karl Lorenz[6], Thomas J Smith[3]

[1]Stanford University School of Medicine, Stanford, CA, [2]Brigham and Women's Hospital, Boston, United States of America, [3]The Johns Hopkins School of Medicine, Baltimore, United States of America, [4]University of New Mexico, Albuquerque, NM, [5]Stanford University School of Medicine, Stanford , United States of America, [6]Stanford University School of Medicine, Stanford, United States of America

Introduction: Although cancer surgery is safer than ever before, perioperative morbidity and mortality are not inconsequential and studies suggest that cancer patients and their families suffer significant psychological and physical symptoms surrounding surgery and for weeks to months after surgery (1-7). Palliative care is patient- and family-centered care that symptomatically and psychosocially supports seriously ill patients and their families and optimizes quality of life, regardless of diagnosis, prognosis, or care goals (8). Studies among medical oncology patients support that proactive palliative care: improves quality of life (9-13), betters physical and psychological symptom management (9-14), betters understanding of prognosis (15), lessens spiritual distress (12), lessens caregiver burden (12), improves caregiver social well-being (16), decreases caregiver psychological distress (13, 16), lowers care costs (14,17,18), decreases aggressive end-of-life care interventions (10,20,21), and may even prolong patient survival (10,20). Despite these benefits, there have been few studies translating proactive palliative care from a medical to a surgical population and none comparing surgeon-palliative care team co-management versus surgeon alone management across patient-reported outcomes (PROs) (21). Indeed, multiple studies even document surgeon and surgical culture resistance to palliative care involvement, particularly any discussions that might concern end-of-life care (22-24).

Methods: Funded by the Patient-Centered Outcomes Research Institute (PCORI), we are currently completing the first ever multi-site randomized controlled trial integrating consultant perioperative palliative care into a surgical setting (NCT03611309; PCORI: IHS 1609-36518-IC). Our study protocol has been published (25) and we are specifically exploring the impact of specialist palliative care on patient and family-reported outcomes in upper gastrointestinal surgical oncology settings. Patients with upper gastrointestinal cancers who are pursuing curative intensive surgery and their family members are eligible for the study. At time of enrollment, patients are randomized to either the control arm (usual care) or the intervention arm (proactive specialist palliative care). From study initiation and for multiple cultural and practical reasons, we expected barriers to enrolling surgical patients in a perioperative palliative care trial. To identify, address, and overcome these barriers, we: (a) convened two stakeholder summits to bring together diverse stakeholders - anesthesiologists, surgeons, palliative care clinicians, oncologists, patients, and family members - to discuss these topics; (b) hold quarterly calls with a diverse professional advisory group with individuals representing the Palliative Care Research Cooperative, the Surgical Palliative Care Task Force within the American College of Surgeons, the Committee for Palliative Medicine with the American Society of Anesthesiologists, the American Academy of Hospice and Palliative Medicine, the Society for Surgical Oncology, and the National Coalition for Cancer Survivorship; and (c) lead weekly phone calls with the study coordinators from each study site and monthly phone calls with all site Principal Investigators.

Results: As of 1/10/2020 and with a goal of 380 patients, we have enrolled 134 patients and 71 family caregivers from four geographically diverse sites in the United States. Barriers to enrollment include: (a) sufficient patients in surgery clinics that meet enrollment criteria; (b) relatively few surgeons at study sites who complete sufficient numbers of surgeries; (c) surgeon comfort with the concept of palliative care and inaccurate conflation of palliative care with hospice care; (d) site study coordinator personnel changes; (e) patient and family member fatigue at time of study enrollment; (f) connecting enrolling study coordinators with potential participant patients and family members; (g) enrolling racially diverse participants; and (h) accommodating preoperative chemotherapy. We have employed multiple methods and incorporated diverse stakeholders to address these barriers.

Conclusion: Specialist palliative care clinical trials are feasible in surgical care settings. Diverse stakeholder teams are essential in addressing and overcoming unique cultural and pragmatic barriers.

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1. Br J Surg 2016; 103:e115-9

2. J Surg Onc 2014; 110:599-610

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4. Surg 2012; 3 Supp 1:S120-7

5. Surg 2012; 16:1727-35

6. Pancreas 2011; 40:938-45

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8. NEJM 2015; 373:747-55

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10. NEJM 2010; 363:733-42

11. Lancet 2014; 383:1721-30

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13. JAMA 2016; 316:2094-2103

14. J Clin Oncol 2004; 22:2008-14

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16. Cancer 2015; 121:3737-45

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19. J Clin Oncol 2012; 30:394-400

20. J Clin Oncol 2015; 22:1438-45

21. JAMA Surg 2016; 151:172-83

22. Crit Care Med 2003; 31:1551-9 23. Crit Care Med 2010; 38:843-8 24. J Am Coll Surg 2002; 194: 665-73 25. J Palliat Med 2019; 22(S1): 44-57

Clinical trials.gov registration: NCT03611309

PCORI identification: IHS 1609-36518-IC

PCORI webpage: https://www.pcori.org/research-results/2017/does-palliative-care-benefit-patients-having-cancer-surgery-and-their-families

Components of Surgeon-Palliative Care Team Co-Management	
TEAM element	**Description**
T – TIME	At least 60 minutes/month devoted to palliative care treatments for the patient and family. Some surgeons may say "I do my own palliative care" but, this intervention requires at least 60 min per month specifically devoted to palliative care communication.
E - EDUCATION	Patients and family members are counselled and educated about their disease, including self-management of symptoms, prognosis, and treatment options.
A – ASSESSMENT	Formal assessment of symptoms including pain, dyspnea, constipation/diarrhea, anxiety/depression, fatigue, and nausea. We will use Edmonton symptom score as a formal assessment.
M – MULTI-DISCIPLINARY	Management must be multi-disciplinary with access to a readily available palliative care team composed of nurse, physician, social worker, pharmacist, and/or chaplain team members.

Table 1: Components of Surgeon-Palliative Care Team Co-Management

Clinical trials.gov registration: NCT03611309

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Table 1: Components of Surgeon-Palliative Care Team Co-Management

	Study design	Participants	Outcomes and Measurement Times
SA1 (months 1-36)	Randomized controlled trial (n=380 patients; n = 304 family members); Outcomes measured at approximately: - enrollment - 1 week after surgery - 1 month after surgery - 3 months after surgery - 6 months after surgery	Patients	(1) **Quality of life - Functional Assessment of Chronic Illness – Palliative Care (FACIT-Pal)**** Subscales: (i) Functional Assessment of Cancer Therapy (FACT-G) (ii) Trial Outcome Index (TOI) (2) Demographics (3) Edmonton Symptom Assessment Score (ESAS)* (4) Functional Assessment of Chronic Illness Therapy – Spiritual Well-being (FACIT-Sp-12)* (5) Mood symptoms including anxiety and depression subscales – PROMIS-29 (6) Health care utilization* (# of post-operative hospitalizations and/or emergency room visits) (7) Presence of advance care planning* (8) Prognostic understanding* (9) Mortality*
		Family members/ Companions	(1) Demographics (2) Zarit Caregiver Burden Scale (ZBI-12)* (3) Mood symptoms including anxiety and depression subscales – PROMIS-29 (4) Functional Assessment of Chronic Illness Therapy – Spiritual Well-being (FACIT-Sp-12) family/companion measure* (5) Prognostic understanding*
SA2 (months 8-16)	In-depth interviews (Approx, n=20 in each arm)	Patients	Patient experiences and beliefs regarding management of symptoms, prognostic clarity, and advance care planning practices and beliefs
	In-depth interviews (Approx. n=20 in each arm)	Family members/ Companions	Family member experiences and beliefs regarding prognostic clarity, caregiver experience, and patient experience of symptoms and advance care planning practices and beliefs
	In-depth interviews (Approx. n=8; all surgeons involved in the trial)	Surgeons	Surgeon experiences and beliefs regarding surgeon alone versus surgeon-palliative care team co-management of perioperative cancer patients and their families.
	In-depth interviews (Approx. n=10-15)	Palliative care clinicians	Palliative care team experiences and beliefs regarding surgeon alone versus surgeon-palliative care team co-management of perioperative cancer patients and their families.

Table 2: Study design, participants, and outcomes for each specific aim (primary outcome, *secondary outcome)**

Perioperative Anesthesia-3 Perioperative colloid choice and effects on bleeding in patients undergoing musculoskeletal surgery

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Introduction: The use of colloids such as hydroxyethyl starch (HES) and albumin is common for intravenous fluid resuscitation in the perioperative period. [1, 2] Meta-analyses comparing albumin with HES (human-derived versus synthetic colloids respectively) in patients with sepsis and in patients undergoing cardiac surgery (with cardiopulmonary bypass) have found that red blood cell transfusions are reduced when albumin is used.[3, 4] However, HES continues to be used worldwide in non-cardiac surgical settings. Our study compares the association of albumin versus HES with major perioperative bleeding in musculoskeletal surgery, the most common surgery performed in the United States.

Methods: In this retrospective cohort study, we extracted data from the Premier Healthcare Database (Premier Inc., Charlotte, NC, USA) between October 2008 and September 2014, a period of time prior to a safety warning about HES in United States (when HES was still widely used). We identified patients who underwent elective inpatient surgery on the musculoskeletal system and received either albumin or hydroxyethyl starch (HES). Patients who received both albumin and HES were excluded from the study. The primary outcome was major perioperative bleeding; secondary outcomes were acute renal failure and prolonged postoperative length-of-stay (>75th%ile), as a surrogate for significant in-hospital complications. We examined differences in baseline characteristics - demographics, comorbidities, and co-treatments. We then conducted propensity-score weighted analysis to ensure comparability of study groups prior to examining outcome differences.

Results: We identified 579,392 patients who underwent surgery in the musculoskeletal system. Only 43,454 received colloids on the day of surgery. After excluding dual colloid recipients (n= 2,243), 41,211 (94.8%) were included in the analysis: 12,803 in the albumin in the albumin group and 28,408 in the HES group. As shown in table 1, there were minor differences between the two groups that were resolved upon propensity-score weighting. This include: van walraven score, which was lower in the albumin group; the higher rate of regional anesthesia (spinal or epidural) that was noted in the albumin vs. starch group; and the use of anti-fibrinolytic medications was noted to be higher in the HES vs. albumin, 19.3% and 13.9% respectively. The propensity-score weighted mean van Walraven score in patients receiving albumin was 0.59, compared to 0.58 in patients that received HES (standardized mean difference= 0.003). There was no difference in the use of anti-platelet medication or anti-thrombotic medication in either group before or after propensity-score weighting. However, the high rate of non-steroidal anti-inflammatory drugs (NSAIDs) usage noted in the albumin group persisted even after propensity-score weighting (standardized mean difference = 0.24 and 0.21 before and after propensity-score weighting respectively). The primary analysis indicated that the rate of major perioperative bleeding was higher in those exposed to HES compared with those receiving albumin . The rate of major bleeding was 16.8% in patients exposed to albumin, compared with 18.5% in those exposed to HES, [Relative Risk 0.89 (95% CI 0.84-0.93)]. We observed no significant difference in secondary outcomes.

Conclusion: Compared with albumin, exposure to HES on the day of musculoskeletal surgery was associated with an increased risk of major perioperative bleeding. Given that HES continues to be used as a colloid in multiple patient populations worldwide, further studies examining the safety of HES solutions are needed.

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3. The Annals of Thoracic Surgery, 72(2), 527-33, 2001.

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Figure 1: Patients undergoing surgery on musculoskeletal system, colloid by type

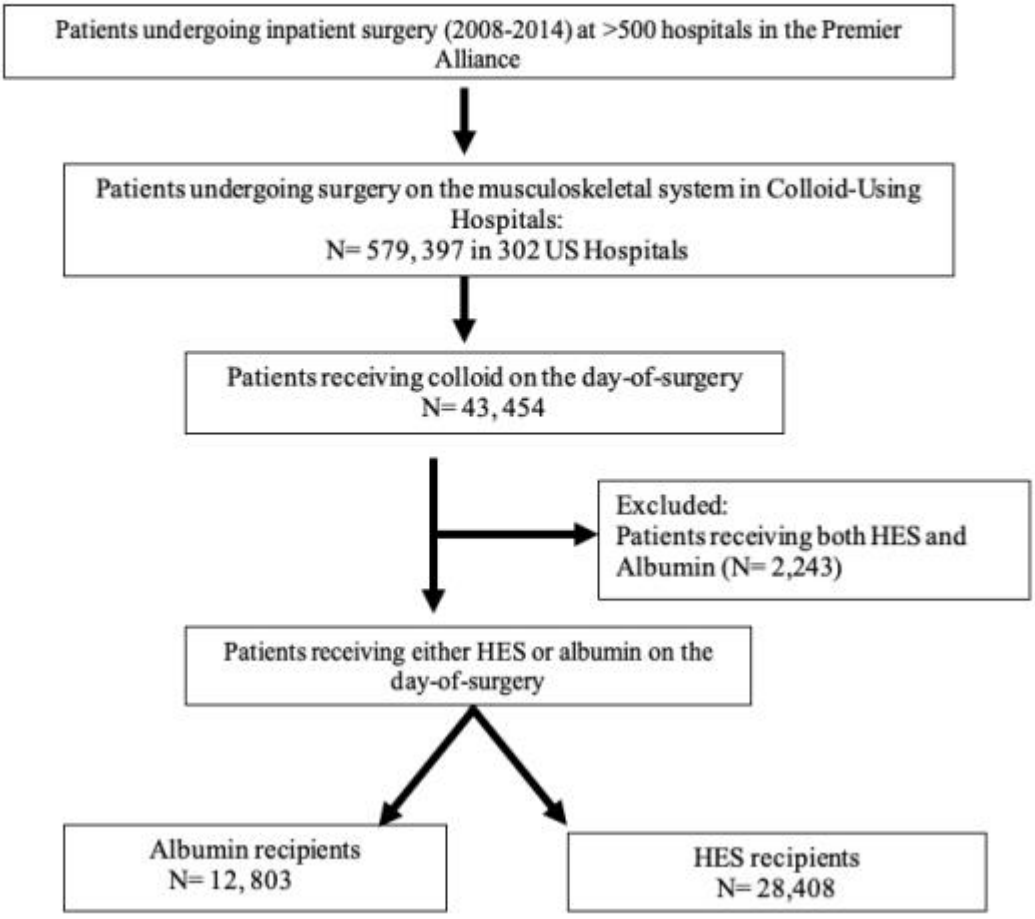

Figure 2: Comparability of patients treated with albumin vs. HES

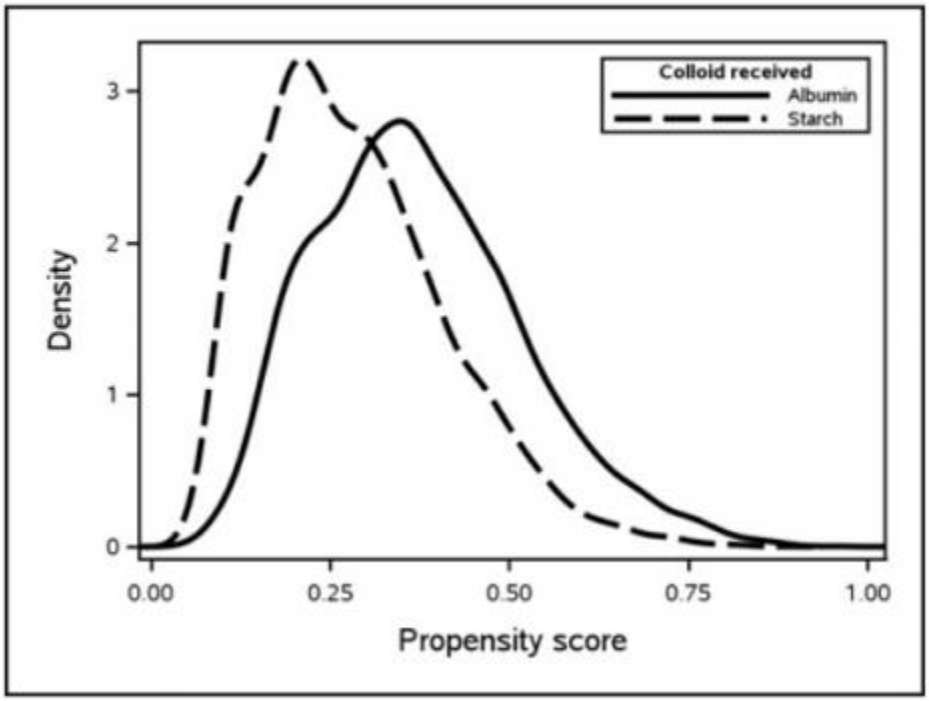

Table 1:

Variable	Albumin (unweighted)	Starch (unweighted)	SAMD (unweighted)	Albumin (weighted)	Starch (weighted)	SAMD (weighted)
Age	65.1 (11.8)	65.4 (12.3)	0.02	65.4 (12.0)	65.4 (12.3)	0.00
Black (ref. white)	7.2%	8.8%	0.06	9.2%	8.8%	0.01
Other race (ref. white)	20.2%	10.2%	0.28	9.8%	10.2%	0.01
Male (ref. female)	41.4%	41.2%	0.00	41.1%	41.2%	0.00
van Walraven score	0.2 (3.6)	0.6 (4.2)	0.10	0.6 (4.0)	0.6 (4.2)	0.00
Anti-fibrinolytic medication	13.9%	19.3%	0.15	18.2%	19.3%	0.03
Anti-platelet medication	2.5%	2.7%	0.01	2.8%	2.7%	0.00
Anti-thrombotic medication	80.6%	78.6%	0.05	78.6%	78.6%	0.00
Analgesia, NSAID, parenteral	40.7%	29.4%	0.24	39.2%	29.4%	0.21
Anesthesia, regional, spinal/epidural	27.1%	13.3%	0.35	14.8%	13.3%	0.04
Anesthesia, epidural	10.2%	4.4%	0.22	5.1%	4.4%	0.03

Perioperative Anesthesia-4 Associations Between Perioperative Crystalloid Fluid Volume And In-hospital Outcomes in Major Spine Surgeries

Fangyu Chen[1], Alan Ellis[2], Karthik Raghunathan[3], Raquel R Bartz[3], Krista L Haines[4], Vijay Krishnamoorthy[3]

[1]Duke University School of Medicine, Durham, United States of America, [2]North Carolina State University, Raleigh, NC, [3]Duke University, Durham, NC, [4]Duke University, Durham, United States of America

Introduction: Major spine surgeries can involve significant changes in circulating blood volume due to intraoperative blood loss and surgical positioning.(1)Perioperative crystalloid fluid management is thus important for optimal patient outcomes. Despite increased interest in Enhanced Recovery After Surgery (ERAS®) protocols(1,2), there is a lack of large randomized controlled trials of different perioperative crystalloid fluid management strategies in spine surgery. In this large observational study, we examine the associations between day-of-surgery crystalloid volume and perioperative outcomes in patients undergoing major spine surgery.

Methods: A retrospective cohort study was conducted using administrative-financial data from Premier Healthcare Database (Premier Inc., Charlotte, NC) between April 2008 - March 2014. The dataset included hospital discharge information and date-stamped itemized charge codes. We included hospitals with crystalloid charges for >90% of patients and identified patients admitted for major spine surgery using ICD-9 procedure codes (3). The primary exposure was total crystalloid volume (TCV) on the day of surgery ascertained using charge codes. The primary composite outcome was hospital length-of-stay > 75th percentile or in-hospital mortality. Postoperative complications (4) are associated with prolonged LOS,(5) and we examined this outcome rather than individual complications. Descriptive statistics were used to examine demographic and clinical characteristics. A generalized additive model (GAM) was used to estimate the optimal crystalloid volume - at which the adjusted probability of adverse outcome adjusted was the lowest. Analyses were controlled for demographics (age, gender, race, marital status, insurance); hospital factors (bed size, teaching status, location); Van Walraven score - 30 comorbidities weighted by mortality risk (6); and co-treatments.

Results: The sample included 135,115 patients. Patients received on average 4L crystalloids on the day of surgery with low amounts of colloid. Administration of red blood cells was associated with a >1L increase in TCV ($p<0.0001$). Most variation in crystalloid volume administered was due to patient (61.6%) factors, although hospital factors did account for substantial variation as well (30.3%). The association between TCV and the probability of composite outcome is approximately J-shaped relationship between crystalloid volume and the composite outcome (Figure 1).

Conclusion: We observed a J-shaped relationship between day-of-surgery crystalloid volume and adverse outcomes in major spine surgery. This supports current recommendations for a more restrictive regimen (<4L). Our findings help fill a significant gap in the spine surgery literature, where large randomized studies of different crystalloid fluid volumes have not been performed.

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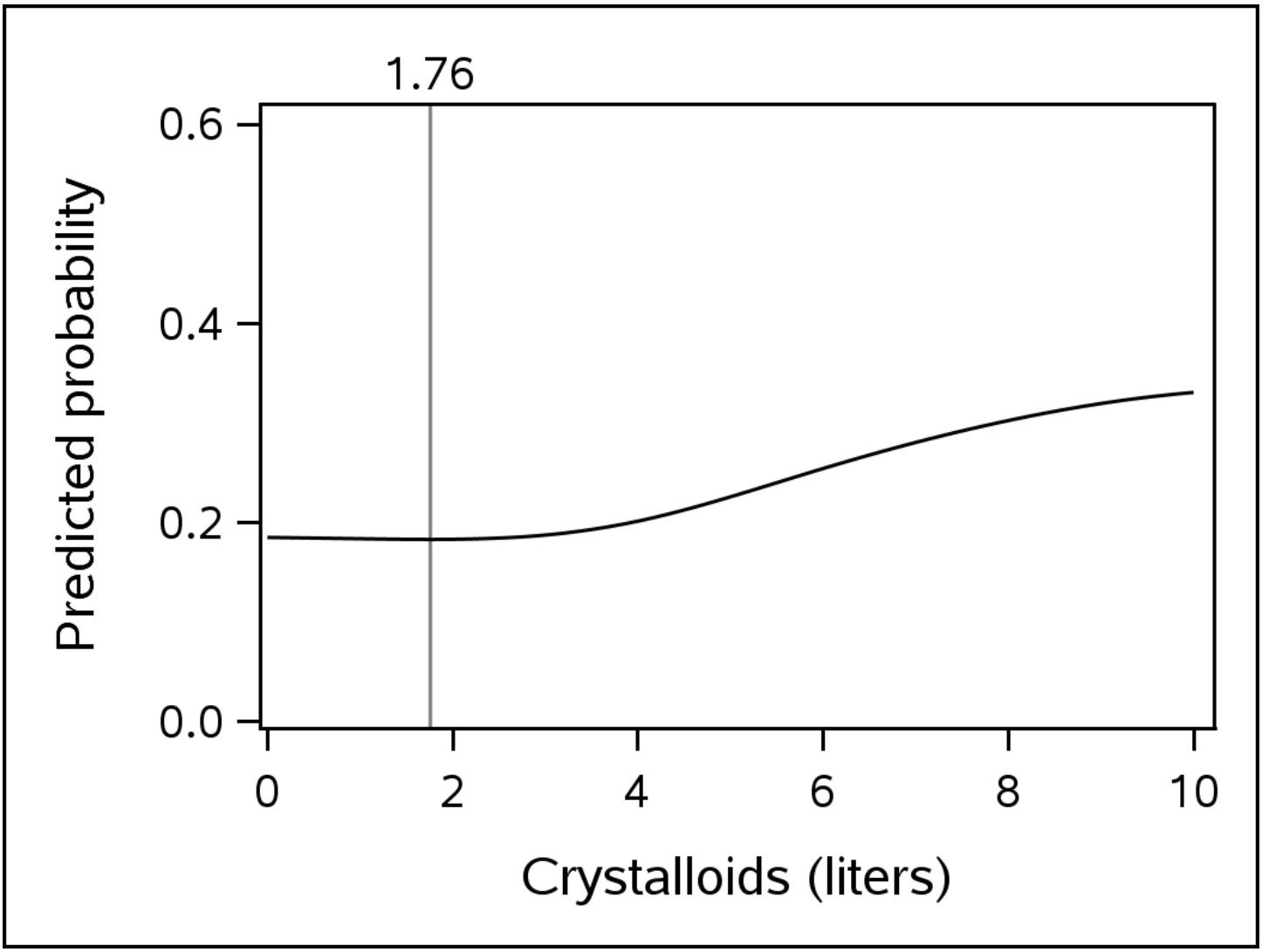
3. Spine (Phila Pa 1976), 39(2), E111-122. doi:10.1097/brs.0000000000000064

4. Neurosurg Focus, 39(2), E4. doi:10.3171/2015.5.focus15157

5. Ann Thorac Surg, 94(1), 109-116. doi:10.1016/j.athoracsur.2012.02.010

6. Med Care 2009;47:626-633.


1.76
0.6
0.4
0.2
0.0
Predicted probability
0
2
4
6
8
10
Crystalloids (liters)

Perioperative Anesthesia-5 Development of a mouse model of Intensive Care Unit postoperative delirium

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[1]University of Virginia, Charlottesville, VA, [2]University of Padova, Padova, Italy, [3]University of Virginia School of Medicine, Charlottesville, VA

Introduction: Intensive care unit (ICU) postoperative delirium (POD) is an acute form of brain failure characterized by fluctuating level of consciousness, inattention, memory deficits and disorganized thinking1-9. Its pathophysiology remains largely unknown, mainly owing to the lack of animal models to study its basic mechanisms2,3,5,9. Hence, we set out to develop a translationally relevant mouse model of delirium that faithfully recapitulates the realism of the perioperative setting by replicating anesthesia, surgery and ICU conditions (A/S/I). We hypothesized that A/S/I would induce changes in mice behavior and gene expression consistent with the features of human delirium.

Methods: Sixty 18-20 month old male mice were tested in the Y-maze, buried food test, simple discrimination task of the attentional set-shifting test and open field test at baseline. The following day they were randomized to A/S/I or control group. A/S/I mice received laparotomy under sevoflurane anesthesia (3 hours), sedation with propofol (2 hours) and ICU conditions, i.e., intermittent lights, sounds and cage shaking (12 hours). Controls did not receive A/S/I. Mice were tested in the Y-maze, buried food, attentional tasks and open field tests at the end of ICU conditions (0h) and every 6 hours up to 24 hours. Mice hippocampi were collected following the behavioral assessments at 24h and processed for qPCR gene expression analysis. Two-tailed Mann-Whitney test was used for statistical analysis. Behavioral data are presented as mean ± S.E.M. Gene data are expressed as fold change relative to controls. Four mice did not survive A/S/I, therefore their data were excluded from analysis. All studies were approved by the Institutional Animal Care and Use Committee.

Results: A/S/I decreased the entries in the Y-maze novel arm at 0h (P=0.001), 6h (P<0.001), 18h (P=0.002) and 24h (P=0.029), and increased the latency to find food in the buried food test at 18h (P=0.035) and 24h (P=0.027). A/S/I increased the trials to criterion in the reverse compound discrimination (P=0.013) and extradimensional shift task (P<0.001) of the attentional test. The changes were independent of motor performance assessed in the open field test (data not shown). A/S/I impaired expression of calcium-independent protein kinase C10 (-4.97 fold change), alpha synuclein11 (-3.78 fold change), tropomyosin receptor kinase A12 (-2.27 fold change) and syntaxin1a13 (-1.50 fold change) relative to controls.

Conclusion: In aged mice, a combination of anesthesia, surgery and ICU conditions induced deficits in memory, attention, thought organization and cognitive flexibility with acute onset and fluctuating course. It also impaired expression of key genes that regulate synaptic exocytosis, synaptic plasticity and memory consolidation in the hippocampus. A/S/I-induced behavioral and gene expression impairments are consistent with the features of human delirium and support the use of our model for mechanistic studies of ICU POD.

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11. J Neurosci 2002; 22(20):8797-8807.
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13. Neuropharmacology 2014; 79:172-9.

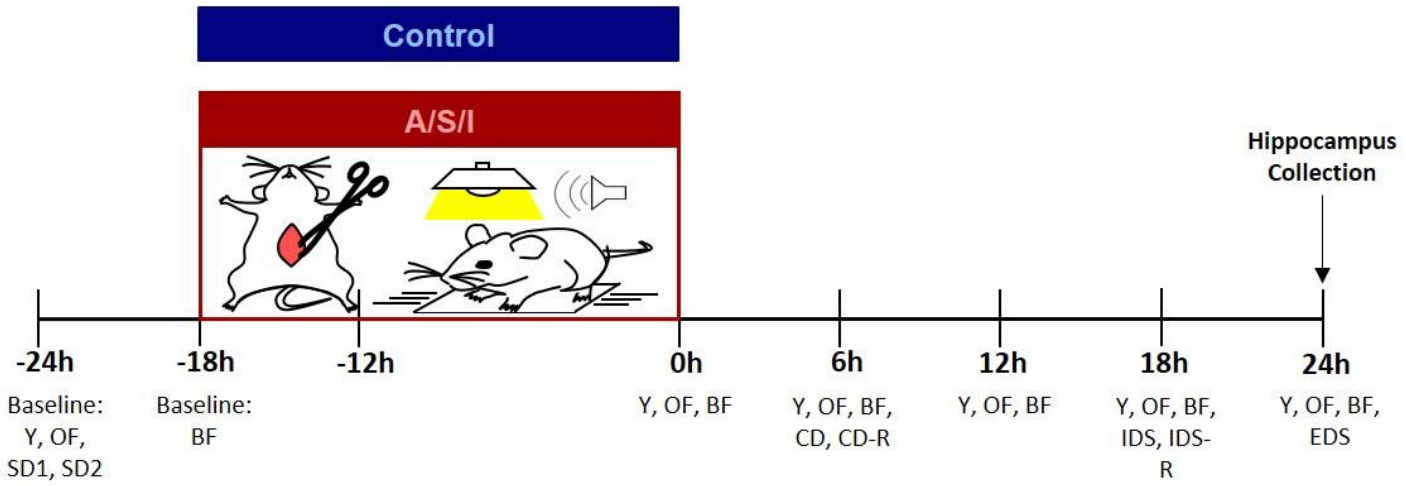

Figure 1. Schematic representation of the experimental design. A/S/I: anesthesia + surgery + ICU conditions. Y: Y-maze test. BF: Buried food test. SD: simple discrimination test. CD: compound discrimination test. CD-R: reverse compound discrimination test. IDS: intra-dimensional shift test. IDS-R: reverse intra-dimensional shift test. EDS: extra-dimensional shift test. OF: open field test.

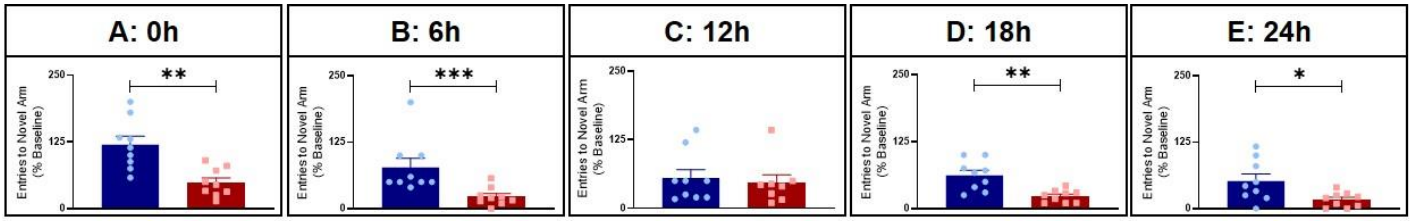

Figure 2. Effects of Anesthesia/Surgery/ICU on mice behavior in the Y-maze. Panels A, B, D and E: A/S/I decreased the number of entries in the novel arm of the Y-maze as compared to controls at 0h (panel A, p= 0.001), 6h (panel B, p<0.001), 18h (panel D, p=0.002) and 24h (panel E, p=0.029). Panel C: there were no differences in the number of entries in the Y-maze novel arm between A/S/I and control mice at 12h (p=0.588). N=9 Control and N=9 A/S/I mice. Time is expressed in hours from the end of ICU conditions.

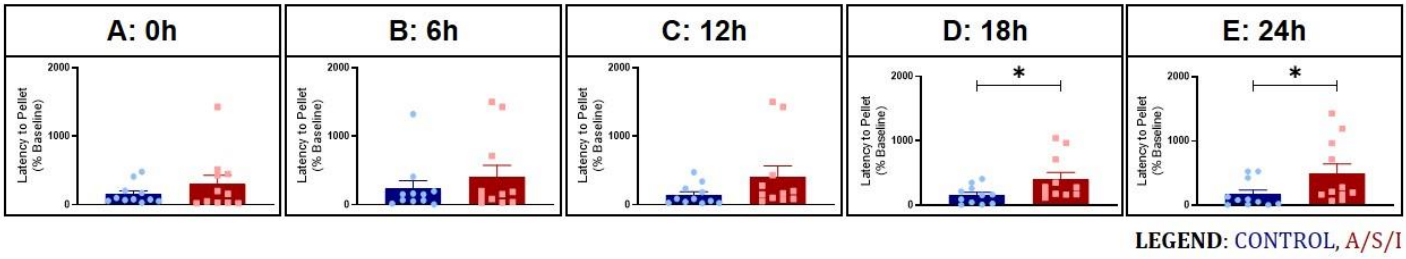

Figure 3. Effects of Anesthesia/Surgery/ICU on mice behavior in the BFT. Panels A-C: there was no difference in the latency to find a buried cereal between A/S/I and control mice at 0h (panel A, P=0.949), 6h (panel B, P=0.478) and 12h (panel C, P=0.116). Panels D and E: A/S/I mice took significantly longer to find a buried sweet cereal compared to control mice at 18h (panel D, p=0.035) and 24h (panel E, p=0.027). N=11 Control and N=11 A/S/I mice. Results are mean ± S.E.M, with individual data represented. Time is expressed in hours from end of ICU conditions.

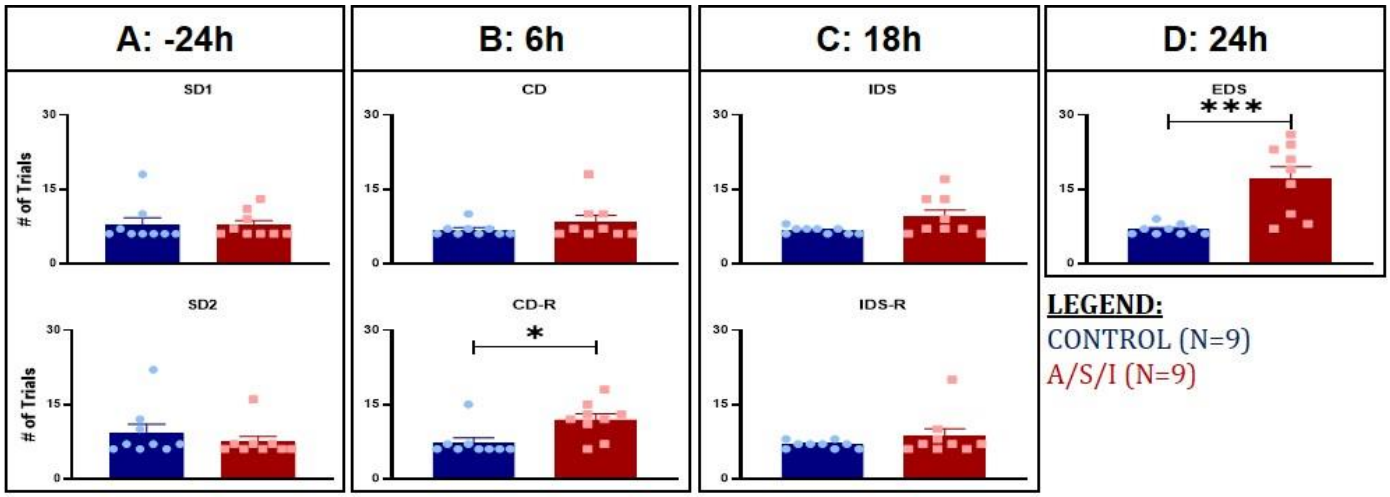

Figure 4. Effects of Anesthesia/Surgery/ICU on mice behavior in the AST. Panel A: there were no differences in baseline performance on the SD tasks between A/S/I and control mice (top panel, P=0.753; bottom panel, P=0.322). Panel B: While A/S/I and control mice performance on the CD task was not significantly different (top panel, P=0.514), A/S/I mice required a significantly higher number of trials to achieve criterion in the CD-R task (bottom panel, P=0.013) compared to controls. Panel C: there were no differences in performance in the IDS and IDS-R tasks between A/S/I and control mice (top panel, P=0.111 and bottom panel, P=0.659). Panel D: A/S/I mice exhibited difficulties finding the reward in the EDS task compared to controls (P<0.001). SD: simple discrimination; CD: compound discrimination; CD-R: reverse compound discrimination. IDS: intra-dimensional shift; IDS-R: reverse intra-dimensional shift. EDS: extra-dimensional shift. N= 9 Control and N=9 A/S/I mice. Results are mean ± S.E.M, with individual data represented. Time is expressed in hours from end of ICU conditions.

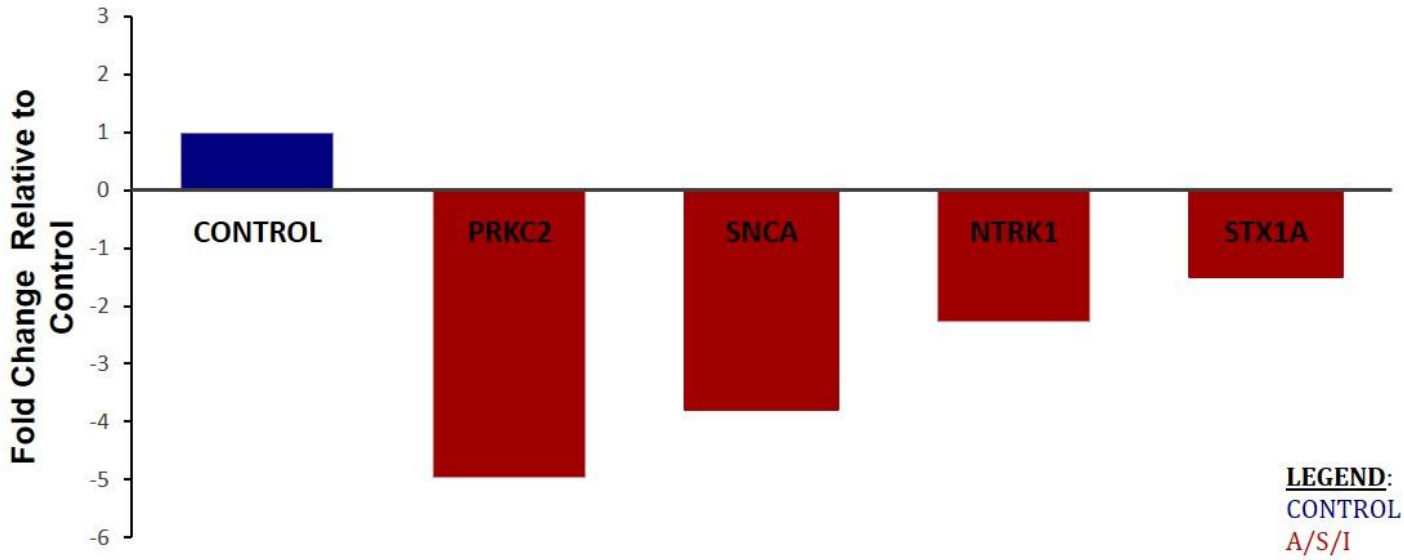

Figure 5. Effects of Anesthesia/Surgery/ICU on hippocampal expression of genes regulating synaptic vesicle exocytosis and plasticity: A/S/I impaired expression of calcium-independent protein kinase C (-4.9 fold change), alpha synuclein (-3.78 fold change), tropomyosin receptor kinase A (-2.26 fold change) and syntaxin1a (-1.49 fold change) relative to controls. N=3 pooled A/S/I hippocampi and 3 control hippocampi. PRKC2: Calcium-independent protein kinase C; SNCA: Alpha Synuclein; NTRK1: Tropomyosin receptor kinase A; STX1A: Syntaxin1A

Perioperative Anesthesia-6 Postoperative Depression after Major Surgery: A Comparative Analysis Using a National Claims Database

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Introduction: Depression is the largest contributor to global disability.1 Aside from surgical disease, major surgery itself could increase the risk of depression. The incidence of postoperative depression has been described in small cohort studies lacking preoperative confounder control or direct comparisons of risk from other surgeries.2,3,4 Given its substantial impact on postoperative recovery we investigated the risk of depression after common major surgeries, hypothesizing that surgeries with higher degrees of stress, pain, complications, or cognitive dysfunction would have an increased risk of postoperative depression.

Methods: Retrospective cohort study with claims from the Optum© Clinformatics® Database of 75 million patients. Cardiac, thoracic, hip, or laparoscopic cholecystectomy (lap CCY) surgery patients between 2004-2019 were screened. Exclusion criteria were previous depression, adjustment disorder, prescription for an anti-depressant or comparator surgery within 365 days before surgery. Death or disenrollment during follow-up (365 days) was censored. The primary outcome was depression, defined by either a new ICD9/10 depression diagnosis code or a new prescription for an antidepressant. A secondary outcome requiring both a diagnosis and a prescription was also analyzed. Covariates included demographics, predictors of depression, and comorbidities. Primary and secondary outcomes were analyzed with multivariate logistic regression. Adjusted analysis included a propensity score matched (PSM) model with preoperative confounders based on prior reports and clinical knowledge. 1:1 matching with a 1% caliper was used. A $P<0.05$ was considered significant. Lap CCY was chosen a priori as the referent group (OR=1). The primary comparison was cardiac surgery versus lap CCY patients. Repeated analyses then explored the risk between thoracic and hip surgery versus lap CCY patients. No adjustments were made for multiple comparisons.

Results: The PSM cohort contained data from 66,097 cardiac surgery (CS) and lap CCY patients (Figure 1, Table 1). The odds of the primary and secondary outcome were significantly higher for CS than for lap CCY patients [OR(95%CI) 1.56(1.50,1.61) $P<0.001$, (1.76(1.63, 1.9), $P<0.001$), respectively] (Table 2). Thoracic (1.33(1.26, 1.41), $P<0.001$) and hip fracture surgery (1.96(1.88, 2.03), $P<0.001$) patients were also at increased risk, however the odds were significantly less for hip replacement patients (0.82(0.79, 0.86), $P<0.001$) (Table 3, Figure 2).

Conclusion: After controlling for preoperative confounders, the odds of developing new depression after cardiac, thoracic, and hip fracture surgery are significantly higher than for patients undergoing lap CCY. Surgery and the associated postoperative period may be uniquely associated with depression, apart from surgical disease. Surgical approach or indication may also influence risk. Further investigation is necessary to identify predictors and preventative targets for postoperative depression after major surgery.

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Table 1 Baseline demographics stratified by surgery type

	Unmatched Cohort			Propensity Matched Cohort		
	Laparoscopic Cholecystectomy	Cardiac Surgery	Absolute Standardized Difference†	Laparoscopic Cholecystectomy	Cardiac Surgery	Absolute Standardized Difference
N	325,952	122,770	-	66,097	66,097	-
Age	51.92 (17.8)	66.8 (12)	0.979	68.1 (13.2)	66.6 (13.2)	0.112
Gender						
Male	113,485 (34.8%)	90,907 (74%)	0.857	45,783 (69.3%)	44,799 (67.8%)	0.032
Female	212,433 (65.2%)	31,838 (25.9%)		20,301 (30.7%)	21,287 (32.2%)	
Low Income Subsidy	11,652 (3.6%)	6,887 (5.6%)	0.112	5,198 (7.9%)	4,483 (6.8%)	0.027
Race						
White	216,376 (66.4%)	89,163 (72.6%)	0.212	46,399 (70.2%)	47,000 (71.1%)	0.028
Asian	7,946 (2.4%)	3,043 (2.5%)		1,849 (2.8%)	1,723 (2.6%)	
Black	27,811 (8.5%)	9,986 (8.1%)		5,379 (8.1%)	5,142 (7.8%)	
Hispanic	44,290 (13.8%)	9,422 (7.7%)		6,099 (9.2%)	5,747 (8.5%)	
Charlson Comorbidity Score*	171.17 (385.31)	338.87 (516.41)	0.368	285.7 (489.4)	268.1 (478.3)	0.036
Angina	8,198 (2.5%)	46,748 (38.1%)	0.986	6,526 (9.9%)	7,550 (11.4%)	0.050
Myocardial infarction	2,693 (0.8%)	25,711 (20.9%)	0.682	2,222 (3.4%)	2,902 (4.4%)	0.053
Percutaneous Coronary Intervention	1,378 (0.4%)	7,204 (5.9%)	0.316	1,329 (2%)	1,805 (2.7%)	0.047
Coronary Heart Disease	1,034 (0.3%)	46,437 (37.8%)	1.087	1,034 (1.6%)	1,711 (2.6%)	0.072
Congestive heart failure	4,342 (1.3%)	15,404 (12.5%)	0.452	3,853 (5.8%)	4,451 (6.7%)	0.037
Smoking	42,486 (13%)	27,378 (22.3%)	0.245	8,974 (13.6%)	9,154 (13.8%)	0.008
Diabetes	42,788 (13.1%)	35,674 (29.1%)	0.398	12,816 (19.4%)	12,181 (18.4%)	0.025
Hyperlipidemia	98,816 (30.3%)	71,404 (58.2%)	0.584	25,172 (38.1%)	25,701 (38.9%)	0.016
Hypertension	111,870 (34.3%)	77,604 (63.2%)	0.604	29,417 (44.5%)	29,377 (44.4%)	0.001
Obesity	47,392 (14.5%)	16,195 (13.2%)	0.039	5,939 (9.0%)	6,151 (9.3%)	0.011
Chronic Kidney Disease	35,247 (10.8%)	27,635 (22.5%)	0.318	11,225 (17%)	10,831 (16.4%)	0.016
Chronic Pulmonary Disease	54,440 (16.7%)	35,188 (28.7%)	0.289	19,163 (29%)	17,687 (26.8%)	0.050
Lung Cancer	1,262 (0.4%)	742 (0.6%)	0.031	514 (0.8%)	424 (0.6%)	0.016
Osteoarthritis	43,779 (13.4%)	22,777 (18.6%)	0.140	14,968 (22.6%)	13,580 (20.5%)	0.051
Cognitive Disorder	3,979 (1.2%)	1,972 (1.6%)	0.033	1,649 (2.5%)	1,392 (2.1%)	0.026
Alcohol Abuse	2,348 (0.7%)	1,536 (1.3%)	0.054	629 (1.0%)	588 (0.9%)	0.006

Values are reported as N (%) or mean (SD) depending on variable type

†Absolute standardized difference is calculated as the difference in group means or proportions divided by the square root of the pooled variance. A value less than 0.1 signifies a negligible difference

**Summed over 365-day period*

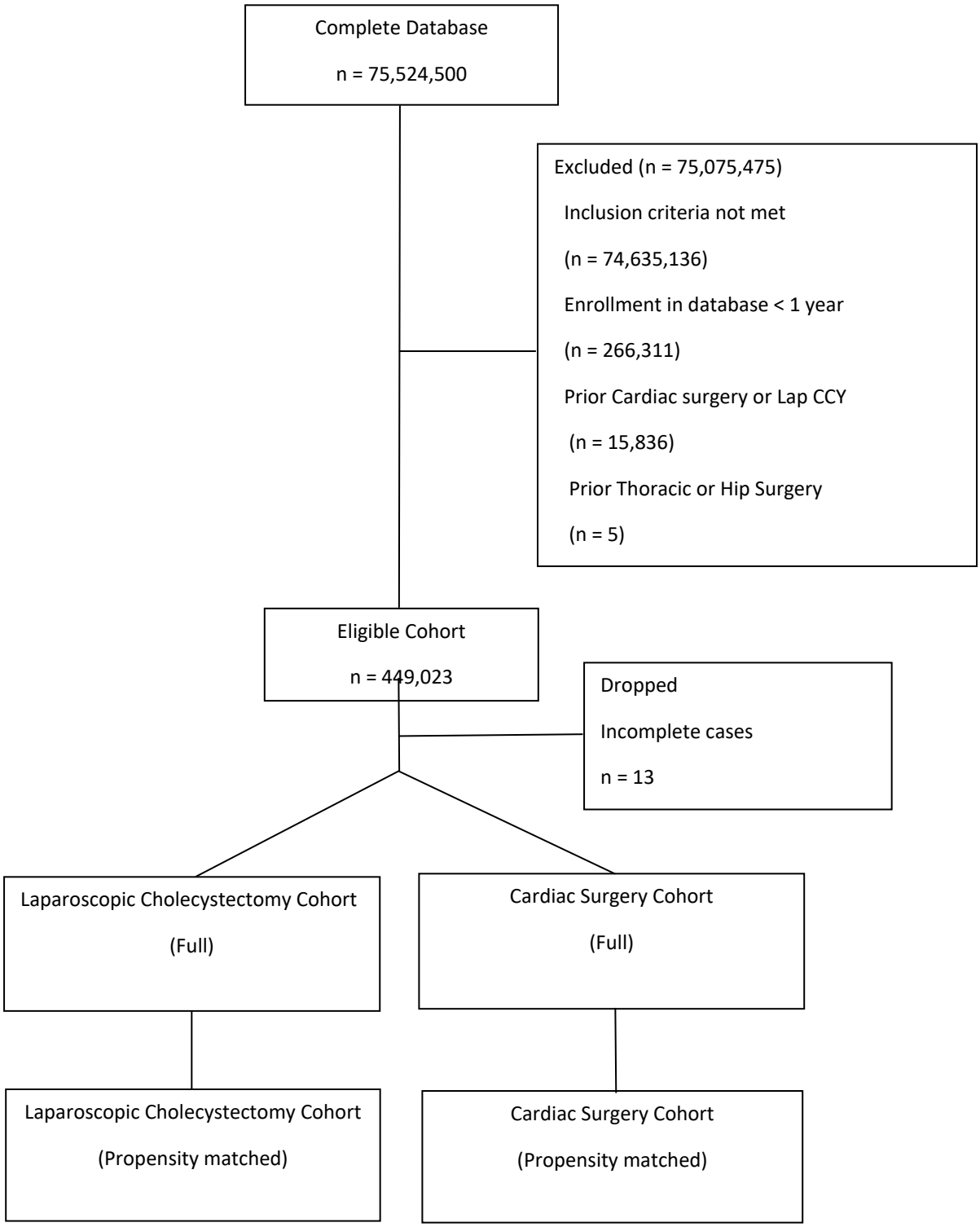
Table 2: Primary and secondary outcomes after cardiac surgery as compared to lap CCY.

	Odds Ratio (95% CI)	P
New depression OR a new prescription		
Unadjusted	1.57 (1.54, 1.60)	<0.001
Propensity score matched	1.56 (1.50, 1.61)	<0.001
New depression AND a new prescription		
Unadjusted	1.60 (1.53, 1.67)	<0.001
Propensity score matched	1.76 (1.63, 1.9)	<0.001

Table 3: Odds of the Primary Outcome for Other Surgeries Compared to Lap CCY

	Odds Ratio (95% CI)	p
Thoracic Surgery		
Unadjusted	1.71 (1.57, 1.72)	<0.001
Propensity score matched	1.33 (1.26, 1.41)	<0.001
Thoracotomy		
Unadjusted	2.09 (1.99, 2.19)	<0.001
Propensity score matched	1.62 (1.49, 1.76)	<0.001
VATS		
Unadjusted	1.57 (1.52, 1.63)	<0.001
Propensity score matched	1.24 (1.16, 1.32)	<0.001
Hip Surgery		
Hip Fracture Surgery		
Unadjusted	2.48 (2.43, 2.53)	<0.001
Propensity score matched	1.96 (1.88, 2.03)	<0.001
Hip Replacement		
Unadjusted	0.81 (0.79, 0.83)	<0.001
Propensity score matched	0.82 (0.79, 0.86)	<0.001

FIGURE 1: CONSORT DIAGRAM – CARDIAC SURGERY VS LAPAROSCOPIC CHOLECYSTECTOMY



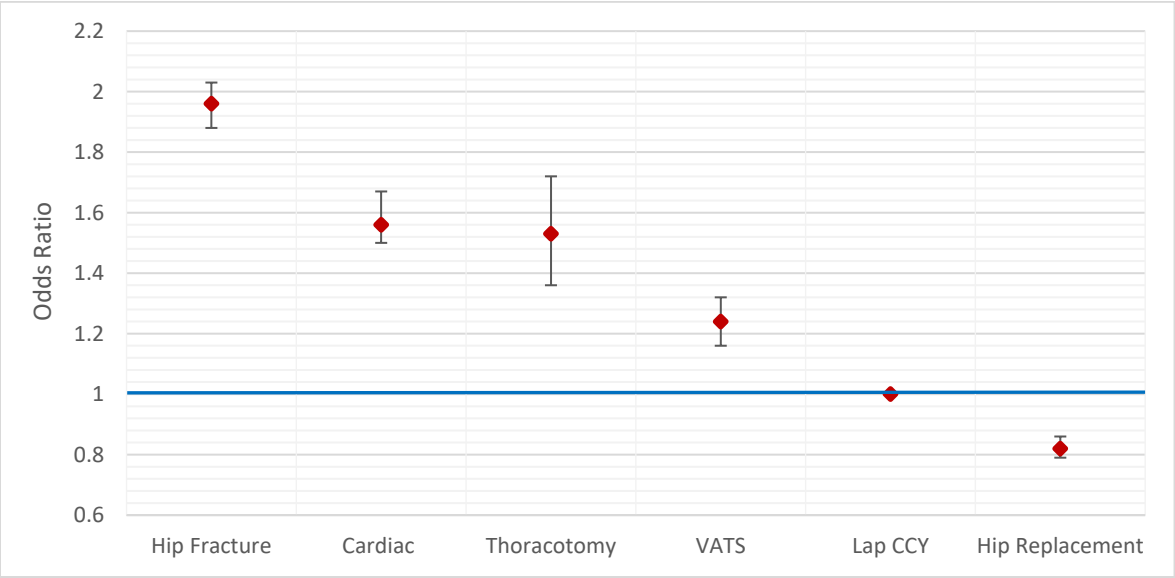


Figure 2: Odds of new depression (diagnosis or prescription) after various major surgeries.
Lap CCY was assigned as referent (OR=1)

Perioperative Anesthesia-7 Establishing the "New Normal': Biostatistics of the Average Patient Undergoing Anesthesia at a University Medical Center

Sean Baskin[1], Malina Varner[2]

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Introduction: Since the 1970s, medical literature has defined the average patient as a 70kg male, however as the population of the United States struggles with increasing rates of obesity, it is unlikely that today's average patient truly weighs 70kg1. In 2017, the National Center for Health Statistics reported an obesity prevalence of 39.8% in the adult population , as well as a 9% increase in obesity rates over a 15-year period (2,3). As such, it is unlikely that 70kg remains an accurate surrogate weight for the average patient. Given this, we sought to identify an observed average weight, as well as other focused health metrics for surgical patients at a single university hospital.

Methods: After obtaining IRB approval, all patients age 18 or older who received anesthetics in an operating environment between January 1 and December 31, 2015 were identified. Extracted data included: medical record number, age, weight, body mass index (BMI), American Society of Anesthesiology (ASA) score and the first recorded set of vital signs limited to heart rate and mean arterial blood pressure (MAP). We excluded patients with an ASA score of 6, and those over 80 years of age due to the disproportionally small number of patients within that group. Patients who had multiple anesthetics were screened to include only their first anesthetic for 2015. Data points for weight, BMI, heart rate, MAP, and ASA score were extracted and imported into the electronic database Research Electronic Data Capture (REDCap). Descriptive statistical analysis was performed looking at the dataset as a whole as well as by gender specific age-by-decades (categories of 19-30, 31-40, 51-60, 61-70, and 71-80), with the exception of the category 'age'.

Results: 19,522 patients were identified who required operative anesthesia during 2015. Females comprised 53.5% of patients and had an average age of 54.7 ± 16 y. The average age for males was 54.7 ± 16 y. Demographic and vital sign data, stratified by both gender and age-by-decade, are shown in Table 1. Similar trends were evident for both females and males when the data was considered by decades of age. For weight and BMI, the 19-30y decade had the lowest average values; and values increased to a high for the 41-50y decade, and then decreased to the 71-80y decade. The average heart rate measured fell within established normal ranges for all decades. There was a steady decrease sequentially from the 19-30y decade (for males, 19-30y and 31-40y decades had similar values) to the 71-80y decade. The MAP value measured also exhibited sequential changes across the decades, increasing from a low for the 19-30y decade to a high for the 71-80y decade. ASA Score: Analysis of ASA status by age-decade is shown in Figure 1. For the 3 lowest age decades, the highest percentage of patients were ASA-2, and patients with ASA status scores ≤ 2 constituted the majority (≥57%). For the three oldest age decades, the highest percentage of patients were ASA status 3, and ASA status scores ≥3 constituted the majority (≥58%). ASA status 5 was <1% for all age decades.

Conclusion: Our data reflects national trends of increasing rates of obesity and hypertension. The average patient weight of 83.5 and 94.1kg for females and males, respectively, is notably higher than the historical average of 70kg1. Additionally, using the Center for Disease Controls (CDC) criteria for obesity (BMI<30kg/m2), the average surgical patient over the age of 31, regardless of gender, would qualify as obese2. Our findings also show that the bulk of our surgical patient population has hypertension when MAP is calculated using the highest allowable blood pressure per the 2017 ACA/AHA Guidelines4. Perhaps the best metric utilized in this analysis for overall health status is the ASA physical status classification system5. ASA-3 status corresponds to 'severe systemic disease', and for all ages above 50, the majority of the surgical patients were ASA status ≥3, as well as 43% of 41-50 year olds. The majority of surgical patients under age 41 were ASA status ≤2, corresponding to 'mild systemic disease', yet even this group demonstrated hypertension. We found that regardless of age or gender, the average patient is likely to weight more than 70kg. Our data also suggests that at equivalent age ranges, males tend to have higher weight, BMI and MAP compared to females. Anesthesia providers should consider current population trends and the potential impact on the delivery of anesthesia.

Reference(s):

1. Evid Based Med. 2013;18(1):21-22.

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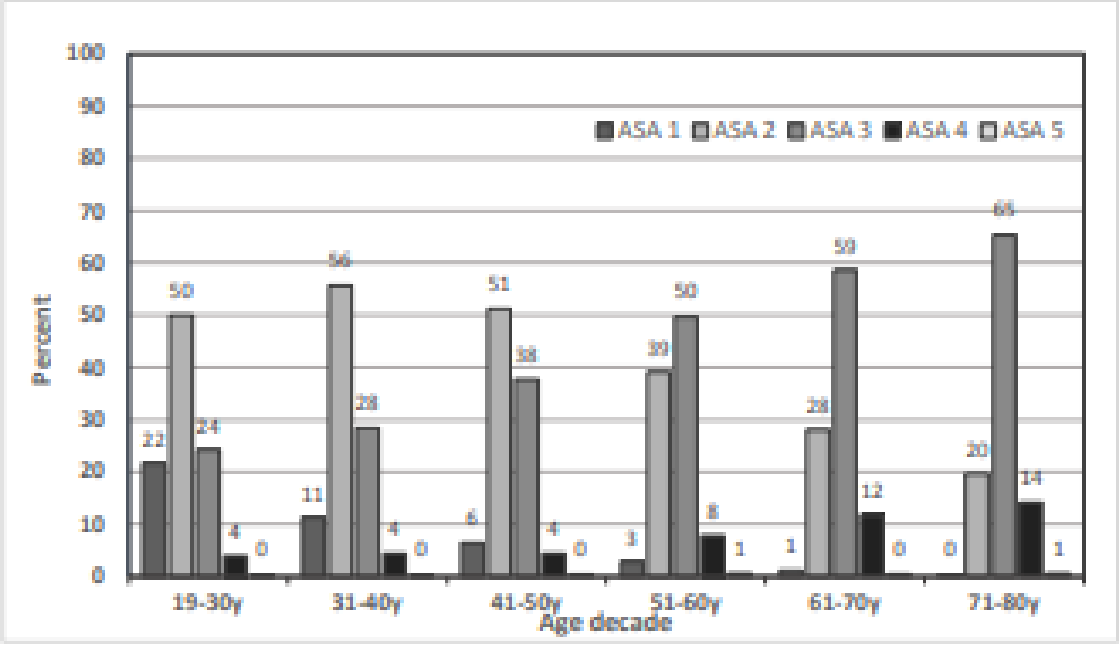
3. NCHS Data Brief No. 288: Prevalence of Obesity Among Adults and Youth: United States, 2015–2016. 2017

Table 1. Demographic and vital sign data by decade and gender

Age (years)	Sex	N	Variable	N	Mean	Std Dev
19-30	Female	1294	Weight (kg)	986	74.9	26.9
			BMI (kg/m^2)	942	28.8	9.7
			First HR (bpm)	1293	83.5	26.6
			First MAP (mmHg)	1283	97.6	14.7
	Male	1068	Weight (kg)	791	80.5	23.1
			BMI (kg/m^2)	765	26.0	7.29
			First HR (bpm)	1066	81.0	28.2
			First MAP (mmHg)	1058	99.1	14.4
31-40	Female	1548	Weight (kg)	1273	84.3	27.1
			BMI (kg/m^2)	1214	31.7	9.9
			First HR (bpm)	1546	80.2	25.5
			First MAP (mmHg)	1542	102.1	15.6
	Male	943	Weight (kg)	641	94.3	28.2
			BMI (kg/m^2)	616	30.0	8.3
			First HR (bpm)	940	81.4	30.3
			First MAP (mmHg)	922	104.4	16.4
41-50	Female	1836	Weight (kg)	1483	87.6	27.5
			BMI (kg/m^2)	1421	32.8	9.9
			First HR (bpm)	1831	78.4	25.8
			First MAP (mmHg)	1824	107.4	16.7
	Male	1091	Weight (kg)	818	100.1	28.2
			BMI (kg/m^2)	786	31.6	8.1
			First HR (bpm)	1087	77.9	29.4
			First MAP (mmHg)	1069	109.9	17.3
51-60	Female	2165	Weight (kg)	1693	86.3	25.7
			BMI (kg/m^2)	1632	32.4	9.3
			First HR (bpm)	2160	76.9	29.5
			First MAP (mmHg)	2139	110.4	17.7
	Male	2061	Weight (kg)	1523	97.4	27.0
			BMI (kg/m^2)	1453	31.1	8.5
			First HR (bpm)	2053	74.1	32.6
			First MAP (mmHg)	2015	111.5	17.4

61-70	Female	2064	Weight (kg)	1575	85.1	25.2
			BMI (kg/m^2)	1518	32.7	9.4
			First HR (bpm)	2058	76.5	31.5
			First MAP (mmHg)	2027	113.9	19.1
	Male	2241	Weight (kg)	1657	96.0	23.8
			BMI (kg/m^2)	1608	31.0	7.4
			First HR (bpm)	2234	72.1	36.4
			First MAP (mmHg)	2186	113.6	18.5
71-80	Female	1525	Weight (kg)	1153	78.3	20.3
			BMI (kg/m^2)	1114	30.7	7.9
			First HR (bpm)	1520	73.4	36.3
			First MAP (mmHg)	1493	116.8	19.8
	Male	1687	Weight (kg)	1201	91.9	19.8
			BMI (kg/m^2)	1162	30.0	6.98
			First HR (bpm)	1684	70.6	40.7
			First MAP (mmHg)	1650	116.0	19.2

Figure 1. ASA Status Class by Age Decade



Perioperative Anesthesia-8 Machine-learning-based algorithm for prediction of postoperative death of non-ICU patients

Simone M Kagerbauer[1], Bernhard Ulm[1], Armin H Podtschaske[1], Manfred Blobner[2], Graessner Martin[1], Andonov Dimislav[1], Bettina Jungwirth[1]

[1]Technical University of Munich, Munich, Germany, [2]Klinikum Rechts der Isar der TUM, Munich, MA

Introduction: Failure to rescue after surgical complications is a major cause of death [1, 2]. About 70% of the patients die on a normal ward and not on an intensive care unit [3]. Therefore, closer postoperative monitoring of patients may improve survival. As critical care capacity is a scarce resource even in high-income countries, it remains essential to identify patients at risk [4]. For this purpose, machine learning models may provide a better prediction of the individual risks than traditional scores.

Methods: After ethical approval, we analysed non-ICU-patients undergoing non-cardiac surgery. We included all preoperative available data of our hospital information and patient data management system from January 2014 to August 2019. 68506 patients (55% male; age 56.2± 21.1 years) undergoing 108457 operations at 94640 unique hospital stays were analysed. In-hospital mortality was 0.3% (n=361). An Extreme Gradient Boosting model was trained on a training set containing 80% of the available data using procedure data (28), surgical codes (>9000), laboratory parameter (988), data from preoperative assessment (181) and medication (201). Area under receiver operating curves (AUROC) for mortality during hospital stay had been calculated. Importance of variables was identified by information gain (IG).

Results: The model predicts in-hospital mortality on 281 of 10921 factors with an AUROC of 92.2 (CI: 89.3 - 95.0, figure 1) in the test dataset. The 5 most important factors were c-reactive protein (CRP, IG 0.09), age (IG 0.08), red blood cell count (RBC, IG 0.03), type of hospital admission (IG 0.03) and BMI (IG 0.02) (figure 2). Thus, the AUROC of our model is better than previously reported AUROCs of POSPOM, Charlson Comorbidity Index (CCI) or Surgical Apgar Score as described in the literature [5].

Conclusion: ML-based models can help to identify high-risk patients in a collective with inexplicit indications for intensive care. Further studies are required to determine their usability as decision support and triage tools for providing optimized patient care at limited critical care capacity.

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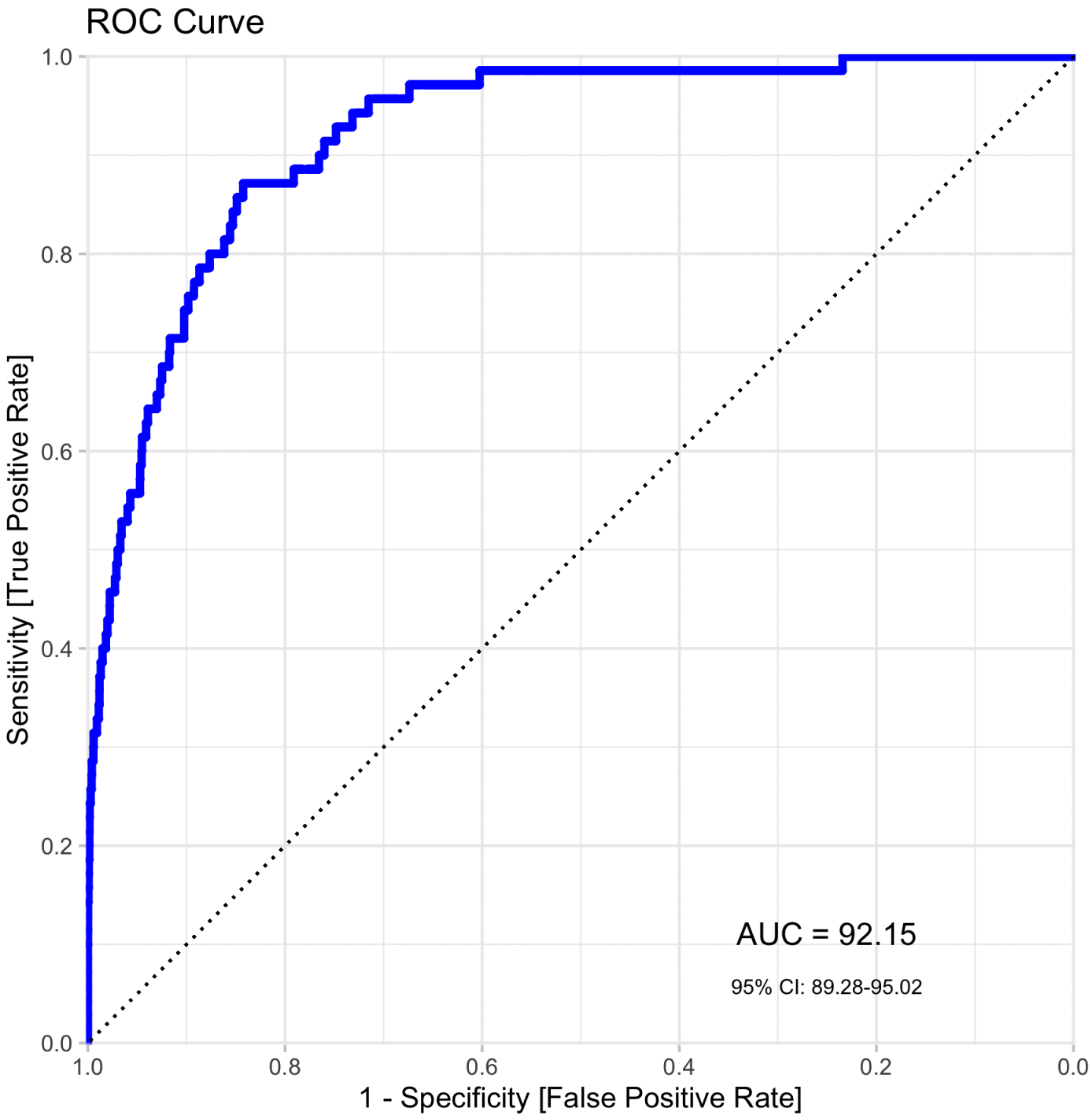
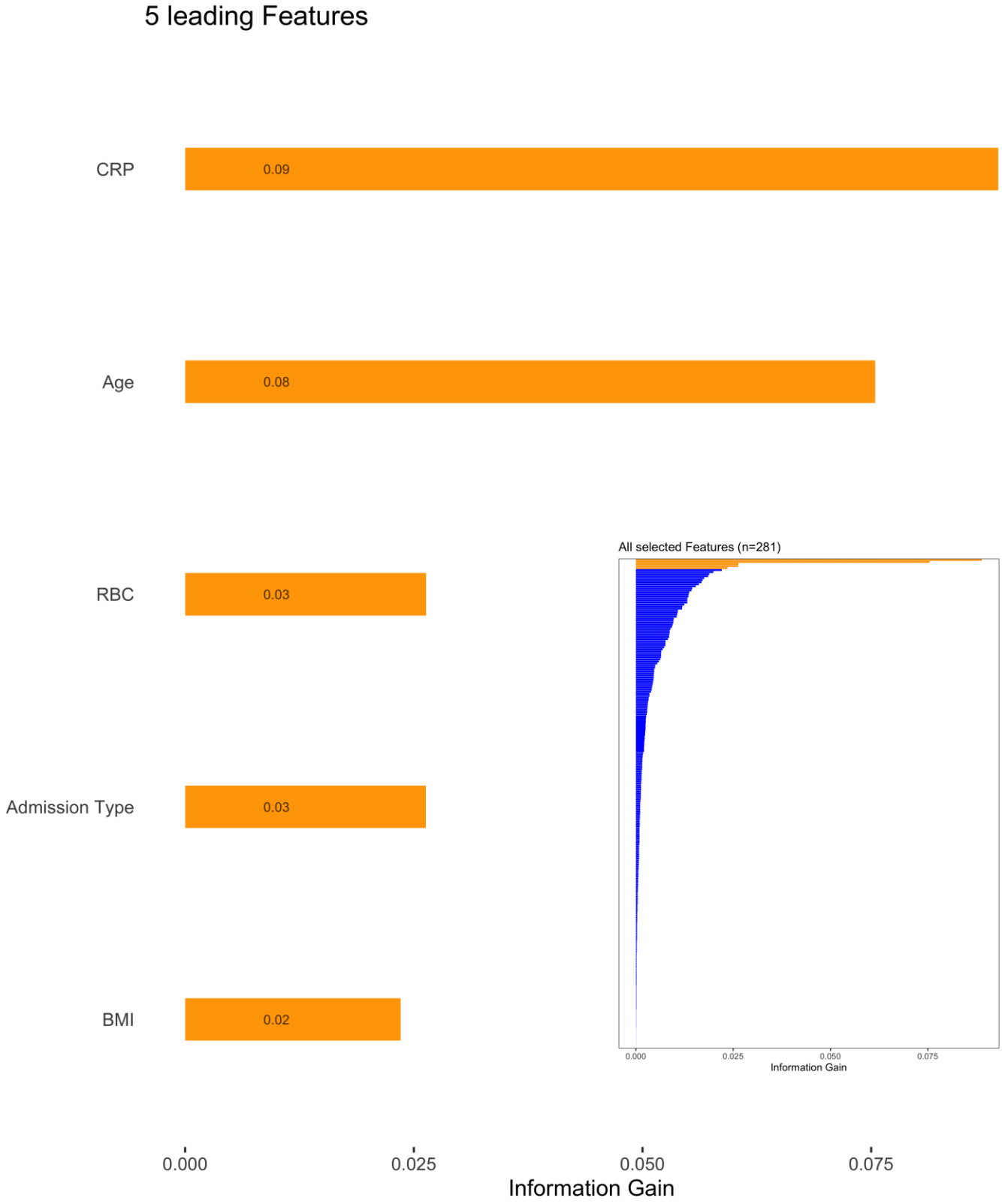

ROC Curve
Sensitivity [True Positive Rate]
1.0
0.8
0.6
0.4
0.2
0.0
1.0
0.8
0.6
0.4
0.2
0.0
1 - Specificity [False Positive Rate]
AUC = 92.15
95% CI: 89.28-95.02


5 leading Features
CRP
0.09
Age
0.08
RBC
0.03
Admission Type
0.03
BMI
0.02
0.000
0.025
0.050
0.075
Information Gain
All selected Features (n=281)
0.000
0.025
0.050
0.075
Information Gain

Perioperative Anesthesia-9 Role of Early Postoperative Use of Oral Nutritional Supplements in Colorectal Surgery Outcomes

David G Williams[1], Tetsu Ohnuma[2], Vijay Krishnamoorthy[2], Karthik Raghunathan[2], Suela Sulo[3], Bridget Cassady[3], Refaat Hegazi[3], Paul E Wischmeyer[4]

[1]Duke University Medical Center, Durham, United States of America, [2]Duke University, Durham, NC, [3]Abbott Nutrition Science, Columbus, OH, [4]Duke University School of Medicine, Durham, NC

Introduction: Postoperative nutritional support is vital in maintaining nutritional status during the catabolic postoperative period and underscored by guidelines encouraging early oral intake following surgery as a routine part of ERAS protocols.1,2 Current nutrition guidelines and small randomized trials examining early use of postoperative oral nutritional supplementation (ONS) suggest clinical outcome benefits following colorectal surgery (CRS).3 However, there is limited real-world evidence of the association between ONS use and improved clinical outcomes in CRS. The aim of this study was to examine the impact of early ONS on post-operative infection and other clinical outcomes in patients undergoing CRS.

Methods: Using a nationwide administrative-financial database (Premier Healthcare Database), this retrospective cohort study examined the association between early ONS use and postoperative clinical outcomes in patients undergoing elective open or laparoscopic CRS between 2008–2014 (total of 61,031 eligible patient encounters in period). Early ONS was defined as the presence of day-stamped hospital charge codes for ONS before postoperative day (POD) 3. The primary outcome was a composite of infectious complications, which was identified using ICD-9 codes. Key secondary (intensive care unit (ICU) admission and gastrointestinal complications) and falsification (blood transfusion and myocardial infarction) outcomes were also examined. Propensity score matching was applied in order to examine outcomes between two comparable patient groups.

Results: ONS was provided in 267 (0.4%) out of 61,031 CRS patients who were eligible to receive ONS by POD 3. Patients receiving early ONS were older, had more comorbidities, were more likely to be Medicare beneficiaries, and had higher rates of malnutrition when compared to non-early ONS recipients. In a propensity-matched sample of early ONS (n=267) versus non-early ONS patients (n=534), infectious complications were significantly lower in early ONS recipients (6.7% vs. 11.8%, P<0.03). Early ONS use was also associated with significantly reduced rates of pneumonia (P<0.04), ICU admissions (P<0.04), and gastrointestinal complications (P<0.05). There were no significant differences in falsification outcomes.

Conclusion: In the overall study population, early ONS following CRS was more likely to be utilized in older patients with a high co-morbidity burden. Despite this, in a well-matched sample of CRS patients, early ONS was associated with reduced infectious complications, pneumonia, ICU admission, and gastrointestinal complications. This retrospective large database analysis provides real-world evidence to suggest improved clinical outcomes from early ONS use in CRS patients.

Reference(s):

1. Osland E, Yunus RM, Khan S, Memon MA. Early versus traditional postoperative feeding in patients undergoing resectional gastrointestinal surgery: a meta-analysis. JPEN Journal of parenteral and enteral nutrition. 2011;35(4):473-487.

2. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. J Gastrointest Surg. 2009;13(3):569-575.

3. Wischmeyer PE, Carli F, Evans DC, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway. Anesth Analg. 2018;126(6):1883-1895.

Perioperative Anesthesia-10 Utilization of Oral Nutritional Supplements in Postoperative Hospitalized U.S. Surgical Patients

David G Williams[1], Tetsu Ohnuma[2], Vijay Krishnamoorthy[2], Karthik Raghunathan[2], Suela Sulo[3], Bridget Cassady[3], Refaat Hegazi[3], Paul E Wischmeyer[4]

[1]Duke University Medical Center, Durham, United States of America, [2]Duke University, Durham, NC, [3]Abbott Nutrition Science, Columbus, OH, [4]Duke University School of Medicine, Durham, NC

Introduction: Perioperative malnutrition is a significant risk factor for increased post-surgical complications.1 To address this risk, postoperative nutrition delivery is an essential component of surgical recovery.1 Yet, dietary intake is often limited following surgery.2-4 Recent surgical guidelines recommend the use of oral nutrition supplements (ONS) to meet nutritional requirements.5 The aims of this study were to: 1) Describe the prevalence of malnutrition in surgical patients in the United States; 2) Examine utilization and variation in early ONS use; and 3) Examine factors associated with early ONS use in selected pre-specified surgeries at known high-risk for poor post-operative nutrition delivery (colorectal/coronary artery bypass grafting (CABG).

Methods: This cross-sectional study was conducted using data on all surgical patients from 655 hospitals in the Premier Healthcare Database (PHD) between October 2008−September 2014. Demographic, clinical, and facility characteristics were examined, and ONS use was identified using day-stamped hospital charge codes. Descriptive statistics were utilized to examine prevalence of malnutrition diagnosis and ONS utilization in patients stratified by surgical type. Multilevel, multivariable logistic regression models were used to examine factors associated with early ONS use in colorectal and CABG surgeries, defined as ONS administered within the first three postoperative days following colorectal surgery and within the first five postoperative days following CABG surgery.

Results: A total of 2,823,532 patients undergoing inpatient surgery were identified across 172 hospitals that had charges for ONS use. Among this population, only 2.4% received ONS. The overall malnutrition prevalence in this population was 4.3%, and only 15% of these patients received ONS. ONS-receiving patients were 72% Caucasian and 65% Medicare patients, with a mean age of 66±16.5 years. Compared to patients not receiving ONS, ONS-receiving patients had higher van Walraven co-morbidity scores (7.3±7.8 vs. 2.3±5.6, $p<0.001$), with comorbidities including: weight loss (18%), diabetes (29%), chronic heart failure (21%), chronic obstructive pulmonary disease (26%), and chronic kidney disease (21%). Individual hospital practice explained much of the variation in early ONS use following colorectal and CABG surgery (45% and 53%, respectively).

Conclusion: In this large surgical population, inpatient ONS use is more common in older, Caucasian, Medicare patients with a high comorbidity burden. Despite an almost 5% prevalence of malnutrition, ONS utilization remained low in this group as well. Our data indicates current ONS utilization in surgical patients is limited, varies substantially at the hospital level, and should be a key target for perioperative quality improvement.

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Perioperative Anesthesia-11 COMPARISON OF THROMBOELASTOGRAPHY WITH CONVENTIONAL COAGULATION TESTS TO EVALUATE THE HAEMOSTATIC PROFILE OF PATIENTS WITH PRIMARY BRAIN TUMOUR UNDERGOING SURGERY

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Introduction: Brain cancer accounts for approximately 1.4% of all cancers and 2.3% of all cancer related deaths(1). Hemostasis is a complex dynamic process involving bleeding and thrombosis as two extreme ends. Traditional plasma-based coagulation assays, provide little information about the dynamics of the clot formation or the quality of clot. Thrombolastography measures viscoelastic changes of the entire clotting process. This study was undertaken to compare thromboelastography with conventional coagulation"¬ tests(PT, aPTT, INR) to evaluate the trends in haemostatic profile and identify specific patterns in coagulation abnormalities if any, of patients "¬with primary brain tumour undergoing surgery."¬

Methods: We designed a prospective observational study in patients with primary brain tumors, undergoing craniotomy for surgical management of the same. Informed written consent was obtained from all the patients enrolled in the study. Forty patients were enrolled from the elective neurosurgical operation list with the diagnosis of supratentorial primary brain tumor. All the patients belonged to American Society of Anesthesiologists (ASA) Physical Status grades I, II& III. All the patients had a Glasgow Coma Scale (GCS) of E4V5M6. A standard anaesthesia regime was followed for all the patients. Samples for thromboelastography (TEG) and conventional tests were taken in the preoperative period, then after removal of tumor, and start of hemostasis and on the first postoperative day. SPSS V.21 statistical package was used.Mean, Mode, Median and Paired t test, Chi square test were done with a $p<0.05$ was taken as statistically significant.

Results: Inclusion criteria included all newly diagnosed patients with primary brain tumours larger than 4 cm in maximum diameter on CT or MRI. Exclusion criteria were patients with a history of haematological or coagulation disorders, those taking anticoagulant therapy, and those with chronic disease-for example, liver cirrhosis or renal failure will be excluded.All 40 patients enrolled in our study had supratentorial brain tumor, of which 22 were glioma and 18 were meningioma. Out of these 40 patients, 20 were male and 20 were female. All the patients were demographically statistically similar. The baseline parameters of all the patients were within normal range and they remained hemodynamically stable through out perioperative period. Intraoperative bleeding was calculated to be 737.7 (±185.6) ml. PRBC were transfused in 17 patients, FFP in 13 but no platelet transfusion was done. In our study we found that there was a universal trend towards hypercoagulability (Persistent decrease in R & K values and Persistent increase in MA &α Angle) in all the TEG parameters measured intraoperatively and post operatively. The conventional tests remained within normal limit except for a slight prolongation in PT, INR and aPTT value intra operatively.

Conclusion: Brain tumors are prone to develop hypercoagulability and are at risk for thromboembolic complications. Thromboelastography maybe useful in identifying these abnormalities. Further evaluation of the role of Thromboelastography in identifying those patients who will be at risk to develop thromboembolic complications can improve our perioperative management of patients with brain tumors.

Reference(s): Ann Card Anaesth. 2018;21:151-157. J Adv Res Med 2018;5: 32-35.

Perioperative Anesthesia-12 Use of BIS in Memory Recall and Recognition

Kimberly Klafta[1], Yaman Kherallah[1], David Glick[2], Michael O'Connor[3]

[1]University of Chicago Pritzker School of Medicine, Chicago, United States of America, [2]University of Chicago, Chicago, IL, [3]The University of Chicago Medicine, Chicago, IL

Introduction: The Bispectral Index Monitor (BIS Medtronic-Covidien, Dublin, Ireland) was developed to monitor the depth of anesthesia and reduce incidence of intraoperative awareness, which studies have shown correlates with the development of posttraumatic stress disorder (PTSD). This study focuses on delineating what BIS readings mean in the context of perioperative memory formation-and subsequent memory retrieval- and the impact BIS monitoring may have on reducing negative sequelae associated with intraoperative awareness.

Methods: Following Institutional Review Board approval, 363 patients undergoing general anesthesia were approached in the pre-op area and provided consent. A total of six words were administered in the preoperative state for later recall and timed with the administration of a physician-determined dosage of midazolam. Words 1, 2, and 3 were given 5 minutes, 3 minutes, and 1 minute prior to the administration; word 4 was given during the administration, and words 5 and 6 were given 1 minute and 3 minutes after the administration of midazolam respectively. At each time point, the patient's BIS score was recorded. Immediately after the operation, patients were approached in the post-op area and asked to recall the six preoperative words given to them. BIS scores for each word were then correlated with the successful or unsuccessful recall of the associated word. Within 24 hours after the procedure, patients were contacted and asked to recall the words given to them and were asked to open an envelope containing 6 study words and 18 other words and identify any words that they had missed. Any word that was only remembered after looking at the list was considered a successful recognition of the word but not a successful recall.

Results: Figure 1 shows rate of recall and recognition by BIS score, stratified into six groups by BIS score. Higher BIS scores correlated with both higher rates of recall and recognition of a word at 24 hours. Rates of recognition were consistently higher than rates of recall among every stratified BIS score group.

Conclusion: By examining the relationship between recall and recognition, we were able to demonstrate consistently higher levels of 24 hour word recognition when compared to word recall. This demonstrates that while some patients may not endorse overt recall of perioperative events, memories of such events can still be triggered with prompting. These findings may help further elucidate the connection between intraoperative awareness events and development of subsequent PTSD due to latent memories.

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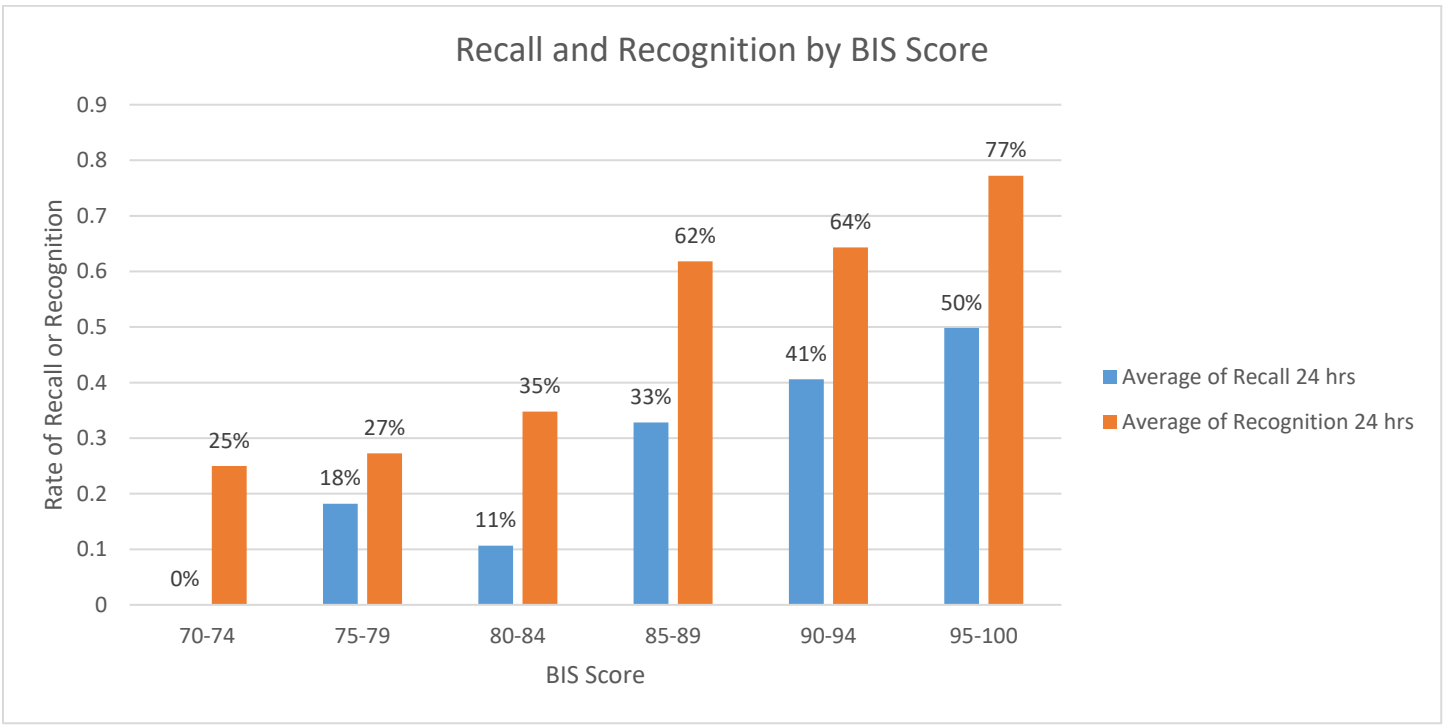
Recall and Recognition by BIS Score
Rate of Recall or Recognition
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0%
25%
18%
27%
11%
35%
33%
62%
41%
64%
50%
77%
70-74
75-79
80-84
85-89
90-94
95-100
BIS Score
Average of Recall 24 hrs
Average of Recognition 24 hrs

Perioperative Anesthesia-13 The Impact of Perioperative Sleep Health on Patient-Centred Outcomes Following Elective Major Joint Arthroplasty - A Systematic Review

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Introduction: Sleep health disruptions have been associated with heightened pain perception and poor quality of life in the general population. However, this association has not been evaluated in the perioperative setting, where surgical trauma and inadequate pain negatively impacts quality of recovery and functional outcomes. The objective of this qualitative systematic review was to evaluate the impact of perioperative sleep health disruption on patient-centred outcomes such as pain control, functional recovery and quality of life following total joint arthroplasty.

Methods: A search of all electronic databases including: Medline, Medline In-Process, ePUB, Embase, CCTR, CDSR, PsychINFO, Biosys Previews, Web of Science (Clarivate), Scopus (Elsevier), PubMed, ClinicalTrials.gov, and WHO ICTRP was conducted from database inception to February 15, 2019. Inclusion criteria were observational studies (including cohort, cross-sectional, and case-control) and randomized controlled trials of patients undergoing major joint arthroplasty in the lower limb with mention of sleep health and pain as measures or outcomes of interest. Article screening and data extraction were conducted by 2 independent reviewers, with all conflicts reviewed and resolved by the principal investigator. Critical appraisal and risk of bias were assessed using the Cochrane Risk of Bias Tool (RCTs) and RoBANS tool (observational studies). Patient-centered postoperative outcomes including sleep, pain intensity and perception for acute and persistent pain, quality of life, functioning, and recovery were extracted. Sleep health domains that were assessed included sleep quality and sleep patterns-total sleep time, sleep latency, night awakenings, and sleep efficiency. Qualitative literature review was performed.

Results: Out of the initial 28,500 studies identified, 17,651 were assessed for eligibility. Of these, 31 articles evaluating 5,247 patients were included. Ten of these articles were randomized control trials RCT and the rest were observational studies. Majority of the studies had a low risk of bias, and high risk of bias resulted mainly for failing to account for confounders such as sleep environment and external factors (Figures 1a and 1b). There was considerable heterogeneity observed in the choice of validated tools used to assess sleep health, pain, functioning, and quality of life (Tables 2a, 2b, and 3). Nevertheless, we aggregated data on sleep health domains to assess their associations with patient-centred outcomes. From the included studies, 29/31 (94%) looked at sleep outcomes [predominantly sleep efficiency (45%), sleep duration (39%), and sleep satisfaction and/or quality (39%)] with 1/31 (3%), 18/31 (58%), and 10/31 (32%) assessing preoperative, postoperative, and intraoperative sleep outcomes, respectively. Most studies (28/31,90%) examined pain outcomes (most commonly pain intensity) with 0 (0%), 12 (39%), and 16 (52%) assessing preoperative, postoperative, and perioperative pain outcomes respectively. Nearly half of the included studies included measures of physical functioning (42%). Poor sleep quality was associated with worse pain and functional recovery outcomes in observational studies (Table 2a and 2b). Of the eight RCTs (Table 3) involving use of a pain intervention post-operatively (i.e. rofecoxib, diclofenac and gabapentin), 4 (50%) reported an improvement in postoperative sleep. Similarly, of the two RCTs involving a sleep intervention (i.e. melatonin, zolpidem), 1 (50%) reported improved postoperative analgesia reported improved analgesia post-operatively.

Conclusion: Significant heterogeneity was observed in the use of validated tools to assess sleep health in the perioperative setting. Furthermore, sleep health disruption, especially patient-reported sleep quality, was associated with worsening of acute as well as persistent post-surgical pain, physical functioning, and quality of life. More research is needed to comprehensively assess sleep health as a predictive factor for relevant patient centred outcomes.

Figure 1a. Risk of Bias Assessment Tool for Non-Randomized Studies Table

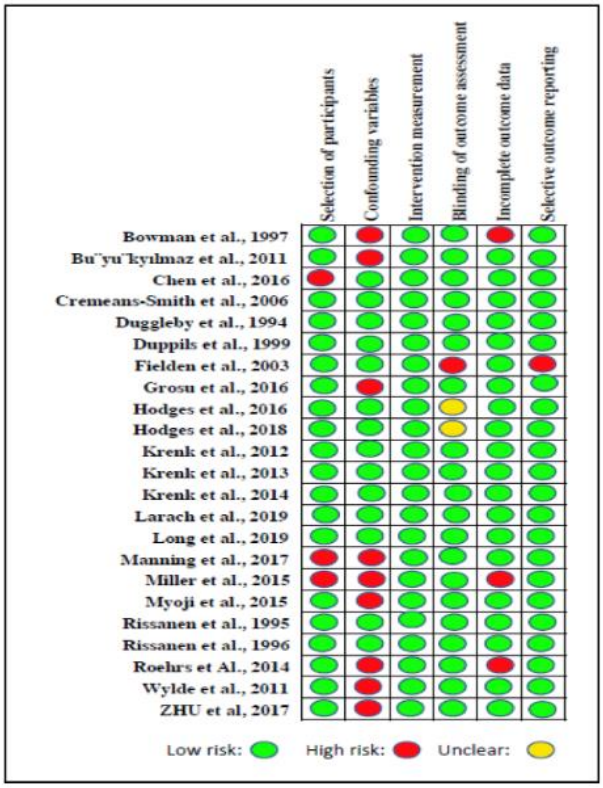

Figure 1a. RoBANS (Risk of bias assessment tool for non-randomized studies) summary table among observational studies evaluating sleep health association, at various different stages of surgical setup, with postoperative pain outcomes and pain-related impacts on physical functioning and quality of life.

Figure 1b. Cochrane Risk of Bias Assessment of Randomized Controlled Trials Table

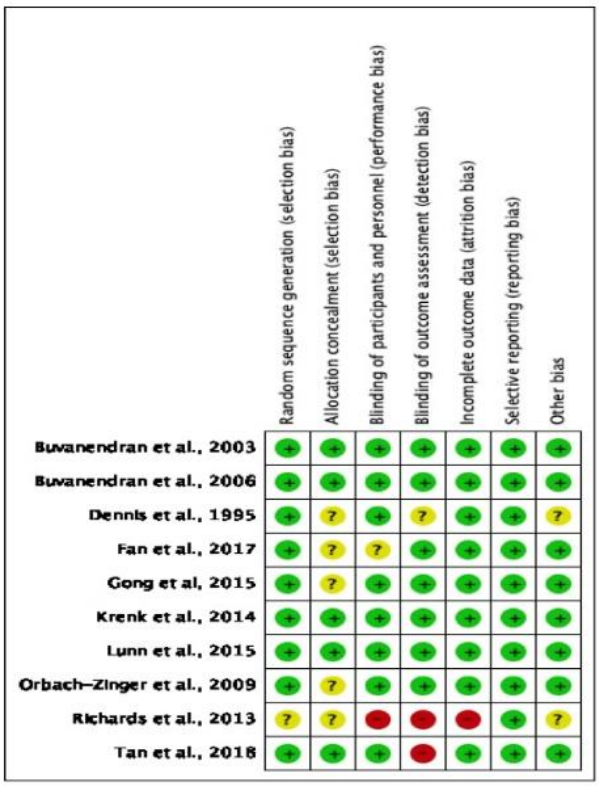

Figure 1b. Cochrane risk of bias summary table among trial evaluating the effects of various interventions in the management of postoperative physical functioning and pain-related sleep disturbance

Table 1. Summary Table of All Included Studies

Study	Study Type		Sleep Domains								Pain Assessment Domains					QOL and Function		
	RCT	Observational	Sleep Quality	Sleep Continuity or Efficiency	Alertness/sleepiness	Sleep Duration (TST)	Pre-operative Sleep	Post-operative Sleep	Sleep Domain Correlation with QOR, QOL, and/or Pain	Validated Tools for Sleep measurement	Pain Intensity	Pre-operative Pain	Post-operative Pain	Pain Correlation with Periop Sleep, Functioning, or QOL	Validated Tools for pain measurement	Overall QOL	Validated Tools for QOL measurement	PhysicalFunctioning
Bowman et al., 1997		*	*					*		*	*	*	*		*			
Buvanendran et al., 2003	*		*	*				*			*	*	*	*	*			*
Buvanendran et al., 2006	*		*					*			*	*	*		*			*
Büyükyılmaz et al., 2011		*	*	*	*	*		*	*	*	*		*	*	*			
Chen et al., 2016		*	*	*	*		*	*		*	*	*	*		*			
Cremeans-Smith et al., 2006		*	*	*	*	*	*	*	*	*	*	*	*	*	*			*
Dennis et al., 1995	*		*	*		*		*			*		*		*			*
Duppils et al., 1999		*																
Fan et al., 2017	*		*				*	*		*	*	*	*		*			*
Fielden et al., 2003		*	*	*	*	*	*	*	*	*								
Gong et al., 2015	*		*	*		*		*	*	*	*		*	*	*			*
Grosu et al., 2016		*	*					*		*	*	*	*	*	*	*		
Hodges et al., 2016		*																
Hodges et al., 2018		*	*			*		*	*		*	*	*	*	*	*		*
Krenk et al., 2012		*	*		*	*	*	*		*	*	*	*		*			
Krenk et al., 2013		*	*			*		*		*	*	*	*		*			*
Krenk et al., 2014	*		*	*		*	*	*		*	*	*	*		*			
Krenk et al., 2014		*	*	*	*	*		*		*	*		*		*			
Larach et al., 2019		*	*				*	*		*	*	*	*		*			*
Long et al., 2019		*																
Lunn et al., 2015	*		*					*		*	*		*		*			
Manning et al., 2017		*	*	*	*	*	*	*		*								
Miller et al., 2015		*		*		*		*		*	*		*	*	*			
Myoji et al., 2015		*	*	*	*	*	*	*	*	*	*		*		*			
Orbach-Zinger et al., 2009	*		*					*					*		*			
Richards et al., 2013	*		*					*		*	*		*	*	*			*
Rissanen et al., 1995		*	*				*	*	*	*	*	*	*	*	*	*	*	*
Rissanen et al., 1996		*	*				*	*		*	*	*	*		*	*	*	*
Roehrs et Al., 2014		*		*	*	*	*		*	*	*	*	*		*			*
Tan et al., 2018	*		*	*				*			*		*	*	*			*
Wylde et al., 2011		*	*	*				*			*	*	*	*	*			
ZHU et al, 2017		*	*					*		*	*		*	*	*			

*RCTs *Observational studies

Table 1. Summary table outlining outcome domains, their correlations, and validated tools used for all included (RCTs and observational) studies.

Abbreviations: QOL- Quality of Life; QOR- Quality of Recovery; RCT- Randomized Controlled Trial; TST- Total Sleep Time

Table 2a. Observational Studies Descriptive Table

Table 2a. Descriptive Summary Table of Observational Studies

Study	Type of Study	Sleep Outcome		Pain Outcome		Results	Confounding (Influencer) Factors
		Measure	Tool	Measure	Tool		
Bowman et al., 1997	Observational: Descriptive Study	Sleep satisfaction	Likert scale (for sleep satisfaction)	Pain perception; Intensity	VAS	Pain scores declined in the postoperative period; intervention worsened delirium, which, inturn, impacted sleep	Cohort type; age; gender; unequal sample sizes
Büyükyılmaz et al., 2011	Observational: Descriptive Correlational (Cohort) Study	Sleep quality, latency, effiency, duration, disturbance,	PSQI	Pain intensity	VAS 10 cm; MPQ-SF; PPI index; BPI	Correlation between postoperative pain intensity and quality of sleep; Most significant contributing factor to poor sleep quality was pain	Variablility in types of surgery
Chen et al., 2016	Observational: Prospective Cohort	latency, effiency, duration, disturbance, daytime sleepiness	PSQI; ESS	Pain intensity	VAS 10 cm	Decrease pain intensity 4-weeks, 6 weeks, 3-mo, 6-mo postoperatively; no correlation between sleep quality and pain; Initial decrease in sleep quality postoperatively with gradual improvement overtime	-
Cremeans-Smith et al., 2006	Observational: Prospective Cohort	Sleep quality, latency, effiency, duration, disturbance, daytime	PSQI	Pain frequency	AIMS2	Positive relationship between postop sleep disurbance, pain intensity, and functioning limitation;: Postop sleep disruption mediated the relationship between pain and functional limitations; increase pain intensity is associated	-
Duggleby et al., 1994	Observational: Cohort	Sleep disturbance	No validated tool	Pain intensity	VAS 10 cm	Decrease in pain and sleep disturbance postoperatively; significant correlation of pain on sleep disturbance	-
Duppils et al., 1999	Observational: Cohort	-	-	-	-	Sleep and pain were not outcomes of assessment in this study	
Fielden et al., 2003	Observational: Cohort	Sleep quality; daytime sleepiness; sleep duration	ESS; Sleep questionnaire			Postoperatively, sleep duration increased by 20 minutes; improvement in sleep quality and sleep effieciency for elderly patients compared to preoperative levels;	-
Grosu et al., 2016	Observational: Prospective Cohort	Sleep quality	BPI	Pain intensity	MPQ-SF; BPI; VDS	Positive evolution of pain intensity postoperatively; Significant correlation between all aspects of postop pain on sleep quality	Depression; gender
Hodges et al., 2016	Observational: Longitudinal Cohort	Not applicable	Not applicable	Not applicable	Not applicable	-	-
Hodges et al., 2018	Observational: Longitudinal Cohort	Sleep quality	Sleep questionnaire	Pain intensity	WOMAC	Postoperative sleep disruption correlated with fatigue; fatigue correlated with QOL; correlation between pain, sleep, fatigue, and	-

Table 2b. Observational Studies Descriptive Table

Table 2b. Descriptive Summary Table of Observational Studies

Study	Type of Study	Sleep Outcome		Pain Outcome		Results	Confounding (Influencer) Factors
		Measure	Tool	Measure	Tool		
Krenk et al., 2012	Observational: Prospective Cohort	Sleep quality	EEG; AASM; hypnogram; PSQI	Pain intensity	VAS	No association between postoperative sleep disturbance and level of pain; postoperative pain affected sleep; sleep quality worsened postoperatively	-
Krenk et al., 2013	Observational: Cohort	Overall sleep	Actigraphy; sleep diary	Pain intensity	10cm VAS	No association between postoperative pain, activity or sleep parameters; inital increase in pain followed by improvement postoperatively; postop increase daytime sleepiness and decrease nighttime sleep duration	-
Krenk et al., 2014	Observational: Cohort	Sleep quality, latency, effiency, duration, disturbance	PSQI	Pain intensity	NPRS	No statistical difference in patients with and without POCD and pain and sleep quality postoperatively	-
Manning et al., 2017	Observational: Prospective Cohort	Sleep quality; disturbance; habits; daytime sleepiness	ESS; Subjective sleep questionnaire			Sleep disturbance increased immediate postop period; improvement in sleep quality gradually chronic postop period;	Gender; patient anticipation of outcome of interest
Miller et al., 2015	Observational: Cohort	Sleep effieciency; duration; quality	Actigraphy	Pain intensity	10cm VAS	Immediate postoperative period- increased pain intensity correlated with decreased sleep duration	Surgery type
Myoji et al., 2015	Observational: Cohort	Sleep duration; sleep-wake rhythm	Actigraphy; questionnaire	Pain intensity	10cm VAS	Pain intensity improved postoperatively from preop levels; postoperative sleep time associated with pain intensity levels; increase sleep time caused decrease in pain intensity	Gender
Rissanen et al., 1995	Observational: Cross-sectional	Sleep quality	NHP	Pain intensity	HRQOL; NHP	Improvement in pain and physical ability in postop group; with inturn improved sleep quality, QOL and physical function (ADL) in postop group vs preop group;	-
Rissanen et al., 1996	Observational: Prospective Cohort	Sleep quality	NHP	Pain intensity	NHP; HRQOL; ADL	Improvements in QOL, functioning ability, pain intensity, sleep quality, and physical ability- gradually following surgery	-
Roehrs et Al., 2014	Observational: Randomized Feasibility Study	Sleep hygiene; sleep-wake timing; TST; TIB; sleep quality; daytime sleepiness	Actigraphy; sleep diary (1 week preop; concurrent); ESS	Pain intensity	10cm VAS	Postoperative pain intensity was lower with sleep extension; Preop sleep exension correlated with (improved) postop pain, physical function, QOL vs no preop sleep extension which resulted in greater postop pain	Duration of study
Wylde et al., 2011	Observational: Cohort	Sleep disturbance	Nonvalidated sleep questionniare	Pain intensity	10cm VAS; MPQ-SF	Pain intensity was greater preop vs postop; postop pain intensity was highest POD1, causing the greatest sleep disturbance; Decline in intensity POD2 POD3; Acute postop pain was associated with sleep disturbance	Gender; Anesthesia type administered
ZHU et al, 2017	Observational: Cross-sectional	Sleep quality; sleep disturbance	BPI questionnaire	Pain intensity	BPI; PPSMB	Greatest postop pain intensity at POD1 with gradual decline thereafter; negative correlation of pain intensity on sleep quality and disturbance: pain induced sleep disturbance	Unequal cohort groups; age; gender

Table 2a and 2b. Brief descriptive table for all included observational, highlighting sleep and pain outcome, the measures evaluated, the tools used for measurement, any confounding factors, and the conclusive result.

Sleep Tools Abbreviations: AASM- American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events; BPI- Brief Pain Inventory questionnaire EEG- Electroencephalogram; ESS- Epworth Sleepiness Scale; NHP- Nottingham Health Profile; PSQI- Pittsburgh Sleep Quality Index

Pain Tools Abbreviations: ADL- Activities of Daily Living; BPI- Brief Pain Inventory questionnaire; HRQOL- Health Related Quality of Life; MPQ-SF- Short-form McGill Pain Questionnaire; NHP- Nottingham Health Profile; NPRS- Numeric Pain Rating Scale; PPI- Present Pain Intensity Index; PPSMB- Postoperative Pain Self-Management Behaviour; VAS- Visual Analog Scale; WOMAC- Western Ontario and McMaster Universities Osteoarthritis Index

Other Abbreviations: POCD- Postoperative Cognitive Decline; QOL- Quality of Life

Table 3. Randomized Controlled Trials Descriptive Table

Desciptive summary of Randomized Contolled Trials

Study	Type of Study	Sleep Outcome		Surgical Time-Period	Pain Outcome		Surgical Time-Period	Results
		Measure	Tool		Measure	Tool		
Buvanendran et al., 2006	RCT	Sleep disturbance	No validated tool	Postoperative sleep (POD 1)	Pain intensity	VAS 10 cm	Preoperative and intraoperative pain (3, 9, 24, and 30-h after surgical incision)	Intervention decreased postoperative pain; positive correlation of VAS scores with CSF PEGE2 and IL-6 levels and negative correlation with postoperative sleep disturbance;
Dennis et al., 1995	RCT	Sleep duration; sleep disturbance	No validated tool	Postoperative sleep (24-hr postop)	Pain intensity	VAS 10 cm	Postoperative pain (24-hrs postop)	No difference in pain intensity before and after intervention; no correlation of sleep and pain; no significance in postoperative sleep
Fan et al., 2017	RCT	Sleep quality	100mm VAS	Preoperative (1 day preop) and postoperative sleep (POD 1,3,5,7)	Pain intensity	VAS 10cm	Preoperative (1 day preop) and postoperative pain (POD 1, 3, 5, 7)	No difference in pain intensity preoperatively and postoperatively between both groups; decrease postoperative sleep quality in placebo group; increase postop sleep quality in intervention group
Gong et al., 2015	RCT	Sleep quality	PSG; objective sleep assessment	Poatoperative sleep (POD 1, 3, 5, 7, 11, 14)	Pain intensity	VAS	Post-operative pain (POD 1, 3, 5, 7, 11,14)	Improved postop sleep quality in intervention group decreased pain intensity; improved pain intensity improved QOR; positive correlation between improved sleep quality and pain on functional recovery
Krenk et al., 2014	RCT	Sleep quality; sleep stages	EEG; self report	Preoperative (1 night, 3 days prior to surgery) and postoperative	Pain	10cm VAS	Preoperative (1 night, 3 days prior to surgery) and postoperative	Postoperative pain intensity and opioid consumption did not change with intervention; no improvement in sleep stages; significant improvement in postop sleep quality and fatigue for intervention group
Lunn et al., 2015	RCT	Sleep quality	11-p NRS	Postoperative sleep (POD 0-6)	Pain intensity; ambulation	100mm VAS	Post-operative pain (4, 6, 24, 28, 32, 48 hours postoperatively & POD 3-6)	No difference postoperatively in pain level and ambulation in both groups; improvement in sleep quality in acute postoperative period for both groups
Orbach-Zinger et al., 2009	RCT	Sleep Quality	Sleep Quality Questionnaire		Pain intensity	VAS		Intervention and placebo showed no improvement in postop pain; no impact on postoperative sleep quality
Richards et al., 2013	Randomized open label	Sleep quality	BPI-SF	Postoperative sleep (0-48 hours after first dose)	Pain Intensity	NPRS, BPI-SF	Postoperative pain (0-48 hours after first dose)	Postoperative pain interference with physical activity, sleep quality, and mood was lower in intervention (morphine) group;
Tan et al., 2018	RCT	Sleep disturbance	non-validated questionnaire	Postoperative sleep (POD 1, 2, 3)	Pain intensity	10cm VAS	Postoperative pain (2, 4, 8, 12, 24, 48, 72 hours postoperatively & upon discharge)	Postoperative pain was lower in femoral nerve block group vs ACB group; positive correlation of pain intensity on improved physical functioning (strength); no impact or association of pain on sleep in both groups

Table 3. Brief descriptive table for all randomized controlled trials, highlighting sleep and pain outcome, the surgical time-period these outcomes were assessed in, the measures evaluated, along with the tools used for the measurements, and the conclusive results.

Sleep Tools Abbreviations: BPI-SF- Brief Pain Inventory-Short-Form; EEG- Electroencephalogram; NRS- Numeric Rating Scale; PSG- Polysomnography; VAS- Visual Analog Scale

Pain Tools Abbreviations: BPI- Brief Pain Inventory; NPRS- Numeric Pain Rating Scale; QOR- Quality of Recovery; VAS- Visual Analog Scale

Other Abbreviations: ACB- Adductor Canal Block; CSF- Cerebrospinal Fluid; IL-6- Interleukin 6; PGE2- Prostaglandin E2; POD- Postoperative Day; RCT- Randomized Controlled Trial

Respiration

Respiration-1 Oral ginger prevents gut microbiome changes in house dust mite (HDM) antigen-induced allergic asthma in mice

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Introduction: Microbial dysbiosis in the gut and the lung is increasingly recognized as being associated with the incidence and severity of asthma [1]. The efficacy of medications, especially orally administered ones, may be influenced by the patient's microbial composition. Despite current treatments for asthma (e.g., β-agonists and inhaled corticosteroids), approximately 40% of severe asthmatics have inadequate control of the disease, and many use alternative medicines, like ginger, for symptom management. Previously, we demonstrated that crude ginger and its purified components, including 6-shogaol, relax airway smooth muscle (ASM) ex vivo [2, 3] and reduce lung inflammation in vivo [4]. We hypothesize that orally administered ginger decreases inflammatory changes in the murine house dust mite (HDM) antigen model of asthma in part by preventing disruption of the commensal gut and lung microbiota.

Methods: Mouse ginger pretreatment and HDM sensitization: All animal studies were approved by the IACUC. Wild-type C57BL/6J 8-12 week-old male mice were co-housed. Mice were briefly anesthetized with isoflurane and pretreated with ginger (40 mg/kg in 2% hydroxypropyl methylcellulose w/v and 2.5% polyethylene glycol w/v) or vehicle via oral gavage once a day for 3 weeks. After this 3-week pretreatment period, mice were randomized to receive intranasal HDM antigen (30 µg in 25 µL PBS) or vehicle once a day, while continuing oral ginger or vehicle twice each day. Fecal pellets were collected at the beginning and end of treatment and stored (-80 [sup]o[/sup]C). Bronchoalveolar lavage: At the end of the treatment period, anesthetized mice were tracheostomized for bronchoalveolar lavage (BAL) (2 mL PBS per mouse). Samples were centrifuged at 800 g x 10 min to remove mucus and cellular debris, and the supernatant was centrifuged at 22 000 g x 30 min to pellet microbial particles, which were resuspended in PBS (100 µL) and stored (-80 [sup]o[/sup]C). Microbiome sample preparation and sequencing: DNA extraction, amplicon library preparation, cleaning, and dilution were performed by the Center for Metagenomics and Microbiome Research (CMMR) at Baylor College of Medicine. Sequence data were analyzed using ATIMA (Agile Tool for Incisive Microbial Analyses).

Results: Intranasal exposure of mice to HDM antigen for 10 days (Fig. 1A) induced a strong inflammatory response characterized by peribronchial and perivascular leukocyte infiltration. HDM also led to increased BAL total cell counts, primarily eosinophils and lymp

Conclusion: Disturbances in the gut microbiome are linked to an increased incidence and severity of asthma. Ginger and its components have been shown to be protective in the allergic inflammatory model of murine asthma [4]. Here we showed that the gut microbial commu

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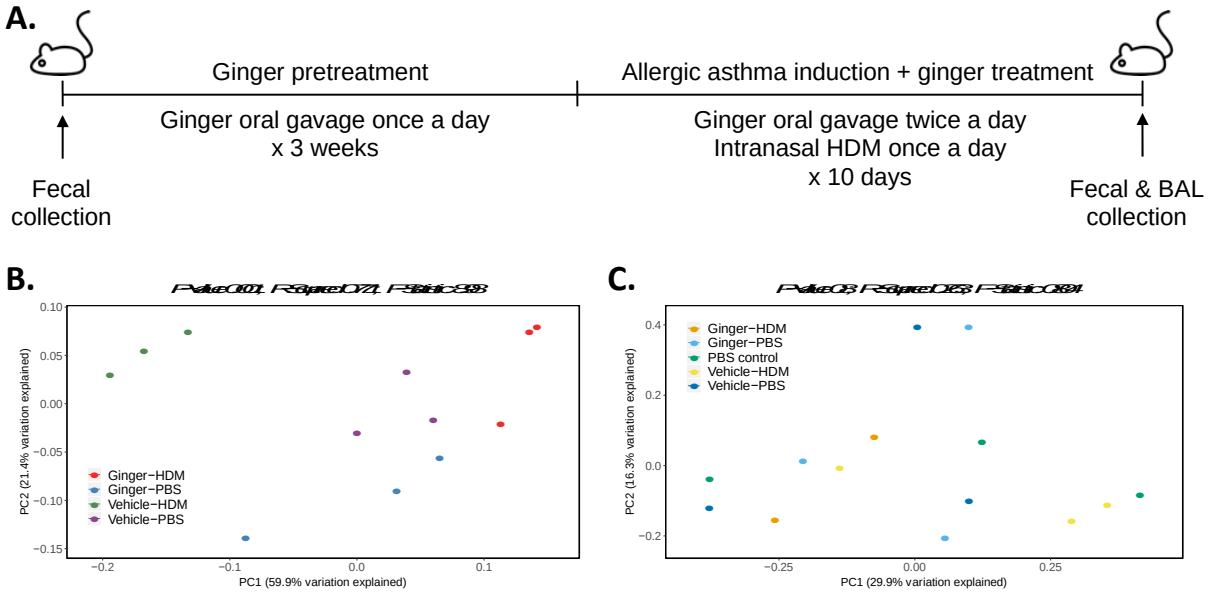

Figure 1. House dust mite (HDM) antigen induces allergic response in lungs and a shift in the gut microbiota, which is reversed with oral ginger. Experimental schematic is shown in A. Principal coordinate analysis (PCoA) of weighted UniFrac distances was performed on controls (Vehicle-PBS), HDM (Vehicle-HDM), ginger (ginger-PBS), and ginger + HDM (Ginger-HDM) samples (B, C). HDM sensitization changes the gut microbiota significantly (B) but not the lung microbiota (C). The closer two points are to each other, the more similar they are. Variance among samples is represented by the X and Y axes, where the percentage noted represents the proportion of all variance represented on that axis. The higher the number, the greater the dissimilarity a given distance along that axis represents. n = 3.

Technology, Computing and Simulation, Equipment Monitoring

Technology, Computing and Simulation, Equipment Monitoring-1 Impact of patient position and artifacts on intraoperative processed electroencephalogram monitoring of burst suppression.

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Introduction: Burst suppression is a waveform pattern observed through electroencephalography (EEG) that is linked to a diminished level of metabolic brain activity [1]. Recent evidence suggests that intraoperative burst suppression during general anesthesia may be associated with a higher incidence of postoperative delirium [2], however the mechanism for this association is undefined. Accurately quantifying burst suppression is important to understanding it's impact on postoperative cognitive outcomes. A previous study [3] suggested that burst suppression determined through a processed EEG is less accurate in predicting postoperative delirium when compared to off-line visual analysis by neurologists. We performed a follow-up study to further investigate the reasons for discordance between burst suppression as measured by a machine vs. neurologist.

Methods: The inclusion criteria were patients ≥ 40 years of age, undergoing major, elective, non-cardiac surgery requiring general anesthesia with an expected hospital stay of at least three days. All patients were monitored intraoperatively with continuous processed EEG using a SEDLine® monitor. The raw EEG data were reviewed visually in an off-line setting by neurologists in 30-second epochs, and each epoch was assigned an estimated duration of burst suppression in whole seconds. Burst suppression was quantified by the SEDLine® monitor in the form of the burst suppression ratio (BSR). A computer algorithm was used to convert the BSR into a raw duration (seconds) of burst suppression and was partitioned into the same 30-second epochs reviewed by the neurologists. SEDLine® generated estimates were considered to be accurate if there was a <10% difference in duration when compared with the neurologists' estimation. Each 30-second epoch was also visually assessed for significant signal artifact (such as wavering baseline, electro-cautery interference, etc.) lasting for ≥3 seconds within a single 30-second epoch.

Results: 23,354 30-second epochs (194 hours) of intraoperative EEG data were reviewed across 45 patients. 84.5% (±17.4%) of the 23,354 epochs analyzed had processed EEG estimates of burst suppression concordant with the neurologists' estimates. Epochs with artifact were significantly more likely to have discordance between the SedLine® and neurologists' estimates (P<0.0001, Table 2). Cases where the patient was prone during surgery had significantly more epochs that were discordant (P<0.0001, Table 3). Prone patients also had a significantly higher incidence of EEG artifact (P<0.0001, Table 4).

Conclusion: Processed EEG monitoring is less accurate in measuring intraoperative burst suppression when there is increased EEG artifact and when the patient is prone, generally as an association of having increased artifact in that position. These are potentially important limitations when using real-time processed EEG for monitoring burst suppression.

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Impact of patient position and artifacts on intraoperative processed electroencephalogram monitoring.

Table 1: Summary		
	Epochs in Agreement (>10% error)	**Epochs with Artifact (>3 second)**
All patients (n=45)	84.5% (±17.4%)	12.1% (±11.3%)
Prone Surgery (n=15)	75.2% (±14.5%)	20.9% (±15.8%)
Supine Surgery (n=30)	91.5% (±10.8%)	7.4% (±4.4%)

Table 2: Chi-square analysis – Artifact presence vs. Epoch Agreement			
Artifact vs. Agreement	**Epochs that Agree** Error ≤ 10% (n = 19618)	Epochs that **Disagree** Error > 10% (n=3736)	**P- Value**
Epochs with Artifact (n=2613)	2043	570	P = 0.0001
Epochs without Artifact (n=20741)	17575	3166	

Table 3: Chi-square analysis - Surgery Position vs Epoch Agreement			
Surgery Position vs. Agreement	**Epochs that Agree** Error ≤ 10% (n = 19717)	**Epochs that Disagree** Error > 10% (n=3637)	**P-value**
Epochs from **Prone Cases** (n=9132)	7010	2122	P < 0.0001
Epochs from **Supine Cases** (n=14222)	12707	1515	

Table 4: Chi-square analysis - Surgery Position vs Artifact Presence			
Surgery Position vs. Artifact	**Epochs with Artifact** (n=2613)	**Epochs without Artifact** (n=20741)	**P-value**
Epochs from Prone Cases (n=9132)	1572	7560	P < 0.0001
Epochs from Supine Cases (n=14222)	1041	13181	

Technology, Computing and Simulation, Equipment Monitoring-2 Lag time in drug delivery by continuous intravenous infusion: direct comparison of peristaltic and syringe pump performance reveals similar effects of dead volume but different startup characteristics

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Introduction: Drug delivery by continuous infusion is prone to time lags between the initiation of an infusion and achievement of the intended delivery rate [1]. At least 3 factors contribute to time lags: 1) dead volume size, (2) the ratio between total system flow and dead volume, and (3) startup delay [2,3]. Dead volume is the total volume contained within catheters, tubing, and connectors from the point where drug and carrier flow streams meet to the patient's blood. Startup delay refers to the intrinsic mechanical properties of the system that the pump must overcome when the pump is turned on [4]. Two common infusion pump types are peristaltic and syringe pumps. Peristaltic pumps use linearly arranged rollers to sequentially compress the tubing of an infusion set, causing forward displacement of fluid in discrete boluses. Syringe pumps use a piston to push a plunger through a fluid-filled syringe. They are preferred for low flow rate delivery (< 5 mL/hr) because continuous flow improves accuracy. The potential clinical impact of long lag times to achieve intended drug delivery rates is a recognized safety concern [5]. We directly compare the performances of a representative peristaltic pump and a representative syringe pump on delivery lag time at clinically relevant flow rates.

Methods: We used established methods [6,7] to quantify delivery of methylene blue (MB, 0.1 mg/mL). Our setup contained two peristaltic pumps (Sapphire; QCOR Medical) or two syringe pumps (Medfusion 2500; Smiths Medical). One pump delivered MB as the model drug, while the other delivered saline as the carrier. In an adult model system, the carrier pump was set to a rate of 10 mL/h and the drug pump was set to a rate of 3 mL/h (5 mcg/min). In a pediatric model system, the carrier pump was set to a rate of 1.5 mL/h and the drug pump was set to a rate of 0.5 mL/h (0.833 mcg/min). A manifold connected the drug and carrier fluid pathways to the distal lumen of a 7Fr triple lumen adult catheter or a 5Fr double lumen pediatric catheter, with manufacturer reported dead volumes of 0.39 mL and 0.26 mL, respectively. MB delivery was quantified by spectrophotometric absorbance. Delivery curves were modeled and compared by multivariable fractional polynomial methods. Post-hoc pairwise comparisons were performed using two sample t-test. The time required to reach 5% (T5), 50% (T50), and 95% (T95) of the intended delivery rate was estimated and reported.

Results: Effects of Startup + Dead Volume The combined effects of startup delay and dead volume on the time required to reach a target delivery rate were studied by turning on the drug pump to initiate MB flow into an ongoing continuous carrier flow. The time required for the drug pump to overcome startup and for the MB to flow through the dead volume to reach the intended delivery rate was measured. Adult Model: The ability to overcome the combined effects of startup delay and dead volume differed between syringe and peristaltic pumps ($p < 0.001$). T5, T50, and T95 were shorter for the peristaltic pump compared to the syringe pump. Pediatric Model: The ability for the pumps to overcome the combined effects of startup delay and dead volume differed between syringe and peristaltic pumps ($p < 0.001$). T50, and T95 were shorter for the syringe pump, while T5 was shorter for the peristaltic pump. Dead Volume Effects To isolate the time lag due to dead volume from that of startup, the carrier and drug infusion pumps were run separately prior to the experimental start. The drug infusion was then directed into the main fluid pathway. The time required for MB to flow through the dead volume and reach the intended delivery rate was measured. Adult Model: The ability for the pumps to overcome dead volume was overall similar between syringe and peristaltic pumps. Pediatric Model: The ability for the pumps to overcome dead volume was overall similar between the two pumps. The T50 was shorter for the syringe pump, while T5 and T95 were similar.

Conclusion: Dead volume and mechanical startup in carrier-based infusion systems cause substantial time lags to reach intended delivery rates when initiating drug infusions. Peristaltic and syringe pumps are similarly susceptible to dead volume effects. Startup performance differed between peristaltic and syringe pumps; their relative performance may be dependent on flow rate. Clinicians must not expect the two types of pumps to perform interchangeably in terms of mechanical startup.

Reference(s):

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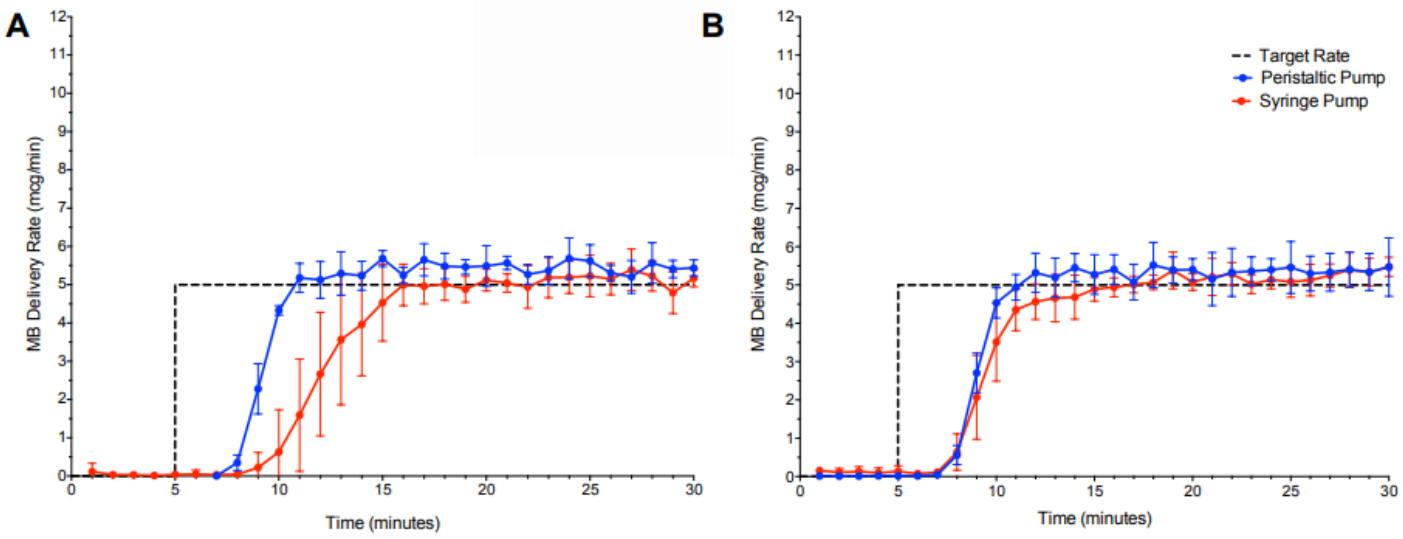

Figure 1. Results from the adult model system. Panel A shows the combined effects of startup delay and dead volume on the initiation of a drug infusion. Panel B shows the effects of dead volume alone on the initiation of a drug infusion.

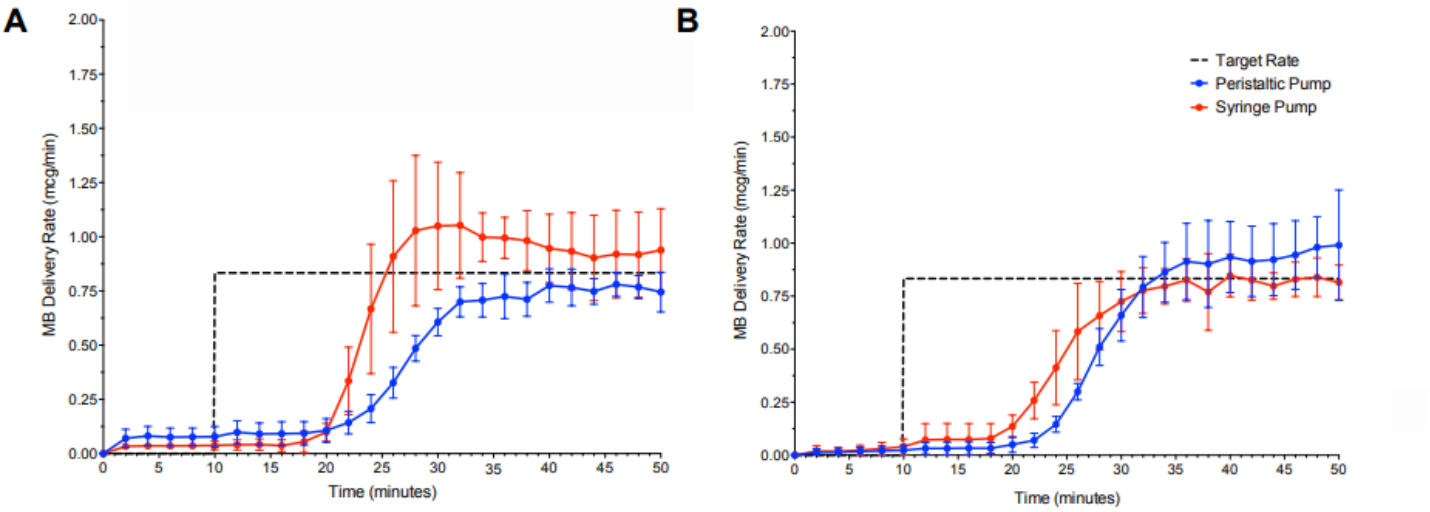

Figure 2. Results from the pediatric model system. Panel A shows the combined effects of startup delay and dead volume on the initiation of a drug infusion. Panel B shows the effects of dead volume alone on the initiation of a drug infusion.

Table 1. Time to achieve 5% (T5), 50% (T50), and 95% (T95) of the intended delivery rate after initiation of a drug infusion in an adult model (13 mL/h total flow)

Startup + Dead Volume Effects		Mean (minutes)		Statistics	
	n	**Peristaltic Pump**	**Syringe Pump**	**Difference [95% CI]**	**P value**
5%	5	2.732	5.064	-3.417 [-4.165, -0.499]	*0.0233*
50%	5	4.104	6.960	-3.687 [-4.974, -0.738]	*0.0196*
95%	5	5.688	10.368	-3.305 [-8.542, -0.818]	*0.0278*
Dead Volume Effects		Mean (minutes)		Statistics	
	n	**Peristaltic Pump**	**Syringe Pump**	**Difference [95% CI]**	**P value**
5%	5	2.476	1.412	1.820 [-0.512, 2.640]	0.138
50%	5	3.928	4.328	-1.315 [-1.191, 0.391]	0.248
95%	5	5.552	6.740	-1.590 [-2.960, 0.584]	0.157

Table 2. Time to achieve 5% (T5), 50% (T50), and 95% (T95) of the intended delivery rate after initiation of a drug infusion in a pediatric model (2 mL/h total flow)

Startup + Dead Volume Effects		Mean (minutes)		Statistics	
	n	**Peristaltic Pump**	**Syringe Pump**	**Difference [95% CI]**	**P value**
5%	8	0.350	4.838	-3.035 [-7.766, -1.211]	*0.0120*
50%	8	17.113	12.909	6.889 [2.905, 5.502]	*< 0.001*
95%	8	29.485	15.987	5.762 [8.192, 18.803]	*< 0.001*
Dead Volume Effects		Mean (minutes)		Statistics	
	n	**Peristaltic Pump**	**Syringe Pump**	**Difference [95% CI]**	**P value**
5%	8	6.810	3.430	1.351 [-2.034, 8.794]	0.200
50%	8	17.255	14.603	3.779 [1.045, 4.260]	*0.00500*
95%	8	24.483	19.437	1.830 [-0.973, 11.065]	0.0926

Technology, Computing and Simulation, Equipment Monitoring-3 Applying Three-Dimensional Multi-Objective Optimization to the Perioperative Services

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Introduction: Although the chief objectives of operating room management are to maximize clinical productivity and minimize under and over-utilized time, multi-objective optimization problems are often very challenging to solve. Despite these challenges, considering multiple criteria undoubtedly leads to better informed decisions. With the advent of data science, multi-objective optimization will enable hospital administrators understand the trade-offs between financial and operational measures. Previously, Tsai et al. demonstrated that it is possible to apply performance frontiers as an economic framework to operating room management metrics of under and over-utilized time [1]. In this article, we expand the previous narrative by using multi-objective optimization to extend the two-dimensional analysis with performance frontiers to three dimensions. Herein, we evaluate the Pareto optimality of an ACS service model on General Surgery (GS) by utilizing three metrics: under-utilized time, over-utilized time, and a financial productivity metric.

Methods: The following monthly summed OR management data were extracted from WiseOR® (Palo Alto, CA), for two years prior and two years after the October, 2015 ACS implementation: out-of-block minutes, after-hours minutes, and opportunity-unused minutes. Monthly block metrics were calculated as follows: Over-utilized time = After-hours minutes + Out-of-block minutes Under-utilized = Opportunity-unused minutes. From financial reports, we obtained monthly work Relative Value Units (wRVUs) and clinical Full Time Equivalents (FTEs) for faculty of the GS service. As Paine et al. did, we used the wRVU/FTE ratio to quantify the financial impact on the GS service of the implementation of the ACS model of care [2]. Under-utilized time, over-utilized time and productivity over the four-year span were then normalized independently of one another to lie between zero and one. Because this multi-objective optimization was performed in the three-dimensional space, the hyperplanes are thus the two-dimensional planes. In three-dimensional space, we randomly assigned underutilization to the x-axis, overutilization to the y-axis, and productivity to the z-axis. Using the programming language Python, the pre-transition and post-transition data were then plotted on the hyperplanes as shown in Figures 1 and 2. The Pareto-optimal sets are the points in which none of the other solutions are superior in the other objectives represented in the space. In both the two-dimensional and three-dimensional multi-objective analyses, the optimal solutions are those that minimize under-utilized and over-utilized time, but maximize productivity, representing the common challenge of conflicting criteria. To address this issue, the direction of the z-axis representing productivity was reversed. Hence, the Pareto-optimal set consists of the outer edge of points closest to the origin (x, z) = (0, 1) and (y, z) = (0, 1) in two-dimensions and (x, y, z) = (0, 0, 1) in three dimensions. The (x, z) and (y, z) coordinates of the pre- and post-transition Pareto-optimal sets were extracted from the two hyperplanes of Figures 1 and 2 to interpolate quadratic surfaces as shown in Figure 3.

Results: The results show that the GS post-transition Pareto-surface is contained within a much smaller volume of space than the GS pre-transition Pareto-surface. In the (x,y) space, the post-transition surface lies closet to the origin representing optimality, however it is higher in its z-elevation, representing lower productivity than the pre-transition surface. This decrease in productivity is due to significant decrease in after-hours case volume. Paine et al. found that over this transition, GS was increased the number of wRVUs generated during normal-hours to compensate for lost after-hours productivity [4]. Hence, the general surgeons were actually more productive during normal hours in the post-transition period [4].

Conclusion: Pareto optimization allows for evaluation of common issues of under-utilized time and over-utilized time in the context of other variables [3]. The Pareto frontier enables operating room managers to track management metrics and their interdependent interactions across time [4]. There is no limitation to the variables that can be analyzed in the context of multi-objective optimization, but it is up to the model user to define the variables based on outcomes that are goals in the context of their healthcare organization.

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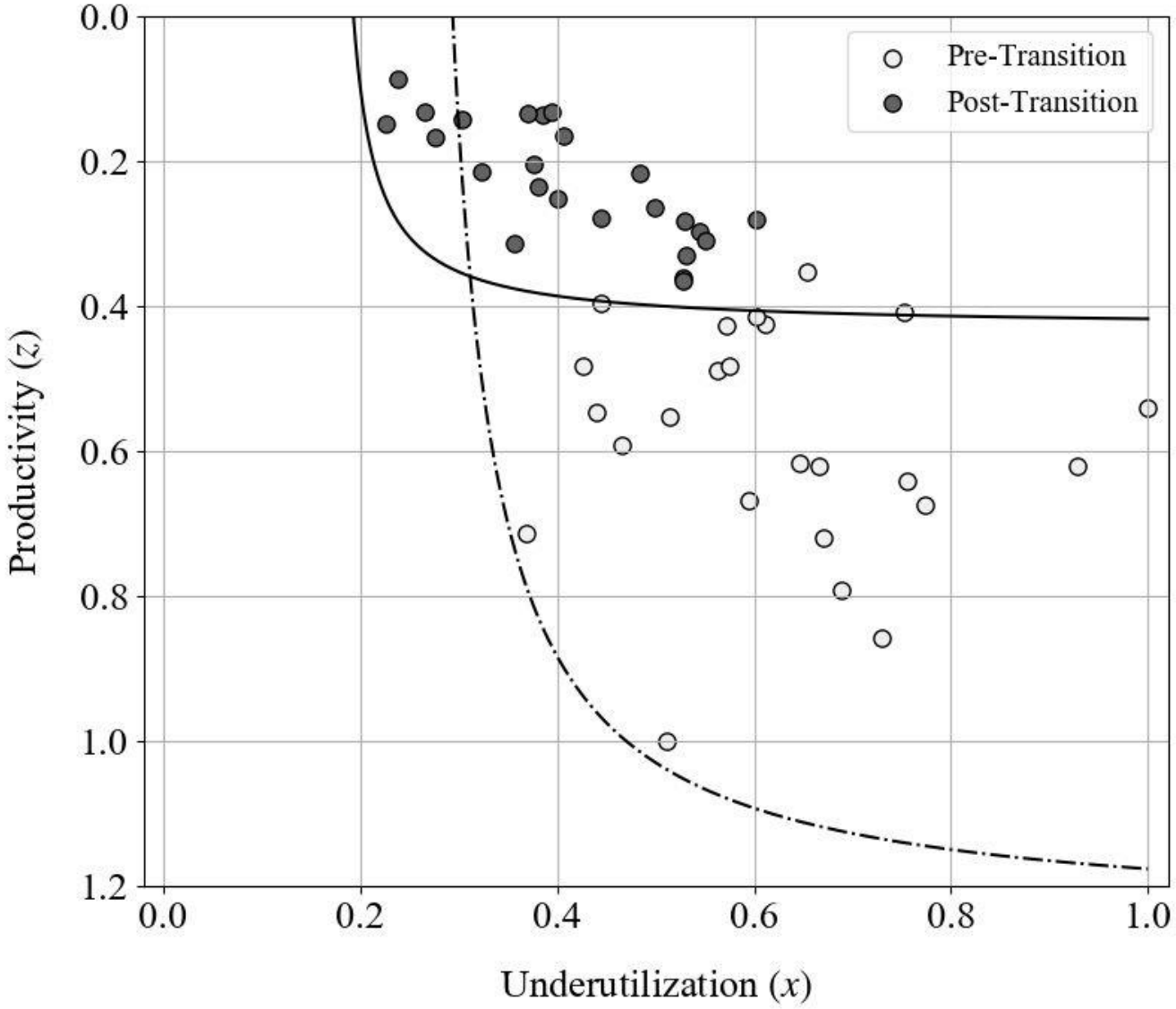
Pre-Transition
Post-Transition
Productivity (z)
Underutilization (x)
0.0
0.2
0.4
0.6
0.8
1.0
1.2

Figure 1

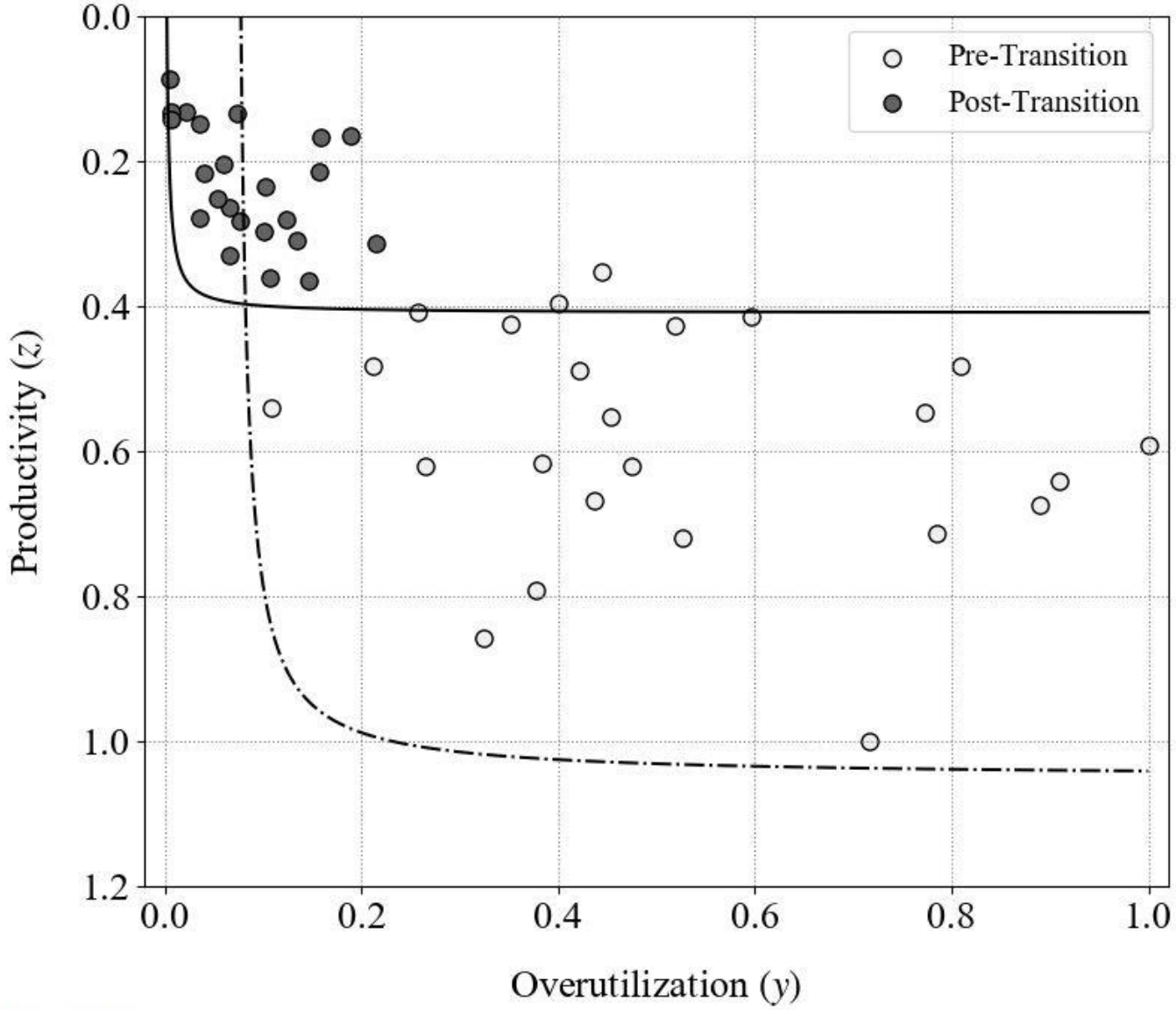
Pre-Transition
Post-Transition
Productivity (z)
Overutilization (y)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
0.0
0.2
0.4
0.6
0.8
1.0

Figure 2

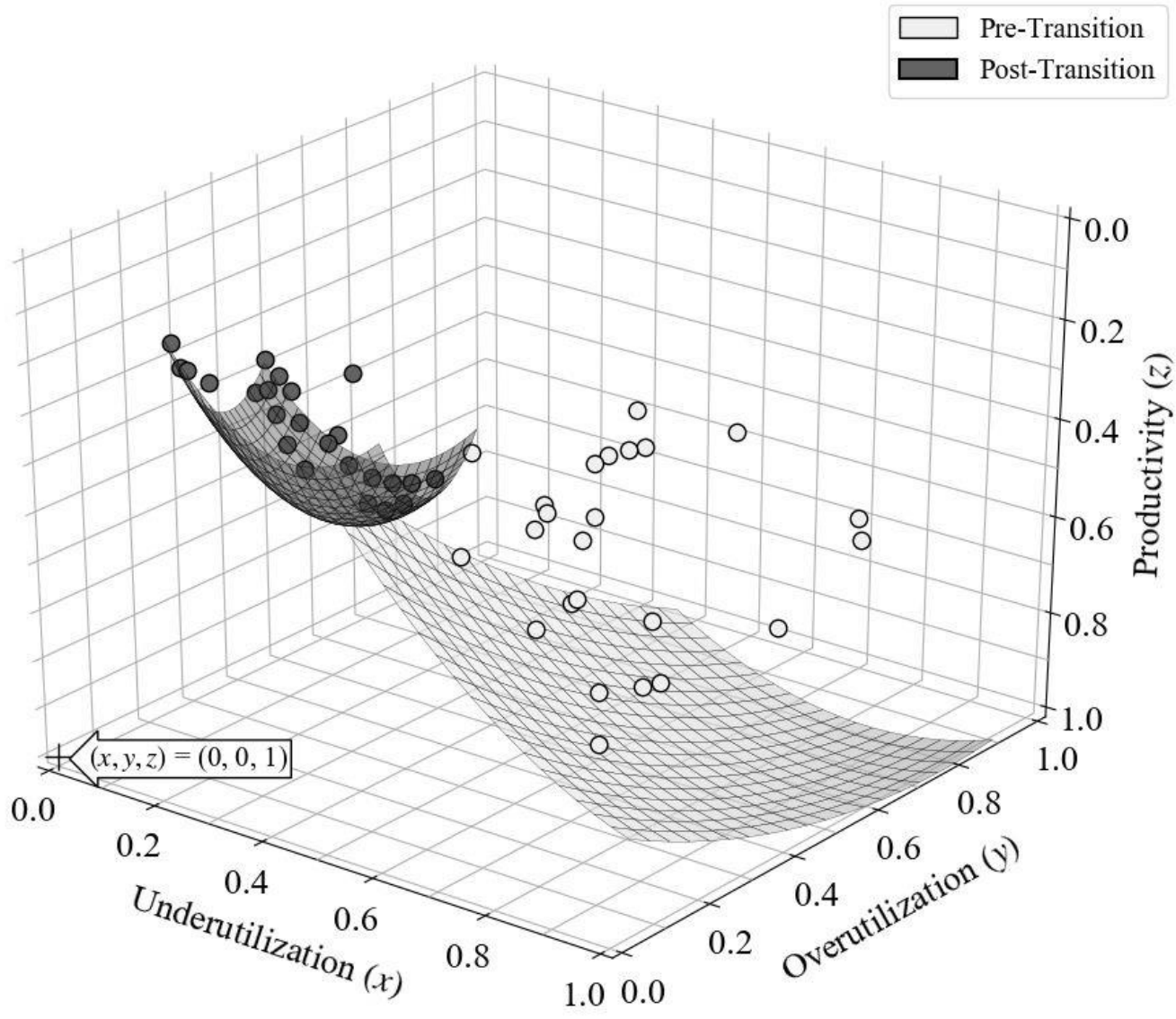
Pre-Transition
Post-Transition
Productivity (z)
0.0
0.2
0.4
0.6
0.8
1.0
(x, y, z) = (0, 0, 1)
Underutilization (x)
Overutilization (y)

Figure 3

Technology, Computing and Simulation, Equipment Monitoring-4 Incidence of Postoperative Residual Neuromuscular Blockade In Cardiac Surgery Intensive Care Unit

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[1]University of Washington, Seattle, WA, [2]University of Washington, Seattle, United States of America

Introduction: There is a paucity of data on the incidence of residual neuromuscular blockade in intubated cardiac surgery patients in the intensive care unit (ICU).(1) The residual neuromuscular blockade is of particular concern for the fast-track cardiac surgery patients, which may increase their risk of post-anesthesia pulmonary complications related to residual paralysis such as hypoxemia and reintubation.(2)

Methods: In a single-center observation study, responses to train-of-four (TOF) stimulation were measured at the time of admission to the cardiothoracic surgery ICU by one of the authors (LB) and before extubation if a trained respiratory therapist was available using an electromyography-based monitor (TwitchView, Blink Device Company, Seattle, WA). The average of two measurements was used for descriptive statistics. The length of mechanical ventilation, communication about neuromuscular blockade to the ICU team, temperature, pH, neuromuscular blocking drug, and reversal drug doses were also recorded.

Results: We measured responses to TOF stimulation in 134 cardiac surgery patients. Eighty-two out of 112 (73%) patients at the time of the arrival to the ICU had a TOF count of 4 (mean TOF ratio 0.76 ±0.26; range 0.11-1.13) while 19 (17%) patients had TOF counts between 1 and 3 and 11 (10%) patients had post-tetanic counts. The mean TOF ratio in 35 patients before extubation was 0.89 ±0.15 (range 0.39-1.05). Forty nine out of 112 (44%) patients had a TOF ratio < 0.9 at the time of arrival to the ICU, while 12 out of 35 (34%) patients had TOF ratio < 0.9 before extubation (Figure). None of the patients were monitored with a twitch monitor or received reversal at the end of their surgery. Thirty-six (27%) out of 134 patients received only an intubating dose of the neuromuscular blocking drug, while 98 (73%) patients received maintenance doses of the non-depolarizing neuromuscular blocking drug in addition to the intubating dose. The mean maintenance dose of vecuronium and rocuronium was 3 ±1 mg and 25 ±7 mg, respectively.

Conclusion: Our study results indicate that residual neuromuscular paralysis in cardiac surgery patients is common at the time of admission to the ICU and before extubation. Our anesthesia providers do not routinely monitor the depth of neuromuscular blockade during cardiac surgery and tend to use large maintenance doses of neuromuscular blocking drugs. Furthermore, our ICU providers do not routinely assess the level of neuromuscular blockade before extubation, which increases the risk of unrecognized residual paralysis in cardiac surgery patients. Assessing the level of neuromuscular blockade with quantitative twitch monitoring in the ICU before extubation and administering reversal drugs when appropriate may eliminate residual neuromuscular paralysis. Alternatively, anesthesia providers should use twitch monitoring during cardiac surgery and reverse patients when appropriate at the end of the case.

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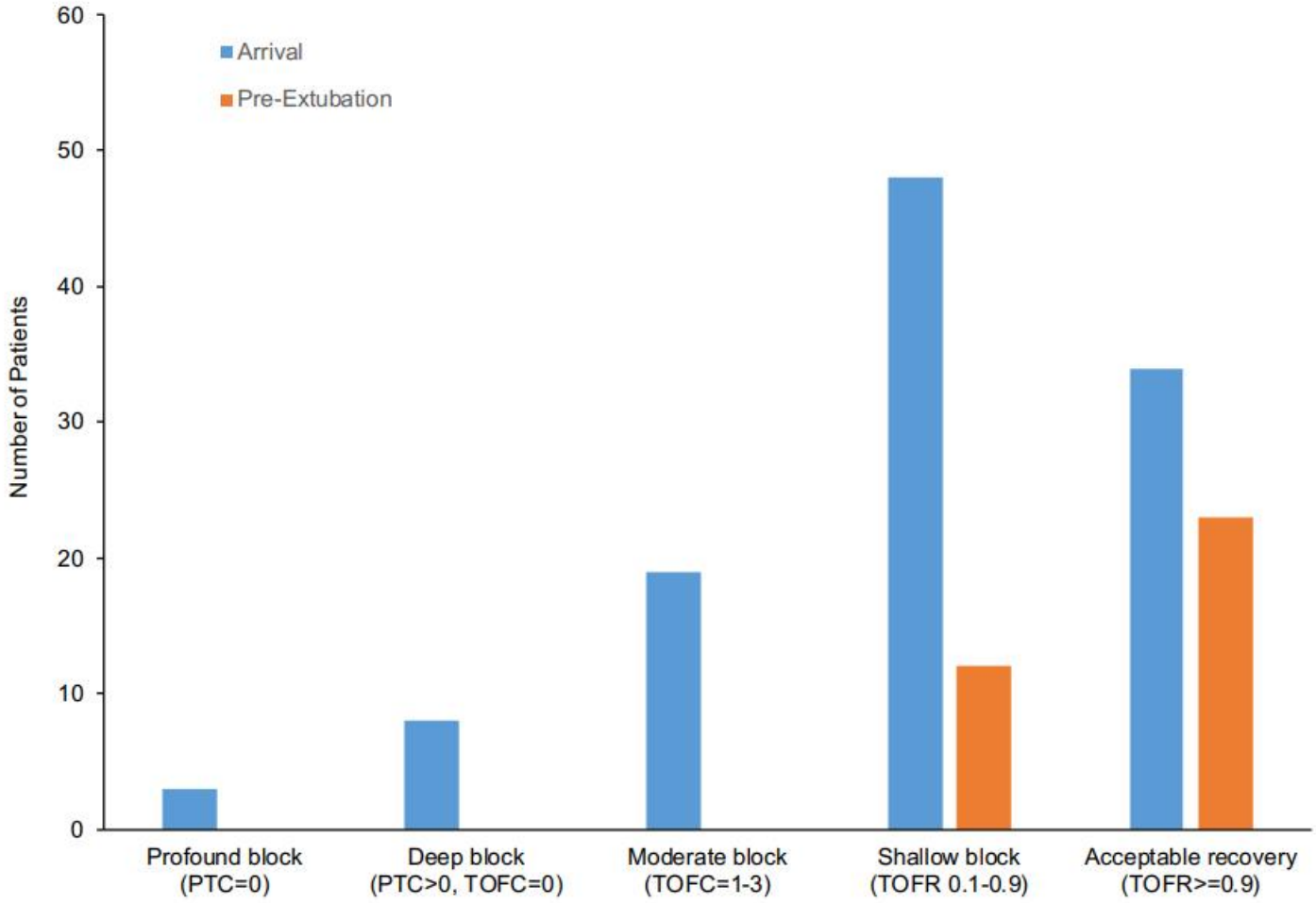
60
50
40
30
20
10
0
Number of Patients
Arrival
Pre-Extubation
Profound block (PTC=0)
Deep block (PTC>0, TOFC=0)
Moderate block (TOFC=1-3)
Shallow block (TOFR 0.1-0.9)
Acceptable recovery (TOFR>=0.9)

Technology, Computing and Simulation, Equipment Monitoring-5 Custom EEG Setup for Direct Comparison of the Patient State Index and Bispectral Index- A Pilot Study

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Introduction: In recent years, the use of processed electroencephalography (EEG) monitors has increased in an effort to closely monitor the impact of anesthetic medications during surgery. Intraoperative use of EEG monitors such as the bispectral index (BIS) and the patient state index (PSI) may be associated with enhanced early recovery times and decreased anesthetic exposure (1,2). Comparative studies between these two indices have applied both commercial sensors simultaneously but size restrictions necessitate that one of the arrays must be placed in a location not consistent with manufacturer recommendations, resulting in compromised accuracy of the collected data (3,4). We present a novel system with a custom-built interface box employing universal neonatal electrodes whose small size allows us to accurately and concurrently compare intraoperative BIS and PSI indices. As proof of concept we present comparative data collected during propofol administration for induction of general anesthesia.

Methods: This was a sponsored, prospective, nonrandomized clinical study that received approval from the Institutional Review Board. All patients provided written informed consent prior to initiation of any study procedures. Data from five adult patients scheduled for elective surgery under general anesthesia were analyzed. Six electrodes (Kendall 1050NPSM Neonatal Electrodes) were applied at locations matching the SedLine sensor array along with five additional sensors applied at BIS Sensor locations (Figure 1). A custom-built interface box was created to allow concurrent use of shared electrode positions and simultaneous connection to the BIS and SedLine monitors. In the operating room, sensors were connected to the interface box. Baseline values were recorded with the patient's eyes closed for 3 min prior to propofol administration. The SedLine Root monitor and BIS system were connected to a computer (Windows Pro PC) for data recording using Masimo Automated Data Collection (proprietary, 2017 version 10.4) and Rugloop (2018 version 10.10) software, respectively. BIS and PSI values were continuously recorded during the induction with propofol.

Results: Three male and two female patients: mean age 65 ± 8.3 years, average weight 88 ± 11.9 kg, average propofol dose 2.78 mg/kg, range 2.38 to 3.10mg/kg were analyzed. PSI, right and left BIS values recorded during the initial 20 minutes of the case are presented in Figure 2.

Conclusion: Our findings demonstrate that this custom interface can provide reliable collection of concurrent BIS and PSI indices in an intraoperative setting. Initial results reveal differences in responses. A larger clinical study utilizing this custom setup is currently underway to characterize differences between PSI and BIS during administration of anesthetic agents over a wide range of EEG activity. This system will allow us to accurately assess the performance of both indices across the entire range of clinical anesthesia.

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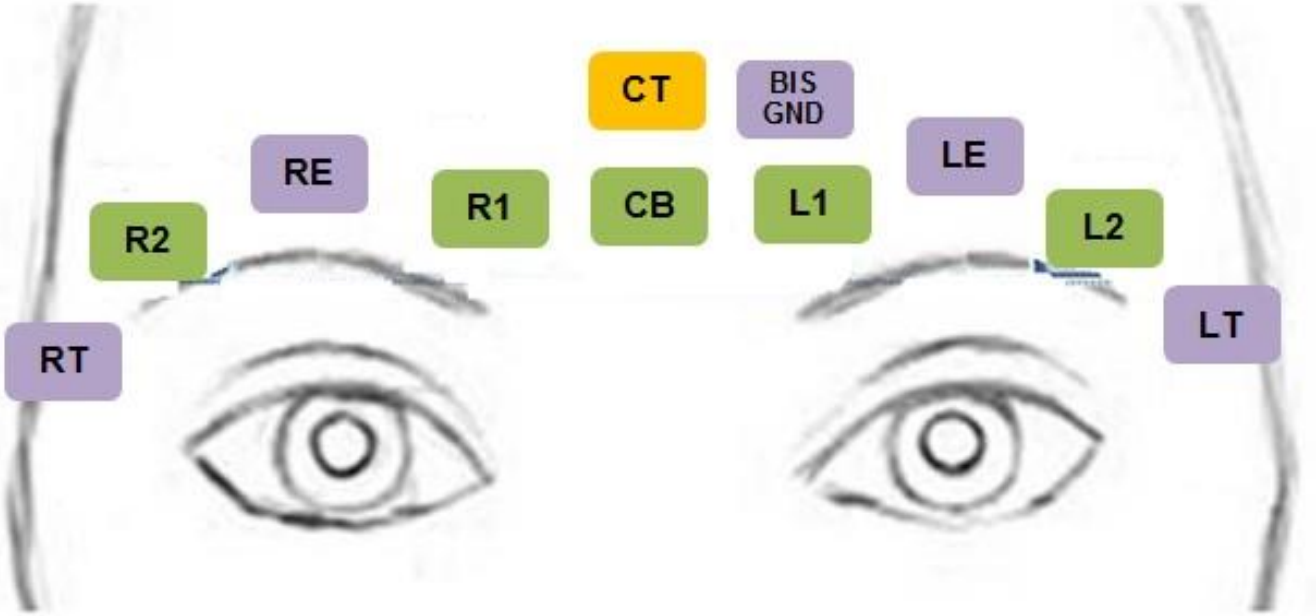
FIGURE 1

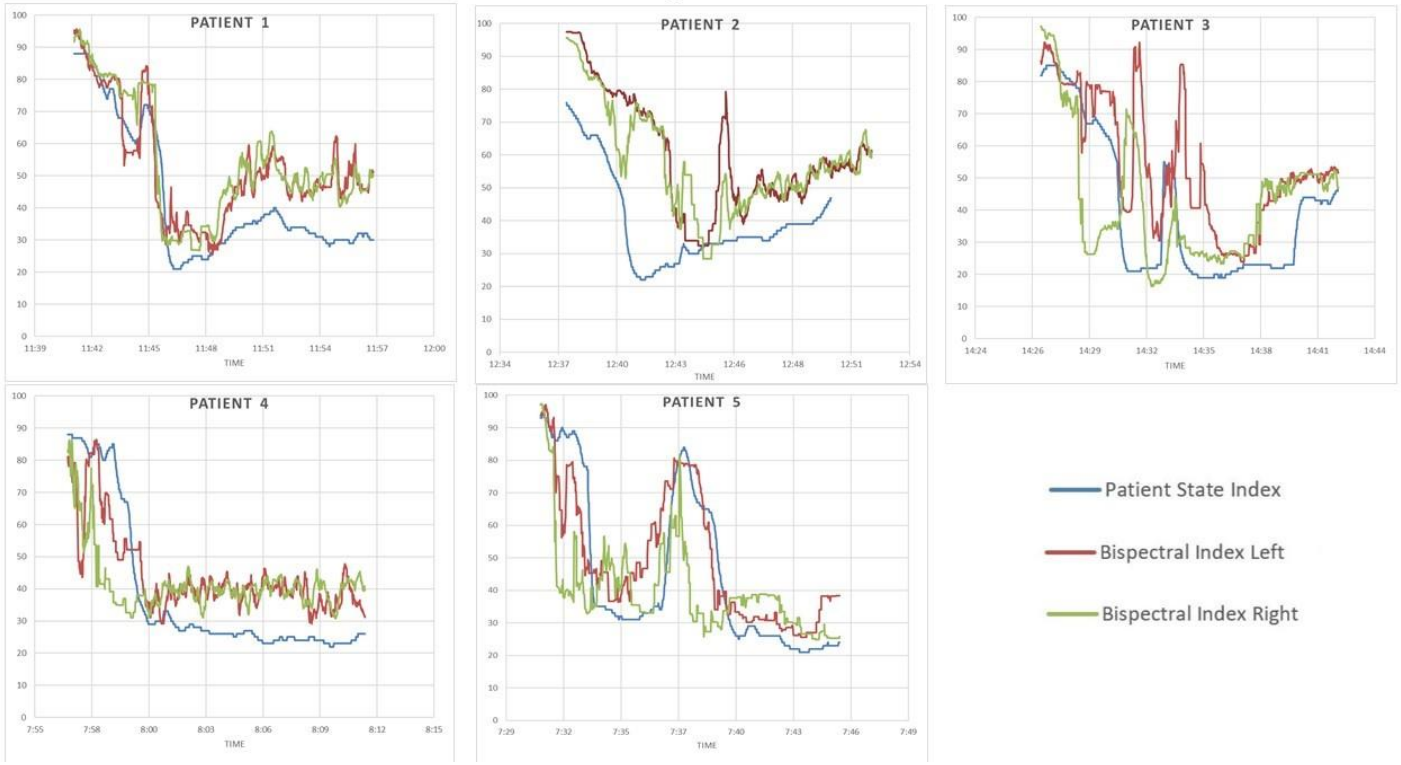


SedLine Electrode Positions

SedLine and BIS Shared Electrode Positions

BIS Electrode Positions

Figure 2


PATIENT 1
PATIENT 2
PATIENT 3
PATIENT 4
PATIENT 5
TIME
Patient State Index
Bispectral Index Left
Bispectral Index Right

Technology, Computing and Simulation, Equipment Monitoring-6 Can machine learning tackle prediction of a rare outcome: Unintended postoperative ICU admissions?

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[1]University of California, San Francisco, San Francisco, United States of America, [2]UCSF, San Francisco, CA, [3]University of California, San Francisco School of Medicine, San Francisco, CA

Introduction: Abbreviations: ICU = intensive care unit, PACU = post-anesthetic care unit, OR = operating room, ASA = American Society of Anesthesiologists, UIAs = unintended postoperative ICU admissions Unintended postoperative ICU admissions (UIAs) are rare but significant events for patients, nurses, surgical and anesthesia teams, and the hospital system [1-4]. Although the incidence of UIAs is reportedly low between 0.2-0.5% of all surgical cases, several groups have studied perioperative circumstances leading to UIAs for quality improvement and development of patient safety protocols [5-6]. Traditional statistics rely on near-normal distribution of input and outcome variables, making prediction models of such rare occurrences (i.e. class imbalance) difficult. With machine learning algorithms, however, it is more possible to tackle class imbalance through data preprocessing and training [7]. This study compares three different machine learning algorithms in predicting UIAs at our tertiary care center and discusses the potential consequences to patient care related to each model.

Methods: This was a retrospective study of all patients >18 years old who underwent surgery at a tertiary care center between December 2016 and December 2019. Neurological and cardiac surgeries were excluded due to a high number of baseline ICU admissions. An unexpected ICU admission was defined as any patient initially admitted to the PACU for postoperative recovery and transferred to the ICU upon discharge from the PACU. Data were preprocessed using a combination of SQLite and Python code. Feature selection was performed using Lasso regression for numeric features and chi-square testing for categorical features. Missing values were filled with the mean value for each feature then scaled from 0 to 1, or labeled as 'missing' then one-hot-encoded for numeric and categorical features, respectively. Classification was performed with both 10-fold cross validation and 80-20% train-test split using Logistic Regression, Gradient Booster, and a 3-layer Neural Network with a densely connected hidden layer and a dropout layer to avoid overfitting [8-9]. Logistic Regression and Neural Network were tested with and without class weight balancing, and oversampling of the minority class was used in Neural Network.

Results: A total of 22,827 cases fit the inclusion criteria, with 446 UIAs (1.95%). More UIAs occurred on Sunday than any other day of the week. The Orthopedic Surgery service had the highest absolute number of UIAs, but Thoracic Surgery service had the highest proportion of UIAs. For all algorithms, the area-under-the-curve metric (true positive vs. false positive) was high (>0.80). However, the precision-recall metric (positive predictive value vs. sensitivity) was poor for all algorithms (<0.40). Use of class weight balancing and oversampling of the minority class for Logistic Regression and Neural Network improved algorithm recall but tended to favor false positive UIAs. Gradient Booster produced the most conservative model in terms of highest accuracy with relatively low false positive rate, with best precision-recall.

Conclusion: Although machine learning algorithms have made predicting rare clinical outcomes much easier, it is extremely important to analyze the outcomes of these models in the context of the patient safety to avoid over- or under-treatment. Users must weigh the benefits and risks of favoring false positives over false negatives. Future work will include continued fine tuning of model parameters and incorporation of real-time data with the goal of real-time, adaptable prediction.

Reference(s):

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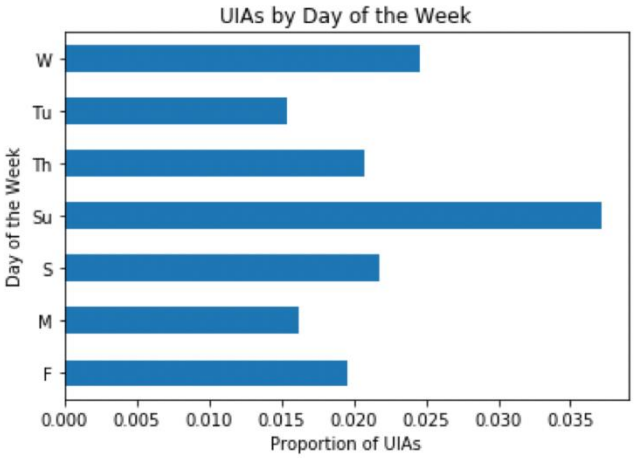
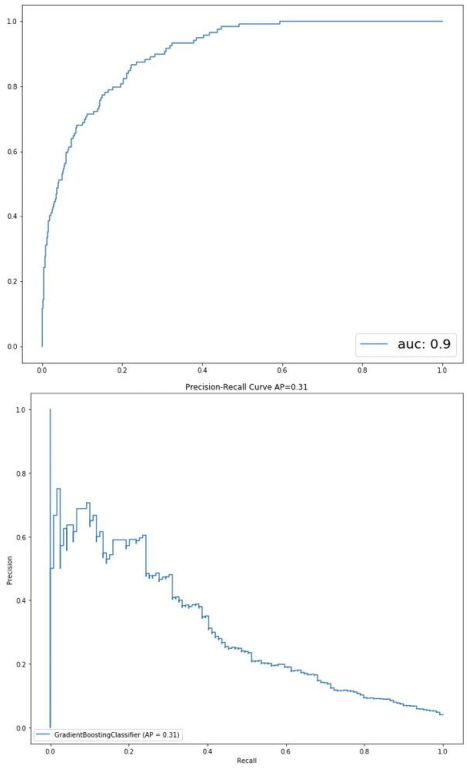


Fig 1. Baseline Metrics.
(*left*) Proportion of UIAs by Day of the Week
(*right*) Proportion of UIAs by Surgical Service

	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4700	8
Actual ICU admission	105	14
Sensitivity=Recall=0.12, Specificity=Precision=0.64, LR+=0.33		

	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4716	13
Actual ICU admission	88	10
Sensitivity=Recall=0.10, Specificity=Precision=0.43, LR+=0.18		



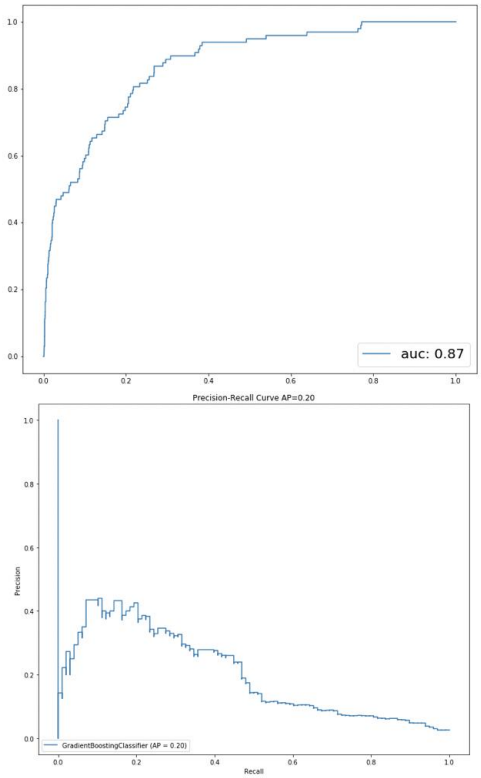


Fig 2. Gradient Booster. (*top) Confusion matrix*, (*middle) ROC curve, (bottom) Precision-Recall curve*
(*left*) Algorithm run with 80-20% train-test split
(*right*) Algorithm run with 10-fold cross-validation

	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4725	12
Actual ICU admission	72	18
Sensitivity=Recall=0.20, Specificity=Precision=0.60, LR+=0.50		

	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4363	374
Actual ICU admission	40	50
Sensitivity=Recall=0.56, Specificity=Precision=0.12, LR+=0.64		

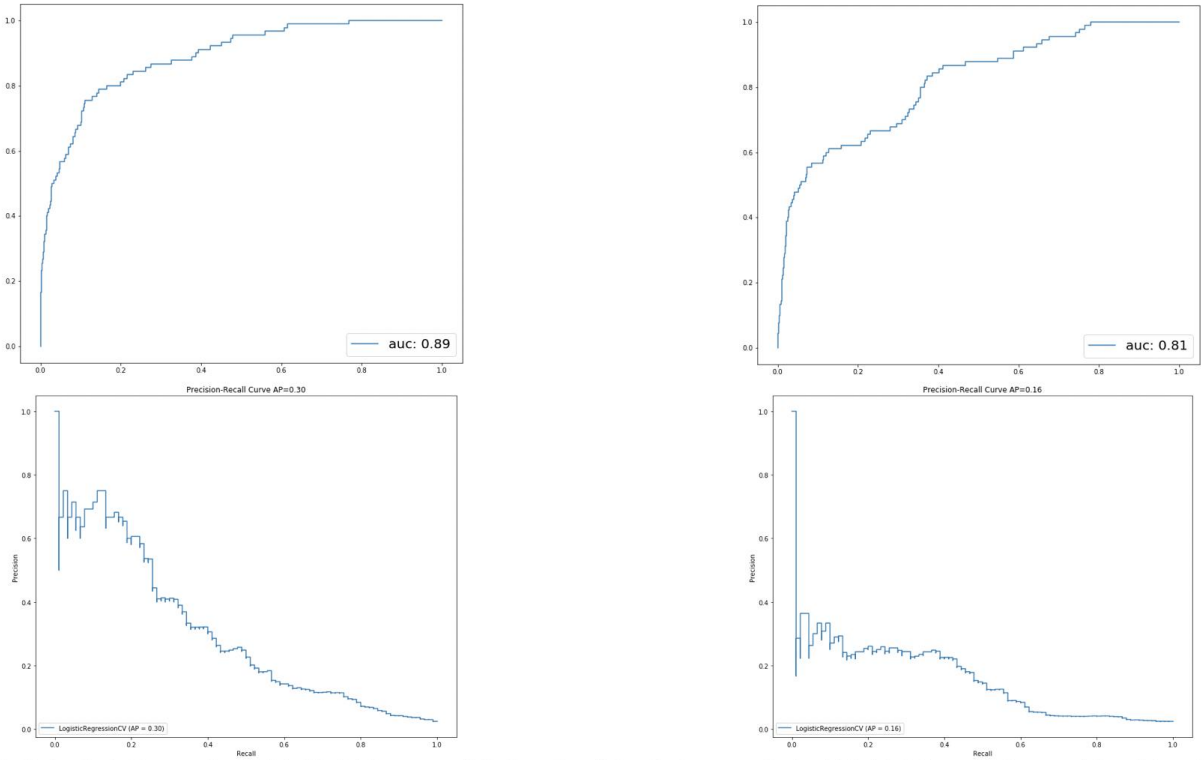
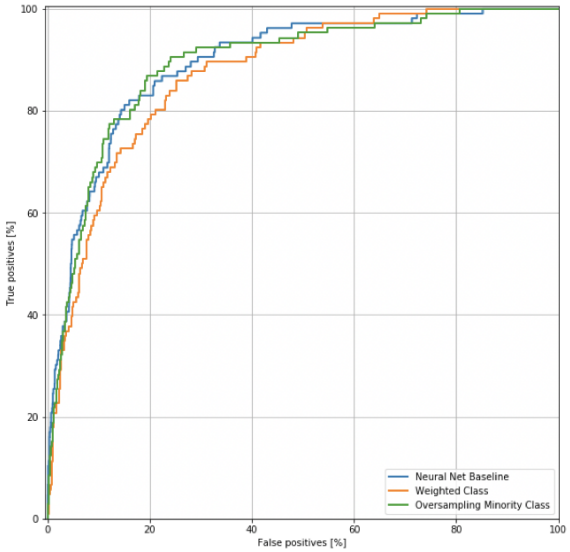


Fig 3. Logistic Regression with 10-fold cross validation. (*top) Confusion matrix*, (*middle) ROC curve, (bottom) Precision-Recall curve*
(*left*) Algorithm without balancing class weights
(*right*) Algorithm run with balancing class weights

Baseline 3-layer Network		
	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4721	0
Actual ICU admission	106	0
Sensitivity=Recall=0.0, Specificity=Precision=0.0, LR+=0		

3-layer Neural Network with Class Weights		
	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	4118	603
Actual ICU admission	33	73
Sensitivity=Recall=0.69, Specificity=Precision=0.11, LR+=0.76		

3-layer Neural Network with Oversampling of Minority Class		
	Predicted non-ICU admission	Predicted ICU admission
Actual non-ICU admission	3857	864
Actual ICU admission	17	89
Sensitivity=Recall=0.84, Specificity=Precision=0.09, LR+=0.92		



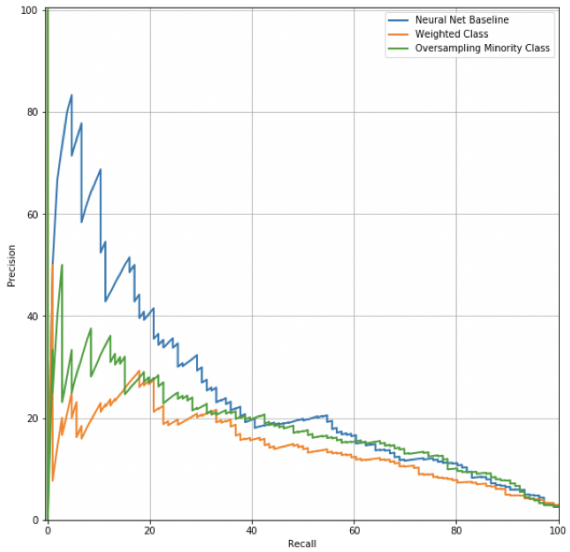


Fig 4. Neural Network
(*left*) Confusion Matrices for 3 different Neural Network algorithms
(*right*) *(top)* ROC curve, *(bottom)* Precision-Recall curve

Technology, Computing and Simulation, Equipment Monitoring-7 The Kaplan-Meier Model Overestimates The Probability Of Healthcare-Associated Infections In ICU Patients

Ksenia Ershova[1], Martin Wolkewitz[2], Oleg Khomenko[3], Olga Ershova[4], Vladimir Zelman[5]

[1]University of Southern California, Los Angeles, CA, [2]Institute of Medical Biometry and Statistics, Freiburg, Germany, [3]Skolkovo Institute of Science and Technology, Moscow, Russian Federation, [4]Burdenko Neurosurgery Institute, Moscow, Russian Federation, [5]Keck School of Medicine, Los Angeles, CA

Introduction: Outcome research in critical care is often focused on the occurrence of complications over time during an Intensive Care Unit (ICU) stay, and the method to do this research is usually a time series analysis. The Kaplan-Meier model is most frequently used to analyze these time series. Used mostly for survival data, it is also popular for evaluating the probability of various complications in the ICU [1]. One important assumption of the Kaplan-Meier model, is that patients who dropped out from the observation, due to discharge or death, have the same risk of complication as those who stayed, which is not accurate for healthcare-associated infections (HAI). There is an alternative model that accounts for competing events, events that preclude the occurrence of complications [2]. It was previously shown that Kaplan-Meier model overestimates the risk of complications in ICU patients [3], however, there is no such data for the risk of HAIs. In this study we compared the performance of the Kaplan-Meier and competing risk models to analyze the probability of HAIs in the ICU.

Methods: An infection surveillance database was prospectively collected in the neurosurgical ICU from 2011-2018. All patients who stayed for >48 hours were included. Three types of HAI were analyzed: urinary tract infections (UTI), ventriculitis/meningitis (HAVM), and pneumonia. The Nelson-Aalen model was used to demonstrate instantaneous hazard. The cumulative probabilities of each infection through day 60 in the ICU estimated by the Kaplan-Meier and competing risk models were compared.

Results: Of the 2,918 included patients, 797 of the patients had UTIs, 307 had HAVMs, and 673 of them had pneumonia. The instantaneous hazard of all three HAIs was non-monotonous over time. It increased rapidly from day 0 to days 10-15 in the ICU and then fluctuated around the higher values of hazard (Figure 1, A1-C1). Cumulative incidence over an eight-year study period calculated per 100 ICU patients was 27.3 for UTI, 10.5 for HAVM, and 23.1 for pneumonia. These values also corresponded to the highest probability of infections in the competing risk model (Figure 1, A2-C2). The Kaplan-Meier model overestimated the cumulative probability of all three infections at day 60 in the ICU: for UTI 2.9 times (0.77 vs 0.27), for HAVM the difference was 4.2 times (0.42 vs 0.1), and for pneumonia 3.2 times (0.72 vs. 0.22), Figure 1, A3-C3. By the end of the study, the at risk number, the number of patients who remained in the ICU by day 60, was 166. This number constituted a significant dropout rate.

Conclusion: We showed that the immediate risk of HAIs in the ICU is non-linear and depends on the number of days patients already spent in the unit. Therefore, it is of interest to study the cumulative probability of HAIs in a time series analysis. As our study demonstrated, in a situation of substantial patient dropout due to discharge or death, the Kaplan-Meier model significantly overestimated a cumulative incidence of UTIs, HAVM, and pneumonia. The competing risk model accounts for the dropout and therefore is recommended when studying the probability of HAIs in the ICU.

Reference(s):

1. Zhang et al. 2019. “The Cumulative Venous Thromboembolism Incidence and Risk Factors in Intensive Care Patients Receiving the Guideline-Recommended Thromboprophylaxis.” Medicine 98 (23): e15833.

2. Fine, Jason P., and Robert J. Gray. 1999. “A Proportional Hazards Model for the Subdistribution of a Competing Risk.” Journal of the American Statistical Association 94 (446): 496–509.

3. Lacny et al. 2018. “Kaplan-Meier Survival Analysis Overestimates Cumulative Incidence of Health-Related Events in Competing Risk Settings: A Meta-Analysis.” Journal of Clinical Epidemiology 93 (January): 25–35.

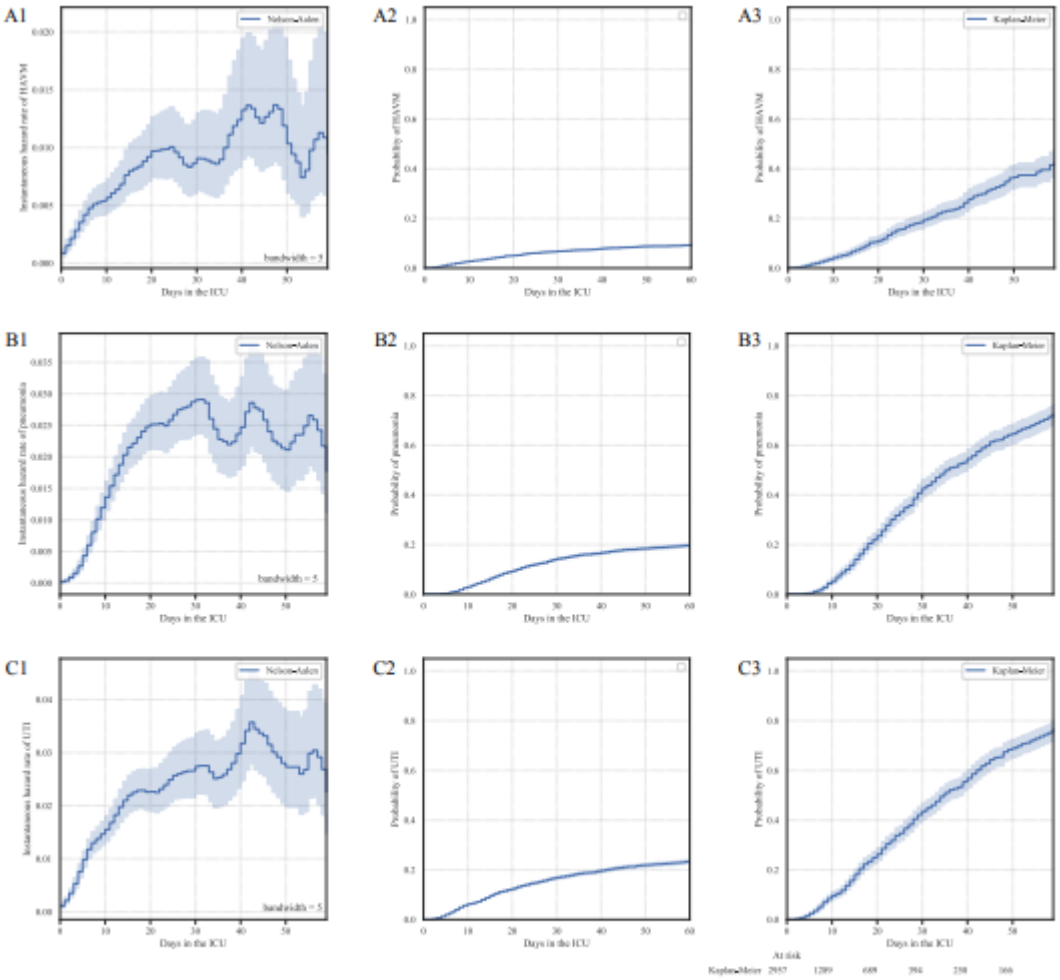


Figure 1. Probability of different healthcare-associated infections in the neurosurgical ICU in 2011-2018. **A1-A3**: Healthcare-associated ventriculitis and meningitis (HAVM); **B1-B3**: Pneumonia; **C1-C3** Urinary tract infections (UTI). **A1, B1, C1**: Kernel-smoothed function of instantaneous hazard of infections depending on the number of days in the ICU, Nelson-Aalen estimate. **A2, B2, C2**: Cumulative probability of infections depending on the number of days in the ICU while accounting for discharge (death) as competing events (competing risk model). **A3, B3, C3**: Cumulative probability of infections depending on the number of days in the ICU when discharge (death) is censored (Kaplan-Meier model).

Technology, Computing and Simulation, Equipment Monitoring-8 High Fidelity CRISPR Libraries to Interrogate Anesthetic Genetic Susceptibilities

Alexendar R Perez[1]

[1]*University of California, San Francisco, San Francisco, CA*

Introduction: CRISPR technology allows for the versatile and permanent modification of DNA through a two component system: a targeting element (Guide RNA) and an endonuclease that cleaves double stranded DNA. CRISPR mediated DNA cleavage allows for the generation of loss-of-function perturbations or precisely engineered modifications of genomic loci. The ease and effectiveness of CRISPR technology in inducing these changes, makes it an ideal tool for genetic screens as it allows for the robust interrogation of virtually any genomic locus. The fidelity of these screens depends on precise targeting by Guide RNAs (gRNA). Guide RNAs must uniquely identify a genetic locus and a complete knowledge of potential off-target sites is essential for precise targeting. Current genome-wide CRISPR libraries contain numerous non-specific gRNAs that create false negatives and false positives in genetic screens. Though the effects of these false negatives and false positives can be corrected computationally, no CRISPR gRNA library currently exists that guarantees high fidelity gRNAs against a broad array of coding sequences. We have utilized our GuideScan software to generate rules defining the design of ultra-specific CRISPR gRNAs libraries for both human and mouse genomes (1). Such libraries are important if investigators utilize CRISPR screens to interrogate the genetic susceptibilities of patients to anesthesia. Recent studies have highlighted the importance of genetics in suggesting new avenues of anesthetic discovery and therapeutic development (2). However, these studies depend on retrospective genotype identification. CRISPR screens, using high fidelity gRNA libraries, allow for prospective identification of genetic targets in human or mouse cells under anesthetic exposure.

Methods: Enumeration of Guide RNA (gRNA) Targets We constructed retrieval trees (tries) consisting of all possible 20mer Cas9 gRNA target sites in the mouse and human genomes as previously published (1). Unlike the original tries reported in GuideScan (1), these were constructed without alternative chromosome data and thus produce a more accurate description of the off-target space of individual gRNAs. To determine the mismatch neighborhood for each gRNA in the library, we traversed each of their sequences through the trie to exhaustively determine all neighbors up to and including Hamming and Levenshtein distances of 3. Specificity scores for each gRNA were computed using Hamming distance neighbors as previously described (1) Computational Adjustment of Off-Target Effects: A computational adjustment that corrects for off-target effects called the CRISPR Specificity Correction (CSC) was developed by training a Gradient Boosted Regression Tree on gRNA library log2 fold change depletion. A total of 426 features were used in learning. Feature importances for this model were extracted and specificity features, which serve as confounders in this setting, were extracted and modeled with a mathematical correction that was demonstrated to robustly eliminate false positive and negatives. Guide RNA Library Design Guide RNA libraries were constructed using the GuideScan software for the selection of uniquely targeting gRNAs. These gRNAs were filtered such that off-target effects, as measured by the degree of computational correction, were minimal. The GuideScan gRNAs were directly compared against published libraries of gRNAs using positive and negative selection screens. Prior to deploying the libraries, global GuideScan specificity scores were computed for each library and directly compared.

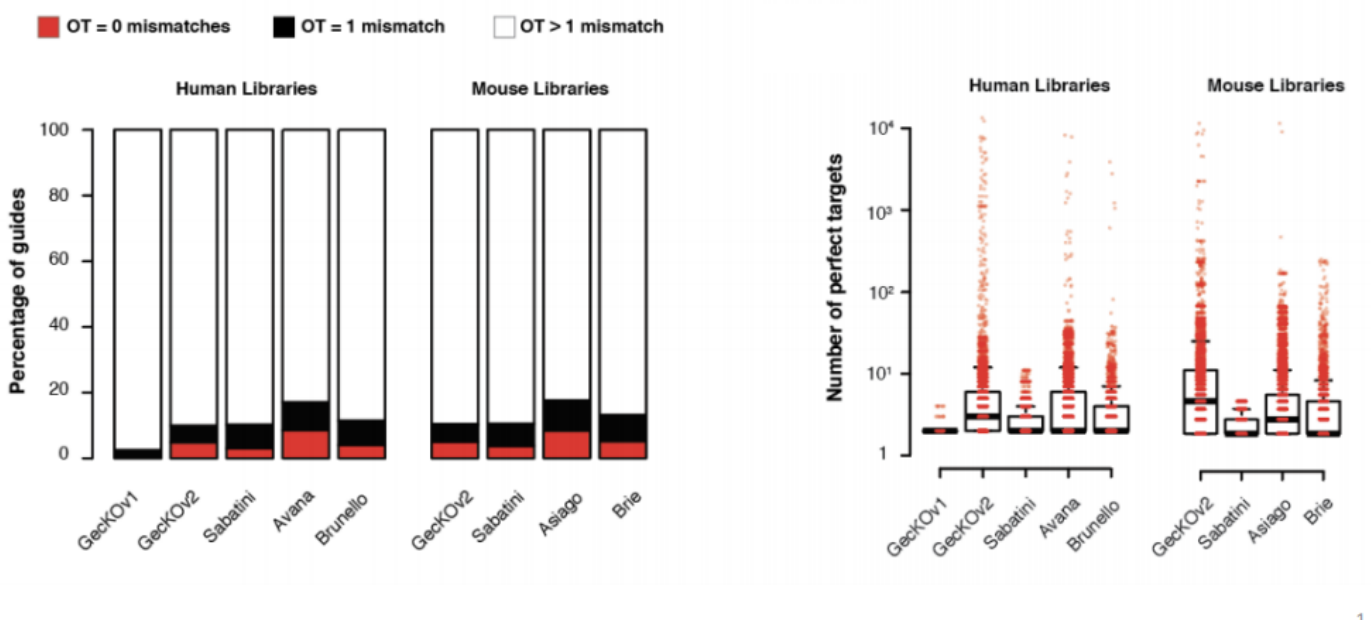
Results: The enumeration and specificity computation of gRNAs allowed for the construction of GuideScan gRNA libraries that were composed exclusively of uniquely targeting gRNAs. Furthermore, the CRISPR Specificity Correction (CSC) was able to robustly account for library gRNA off-target effects. Overall, GuideScan gRNA libraries showed the highest and most robust specificity in targeting genomic loci.

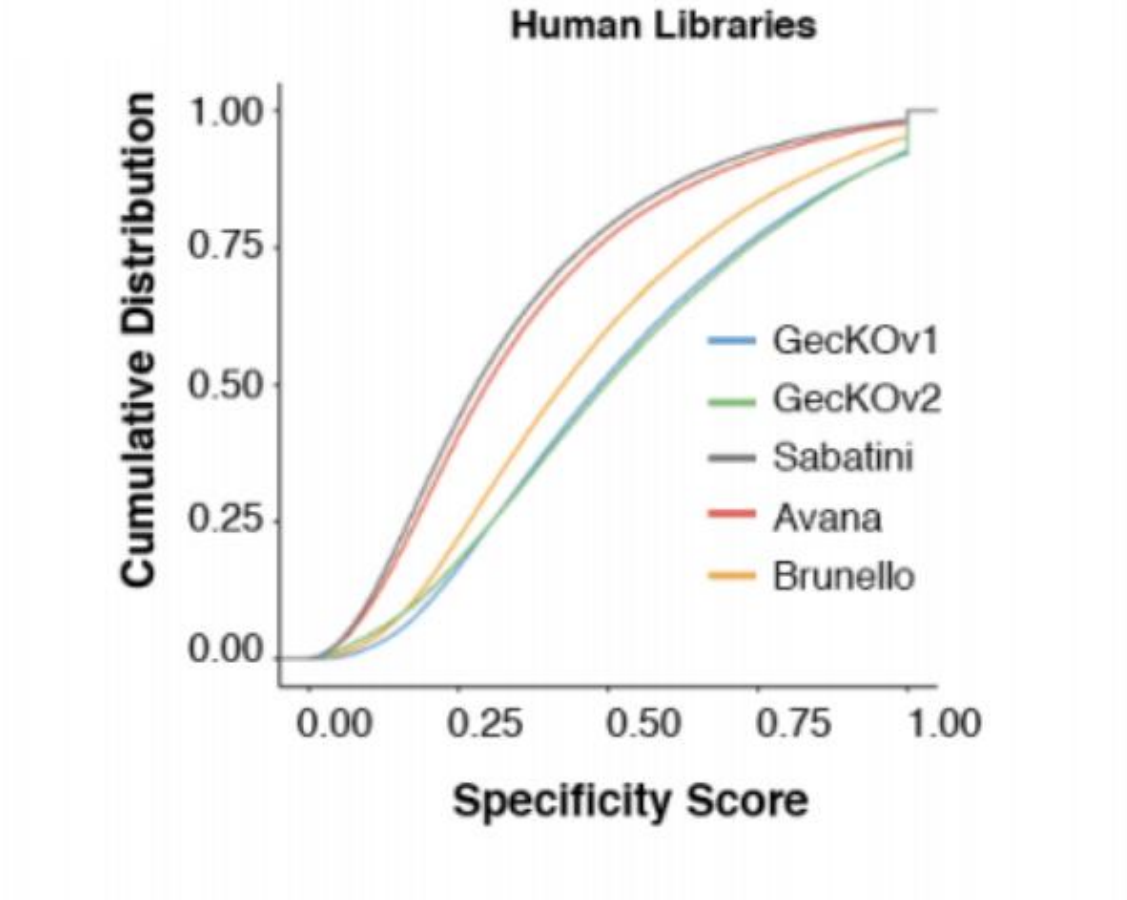
Conclusion: GuideScan libraries contain the most specific gRNAs reported to date and allow for highly precise targeting of loci. These libraries will be deployed to precisely screen for novel genetic susceptibilities to anesthesia.

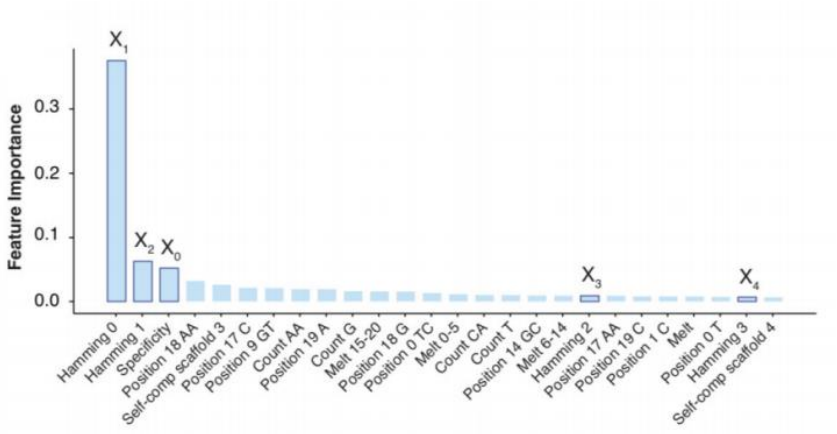
Reference(s):

1: GuideScan software for improved single and paired CRISPR guide RNA design, Nature Biotechnology, 35, 347, 2017

2: Microdeletion in a FAAH pseudogene identified in a patient with high anandamide concentrations and pain insensitivity, British Journal of Anaesthesia, 123, 249-253, 2019


OT = 0 mismatches
OT = 1 mismatch
OT > 1 mismatch
Human Libraries
Mouse Libraries
Percentage of guides
100
80
60
40
20
0
GecKOv1
GecKOv2
Sabatini
Avana
Brunello
GecKOv2
Sabatini
Asiago
Brie
Number of perfect targets
10^4
10^3
10^2
10^1
1


Human Libraries
Cumulative Distribution
1.00
0.75
0.50
0.25
0.00
GecKOv1
GecKOv2
Sabatini
Avana
Brunello
0.00
0.25
0.50
0.75
1.00
Specificity Score


Feature Importance
0.0
0.1
0.2
0.3
X1
X2
X0
X3
X4
Hamming 0
Hamming 1
Specificity
Position 18 AA
Self-comp scaffold 3
Position 17 C
Position 9 GT
Count AA
Position 19 A
Count G
Melt 15-20
Position 18 G
Position 0 TC
Melt 0-5
Count CA
Count T
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Hamming 2
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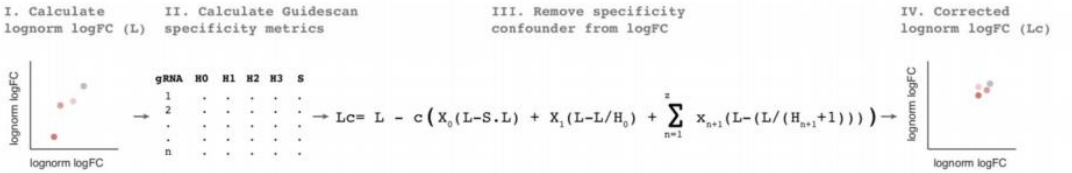
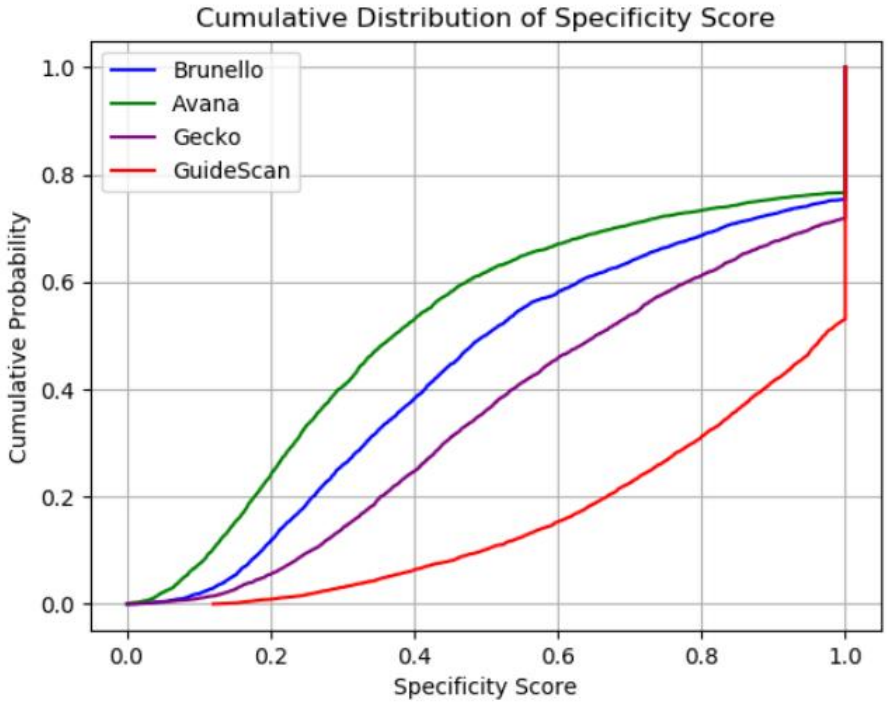
Melt
Position 0 T
Hamming 3
Self-comp scaffold 4


I. Calculate lognorm logFC (L)
II. Calculate Guidescan specificity metrics
III. Remove specificity confounder from logFC
IV. Corrected lognorm logFC (Lc)
lognorm logFC
lognorm logFC
gRNA H0 H1 H2 H3 S
1
2
n
Lc= L - c(X0(L-S.L) + X1(L-L/H0) + Σ Xn+1(L-(L/(Hn+1+1))))
lognorm logFC
lognorm logFC


Cumulative Distribution of Specificity Score
Brunello
Avana
Gecko
GuideScan
Cumulative Probability
0.0
0.2
0.4
0.6
0.8
1.0
Specificity Score
0.0
0.2
0.4
0.6
0.8
1.0

Technology, Computing and Simulation, Equipment Monitoring-9 The Rapid Pulse Confirmation Device: An observational study of a prototype device designed to detect return of spontaneous circulation (ROSC) and quantify chest compression efficacy

Jonathan Bond[1], Michael Ritchie[1]

[1]West Virginia University, Morgantown, WV

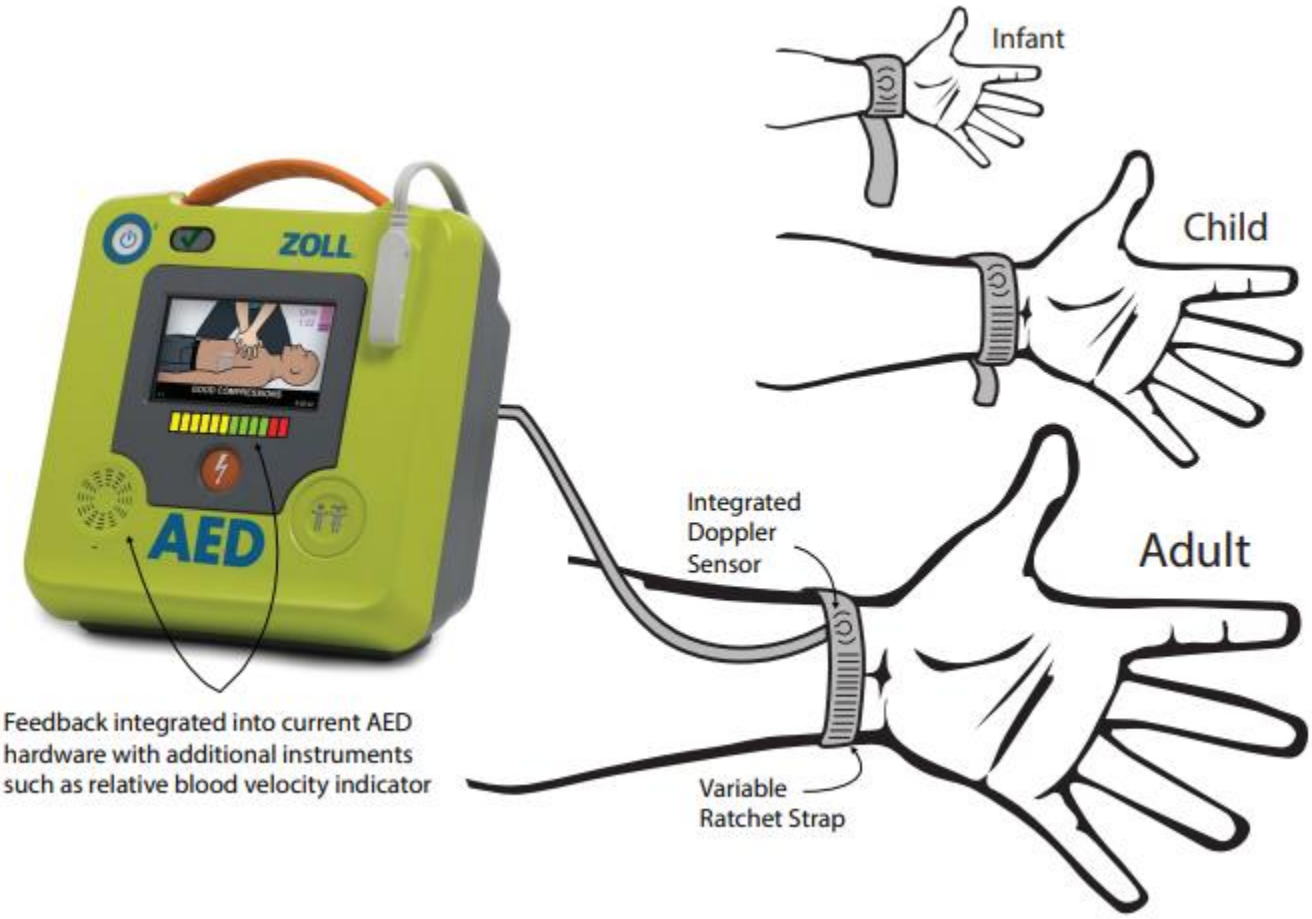
Introduction: Effective chest compressions are essential to the survival of a cardiac arrest requiring cardiopulmonary resuscitation (CPR). Major challenges to providing effective chest compressions are frequent interruption of compressions, insufficient force applied to the chest and low rate of compression. To potentially solve the issues of evaluating the chest compression effectiveness and minimization of the time interval of pulse checks, the authors have constructed a novel device that can be rapidly applied to an arresting patient and evaluate the current state of the circulatory system using a processed Doppler signal. It is designed to be applied over a major artery and detects the Doppler shift of red blood cells to gauge red blood cell velocity and rate of pulsation during compressions and pulsatile blood flow indicative of ROSC during pulse checks. The overall goal of the device is to provide feedback on compression efficacy beyond the American Heart Association depth based approach and increase accuracy while decreasing time required for pulse checks.

Methods: The observation study was designed to assess the viability and functionality of the RPC device prototype in a controlled cardiac arrest environment. Specifically, the data was obtained with the goal being to evaluate initial device performance with the specific observation of the device's ability to detect pulsatile blood flow in comparison with indwelling brachial arterial catheter tracings. Secondary data collected for comparison of RPC device feedback in relation to TEE, pulse oximetry, and ECG. Patients were assessed for inclusion and exclusion criteria in the pre-operative area on the morning of the scheduled cardiac surgery. The left carotid artery was selected due to the convenience of access near the head of the bed and way from the draped sterile field. After the patient had been rewarmed, the RPC device, brachial arterial catheter tracing, and the pulse oximeter were observed for the detection of pulsatile blood flow. The time of detection of the RPC device and the invasive arterial blood pressure were recorded. Observations were made concerning device audible and visual feedback of pulsatile blood flow as well as correlation with other clinical monitors including ECG, transesophageal echocardiography and pulse oximetry. Cardiopulmonary bypass pump flow was recorded if applicable.

Results: The population studied were patients > 18 years of age undergoing valve repair/ replacement surgery, coronary artery bypass surgery or a combination of the procedures who required cardiopulmonary bypass. Further inclusion and exclusion criteria can be seen in Figure 2. A total of 10 patients were enrolled according to the inclusion and exclusion criteria above. BMI range from 24.8 to 39.9 representing patients of normal body habitus to obese body habitus. The average detection time of the RPC device was within one minute of the brachial artery catheter with an SD of 1 minutes. The difference in RPC pulse rate reading and arterial line pulse reading was 3 beats per minute with a standard deviation of 14. Average blood pressure values at the time of detection of ROSC was systolic blood pressure of 77 millimeters of mercury (mmHg) with an SD 11 mmHg and mean arterial pressure of 57 mmHg with an SD 13 mmHg. The data is summarized in Figure 3.

Conclusion: A device that can be quickly applied during a cardiac arrest that would give meaningful feedback about the efficacy of circulation during chest compression as well as substantially reduce pulse check interval could prove beneficial to cardiopulmonary resuscitative efforts both in and outside the hospital. The goal of this quasi-experimental observational study was to assess the ability of the RPC device to detect the return of spontaneous circulation. A patient preparing to separate from CPB often has a lower body temperature, requires ionotropic and/or vasopressor support, has 'stunned' myocardial tissue, and may have fluctuating effective circulatory volume. Many parallels can be drawn between the patient state described above and that of a spontaneous cardiac arrest patient. The observations made in this study showed the device to be able to detect return of pulsatile flow within an average of one minute of detection by an indwelling brachial arterial line. We plan to expand study of the device to spontaneous arresting patients as well as to an animal model to determine limits and significance of detection data.

Reference(s): Dick, Wolfgang F., et al. 'The carotid pulse check revisited: what if there is no pulse?.' Critical care medicine 28.11 (2000): N183-N185. Kleinman, Monica E., et al. '2017 American Heart Association focused update on adult basic life support and cardiopulmonary resuscitation quality: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care.' Circulation 137.1 (2018): e7-e13. Adedipe, Adeyinka A., et al. 'Carotid Doppler blood flow measurement during cardiopulmonary resuscitation is feasible: a first in man study.' Resuscitation 96 (2015): 121-125. Zengin, Suat, et al. 'Comparison of manual pulse palpation, cardiac ultrasonography and Doppler ultrasonography to check the pulse in cardiopulmonary arrest patients.' Resuscitation 133 (2018): 59-64 Kucewicz, John C., et al. 'Towards a non-invasive cardiac arrest monitor: An in vivo pilot study.' Resuscitation 134 (2019): 76-80.


Infant
Child
Adult
ZOLL
AED
Integrated
Doppler
Sensor
Variable
Ratchet Strap
Feedback integrated into current AED
hardware with additional instruments
such as relative blood velocity indicator

Inclusion:

18 or older

Left ventricular ejection fraction (LVEF) >40% on pre-operative echocardiogram

Patient with single cardiac valve disease to be repaired during a scheduled surgery

Patient undergoing coronary artery bypass

A combination procedure of criteria 3 and 4

Exclusion:

Redo procedure

Emergency procedure

Arterial stents in the radial, ulnar, brachial, femoral, or carotid arteries

History of peripheral arterial bypass

History of any degree of carotid artery stenosis

Thoracic outlet syndrome

Valvular heart disease NOT being repaired day of surgery

Heart rhythm other than sinus before the scheduled procedure (occasional PVC's ok) as determined by pre-operative EKG

Figure 2- Inclusion and Exclusion Criteria

Subject Number	Sex	BMI	Difference in Time (mins) RPC vs BAC	Difference in Time (mins) pulse oximeter vs RPC	Pulse Difference RPC vs BAC (BPM)
1	male	27.01	-1	-4	0
2	male	24.85	0	-13	-1
3	male	39.69	-3	-14	2
4	female	29.74	-4	-5	0
5	male	30.29	-2	-3	9
6	female	33.15	0	-12	-16
7	female	24.79	0	-2	0
8	female	33.01	0	2	40
9	male	39.9	0	0	-2
10	male	27.82	0	-1	2

Figure 3- Observations of the function of the RPC device versus brachial artery catheter and pulse oximeter in time of detection of pulsatile flow in minutes and beats per minute (BPM) pulse reading.

Patient	Sex	BAC Systolic Pressure (mmHg)	BAC Diastolic Pressure (mmHg)	BAC Mean Arterial Pressure (mmHg)
1	male	62	48	52
2	male	84	37	52
3	male	90	63	72
4	female	75	39	51
5	male	87	65	72
6	female	89	76	80
7	female	74	67	69
8	female	60	53	55
9	male	88	74	78
10	male	69	51	57

Figure 4- The blood pressures (systolic, diastolic, and systolic) at time of BAC detection of pulsatile flow are included to assess device performance at hypotensive pressures.

Technology, Computing and Simulation, Equipment Monitoring-10 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 for 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.

Medically Challenging Cases

Airway Management

Airway Management-1 Percutaneous Tracheostomy: Don’t Re-intervene Without Help!

Melissa Murray[1], Micah Long[2]

[1]University of Wisconsin School of Medicine and Public Health, Madison, WI, [2]University of Wisconsin, Madison, United States of America

Introduction: It is widely accepted that bedside percutaneous tracheostomy (PCT) is a reasonable alternative to surgical tracheostomy in critically ill patients in the ICU1. Although recent studies suggest that bedside percutaneous tracheostomy can be performed safely without bronchoscopic guidance2, many of these studies excluded patients with suspicion of difficult anatomy, prior history of airway problems and those with previous tracheostomy. Thus, some argue that bronchoscopic guidance improves safety3. Nonetheless, due to the expanded utilization of percutaneous, non-bronchoscopically guided techniques, some providers may also manipulate new, but problematic, tracheostomy tubes without bronchoscopic guidance, for problems such as cuff rupture, and this poses severe risk to patients.

Case Report: The patient was a 69-year-old man with history of severe COPD, coronary artery disease, TIA, and hypertension presenting with symptomatic type-IV thoracoabdominal aortic aneurysm requiring operative repair. Post-operative course included massive PE and two extubation failures requiring bronchoscopically guided percutaneous tracheostomy with placement of an 8.0 cuffed Shiley. Two days later, he had a slow continuous leak from tracheostomy cuff, attributed to small puncture hole. After confirmation that the cuff was not hyperinflated, it was elected to replace the tracheostomy under bronchoscopic guidance facilitated with sedation in the intensive care unit. He had no external neck swelling, edema or anatomic abnormalities and he was actively vocalizing around the tracheostomy. Further, his prior airways were performed with indirect laryngoscopy showing easy views of normal anatomy. Nonetheless, bronchoscopic visualization of the upper airway was extremely challenging and would have precluded direct or indirect laryngoscopy guided orotracheal reintubation of the airway (Figures 1 & 2). To maintain adequate gas exchange and cardiovascular homeostasis, we loaded an endotracheal tube over a bronchoscope, entered the airway and performed the procedure under indirect visualization. This enabled orotracheal reintubation rescue via the bronchoscope, where an endotracheal tube could be placed distal to the tracheostomy site. The procedure was uncomplicated and a new Shiley tracheostomy tube was placed using repeat dilation and the recommended Seldinger technique4.

Discussion: A tracheostomy cuff leak can be sudden or insidious. Unappreciated etiologies include hyperinflation of the cuff or cephalad positioning resulting in the cuff opening the vocal cords and offering air passage through the glottic inlet. Once it is decided to replace a tracheostomy, added caution is required to ensure safety. Replacement of the tube through the stoma can be impossible even for experts in open surgical tracheostomies, especially for patients with recent tracheostomies5. Failure of tube replacement prompts intervention 'from above,' and with recent airway manipulation, airway edema, or an unsafe primary airway, this is challenging. Rescuing the failed attempt may require direct or indirect laryngoscopy. The assumption that orotracheal airway rescue is possible via direct or video laryngoscopy, particularly without expert presence, should be abandoned. As we have shown, even with previously unremarkable intubations and airway anatomy, tracheostomy placement can cause or coincide with glottic edema making sedated or anesthetized airway interventions from above impossible. While rare, this catastrophic complication can be avoided by the simple use of bronchoscopy with a loaded endotracheal tube.

Reference(s):

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Figure 1

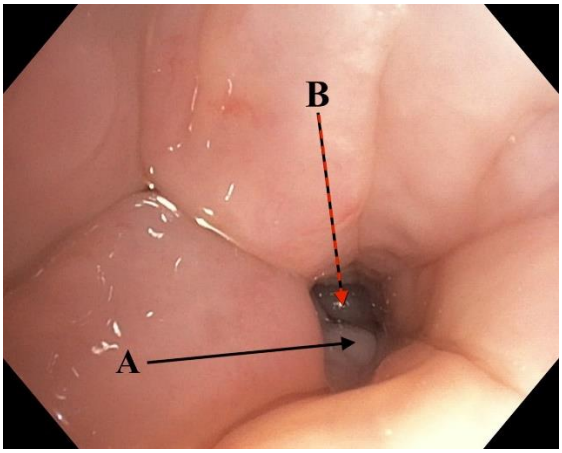

Figure 2

Airway Management-2 Severe Orolingual Angioedema After Thrombolytic Therapy In A Stroke Patient: A Case Report

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Introduction: Tissue plasminogen activator (tPA) is a fibrinolytic agent that serves as first-line therapy for acute ischemic stroke. Despite its therapeutic efficacy, it is widely associated with intracerebral hemorrhage as a potential adverse effect. A rare and under-appreciated complication of tPA administration is angioedema. The mechanism of tPA induced angioedema is hypothesized to be excessive bradykinin production and activation of the complement cascade. Moreover, there is an observed increase in risk of tPA induced angioedema in patients who also take angiotensin-converting enzyme inhibitors (ACEI). While angioedema following tPA administration may occur with or without concomitant use of ACEI, the management of patients who have received both medications demands heightened awareness of their airway integrity and hemodynamic status.

Case Report: A 48-year-old obese African American man with a past medical history of Down syndrome, Diabetes Mellitus, and hypertension managed with an ACEI, was referred to our facility from an outside hospital where he was brought by his father after being found down at home. His initial presentation featured right-sided weakness, right-sided facial droop, aphasia, and left-sided gaze deviation. Telestroke service was consulted, and based on their recommendations, a bolus of tPA was administered followed by transfer to a tertiary care hospital for further management. His initial vital signs upon presentation to our emergency department included a blood pressure of 205/114, heart of 99 bpm, respiratory rate of 22/min, and an oxygen saturation of 100% on 15 liters via a non-rebreather mask. Physical exam revealed marked swelling of the tongue, which was not present prior to administration of the tPA bolus (as seen in figure I). Repeat imaging of head & neck revealed proximal occlusion of the left middle cerebral artery. Anesthesiology was consulted for intubation in the setting of impending respiratory failure secondary to patient's newly discovered severe angioedema. A fiber-optic bronchoscope was used for nasal intubation after applying 2% lidocaine to nares and administration of 8mcg of Dexmedetomidine. Under direct visualization of glottic opening, a 6.5 mm cuffed endotracheal tube was passed through the vocal cords, and placement was confirmed by a positive color change on a colorimetric device and auscultation. Bite blocks were placed to prevent the patient from biting on his tongue. Subsequently etomidate, dexmedetomidine, and rocuronium were given. Neurosurgery team performed an emergent thrombectomy. Postoperatively the patient's persistent angioedema was managed using a combination of racemic epinephrine, hydrocortisone, methylprednisolone, dexamethasone, and antihistamines. On hospital day 8, the patient underwent tracheostomy by Otolaryngology team due to continued angioedema. During the next several days, he underwent botulinum toxin injections in the medial pterygoid muscles and a tongue biopsy, which revealed extensive acute on chronic inflammation of the tongue along with tissue necrosis. The patient's family was offered the choice between partial glossectomy and conservative therapy, of which they opted for the latter. The patient was discharged to a long-term acute care facility after a 52-days inpatient stay.

Discussion: Our case describes the occurrence of severe angioedema in a stroke patient following tPA administration, subsequently requiring emergent intubation. Mild- moderate angioedema is reported in 1.3% to 7.9% of patients given tPA for treatment of ischemic stroke, and the incidence of severe angioedema requiring surgical intervention is even lower. It is hypothesized that that there is an increase in bradykinin released by brain tissues following ischemic insult, along with up-regulation of kinin-B2 receptors in dying cells. tPA also leads to increased bradykinin due to activation of plasmin and complement cascade. Furthermore, a comprehensive medical history and updated medication lists should be obtained as patients taking ACEI who are given tPA are at even higher risk of severe angioedema. Thus, anesthesiologists tasked with the management of airway in a patient presenting with acute ischemic stroke must be vigilant about the risk of severe orolingual angioedema in stroke patients who have undergone tPA therapy.

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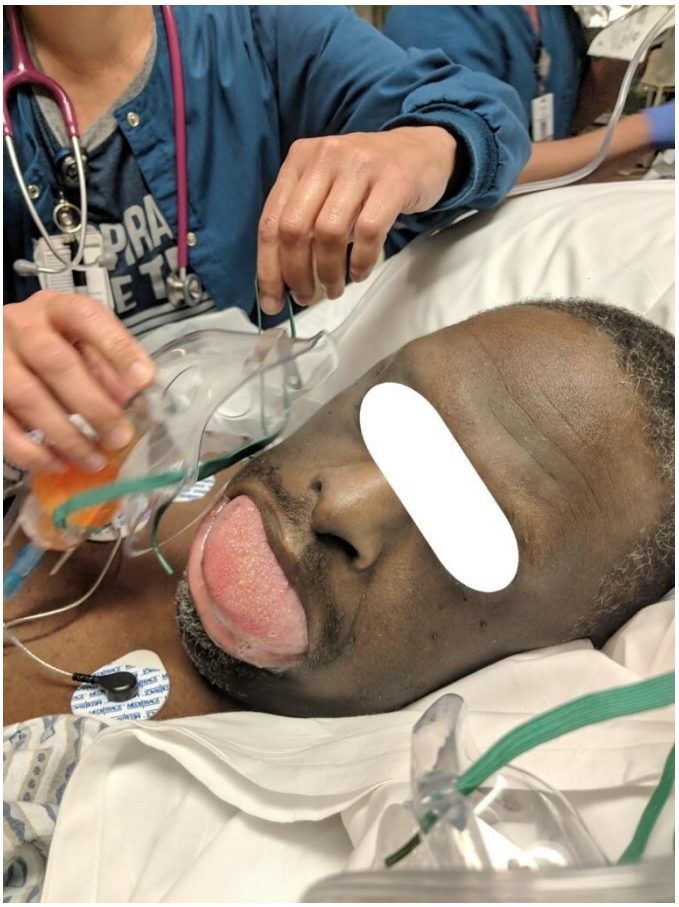

Ambulatory Anesthesia

Ambulatory Anesthesia-1 Cerebral Air Embolism During Esophagogastroduodenoscopy and Esophageal Balloon Dilatation: A Case Report

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Introduction: With its minimally invasive nature and low complication rate, esophagogastroduodenoscopy (EGD) has become an invaluable tool for both diagnostic evaluation and therapeutic intervention. Common complications associated with EGD are airway obstruction, esophageal perforation, and bleeding. Cerebral air embolism (CAE), however, is a rare event that has a wide range of presentations from subclinical to devastating neurologic compromise and death. Our literature search yielded 31 cases of CAE associated with EGD.1 Diagnostic tests include echocardiography, abdominal and cerebral computed tomography (CT) and magnetic resonance imaging (MRI). Treatment consists of maintaining hemodynamic stability, proper patient positioning and hyperbaric oxygen therapy (HBOT).

Case Report: A 79-year-old woman with a history of a Schatzki's ring presented for esophageal balloon dilation. She was placed in the left lateral decubitus position and received intravenous fentanyl 50mcg, lidocaine 40mg, and propofol 20mg. The endoscopist proceeded with the EGD using air for insufflation. A Schatzki ring was identified in the proximal esophagus 15cm from the incisors and dilated using a 10mm balloon dilator. In addition, many bleeding esophageal ulcers were identified. Upon completion 11 minutes later, the patient was unresponsive to tactile stimuli with a significantly elevated blood pressure of 204/121mmHg. The decision was made to intubate the trachea for airway protection and obtain a brain CT which revealed multiple foci of air within the brain parenchyma bilaterally and loss of gray-white differentiation in the left frontal lobes compatible with acute infarct. The patient was admitted to the intensive care unit and a follow-up brain CT after 24 hours showed cerebral edema and multiple large acute infarcts involving considerable portions of the cerebral and the cerebellar hemispheres. A transthoracic echocardiogram (TTE) with bubble study did not show evidence of an atrial septal defect (ASD) or patent foramen ovale (PFO). Given the patient's poor prognosis, the family decided to withdraw care.

Discussion: Although rare, a CAE during endoscopy may lead to a catastrophic outcome if not recognized promptly. It is suggested that air insufflation in the presence of a mucosal barrier disruption leads to a significant pressure gradient that entrains air into the vasculature.2 Of note, most insufflation regulators do not measure the volume of gas used.3,4 In our case, the ulcers were likely the point of entry for the air. Once in the circulation, air is removed by diffusion across the arteriolar wall through the alveolar space. However, once this capacity is exceeded, air can enter the arterial circulation through a right-to-left intracardiac shunt, intrapulmonary shunt, a gastrointestinal arteriovenous malformation (AVM), or insufficient filtration by the pulmonary capillaries.5,6 Cerebral hypoperfusion is the eventual result of strain on the right ventricle and decreased cardiac output. Air bubbles also cause a physical obstruction (gas-air lock) and inflammation, both of which lead to ischemia. Subsequent bronchospasm and V/Q mismatch will cause worsening hypoxemia, hypercarbia, and acidosis.7,8 As neurologic symptoms are hard to discern in anesthetized patients, an acute drop in end-tidal CO2 may warn of an embolism.9,10 Once a CAE is suspected, the procedure should be aborted and 100% oxygen should be administered. Other recommendations include placing the patient in the left lateral decubitus and Trendelenburg position to minimize entry of air into the brain.11 Immediate CT scan of the brain may reveal gas bubbles. Echocardiography may demonstrate air in the right ventricle and rule out an intracardiac shunt.12 HBOT should be initiated within 5 hours and can minimize the size of the bubbles, increase the diffusion gradient, and decrease cerebral edema.13,14 Potential mitigating factors include using CO2 instead of air, reducing the maximal insufflation pressure, and limiting the volume of insufflated gas. In conclusion, providers must remain vigilant and recognize a CAE during endoscopy to minimize patient morbidity. Upon recognition, 100% oxygen should be applied, the patient must be properly positioned, and HBOT should be initiated within 5 hours.

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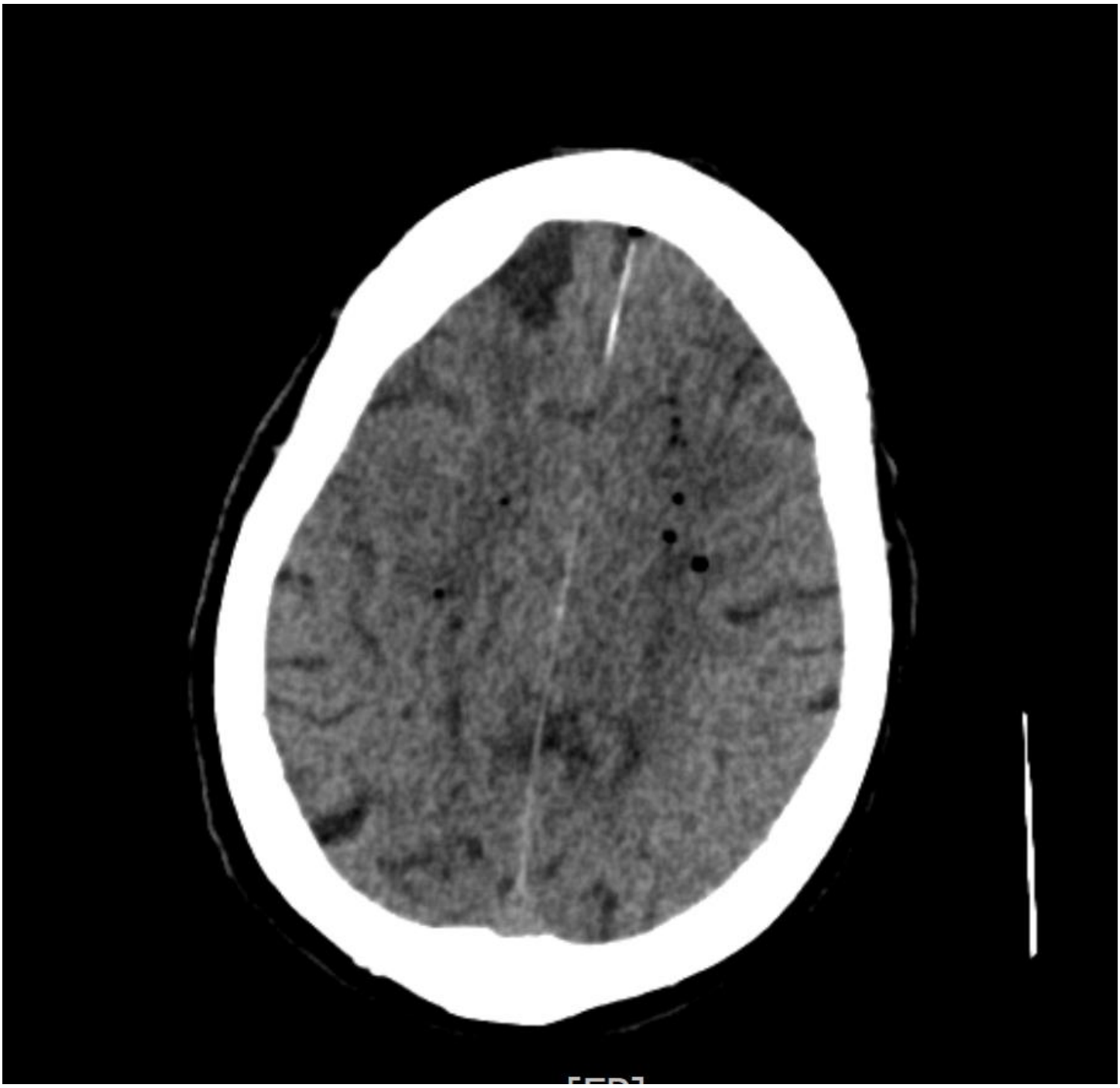

Initial CT scan with focal multiple foci of air.

Cardiovascular Anesthesiology

Cardiovascular Anesthesiology-1 Severe Non-Cardiogenic Pulmonary Edema Following Protamine Administration: A Rare Case of Type 3 Protamine Reaction

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Introduction: The use of heparin for cardiopulmonary bypass (CPB) requires reversal to prevent significant bleeding. Despite known complications related to protamine, it remains the reversal agent of choice. Positively charged protamine isolated from fish sperm binds and inactivates heparin. Acute protamine reactions range from mild hypotension from histamine release to complete cardiovascular collapse (1). Harrow classified protamine reactions as three main types (2). Type 3 is associated with catastrophic pulmonary vasoconstriction (2). Severe protamine reactions during cardiac surgery are rare with an incidence of 0.13% and result in high mortality (3). Risk factors for severe protamine reactions include neutral protamine Hagedorn (NPH) insulin use, previous protamine exposure and history of vasectomy (3, 4, 5). We discuss a patient who developed severe non-cardiogenic pulmonary edema and pulmonary hypertension following protamine administration during cardiac surgery.

Case Report: A 61-year-old male with hypertension, congestive heart failure, and history of vasectomy developed severe prosthetic paravalvular aortic regurgitation and underwent mechanical aortic valve replacement. CPB lasted approximately 204 minutes and aortic cross clamp time was 176 minutes. Following uneventful separation from CPB, protamine was administered. Twenty minutes following administration of protamine, the patient became acutely hypoxic and was very difficult to oxygenate. For the next 45 minutes, the patient underwent aggressive medical management and received antihistamines, high dose steroids and epinephrine. Approximately one liter of pink frothy fluid was suctioned out of the endotracheal tube. Eventually the patient was placed back on CPB. His cardiopulmonary status improved and coming off bypass he was noted to have significantly elevated pulmonary artery pressures which had changed from his baseline. Inhaled nitric oxide (iNO) was started with improvement in his pulmonary artery pressures. He required significant hemodynamic support to come off CPB. Figure 1 and 2 are the preoperative and immediate postoperative chest radiographs showing the severity of the acute pulmonary edema. His postoperative course was complicated by prolonged intubation, slow iNO wean with transition to sildenafil, several blood transfusions, acute kidney injury requiring temporary dialysis, severe delirium, atrial fibrillation, and embolic ischemic injury to his right forefoot resulting in right transmetatarsal amputation. He was discharged postoperative day 36 to a long term care facility for further rehabilitation.

Discussion: Non-cardiogenic pulmonary edema and acute severe pulmonary hypertension as a result of protamine administration is very rare and carries a high morbidity and mortality. Prompt recognition and aggressive supportive care are imperative. A high level of vigilance is especially important in patients with multiple risk factors including NPH insulin use, history of vasectomy, fish allergy, and previous protamine exposure.

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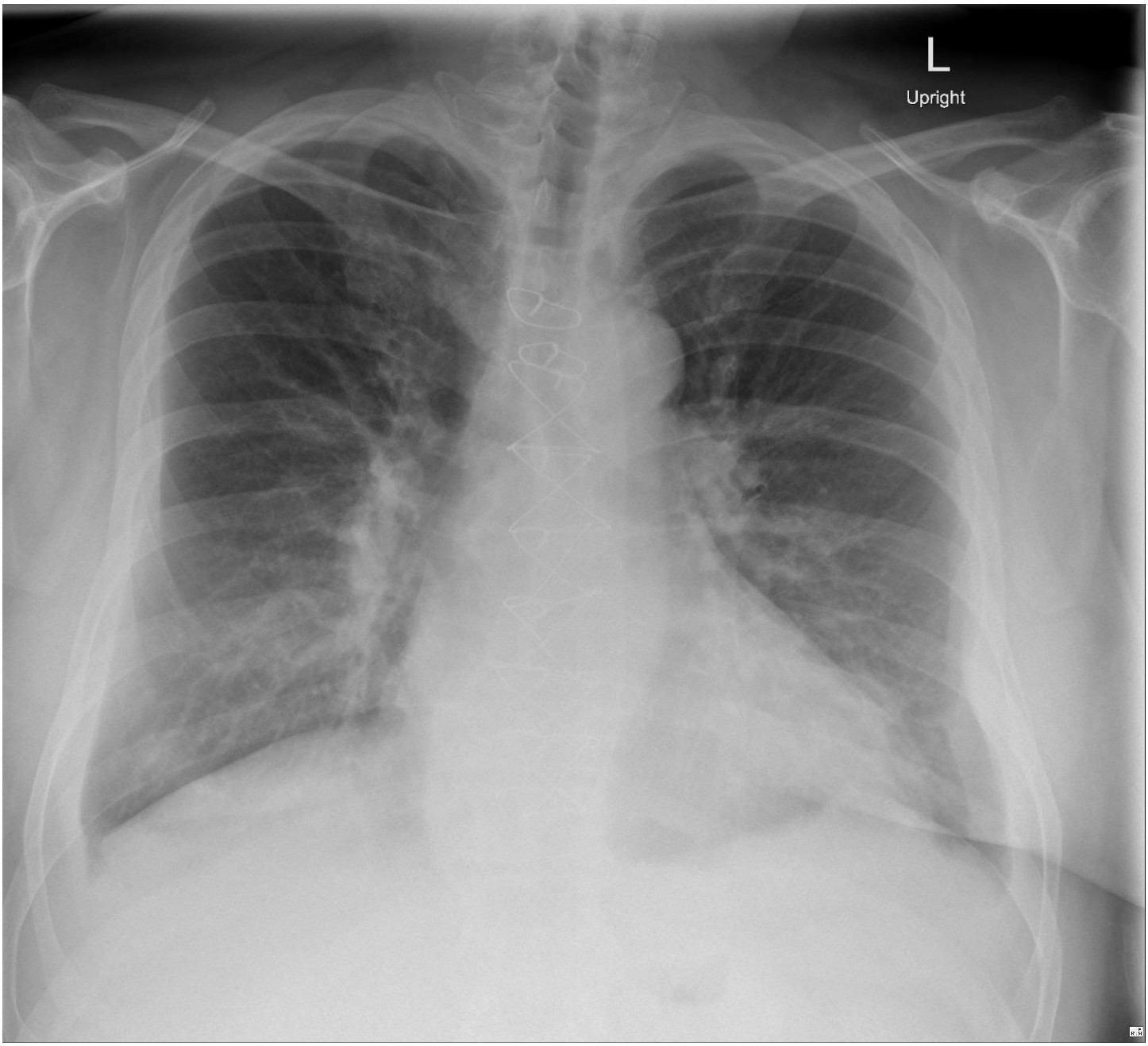

Figure 1: Preoperative chest radiograph

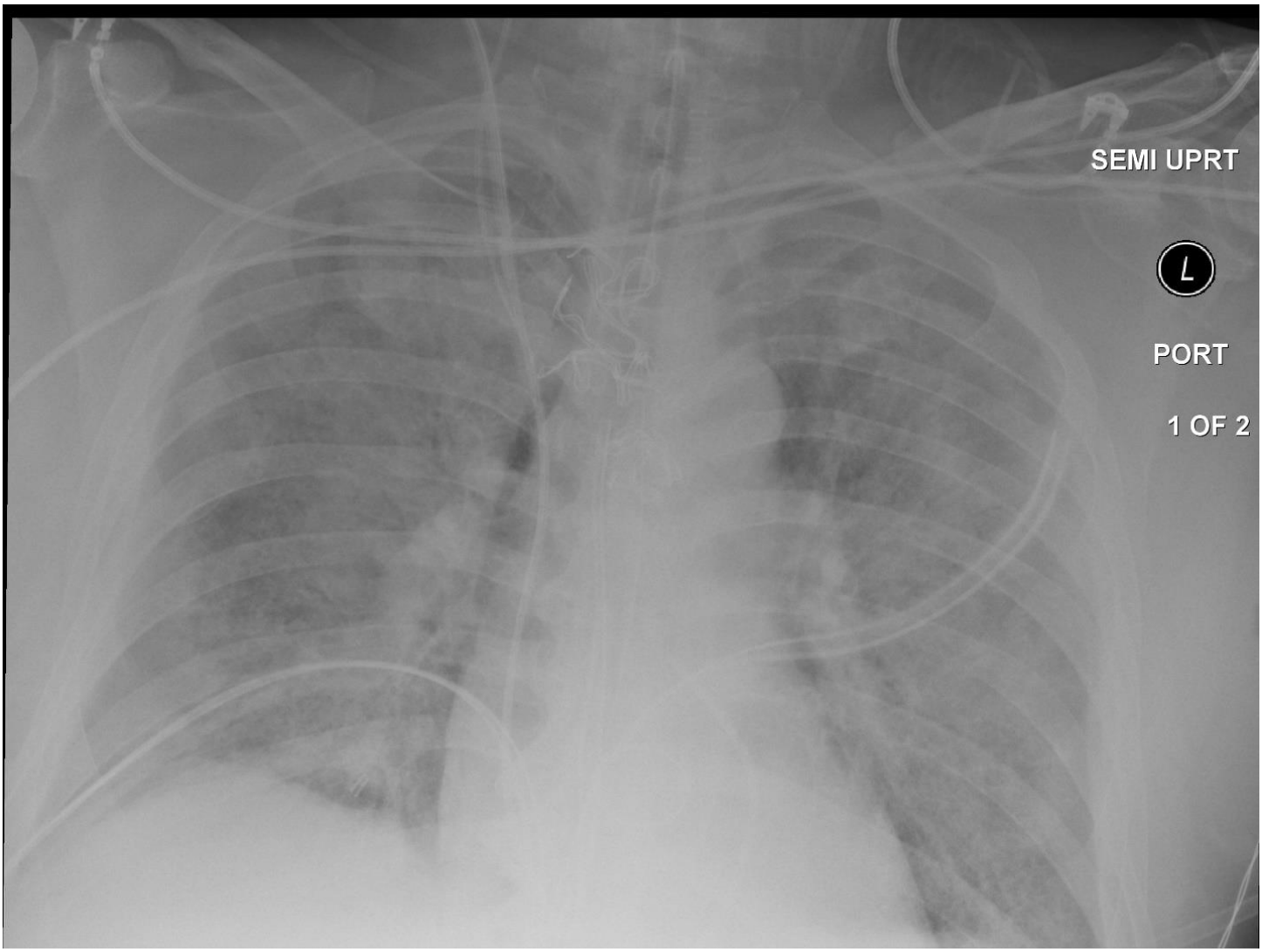

Figure 2: Immediate post-operative chest radiograph

Cardiovascular Anesthesiology-2

Immunosuppression Management After Hemorrhage in Post-Cardiac Transplant Patients

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Introduction: Perioperative management of heart transplant patients for non-cardiac surgery focuses on screening for evidence of rejection, pharmacodynamics of the denervated heart, and avoidance of CMV exposure or sensitization from blood products. Complications due to anticoagulation, steroids and diuretics have also been discussed.1,2,3 Rarely do heart transplant patients present for surgeries with expected large volume resuscitation such as trauma or major vascular surgery. In this case series, we describe two cardiac transplant patients undergoing elective abdominal aortic aneurysm repair who were followed postoperatively by the cardiac transplant team, and discuss management of anti-rejection medication in the setting of blood loss and transfusion.

Case Report: Case 1 A 73 year old male 4 years status post orthotopic heart transplant presented for transcutaneous endovascular repair of a type B aortic dissection. His intraoperative course was notable for 750 milliliters estimated blood loss and 3 liters (L) crystalloid administration. He received 3 units of leuko-reduced red blood cells over his postoperative course, with a hemoglobin nadir of 6.8 g/dL. He continued on his maintenance prednisone and mycophenolate, but tacrolimus was increased after a subtherapeutic level of 3.5 ng/mL on post-operative day two, rising to 7.8 ng/mL three days later. Approximately two weeks after discharge, the patient reported worsening fatigue and dyspnea on exertion. Tacrolimus level was found to be 3.9 ng/mL. Endocardial biopsy confirmed 3R/2R rejection. Case 2 A 70 year old male 12 years status post orthotopic heart transplant presented for open suprarenal abdominal aortic aneurysm repair. Coagulopathic bleeding persisted throughout the procedure with 3 L estimated blood loss. Resuscitation included 2 L autologous red blood cells, 6 units fresh frozen plasma, 3 units platelets, 6 packs of cryoprecipitate, 6.5 L crystalloid, tranexamic acid and factor VIIa. The primary concern was to prevent graft rejection in the setting of large volume resuscitation. Methylprednisolone 500 mg was administered and tacrolimus and mycophenolate levels were drawn mid-resuscitation. Mycophenolic acid level dropped from 81 to 40 mcg/mL. Tacrolimus titers decreased from 9.6 to 6 ng/mL, and remained subtherapeutic between 2.5 and 5.1 ng/mL until postoperative day 23. High dose steroids were continued until therapeutic trough level was achieved. Sublingual tacrolimus was given until return of bowel function indicating reliable oral absorption. Mycophenolate was restarted prior to discharge.

Discussion: The prevention of acute rejection in the second case, despite significantly higher transfusion requirement was attributed to pulse dosing of methylprednisolone and close monitoring of tacrolimus levels. Steroid administration must be weighed against the risk of infection and delayed wound healing. Tacrolimus toxicity is another concern with hypovolemia, however monitoring tacrolimus and mycophenolate levels perioperatively illustrated rapid dilution during resuscitation. Pulse dose methylprednisolone continued in the early postoperative period was protective until immunosuppressant titers stabilized. Collaborative management of anti-rejection regimen with the cardiac transplant team in post-transplant patients with anticipated blood loss and transfusion requirement is a critical component of perioperative care.

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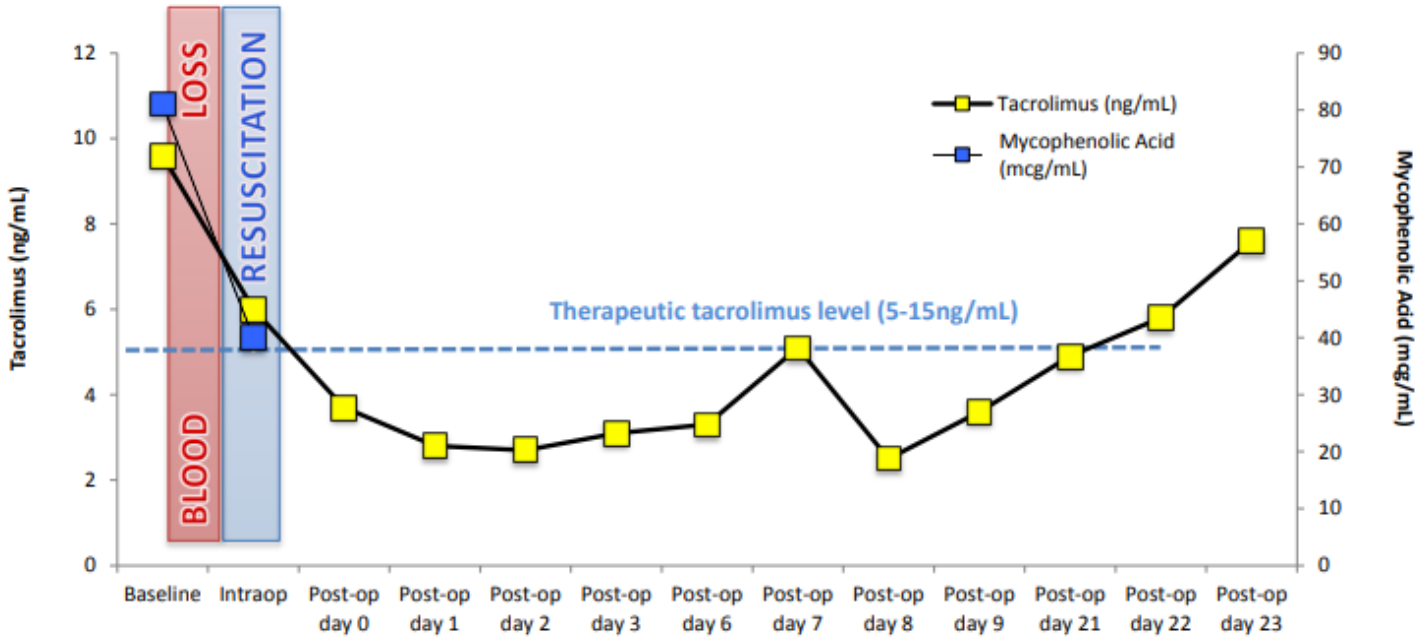
Perioperative Serum Tacrolimus & Mycophenolic Acid Levels for Case 2



Cardiovascular Anesthesiology-3 Cor Triatriatum Dexter and Patent Foramen Ovale Discovered Following Cardioembolic Stroke

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Introduction: Cor triatriatum (CT) is a rare congenital cardiac anomaly with fewer than 250 cases reported within existing literature (1). It is defined by the presence of an abnormal flap or septation within either the left atrium (cor triatriatum sinister (CTS)) or right atrium (cor triatriatum dexter (CTD). CT may exist as an isolated anomaly or in combination with additional congenital cardiac abnormalities. Most cases of CT are found in early infancy. However, few cases may remain asymptomatic until adulthood or be discovered post-mortem (2). The septation created by CT impedes filling of the corresponding ventricle, with CTS and CTD symptomatically resembling mitral or tricuspid valvular stenosis respectively (2). Additional CT related complications include pulmonary hypertension, heart failure, atrial fibrillation, syncope, thrombus formation, and sudden caidiac arrest (3). Several existing case reports describe cardioembolic stroke or cerebrovascular accident (CVA) in the context of left-atrial CTS (4-8). However, to our knowledge no existing case report describes CVA in a patient affected by right atrial CTD. Here, we describe a case of cardioembolic CVA in a patient with CTD and a patent foramen ovale (PFO).

Case Report: A 36-year-old female with a past medical history of peripheral scleroderma, renal cell carcinoma s/p partial nephrectomy, childhood Ewing sarcoma s/p chemotherapy, and recent cardioembolic stroke s/p intracranial thrombectomy by interventional radiology presented for cardiac surgery. The patient displayed no residual neurological deficits after cerebral thrombectomy. However, her stroke workup was notable for a transesophageal echocardiogram (TEE) revealing severe mitral regurgitation, mild aortic incompetence, mild tricuspid regurgitation, patent foramen ovale, and right atrial cor triatriatum. The patient had a preserved left ventricular ejection fraction of 65%. No masses or thrombi were identified within the left or right atrium. Rheumatologic evaluation determined that the patient's scleroderma was isolated to the periphery without evidence of systemic or cardiovascular involvement. The patient also denied a history of transient ischemic attack, syncope, chest palpitations or diagnosis of atrial fibrillation. Additional workup, including carotid arterial duplex and Holter monitor evaluation were unremarkable. Cardiogenic embolism was suspected, and the patient presented for minimally invasive mitral valve repair, resection of right atrial membrane, closure of the PFO, and ligation of the left atrial appendage, which proceeded uneventfully. She recovered well post-operatively and was free from residual neurologic symptoms or subsequent cerebrovascular events at 2-month outpatient follow-up. Images 1-3 were obtained by the patient's anesthesia providers following the induction of anesthesia and prior to surgical correction of her cardiac malformation. Image 1 is a TEE image demonstrating CTD with a PFO. Figure 2 is a TEE image with color flow doppler demonstrating blood flow from the right atria into the right ventricle. Figure 3 is a static image taken from a TEE video recording with color flow doppler demonstrating interflow between right atria.

Discussion: Cor triatriatum is a rare congenital cardiac anomaly. Few affected patients progress to adulthood without symptomology or diagnosis. Classical CT is defined as isolated CT in the absence of other congenital cardiac malformations. However, most patients present with coexisting congenital cardiac malformations (1). The most frequent coexisting cardiac anomalies included atrial septal defect, PFO, tricuspid regurgitation, and myxomatous mitral valve disease (3). Though CT remains rare, existing evidence suggests that our patient's simultaneous CT, PFO, and valvular disease may be consistent with known presentations of the anomaly. A review of existing literature reveals several reports of CT-related cardioembolic stroke (4-8). However, each case describes cardioembolic stroke in the context of CTS, a left-sided atrial malformation. To our knowledge, no existing report describes a case of cardioembolic stroke with CTD, a right-atrial malformation. Our patient's PFO may have made passage of a right atrial thrombus to the left atrium, ventricle, and systemic circulation possible. However, the exact etiology of our patient's CVA remains unknown and her complex medical history should not be overlooked.

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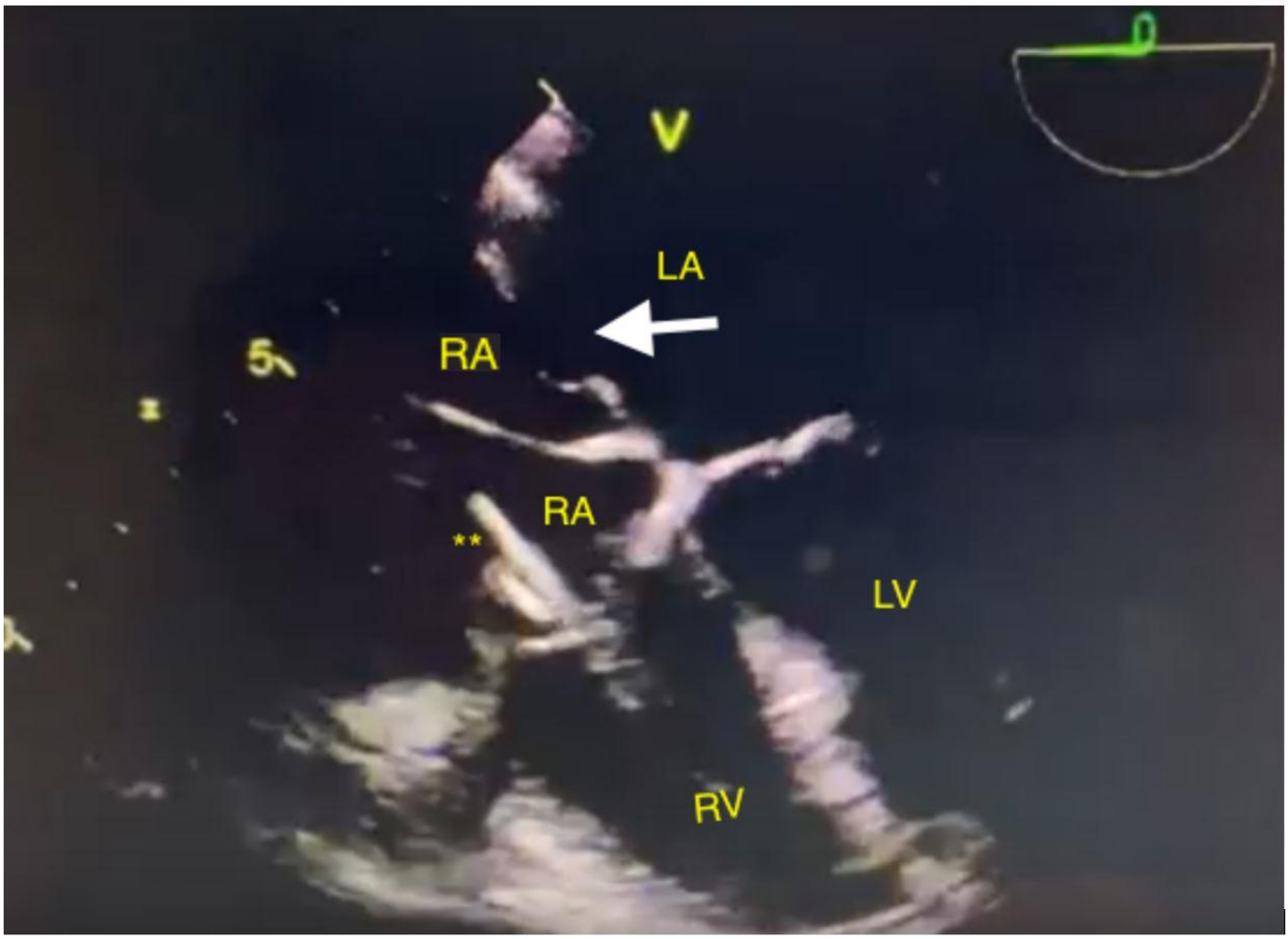
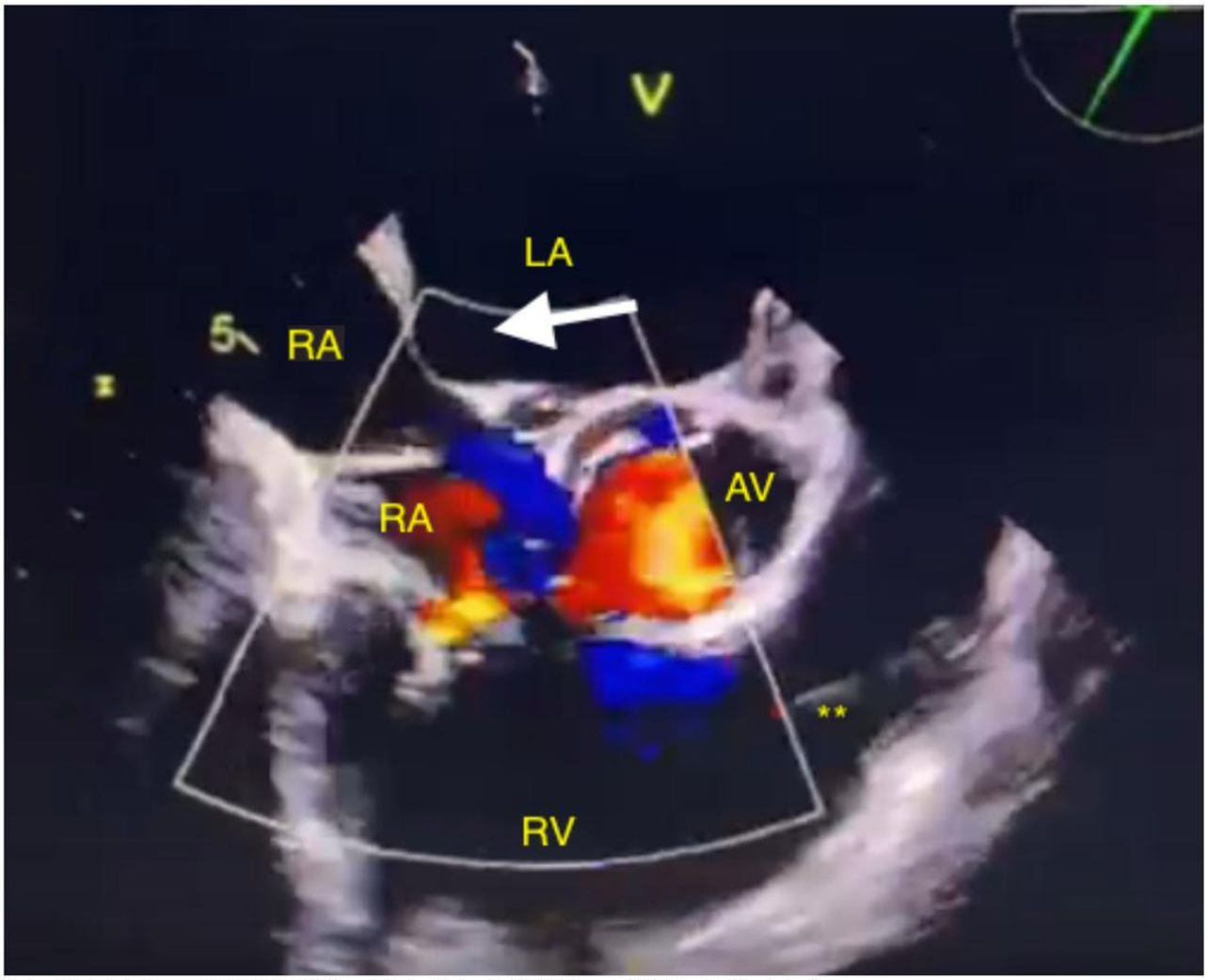
Figure 1: Transesophageal Echocardiogram demonstrating Cor Triatriatum Dextran with a Patent Foramen Ovale.



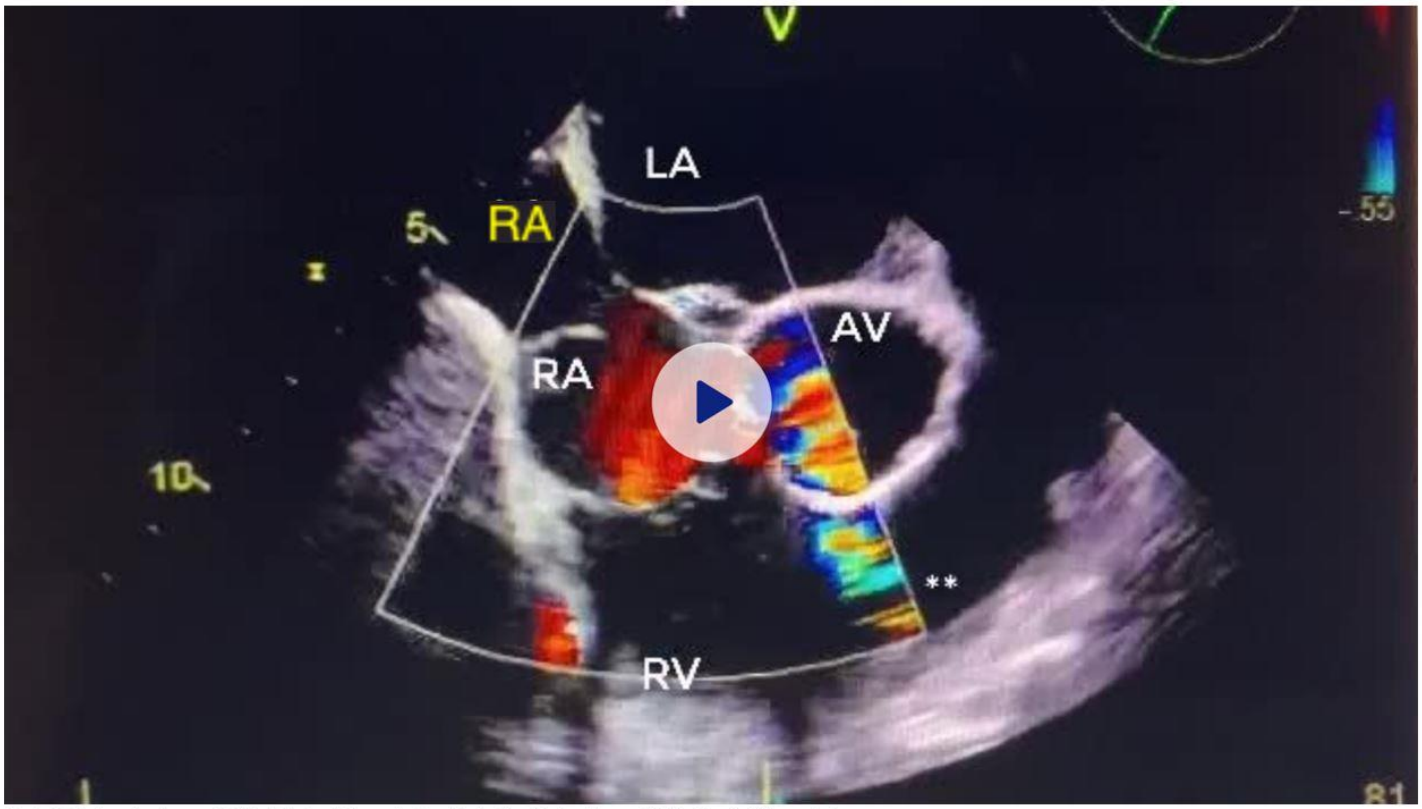
RA: Right Atrium; RV: Right Ventricle; LA: Left Atrium; LV: Left Ventricle

Figure 2: Transesophageal Echocardiogram with color flow doppler demonstrating Cor Triatriatum Dextran with blood flow into the right ventricle.



RA: Right Atrium; RV: Right Ventricle; LA: Left Atrium; LV: Left Ventricle

Figure 3: Transesophageal Echocardiogram with color flow doppler demonstrating Cor Triatriatum Dextran with blood flow between right atria. A small patent foramen ovale is also visible between right and left atria.



RA: Right Atrium; RV: Right Ventricle; LA: Left Atrium; LV: Left Ventricle

Cardiovascular Anesthesiology-4 Incidental PFO With Flow Reversal Causing Hypoxia: A Case Of Arduous Separation From Cardiopulmonary Bypass Made Possible With Inhaled Nitric Oxide

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Introduction: Patent foramen ovale (PFO) is a remnant of the fetal circulation that is present in 25% of adults (1) with incidence of intraoperative previously undiagnosed PFO during cardiothoracic surgery is 17%(2). Presented here is a case of incidentally discovered PFO during coronary artery bypass grafting on pump leading to severe hypoxia in setting of reduced right heart function, pulmonary hypertension and COPD.

Case Report: 83 year-old gentleman with diabetes, hypertension, chronic obstructive pulmonary disease on 4L O2 at home, obstructive sleep apnea, and hyperlipidemia who presented with new onset chest pain and shortness of breath. EKG showed sinus tachycardia with an incomplete RBBB and inferior Q waves but no dynamic ST/T wave changes. Labs were positive for troponin leak. CT PE was negative. Preoperative hypotension was treated with fluid resuscitation and vasopressor support. A complete heart block was observed on telemetry, resulting in inotropic support and a transvenous pacer. TTE demonstrated LVEF of 60%, normal RV function, RA pressure 8mmHg and no valvular or regional wall motion abnormality. Cardiac catheterization revealed severe three-vessel disease and he was taken to the operating room to undergo on pump CABG for revascularization. After induction, intubation, and central line placement a TEE was performed that revealed a patent foramen ovale. The operative course was unremarkable but liberation from bypass resulted in profound hypotension, elevated PA pressure, hypoxemia, moderately reduced RV function, mild TR, and worsening right to left shunt across the PFO. Hypoxemia showed minimal signs of improvement despite starting milrinone and vasopressin. Inhaled nitric oxide was initiated to reduce pulmonary vascular resistance. The patient's hemodynamics and oxygenation improved facilitating independence from cardiopulmonary bypass. The patient was then transferred to ICU. Patients with PFO are usually asymptomatic because the defect is flap-like and pressure in the left heart is normally greater than right limiting significant shunting. However, conditions that result in higher than normal right heart pressure can cause flow reversal leading to hypoxia. Several factors were identified in our patient that could have increased the right heart pressure instigating hypoxemia in presence of a PFO. Hypoxia in turn, made the separation from cardiopulmonary bypass difficult. This patient had history of COPD and OSA, which can lead to hypoxia-induced pulmonary vasoconstriction, increasing right atrial pressure (3). Hypoxia driven rise in right sided pressure with right to left shunting through the PFO can be minimized with the use of inhaled nitric oxide, or a phosphodiesterase (PDE)-5 inhibitor (3). Additionally the patient developed right heart failure and subsequent elevated pressure possibly resulting from reduced coronary perfusion pressure to the right ventricle due to reduction in mean arterial pressure caused by anesthetic agents, cardiopulmonary bypass associated systemic vasodilation and positive pressure ventilation-induced elevation in peripheral vascular resistance (4).

Discussion: PFO can potentially allow means of right to left shunt causing hypoxia in patients with elevated right heart pressure, preventing weaning from cardiopulmonary bypass. Inhaled Nitric Oxide can be used to diminish shunting across the PFO.

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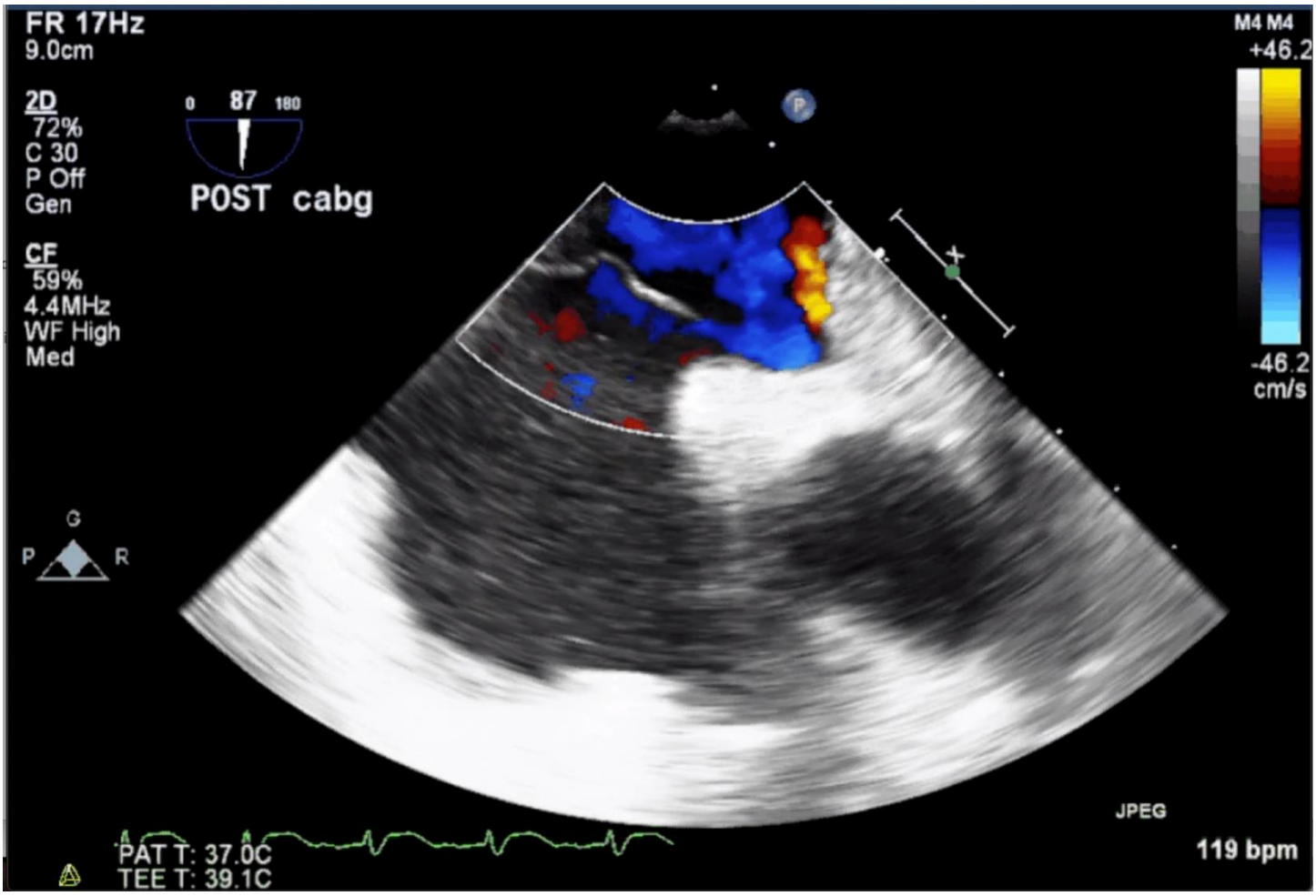
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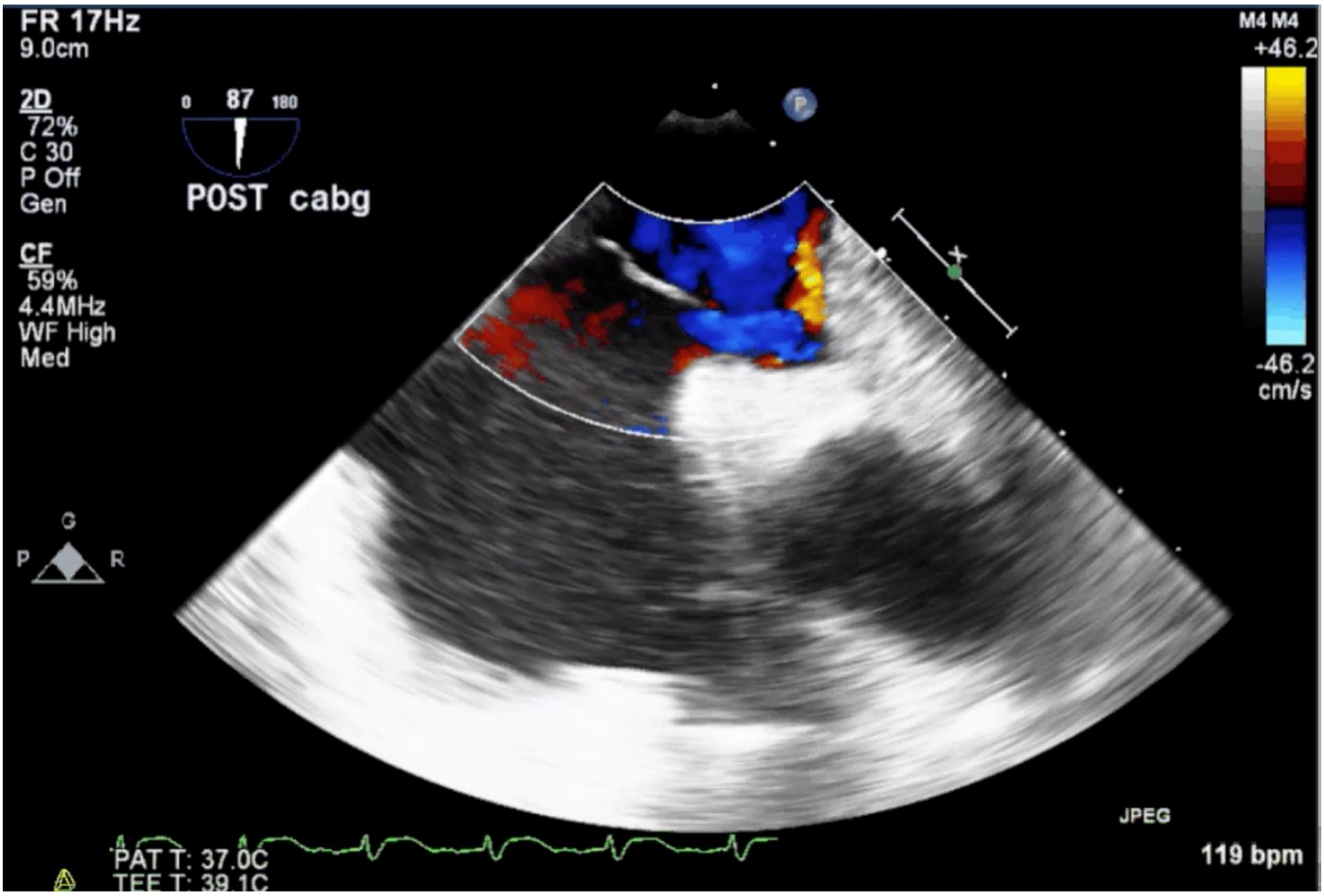
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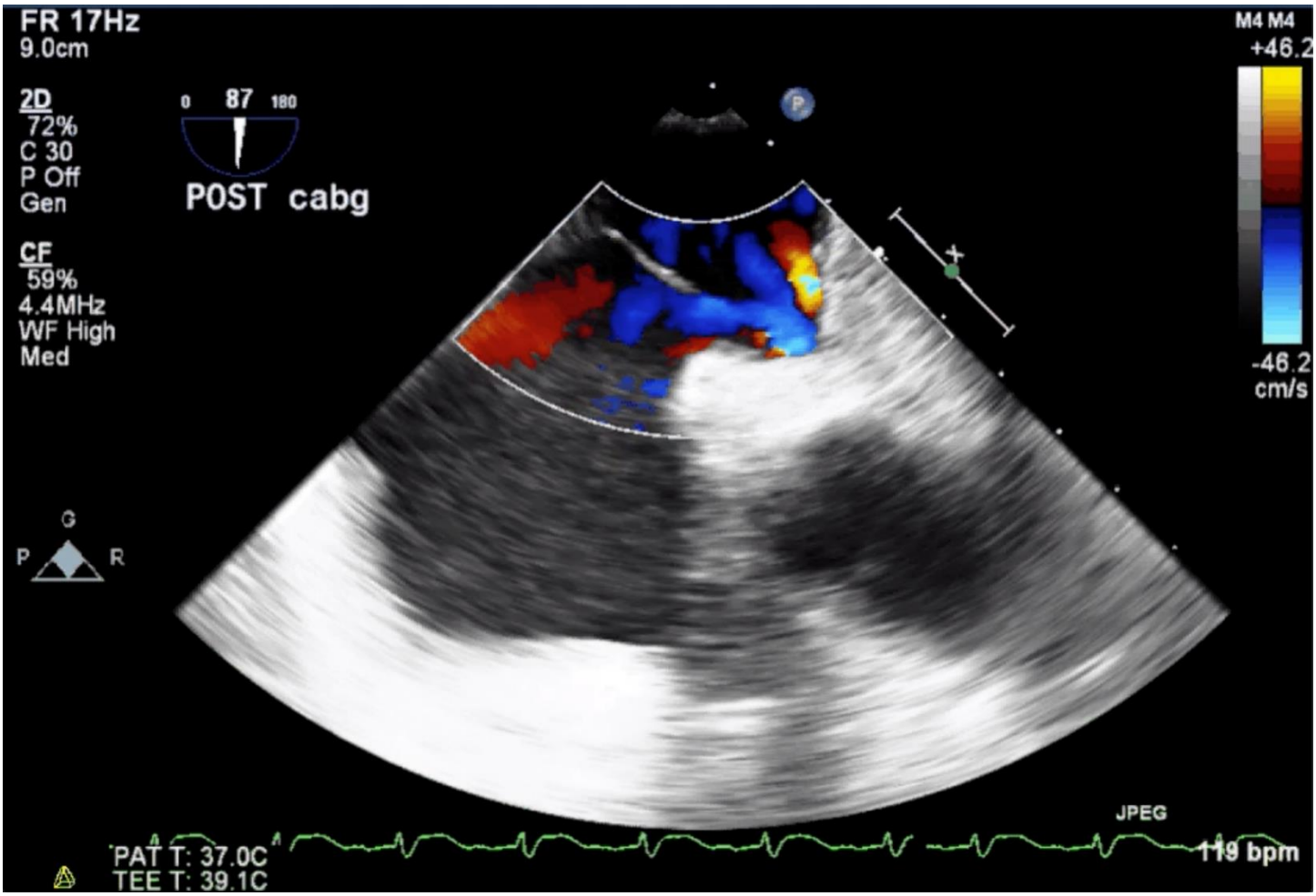
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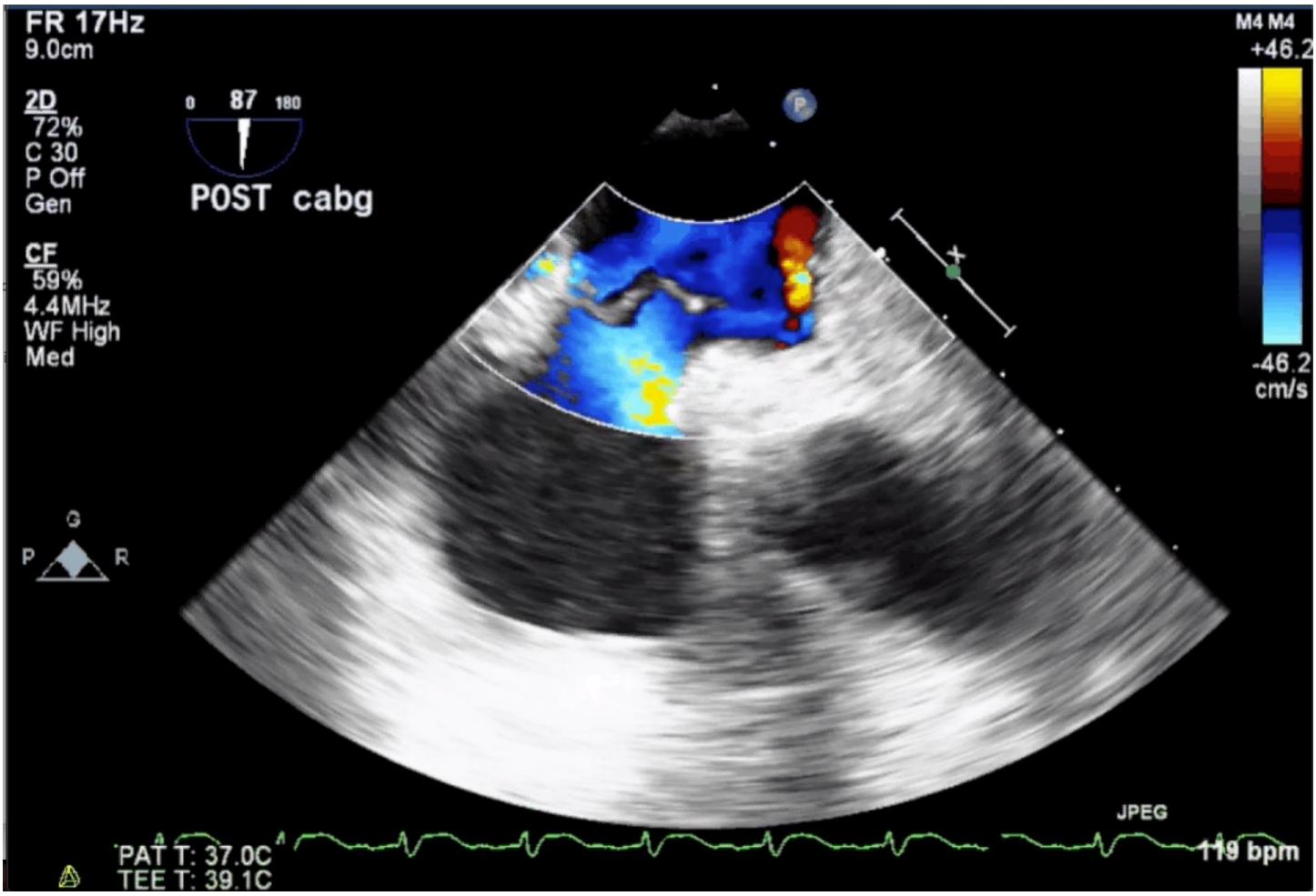
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Cardiovascular Anesthesiology-5 A Multidisciplinary Approach to a Case of Peripartum Cardiomyopathy

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Introduction: The incidence of peripartum cardiomyopathy (PPCM) is 0.001 to 0.0003 live births.(1) This number is increasing in part due to improved diagnostic tools, awareness, increasing maternal age, and multifetal pregnancies.(2) Moreover, in California 2004-2006, peripartum cardiomyopathy was the leading cause of maternal mortality. The etiology is unclear although race and presence of preeclampsia are major contributing factors to disease pathophysiology and morbidity. Signs and symptoms include left ventricular enlargement, peripheral edema, shortness of breath, elevated brain naturetic peptide and troponins.(3) This report details a case of antenatal cardiomyopathy.

Case Report: The patient is a 25-year-old female G1P0 31 5/7 weeks with no significant past medical history presenting with lower extremity edema and proteinuria. Upon workup she was found to have preeclampsia with severe features and intrauterine growth restriction. CT scan showed a small subsegmental pulmonary embolus, cardiomegaly, and minimal pericardial effusion. Echocardiogram showed an ejection fraction (EF) of 20% and spherical geometry of her left ventricle, concerning of a chronic cardiomyopathy. Right ventricular function was normal. Right ventricular systolic pressures were estimated to be 40-50 mmHg. A multidisciplinary team comprised of obstetricians, obstetric and cardiac anesthesiologists, and advanced heart failure cardiologists transferred her to the cardiac care unit the night before a contraction stress test (CST). Prior to the CST, the patient had an epidural, an arterial line, a right internal jugular vein introducer and a pulmonary artery catheter placed. The CST had to be halted and the patient was planned for emergency cesarean section (c-section) due to fetal decelerations. Lidocaine with epinephrine was utilized to rapidly obtain a surgical level of epidural anesthesia, with preemptive dobutamine and norepinephrine used for hemodynamic perturbation associated with the technique. The c-section was performed in a hybrid cardiac catherization lab to allow for rapid deployment of mechanical circulatory support should it have been necessary. A repeat vertical incision was made from the patient's prior surgery for ovarian torsion. The baby was delivered within ten minutes. Dobutamine and norepinephrine were maintained throughout her delivery and left on at the end of the case for cardiac support. Oxytocin and carboprost were administered to treat uterine atony and she was uneventfully transferred back to the cardiac care unit where her inotropes and vasopressors were weaned off over several days. After successful diuresis and ICU monitoring for post-operative volume shifts, she was discharged home in good condition. After discharge she was maintained on metoprolol, losartan, furosemide, and warfarin.

Discussion: There are a limited number of randomized controlled trials on treatment strategies for PPCM. Therapy focuses on controlling systolic heart failure, volume status, neurohormonal responses, arrhythmias, and thromboembolic events. Most instances occur postpartum; however, this case took place antenatally without a previous diagnosis of preeclampsia or hypertension during the pregnancy until her initial presentation. This highlights a challenge with the management PPCM as many patients may go undetected with little time for medical optimization. Given this patient's nadir EF of 20%, classifying her as mWHO IV (modified World Health Organization classification of maternal cardiac risk grade IV) her risk of serious maternal cardiac event or mortality was 40-100%. Fortunately, this patient had a favorable outcome due to a quickly assembled multidisciplinary team. Her care was facilitated by the use of invasive hemodynamic monitoring, anticipating an autobolus with preemptive dobutamine administration, minimizing fluid administration, and early vasopressor support upon assurance of adequate cardiac output. Postpartum, patients normally proceed to full recovery. In approximately 70% of patients, EF returns to >50% after 6 months.(5) Given the spherical geometry of her myocardium, acute on chronic decline in ejection fraction is suspected and this patient's EF may not return to normal after her pregnancy.

Reference(s):

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4. Scientific Document Group, 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy: The Task Force for the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC), European Heart Journal, Volume 39, Issue 34, 07 September 2018, Pages 3165–3241

5. Clinical Outcomes for Peripartum Cardiomyopathy in North America: Results of the IPAC Study (Investigations of Pregnancy-Associated Cardiomyopathy).J Am Coll Cardiol. 2015; 66:905–914

Cardiovascular Anesthesiology-6 Detection of seizure activity during cardiac surgery: Should electroencephalographic monitoring be a standard monitor?

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Introduction: Monitoring cerebral perfusion and state of neurologic and hypnotic status during cardiopulmonary bypass (CPB) remains an active area of research. Besides monitoring depth of anesthesia, non-invasive monitors of brain activity can provide early information about cerebrovascular events like ischemia, hemorrhage, etc. and influence both intra-operative and post-operative management.

Case Report: A 60-year old male with a history of hypertension and severe eccentric mitral regurgitation thought be due to P1/P2 flail and ruptured posterior chordae presented for minimally invasive mitral valve repair on CPB. After 2mg of midazolam as anxiolysis, anesthesia was induced with 2 mg/kg of propofol, 3 mcg/kg of fentanyl and 1mg/kg of rocuronium. Aminocaproic acid was used for anti-fibrinolytic therapy. In addition to a continuous cardiac output Swan-Ganz catheter, cerebral oximetry and hypnotic monitoring (SedLine) was used for the case as is standard for procedures involving CPB at our institution. Lung isolation was achieved via a 37 Fr left-sided double lumen tube and a mitral annuloplasty ring was placed with no residual MR. The patient was weaned off CPB on 0.03 mcg/kg/min of epinephrine and inhaled epoprostenol 0.05 ng/kg/min. The total CPB time was 71 minutes and the aorta was cross-clamped for 54 minutes. Approximately, 15 minutes after liberation from CPB the patient was noted to have rhythmic electrical activity seen on the SedLine that lasted 3 minutes before it was terminated with a 3mg midazolam bolus. The cerebral oximetry was stable during this time though it had a symmetric dip after weaning CPB as is expected. There were no new drugs given around this time but the patient did receive a 50mg ketamine bolus while on CPB about an hour prior to this event. The remainder of the procedure was uneventful and the patient was successfully extubated the same day in the intensive care unit with a normal neurological examination.

Discussion: The differential diagnosis of seizures during CBP includes reduction in cerebral perfusion pressure leading to cerebral ischemia, pump-generated emboli, atheromatous emboli from aortic cannulation in diseased aorta, air embolism during liberation from CPB in an open chamber procedure when the myocardium is closed and defibrillated (1), use of high-dose tranexamic acid as an anti-fibrinolytic (2), major electrolyte disturbances (ex: rapid sodium correction), and CPB-related alterations in cerebral physiology. It is likely that the incidence of seizures under CPB is under-reported because most of the time the patients are under a full MAC of isoflurane, may have neuromuscular blockade on board which may mask the physical manifestations of seizure activity, and most importantly because electroencephalographic (EEG) data is not routinely monitored intraoperatively. Post-operative seizure activity is strongly associated with increase rates of neurologic morbidity (3) and is frequently related to an intraoperative adverse event. The event witnessed in our patient suggests that our current monitoring strategies may be possibly missing key events that are contributing to poor post-cardiac surgical neurologic outcomes. Identification of these events in real time is critical to understanding their significance and developing strategies to avoid them and the related post-operative sequelae. This also calls into question whether standardized EEG monitoring along with cerebral oximetry should be the standard of care for patients undergoing cardiopulmonary bypass.

Reference(s):

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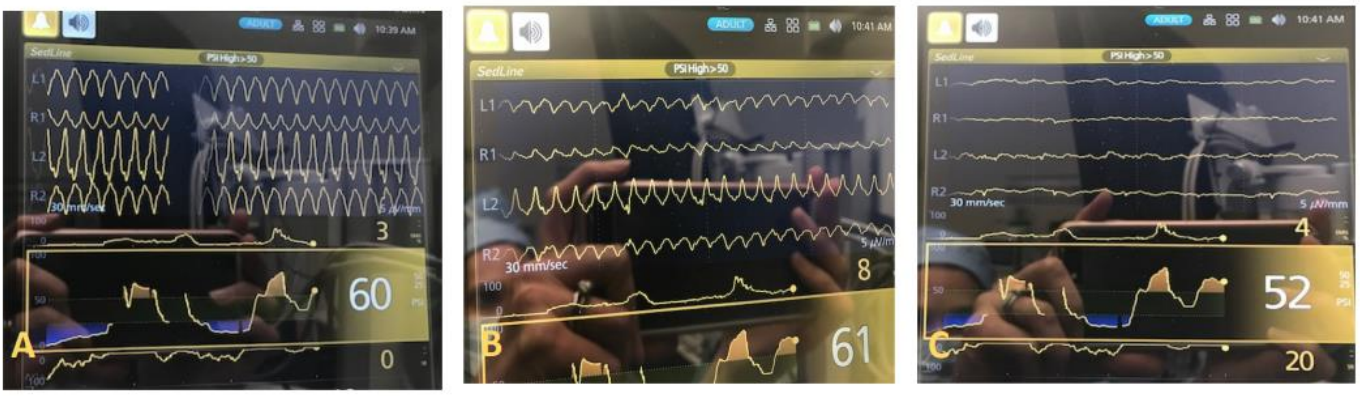

Images: ***(A-B)*** Capture sudden onset rhythmic discharge pattern with increasing ***Patient State Index (PSI)***. This activity persisted for about 3 minutes at which point 3mg of midazolam were administered with subsequent resolution of the rhythmic activity in very low-voltage low-frequency activity ***(C)***. The PSI was noted to trend down but not captured in the panel above due to time-delay in the algorithm that processes these waveforms.

Cardiovascular Anesthesiology-7

Ascending the Ladder of Mechanical Support

Emily Naoum[1], Douglas Colquhoun[1]

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Introduction: Patients with decompensated heart failure and cardiogenic shock may be refractory to medical therapies and require mechanical circulatory support.

Case Report: A 51 year old woman with a history of peripartum dilated cardiomyopathy with an LV EF 10% and end stage renal disease on hemodialysis was found to have elevated biventricular filling pressures with reduced cardiac output. She was admitted for volume optimization and inotropic support while evaluation for heart-kidney transplant was ongoing. She was volume optimized with aggressive diuresis, but remained symptomatic. Inotropic support was limited by malignant arrhythmias. The patient underwent placement of an Impella 2.5 for LV support, however, it was found to be dislodged shortly after placement. She returned to the catheterization lab and underwent placement of a TandemHeart with a transseptal left atrial inflow cannula (21Fr) and right femoral outflow cannula (15Fr). On the evening after placement, the patient began to experience atrial arrhythmias, decreased systemic blood pressures and low Tandem flow. Based on the clinical picture and TTE findings, it was felt the patient's poor cardiac output was related to insufficient RV support. A 23Fr femoral venous cannula was placed bedside and spliced with the TandemHeart LA drainage cannula. The TandemHeart pump was discontinued and cannulas were connected to a Maquet Cardiohelp ECMO system. The existing femoral arterial cannula was used for blood return. Throughout her VA ECMO course, she maintained 0.8-1.1L of flow from the LA cannula and 1.1-1.3L flow from the femoral venous cannula. Addition of the femoral venous cannula allowed decompression of the RA and rapid initiation of biventricular support utilizing the two existing cannulas. There was significant flow in the LA venous catheter that suggests there was some maintained native RV function with partial offloading by the additional femoral venous catheter. Mechanical support must be managed carefully as VA ECMO may increase LV afterload and in profound LV dysfunction increase LV end diastolic and PA pressures and worsen global cardiac function.(1) A similar cannulation strategy, by adding a transseptal LA catheter, has been described in a case of a patient on VA ECMO who subsequently developed an LV thrombus, in which a TandemHeart transseptal cannula allowed for LA decompression.(2)

Discussion: This case illustrates a spectrum of percutaneous mechanical support strategies culminating in VA ECMO for potential bridge to transplant. Familiarity with the different methods of mechanical circulatory support and an understanding of the anatomical location of cannula placement and functional implications allows providers to escalate and combine support as clinically indicated.

Reference(s):

1Sultan I, Kilic A, Kilic A. Short-Term Circulatory and Right Ventricle Support in Cardiogenic Shock: Extracorporeal Membrane Oxygenation, Tandem Heart, CentriMag, and Impella. Heart Fail Clin. 2018 Oct;14(4):579-583.

2Jumean M, Pham DT, Kapur NK. Percutaneous bi-atrial extracorporeal membrane oxygenation for acute circulatory support in advanced heart failure. Catheter Cardiovasc Interv. 2015 May;85(6):1097-9.

Cardiovascular Anesthesiology-8 The Perfect Storm: Pulmonary Hypertension in the setting of Perioperative Thyrotoxicosis

Tim Shutter[1], Jun Sasaki[1]

[1]UT Southwestern Medical Center, Dallas, TX

Introduction: Thyroid storm or thyrotoxic crisis is a hypermetabolic state due to an overabundance of circulating thyroid hormone often associated with increased morbidity and mortality in the perioperative and postoperative setting (Miller RD., 2010). Pulmonary hypertension is associated with high morbidity and mortality, associated with right ventricular failure, arrhythmia, myocardial ischemia and intractable hypoxia (Sarkar and Desai, 2018). Multiple case studies suggest an association between pulmonary hypertension and a hyperthyroid state with hemodynamic and symptomatic recovery occurring when normal thyroid function is restored (Virani et al., 2003, Rashidi et al., 2017, Ganeshpure et al., 2012, Sugiura et al., 2015).

Case Report: A 40-year-old Hispanic female with significant history of morbid obesity and hyperthyroidism presents to the emergency department with two days of pelvic pain and findings of hydrosalpinx, scheduled for ovarian cystectomy and oophorectomy. Diagnosed with Graves disease six months previously, she was prescribed methimazole and nebivolol by an endocrinologist. Patient confirmed adherence to medication on the morning of surgery. She remained afebrile but moderately hypertensive and tachycardic throughout the procedure needing intermittent esmolol boluses. Upon extubation, patient developed severe tachycardia unresponsive to beta blocking medication. After recovering from anesthesia, she appeared confused and restless, complaining of nausea and heart palpitations. Upon further questioning, patient stopped home medications for greater than two weeks due to financial limitations. She was provided intravenous propylthiouracil and hydrocortisone along with oral propranolol for assumed thyrotoxicosis with admission to the surgical intensive care unit. Post operation lab work showed indeterminable elevated values outside the range of testing for TSH, free T3 and T4 along with an elevated lactate. Patient was diagnosed with thyroid storm needing over 2 weeks of hospitalization for recovery. Transthoracic echocardiogram during admission showed severely elevated right ventricular systolic pressures, a dilated pulmonary artery and systolic flattening of the interventricular septum consistent with right ventricular pressure overload with pulmonary hypertension. Her heart dysfunction was postulated to be due to inconsistent treatment of her hyperthyroidism. She was continued on methimazole and propranolol with improved heart rate and baseline mentation a week after her original surgery. The patient was discharged home with planned follow up echocardiogram to assess improvement of PH with compliance of prescribed medications.

Discussion: Though literature suggests a possible link between PH and hyperthyroidism, no clear mechanism has been identified. Proposed mechanisms include increased catecholamines causing vasoconstriction of pulmonary vasculature, increased metabolism of intrinsic pulmonary vasodilating substances or impaired metabolism of vasoconstrictors, or an autoimmune process inducing direct endothelial damage (Marvisi et al., 2013). In the United States, roughly 1.2% of the population has a formal diagnosis of hyperthyroidism with many appearing for elective surgery each day (Kravets I, 2016). Patients with known pulmonary hypertension are considered high risk candidates for surgical intervention. In the future, echocardiogram may be warranted for evaluation of PH in this population.

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Cardiovascular Anesthesiology-9 The Utility of Real-Time 3D in Diagnosing Acute Dysfunction of Bioprosthesis

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[1]Augusta University Medical Center, Augusta, GA, [2]Augusta University, Augusta, GA

Introduction: Bioprosthetic valves structures degenerate gradually over time. The failure of a bioprosthetic valve immediately after implantation is infrequent (1). Possible causes include valvular leaks (paravalvular or intravalvular) or leaflet dysfunction, usually caused by an obstruction or entrapment by suture loops. The Intraoperative impact of transesophageal echocardiography (TEE) has been established since it contributes to diagnostics and therapeutic management in valve replacement surgery (3). We present a case where the use of real-time 3 dimensional (3D) TEE was found to be highly effective in the evaluation of acute bioprosthetic failure.

Case Report: A 73-year-old M admitted for endocarditis. He had a history of hypertension, Diabetes Mellitus type I, a previous mitral valve replacement (mechanical), and multiple urinary tract infections (E. faecalis). Echocardiography revealed a vegetation in the mitral valve that obstructed the Left ventricular outflow tract (LVOT), as well as moderate to severe Tricuspid regurgitation and moderate to severe pulmonary hypertension. He was scheduled for a redo mitral valve replacement. Following a very surgically challenging debridement and resection of the mitral valve annulus and vegetations. A 31mm bioprosthetic valve was implanted. Positioning was determined by transesophageal echocardiogram (TEE) with real-time imaging for cardiac navigation and was considered satisfactory. However, we recognized the presence of a severe intravalvular leak in 2D TEE (Fig. 1). To better localize and identify the mechanism of this leak, we rely on real-time 3D TEE on the dual volume layout view (fig. 2 and 3). Utilizing this mode, we identify a residual suture that was interrupting the mobility of the posterior leaflet in the new valve, causing a severe Mitral regurgitation (MR) (vena contracta 0.65cm). Knowing the mechanism, severity, and location of the intravalvular leak, the surgical team decided to arrest the heart and attempt a repair. Guided by echocardiography, the surgeon was able to successfully repair the intravalvular leak with complete resolution of the severe MR. However, at this point, our patient was coagulopathic (most likely due to prolonged pump time), and we were able to come off bypass only after the placement of an Intra aortic balloon pump for hemodynamic control. He was transferred to the critical care unit with an open chest and expired on his post-operative day 4.

Discussion: The use of real-time 3D TEE provides additional information and different perspectives seen from the atrial (surgeon's view) and the ventricular side. In addition to the diagnosis, it is of great aid to implement an appropriate intervention strategy (2) . When compared to traditional 2D TEE, it provides a unique visualization and a better and more precise understanding when evaluating an implanted bioprosthetic.

Reference(s): Shapira Y, Vaturi M, Weisenberg DE, et al. Impact of intra-operative transesophageal echocardiography in patients undergoing valve replacement. Ann Thorac Surg 2004;78: 579–83. Real-Time three-dimensional Transesophageal Echocardiography in Valve Disease: Comparison with Surgical Findings and Evaluation of Prosthetic Valves. Singh A, Nanda NC, Kirklin JK. Intraoperative trans- esophageal echocardiographic diagnosis of a stuck bio- prosthetic mitral valve leaflet. Echocardiography 2007;24: 436–8.

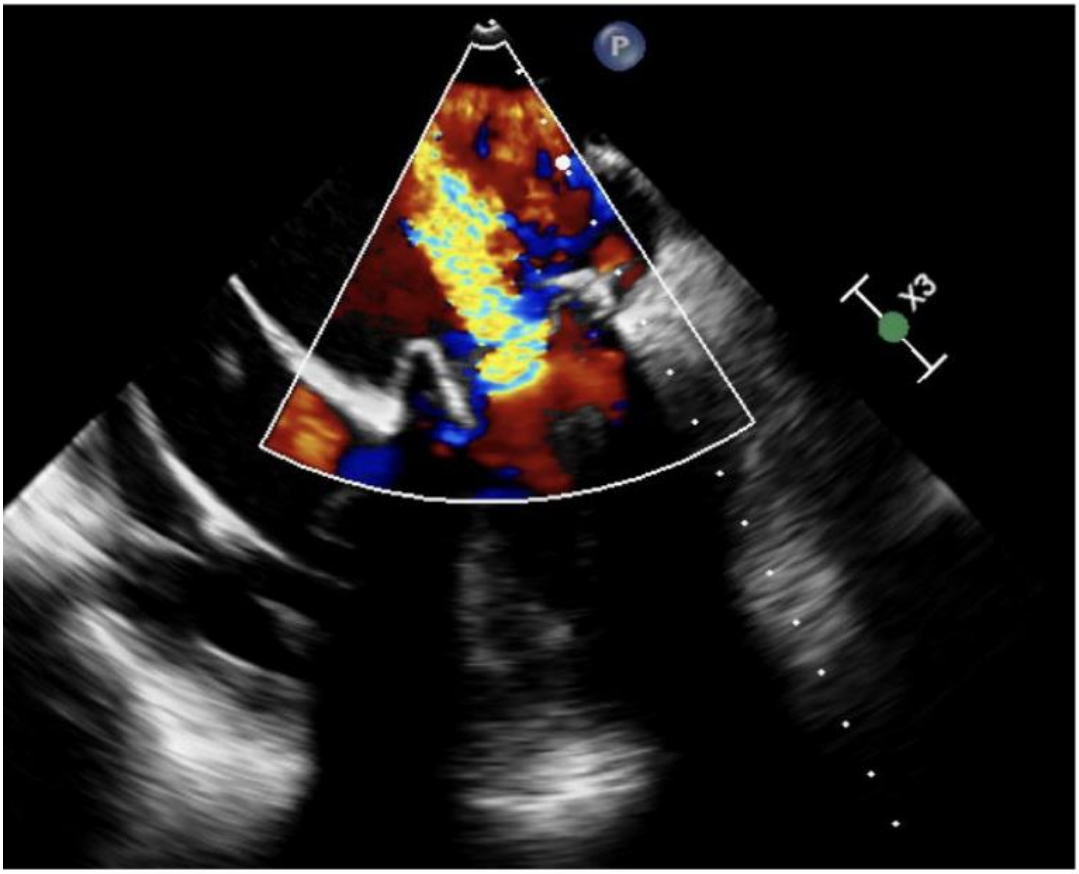

Fig. 1. Midesophageal 4 chamber. 2D TEE.
Severe Mitral Regurgitation

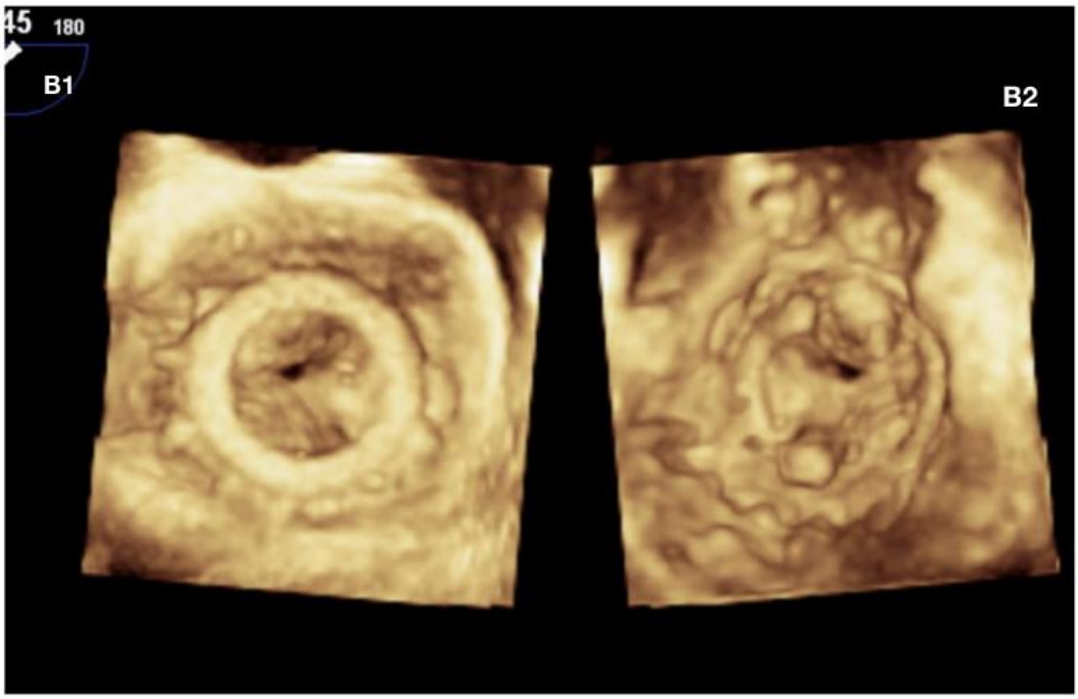

Fig. 2. 3D TEE Mitral valve.
B. Dual volume layout view
B1. Surgeons view
B2. arrow demonstrating residual structure on ventricular view.

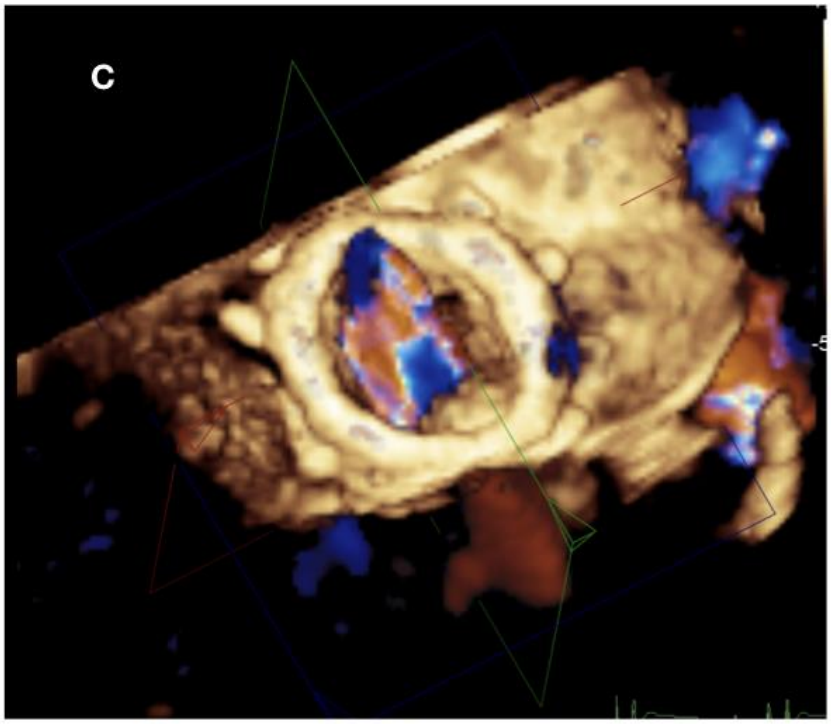

Fig.3. 3D Mitral valve reconstruction with color doppler
Revealing severe MR jet

Critical Care

Critical Care-1 Hemorrhagic Shock in End-Stage Liver Disease: A Case Study for Consideration of Non-Portal Hypertensive Etiologies

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[1]Mayo Clinic, Rochester, MN

Introduction: Patients with liver cirrhosis are prone to bleeding. As such, it is crucial that intensivists recognize common and uncommon etiologies for life-threatening hemorrhagic shock.

Case Report: A 54 year old male with end-stage liver disease and portal hypertension from hepatitis C with progressive hepatocellular carcinoma despite chemoembolization was transferred to the Emergency Department unresponsive in profound shock with agonal respirations. Endotracheal intubation was emergently performed, which was notable for brisk oropharyngeal bleeding. Arterial blood gas revealed severe mixed metabolic and respiratory acidosis with hematocrit < 15%. Massive transfusion was initiated for presumed variceal bleeding. Point-of-care ultrasonography was notable for large-volume ascites, central hypovolemia, and hyperdynamic cardiac function. Upper endoscopy revealed substantial pooling of blood in the posterior oropharynx, but no active bleeding from known esophageal and gastric varices. Flexible naso-oropharyngoscopy revealed a supraglottic mucosal disruption as the source of bleeding, presumably from traumatic endotracheal intubation, which was managed with oropharyngeal packing. However, the patient continued to have marked hemodynamic instability, diffuse coagulation derangements, and severe anemia requiring large-volume transfusion out of proportion with what would be anticipated by an oropharyngeal disruption. A paracentesis was performed given worsening tense ascites, revealing frank bloody drainage. Surgical and procedural interventions were considered, but ultimately the patient was deemed to have a non-survivable intra-abdominal catastrophe. Autopsy confirmed massive intra-abdominal hemorrhage secondary to a spontaneous rupture of hepatocellular carcinoma.

Discussion: Traumatic intubation may mimic variceal bleeding but is unlikely to progress to hemorrhagic shock. Although gastroesophageal variceal bleeding remains among the most common and deadly complications of patients with cirrhosis and portal hypertension, it is not the sole cause(1,2). Importantly, most non-portal hypertensive associated bleeding etiologies, apart from major trauma, are unlikely to result in massive acute blood loss. Hepatocellular carcinoma tumor rupture is an uncommon cause of hemorrhagic shock in developed nations, though it carries high mortality(3). Diagnosis is typically confirmed by axial imaging, which may be difficult to obtain in the critically ill patient. Management is based on supportive care, including massive transfusion and correction of coagulopathy, and emergent procedural intervention, including transarterial embolization, perihepatic packing, suture plication, hepatic artery ligation, alcohol injection, or surgical resection(4).

Reference(s):

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(4) Spontaneous rupture of hepatocellular carcinoma: a systematic review. Arch Surg. 2006;141(2):191–198.

Critical Care-2 ACUTE RADIAL ARTERY THROMBOSIS AFTER ARTERIAL LINE PLACEMENT IN ICU: A CASE REPORT

ROSA LOPEZ-RINCON[1], MIGUEL PLAZA-LLORET[2], Vikas Kumar[3], Manuel Castresana[4]

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Introduction: Radial artery thrombosis may be caused due to a wide variety of causes including iatrogenic cannulation, atherosclerosis, trauma or even emboli. Cannulation of the radial artery in the critically ill patient is a common procedure that is usually related to endothelial injury, exposing subendothelial collagen leading to platelet adherence and subsequent thrombus formation. There are many studies that have shown this to occur in up to 40% to 60% of cases (1)(5). The following case presentation includes a case of acute thrombosis of the radial artery following the cannulation and discusses the medical implications and therapeutic options available.

Case Report: A 62-year-old male with PMH of CAD, DM, HTN, COPD, hypothyroidism and multiple attempted ventral hernia repairs, admitted to the ICU as a level 1 trauma following a penetrating injury to the abdomen. During his ICU-hospital course had a radial arterial line placed on his right hand for hemodynamic monitoring for 4 days. Seldinger technique was performed with ultrasound (US) guidance for arterial cannulation without any complications reported. During morning rounds his right hand was found to be relatively cooler than the left hand, the patient denied pain but he was not oriented enough for a full systematic review and was uncomfortable in his bed in the ICU. According to his physical examination RUE: + radial signal, + ulnar signal, + palmar arch motor sensory intact, hand relatively cool compared to L hand, palpable brachial artery. LUE, RLE, and LLE: Palpable radial and femoral, good capillary refill < 2 seconds, motor-sensory intact. Following this, multiplanar US images of the right upper extremity arterial vasculature were performed with the use of color Doppler overlay and spectral Doppler waveform analysis (Image 1). It showed a distal occlusion of the right radial artery (Image 2 and 3), also showed superficial venous occlusion. The rest arteries including the mid aspect of the radial artery (Image 4), right proximal radial artery (Image 5) and right ulnar artery were patent and demonstrate normal triphasic spectral Doppler waveforms. Vascular surgery was consulted shortly after the results came back. They recommended no need for acute surgical interventions, start therapeutic low-intensity heparin iv infusion, vascular checks every 4 hours and keep hand warm and level with the body. After 2 weeks of treatment, his right hand became warmer and a new US study showed that the obstruction was resolved.

Discussion: Radial artery thrombosis incidence ranges between 5 and 30%. This wide range is probably created by the fact, that radial occlusion is not symptomatic in most patients because of the dual blood supply of the hand and that US assessment is not a standard procedure after cannulation (3). Looking at the two different techniques performed, the Seldinger technique and the 'transfixion' technique, curiously there does not appear to be any major difference between thrombotic complication rates for either technique. Shorter compression time during hemostasis was shown to reduce radial thrombosis (4). Several strategies have been reported to help the recanalization of the artery if acute artery thrombosis is diagnosed adequately early. Percutaneous recanalization and ulnar artery compression have all been described in the literature. To date, there is no agreeable evidence to recommend the routine use of any of the above approaches. Anticoagulation iv serves as the gold standard in thrombotic arterial occlusions so far. Thus, the addition of vasoactive medication does not lead to further beneficial effects (3). Identification and surveillance of complications associated with arterial line placement are an essential component of safe critical care practice. A usually noiseless complication after arterial line cannulation is radial artery thrombosis. It is thought that it is related to the hemostasis technique after the procedure. That apparently harmless procedure for close hemodynamic monitoring, very common in the ICUs, can have severe consequences. Not only related to the limb viability, but also related to its management. Radial artery occlusion should be treated with anticoagulation to regain patency, increasing patient morbidity, and bleeding risk. Thus, it is crucial for all medical staff to understand that a routine procedure in the clinical management of critically ill adults, can be dangerous and a careful review of the indications needs to be in mind before proceed.

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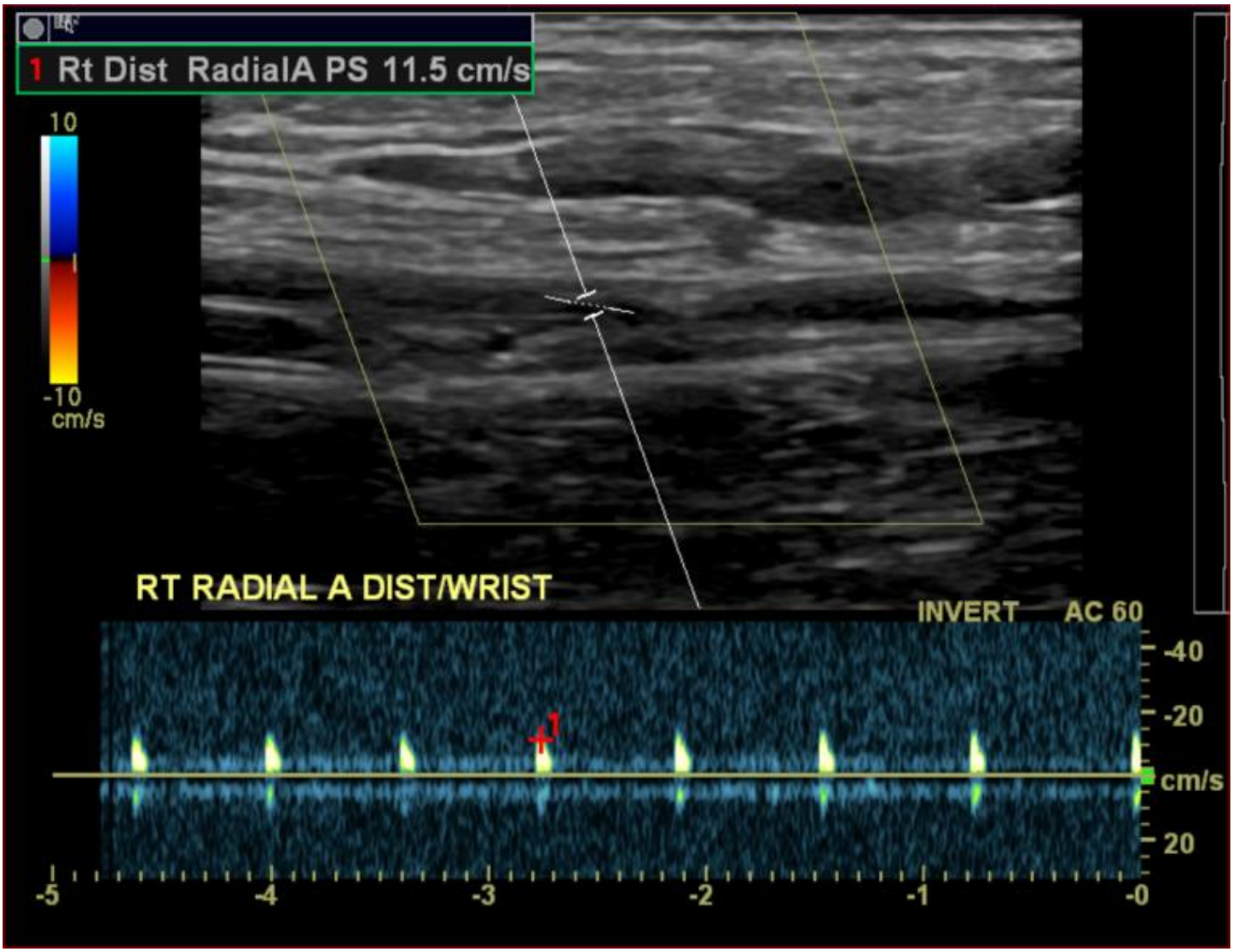
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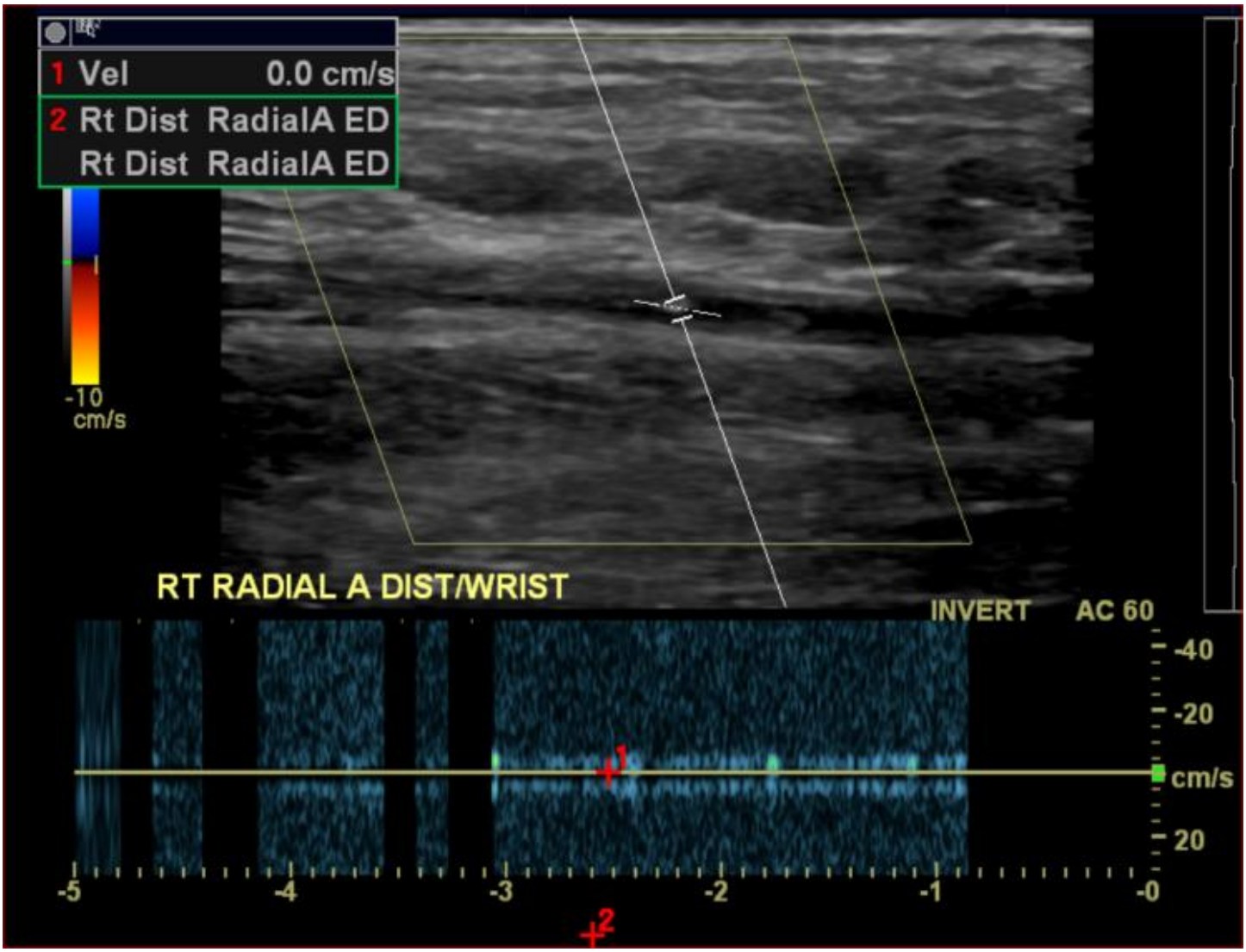
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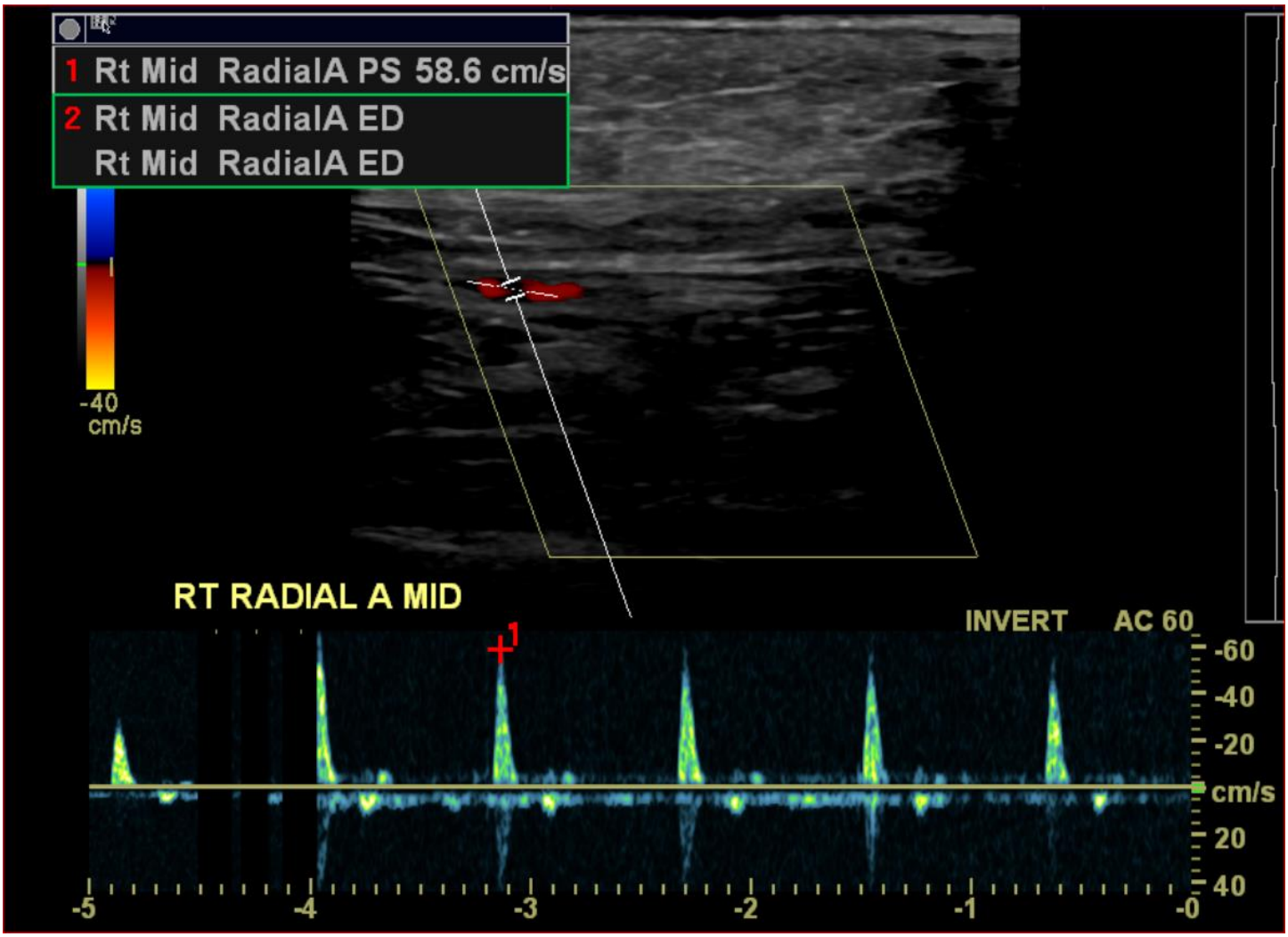
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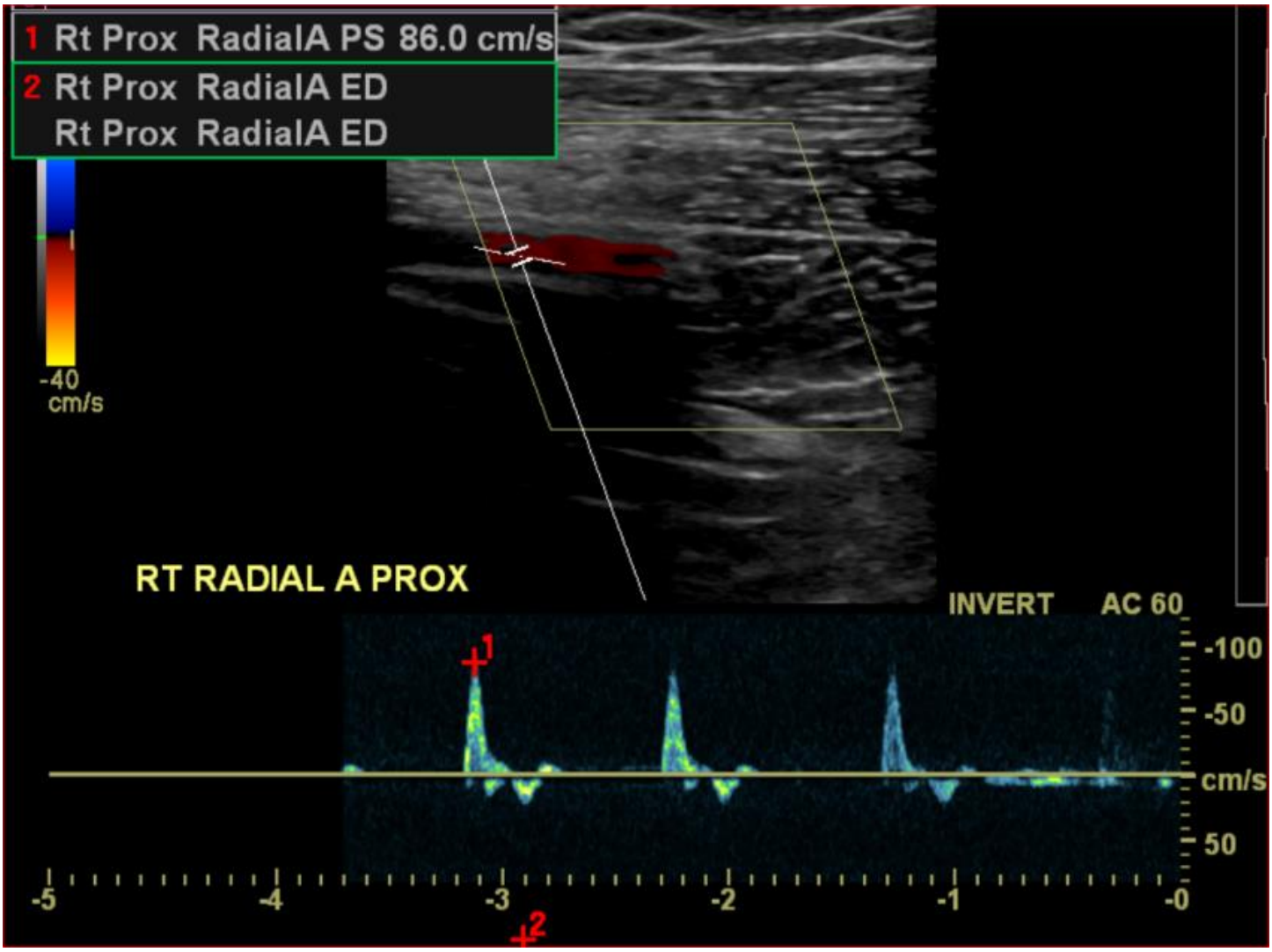
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Critical Care-3 A mysterious case of persistent ketoacidosis, the culprit- Empagliflozin!

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Introduction: Empagliflozin inhibits the sodium glucose cotransporter 2 (SGLT2) in the proximal tubule thereby blocking reabsorption of glucose. It has been shown to improve glycemic control and decrease in diabetics with concomitant heart failure (1-2). Given the favorable clinical profile, SGLT2 inhibitor use is on the rise as is one of its rare but life-threatening adverse effects: diabetic ketoacidosis. SGLT2 inhibitor-induced DKA can be difficult to recognize as its presentation is one of a severe anion gap acidosis in the setting of a normal or mildly elevated blood glucose level. We present a peculiar case of a patient with SGLT2 inhibitor-induced DKA in the hope of raising awareness of this emerging condition.

Case Report: 69 year-old female with obesity status post gastric bypass and DM2, who presented with complaints of nausea, vomiting, and confusion. Five days prior, she was taken off insulin and started on empagliflozin. Initial labs revealed pH 6.8, bicarbonate 4 mmol/L, anion gap 29, blood glucose 343 mg/dl, lactate 6.2 mmol/L, creatinine 1.69mg/dl, and beta-hydroxybutyrate 2 mmol/L. Urinalysis demonstrated mild pyuria but culture was negative. Broad-spectrum antibiotics were started. Blood cultures, EKG, CT chest/abdomen/pelvis were unrevealing for source of DKA. Aggressive IV fluid administration and insulin infusion were started. Within 4 hours, blood glucose and lactate normalized, but pH remained 6.8 with anion gap of 30. At this point she was administered a more concentrated dextrose source to facilitate increasing her insulin infusion to close the gap. A bicarbonate infusion was started given concern for respiratory fatigue. Anion gap normalized 24 hours later, but beta-hydroxybutyrate remained persistently elevated at >2 mmol/L for 72 hours. She was transitioned to subcutaneous insulin regimen and discharged home on day 7. Discussion: The FDA Adverse Event Database identified 73 cases of DKA linked to SGLT2 inhibitors between 2013 and 20153. In many cases, DKA was not initially suspected because blood glucose levels were below those typically expected in DKA (3). The proposed mechanism of SGLT2 inhibitors causing DKA include indirect effects on reducing endogenous insulin levels and enhancing glucagon secretion while also reducing renal ketone clearance (4). In our patient, the anion gap metabolic acidosis was attributed to DKA. The persistent acidosis and large anion gap despite initiation of therapy and correction of hyperglycemia was unusual. The likely precipitating factors were a combination of hypovolemia from probable gastroenteritis and cessation of insulin and initiation of empagliflozin. These are consistent with triggering factors identified in the literature (5).

Discussion: It is important to recognize ketoacidosis with mild hyperglycemia as a result of SGLT2 inhibitor use and identify factors that might predispose to its development.

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Critical Care-4 Bedside TTE to Diagnose Impella Device Thrombosis in a Patient with Acute Myocardial Infarction-Related Cardiogenic Shock

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Introduction: Although advances in the treatment of acute myocardial infarction-related cardiogenic shock have been significant, overall mortality remains up to 50%[1]. One such area of advancement is the expanding role of temporary percutaneous mechanical circulatory support devices. The theoretical benefits of these devices are numerous and include improving vital organ and coronary artery perfusion to reducing myocardial oxygen demand through intracardiac pressure modulation. Over the past two decades the use of these devices in cardiogenic shock, including the Impella (Abiomed, Danvers, MA), has risen sharply in the United States[2]. The Impella has been shown to offer superior hemodynamic parameters in cardiogenic shock when compared to the intra-aortic balloon pump; however, an improvement in mortality has yet to be demonstrated3-5. Overall, the Impella has been found to be relatively safe, with the most common complications being related to vascular injuries or hemolysis6,7. Reports of device malfunction have been varied: some studies reporting rates as low as 0.16% while others have seen device failure up to 17% of cases8,9. Although reported infrequently in the literature, pump thrombosis has started to surface as a cause of Impella device failure in recent years10-12. Here we present a case of Impella pump thrombosis causing abrupt device failure in a patient on systemic anticoagulation, diagnosed immediately by bedside transthoracic echocardiography.

Case Report: A 78-year-old female with history of essential hypertension and hyperlipidemia presented to an outside hospital with dyspnea and worsening chest pressure. Upon arrival to the emergency room she was found to have an acute ST-elevation myocardial infarction and was taken emergently to the cardiac catheterization lab. During the course of her procedure the patient became hypotensive and altered, requiring intubation for airway protection and vasoactive medications for hemodynamic support. Transthoracic echocardiography revealed the patient to have a left ventricular ejection fraction (LVEF) of approximately 5%. The left femoral artery was accessed for placement of an Impella CP device to help facilitate coronary catheterization and possible intervention with subsequent improvement of LVEF to approximately 20%. Heparin was started both systemically at 500 U/hr and through the purge solution and continued throughout the entirety of her hospital course. Coronary angiography was consistent with complete occlusion of the left main coronary artery into the ostial potion of the left circumflex artery. One drug eluting stent was placed in the left main coronary artery; however, the left circumflex artery was unable to be intervened upon and remained occluded. After cardiac catheterization the decision was made to transfer the patient to a tertiary care center for consideration of veno-arterial ECMO for longer term circulatory support. She was airlifted to the University of Michigan Hospital several hours later. Upon arrival the patient was hemodynamically stable and the blood flow through the Impella device remained constant at 2.9-3.4 L/min. Approximately four hours after arrival, the flow on the Impella device abruptly decreased to 0.1L/min. Bedside transthoracic echography revealed appropriate device position, adequate left ventricular volume and a 1cm by 0.5cm mobile mass on the ventricular portion of the cannula. The mass was best characterized on an apical five chamber view which scanned across the plane of the Impella device. Partial thromboplastin time was greater than 120 seconds and anti-Xa unfractionated heparin level was greater than 1.5 IU/ml at the time of the event. The patient became hemodynamically unstable shortly thereafter despite escalating inotropic and vasoactive support. She was ultimately taken to the operating room for VA ECMO cannulation.

Discussion: Thrombosis at the inflow site of the Impella pump is an apparent complication which can result in immediate failure of the device, even in fully anticoagulated patients. Inflow thrombosis may become a more frequently diagnosed complication of Impella placement as its clinical use continues to expand. Bedside transthoracic echocardiography may be useful in expediting this diagnosis and planning alternative means to support patients with myocardial infarction-related cardiogenic shock.

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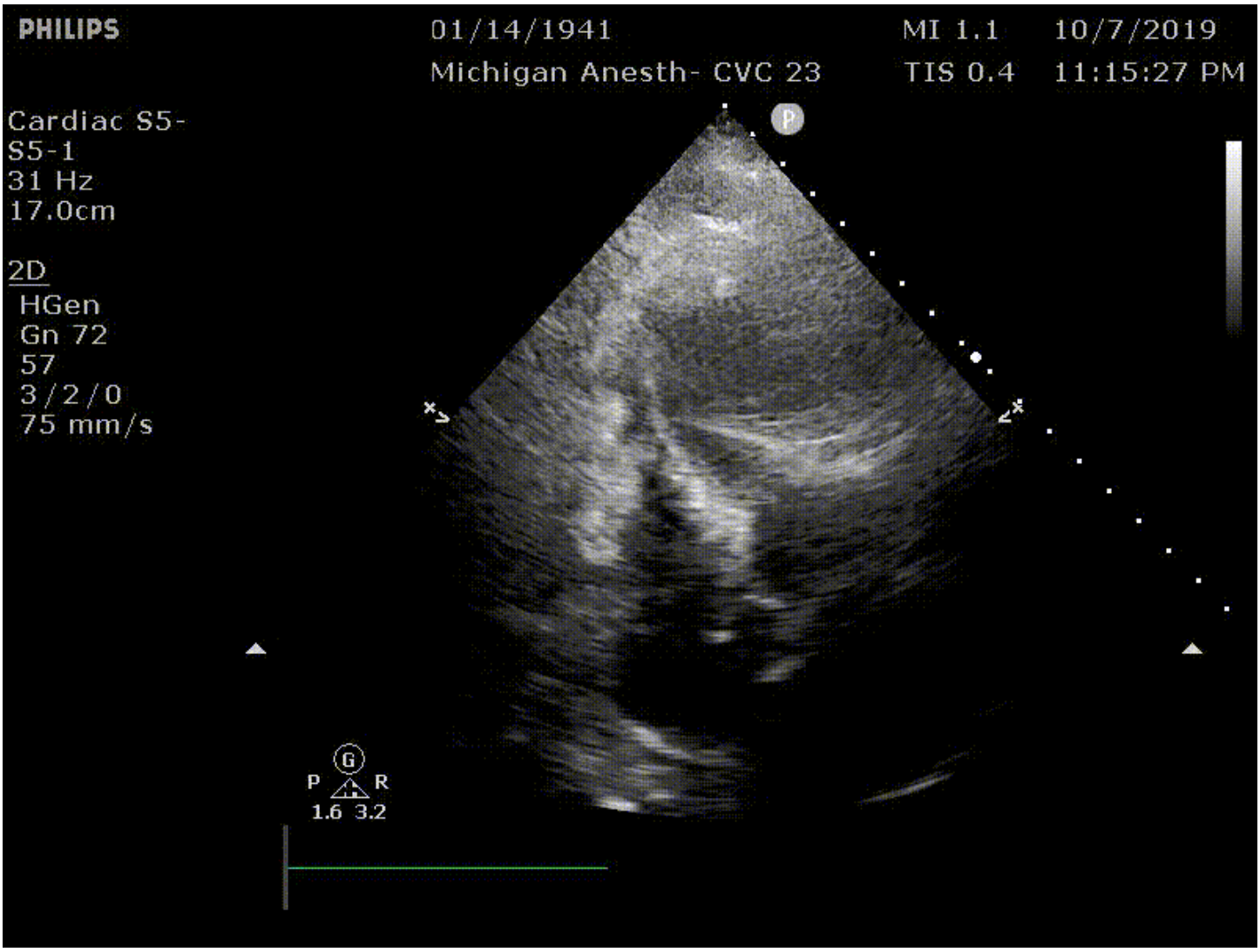
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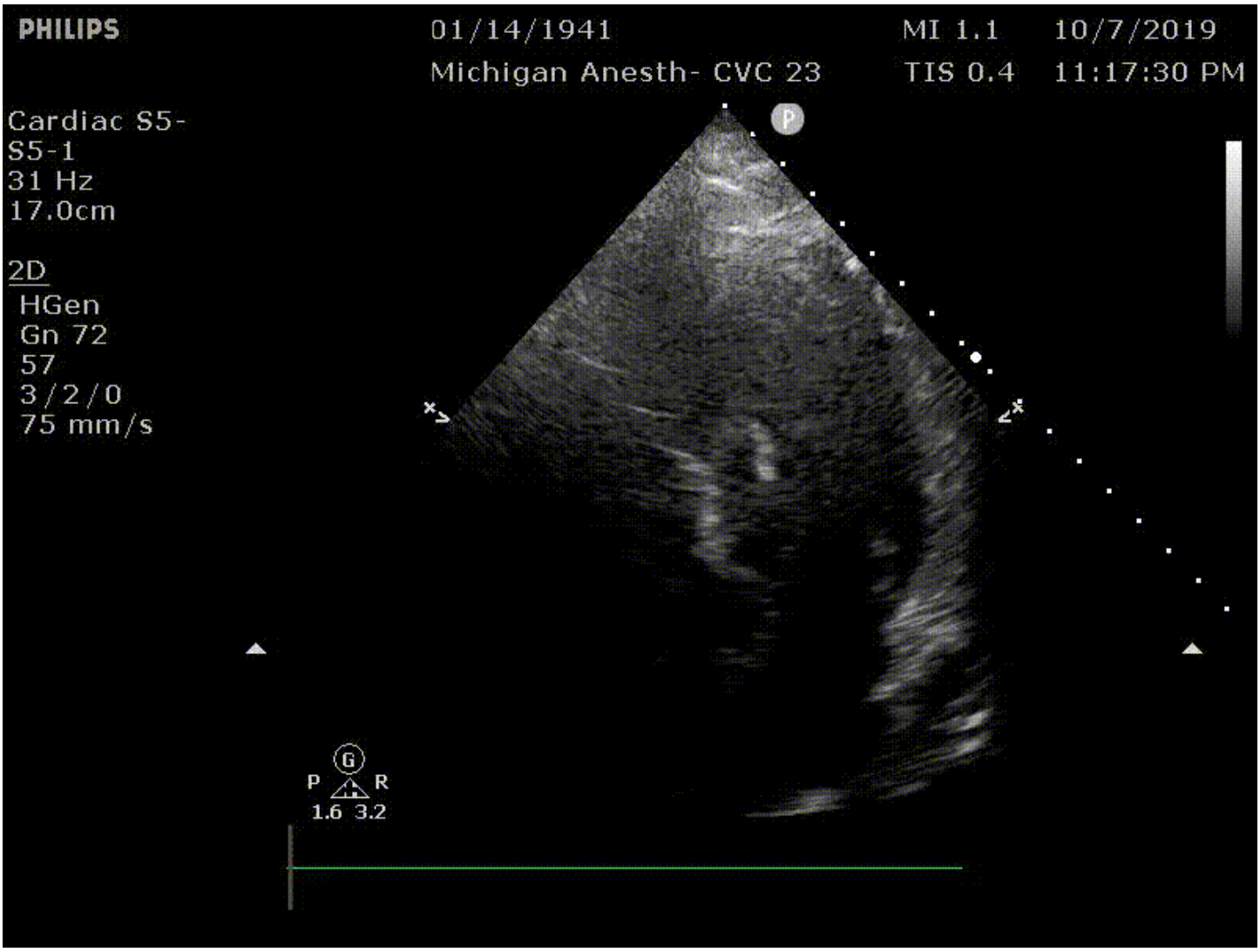
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Critical Care-5 Malignant Catatonia in a 19-Year-Old Male Treated with Electroconvulsive Therapy

Nicholas Eglitis[1]

[1]*OHSU, Portland, OR*

Introduction: Malignant catatonia is a rare clinical entity. This condition is clinically indistinguishable from the neuroleptic malignant syndrome (NMS)1 and is characterized by catatonia, muscle rigidity, fever, and autonomic instability.

Case Report: A 19-year-old male with recently diagnosed schizophrenia was admitted for catatonia from an inpatient psychiatric facility. He developed subacute muscle rigidity over the preceding week followed by acute onset hypertension, tachycardia, and diaphoresis. The psychiatric team had a high suspicion for progression to malignant catatonia. The patient was transferred to the intensive care unit where he had an awake fiberoptic intubation for severe muscle rigidity and trismus followed by emergent electroconvulsive therapy (ECT) and post-procedural extubation. Immediately after the first treatment, the patient was more interactive, less rigid, and less tachycardic and hypertensive. The following day, the patient had returned to his highly rigid state, so he underwent a second awake fiberoptic intubation followed by repeat ECT and extubation. The next day he was noticeably less rigid, more communicative, able to eat independently, and stand and pivot to a chair. He was able to tolerate further twice weekly ECT treatments with a natural airway given the resolution of his rigidity. At the time of discharge the patient was back at his baseline level of functioning.

Discussion: Malignant catatonia is a true psychiatric emergency. Catatonic states can progress toward malignant catatonia once hemodynamic instability, rigidity, and fevers present. If not treated with ECT, mortality is reported as high as 75-100%2. Malignant catatonia remains a rare but serious condition given its overlap with the NMS and its mimicking of other common disorders in critical care settings such as sepsis with delirium. Reduction in mortality requires rapid identification, supportive critical care, withdrawal of antidopaminergic agents, and early initiation of ECT. Many patients with simple catatonia can be treated with early benzodiazepine therapy and ECT3, which would limit their progression toward malignant catatonia. However, most catatonic patients are unable to consent for ECT given mutism, extreme negativism, stupor, and delusions. One other potential barrier to effective treatment regards the varying state laws surrounding ECT and even more so surrounding involuntary ECT4. These barriers to care can have unfortunate negative outcomes for these patients.

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Critical Care-6 Rasburicase induced Methemoglobinemia Complicated by Undiagnosed Glucose-6-Phosphase Deficiency

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Introduction: Tumor lysis syndrome (TLS) occurs when large numbers of neoplastic cells lyse, releasing cellular components. Electrolyte derangements include hyperkalemia, hyperphosphatemia, hypocalcemia and hyperuricemia; the latter of which can cause renal failure1. Rasburicase is a medication that increases the solubility of uric acid, thereby allowing for excretion. A rare side effect is methemaglobinemia, for which the treatment can be Methylene Blue or Ascorbic acid2. Due to the promotion of hemolysis, both therapies are contraindicated in patients with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, although this represents a population especially susceptible to Rasburicase-induced methemaglobinemia3. We present a case of Rasburicase-induced methemaglobinemia in a patient with unknown G6PD status and delayed hemolysis treated effectively with supportive care.

Case Report: We present a 77 year old male with chronic lymphocytic leukemia and chronic-obstructive pulmonary disease who presented with tachypnea, hypoxemia, and cough. He was febrile with a leukocytosis, positive for Influenza A, started on Oseltamiver and admitted to the intensive care unit for management of hypoxemia and a new oxygen requirement. He was hyperkalemic, hyerphosphatemic, uricemic, and had acute worsening of renal function for which Rasburicase (6mg dose) was given out of concern for TLS. Within 24-hours, he developed worsening hypoxemia and a mixed respiratory/metabolic acidosis. Oxygen saturation decreased to 84-87% despite maximal non-invasive ventilatory support. Co-oximetry testing revealed a methemoglobin level of 14%. Prior to administration of Methylene Blue, testing for G6PD deficiency was performed despite a normal haptoglobin and no evidence or history of hemolysis. He was started on ascorbic acid and over the next 24-hours, decreasing hematocrit and haptoglobin levels demonstrated evolving hemolysis requiring multiple blood transfusions. Worsening acidosis due to progressive renal failure necessitated continuous renal replacement therapy and hypercarbic respiratory failure required intubation and mechanical ventilation. Given the evolving hemolysis, a presumptive diagnosis of G6PD deficiency was made, plans for methylene blue were aborted, ascorbic acid was discontinued and supportive care, including blood transfusion and mechanical ventilation was continued. Serum haptoglobin, methemaglobin and SpO2 levels were trended with a peak methemaglobin level of 17 (Figures 1,2). After 72 hours, his G6PD resulted as deficient, however by this time his methemaglobin level was under 10%. By ICU day 5, his methemaglobin level was under 5%, his SpO2 was>92% and he was subsequently extubated on ICU day 6.

Discussion: Rasburicase is effective in reducing kidney injury in TLS, but can cause methemaglobinemia, the treatments for which (methylene blue or ascorbic acid) are contraindicated in G6PD deficiency1-3. Although our patient did receive ascorbic acid, but not methylene blue, he nevertheless developed a delayed, significant hemolysis requiring blood transfusions. This case demonstrates that not only can hemolysis have a delayed presentation but that supportive care alone is effective for treatment of Rasburicase-induced methemaglobinemia in patients with G6PD deficiency. Clinicians should be cautious when administering Rasburicase, and consider withholding methylene blue for methemaglobinemia until G6PD status is known.

Reference(s):

1- JAMA Oncol. 2018;4(6):895

2- West J Med. 2001 Sep; 175(3): 193–196

3- Clin Case Rep. 2016;4(4):315–319

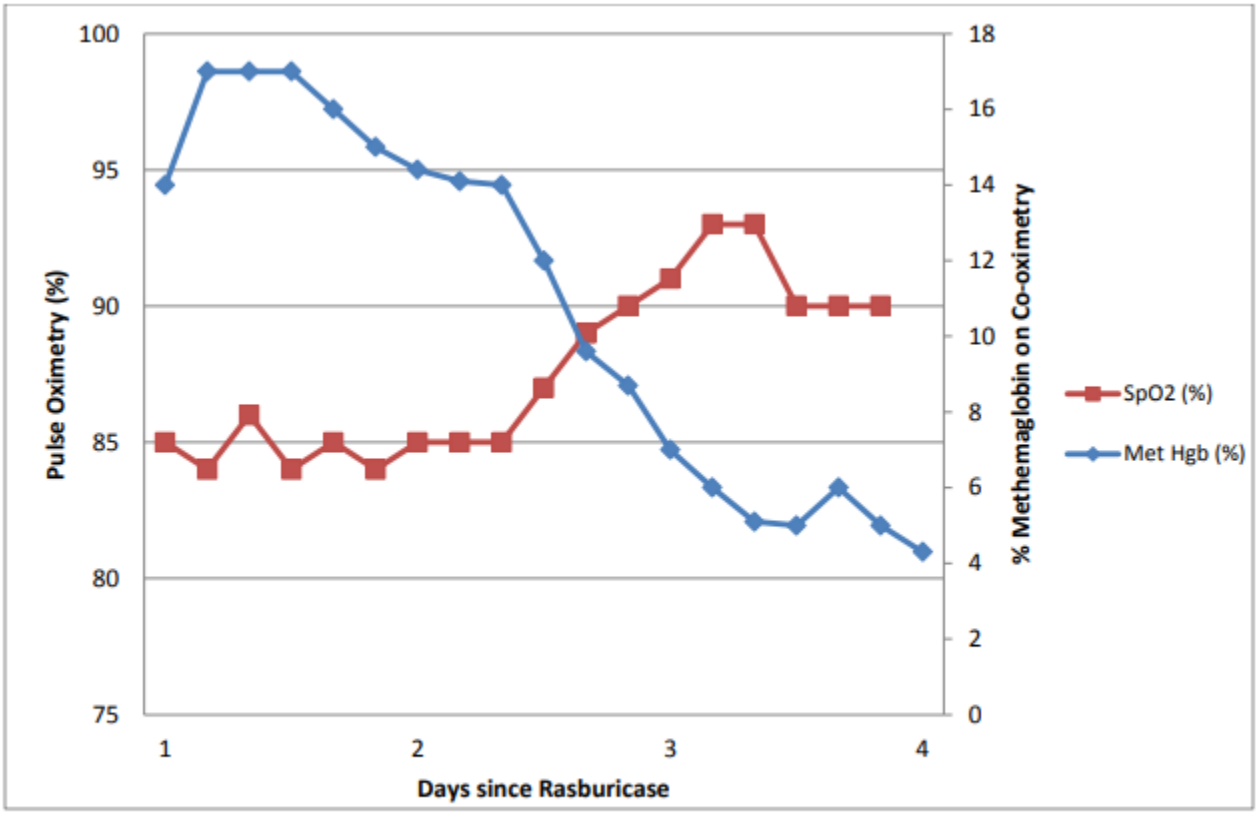

Figure 1: Trend of Methemaglobin (%Met Hgb) and Pulse Oximetry (%SpO2) after administration of Rasburicase

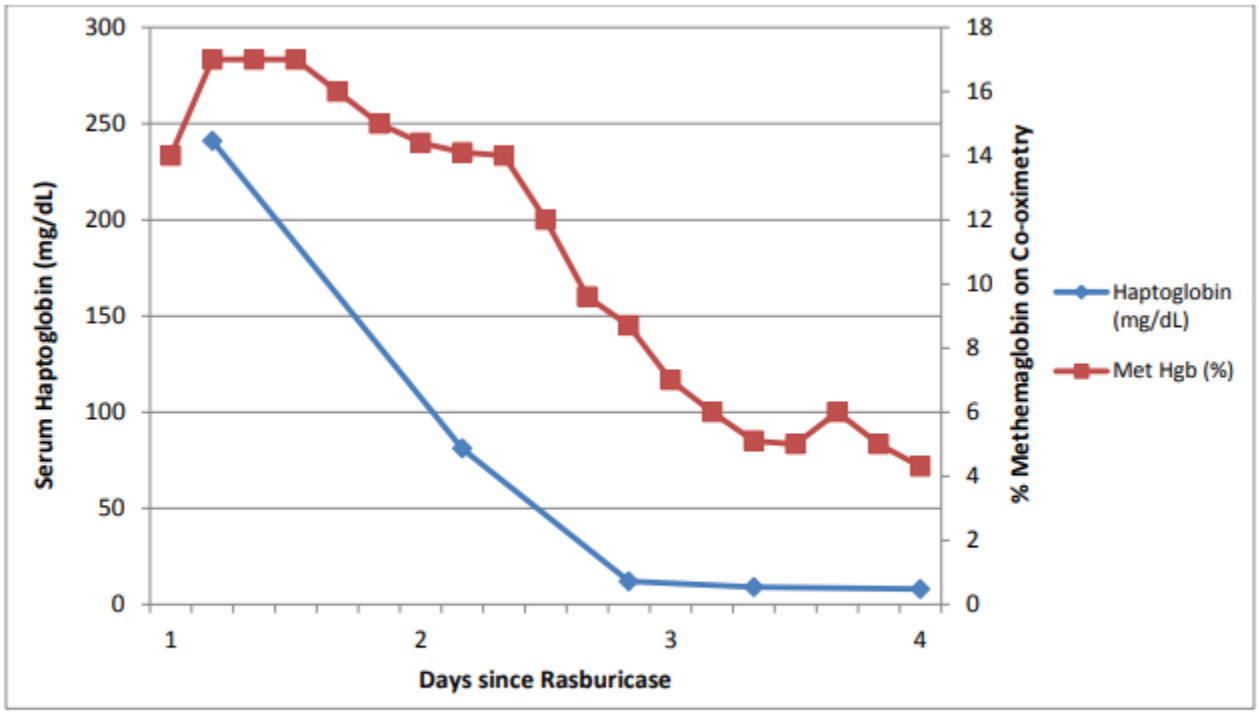

Figure 2: Trend of Methemaglobin (% Met Hgb) and Serum Haptoglobin (mg/dL) after administration of Rasburicase

Critical Care-7 Complex Management of V-V ECMO for Status Asthmaticus After Failed Medical and Volatile Anesthetic Therapy

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Introduction: Status asthmaticus (SA) is a life-threatening condition, occurring when an acute asthma exacerbation fails to respond to standard treatment with corticosteroids and bronchodilators. Hypercapnia in SA is a late stage indicator with increased arterial carbon dioxide (PaCO2) when breathing becomes so exhausted that respiratory failure occurs. Mechanical ventilation (MV) in SA must be weighed carefully with overall risks and is rarely needed in patients without hypercapnia. MV is indicated when a patient has a change in mental status, hemodynamic collapse, or exhaustion of respiratory muscles with life-threatening hypercapnia and acidemia.(1) When MV fails, clinicians must consider other therapies, such as inhaled anesthetics or ECMO. In this case, a patient with refractory SA received inhaled isoflurane followed by V-V ECMO as rescue therapy.

Case Report: A 38 year-old male presented with acute hypercarbic respiratory failure and SA. He failed nebulizer and Bi-PAP therapy and was intubated. Post-intubation, he required pressure-control ventilation mode (50/5). ABG showed pH=6.8 and paCO2=114. Medical therapy consisted of albuterol, ketamine, propofol, magnesium, methylprednisolone, bicarbonate, and vecuronium. He remained hypercapnic despite comprehensive medical therapy and multiple different ventilator strategies (ABG pH=7.04, paCO2=100). Oxygenation was adequate with FiO2=0.60. Due to continued hypercapnia and acidemia, Anesthesiology was consulted to administer inhaled isoflurane in the ICU. Epinephrine was started to assist with bronchodilation. After 12 hours of inhaled isoflurane, he had no improvement in acidemia or hypercapnia (pH=7.2, paCO2=128). The patient was placed on V-V ECMO using a 30-Fr CrescentTM dual lumen catheter in the RIJ vein. Flow was set at 5L/min. Hypercapnia improved (PaCO2=52), but worsening hypoxemia (PaO2=45) was seen. This hypoxia was likely due to a mismatch between maximum cannula flow rate and the patient's intrinsic cardiac output. Epinephrine was discontinued to decrease cardiac output, resulting in increased oxygenation to an adequate level. The patient remained on V-V ECMO for 3 days and was subsequently extubated 6 days later. He was discharged on hospital day 12 to an acute rehab facility.

Discussion: The use of inhaled anesthetics (IA) for SA has resulted in improvement in ventilation for patients with refractory bronchospasm.(2) The difficulty in initiating IAs in the ICU is often related to lack of resources such as equipment or trained personnel. In an already intubated patient, the use of IA is a non-invasive treatment modality with minimal long-term side effects, therefore it may be worthwhile to attempt using IA prior to trying ECMO. An increasing number of reports also suggest that ECMO has been used successfully to treat SA in patients who have failed to improve on maximal medical treatment and ventilator therapy alone. V-V ECMO allows for clearance of CO2 and assists oxygenation without relying on aggressive mechanical ventilation strategies which may result in barotrauma or other ventilator-induced lung injuries.(3) However, initiating ECMO can be a complex process and potential complications include hemorrhage, infection, vascular or neurologic injury and equipment malfunction. Since SA in itself is not an indication for ECMO, the appropriate timing for proceeding with cannulation is not well defined. However, in patients who are persistently hypoxemic, acidotic or with significant hemodynamic instability despite maximal mechanical ventilation strategies, it may be prudent to consider ECMO as a rescue therapy. Arterial oxygenation for V-V ECMO patients depends on the pump flow relative to the patient's cardiac output. If cardiac output is higher than pump flow, not all blood will be oxygenated.(4) Our patient was persistent hypoxemic despite maximum ECMO flow for the cannula size. Discontinuation of epinephrine resulted in improved oxygenation as the cardiac output decreased. Both IA and ECMO are not standard therapies for SA, but may be utilized in refractory SA.

Reference(s):

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3) Critical Care. (2017); 21: 297

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Critical Care-8 Passenger Lymphocyte Syndrome in a Patient following Orthotopic Liver Transplant

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Introduction: Passenger Lymphocyte Syndrome (PLS) is a well described type of immune-mediated hemolysis following solid organ transplantation that is primarily due to a minor ABO mismatch, although case reports of non-ABO PLS exist. Minor ABO mismatch is commonly encountered in transplantation because of the high demand for organs (1). PLS-related hemolysis can range from mild and clinically irrelevant to severe with multiorgan failure and death. Severity correlates with the quantity of viable donor B lymphocytes and isohemagglutinins that are carried with the organ to be transplanted--hence the name 'Passenger Lymphocyte Syndrome.' Hemolysis occurs due to donor B lymphocytes producing antibodies against recipient or transfused red blood cells (2). Fortunately, this is a self-limited disease that starts one to three weeks following organ transplant and resolves within three months. Management includes escalation of immunosuppression, or immune modulation with IVIG or monoclonal antibody therapy. Supportive care is primarily red blood cell transfusion, typed to the organ donor ABO group (2,3). Regarding PLS in liver transplant, biochemical evidence of antibody formation and hemolysis has been described to occur in over half of all patients, however only very few cases proceed to moderate-to-severe hemolysis. Below we present a case of Severe PLS-related hemolysis in an orthotopic liver transplant patient.

Case Report: A 68 year-old, ABO group A+ man with a history of NASH cirrhosis, hepatocellular carcinoma and Type 2 Diabetes Mellitus underwent OLT from an O+ donor. His preoperative antibody screen was negative. His intraoperative course was benign, requiring an acceptable amount of blood product transfusion, but post-operatively developed a perihepatic bleed and a biliary leak. On post-operative day (POD) 10 he developed acute anemia requiring transfusion, and acute renal failure requiring renal replacement therapy. He further developed septic shock and there was concern for cholangitis on CT imaging. He was taken to the operating room for exploratory laparotomy, abdominal washout, and biopsy-which was found to be negative. Despite surgical hemostasis he continued to require daily blood product transfusions, and developed significant hyperbilirubinemia. On POD 22, a full hemolysis work-up was initiated with a subsequent positive direct Coombs test for IgG and C3d and indirect Coombs test for the development of an acquired anti-A alloantibody. Importantly, he was transfused with recipient-matched blood products during this time. Hematology was consulted for further evaluation of ongoing hemolysis. A differential diagnosis of PLS vs. Hemophagocytic Lymphohistiocytosis was made (HLH), however, despite equivocal liver and bone marrow biopsies, HLH-specific tests were negative. PLS was confirmed and further transfusions were done with O+ product, consistent with the donor ABO type. Following transfusion with O+ type blood, his hemolytic anemia resolved and the need for transfusion diminished. His renal dysfunction progressed to end-stage renal disease (ESRD) requiring renal replacement therapy (RRT). On POD 52 he was discharged to a rehabilitation facility. Unfortunately, he returned two days later with sepsis due to an intraabdominal abscess, and remained hospitalized for two months requiring placement of intraabdominal drain by IR. He is scheduled for outpatient fistula formation for ESRD in January 2020.

Discussion: PLS due to minor-ABO mismatch can lead to devastating immune-mediated hemolysis post-liver transplant caused by donor lymphocyte antibody production against recipient red blood cells. The risk of PLS is noted to be greatest in a blood-type O donor and blood-type A recipient (1), as described in this case. The diagnosis is made by direct and indirect antiglobulin testing, as well as antibody screening. Care is supportive with blood product transfusion matched to the donor ABO type being the mainstay treatment. Immunosuppression regimens may be increased or augmented to mitigate hemolysis. Renal failure requiring RRT may be necessary, as seen here, but the disease itself is self-limited, resolving in several months. Given the numerous post-operative complications associated with liver transplants it is important to pursue PLS as a possible diagnosis for ongoing anemia that does not improve with blood transfusion.

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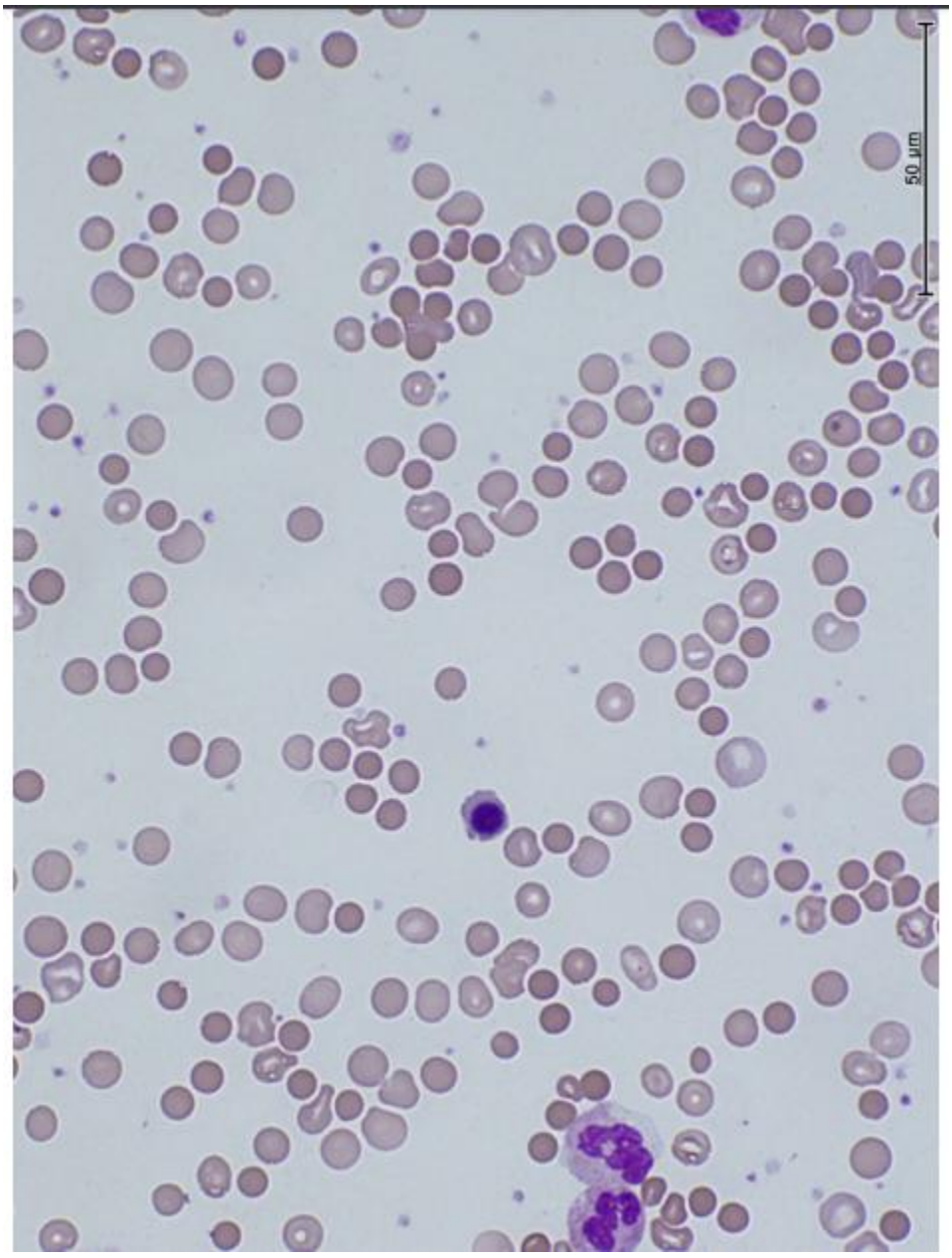
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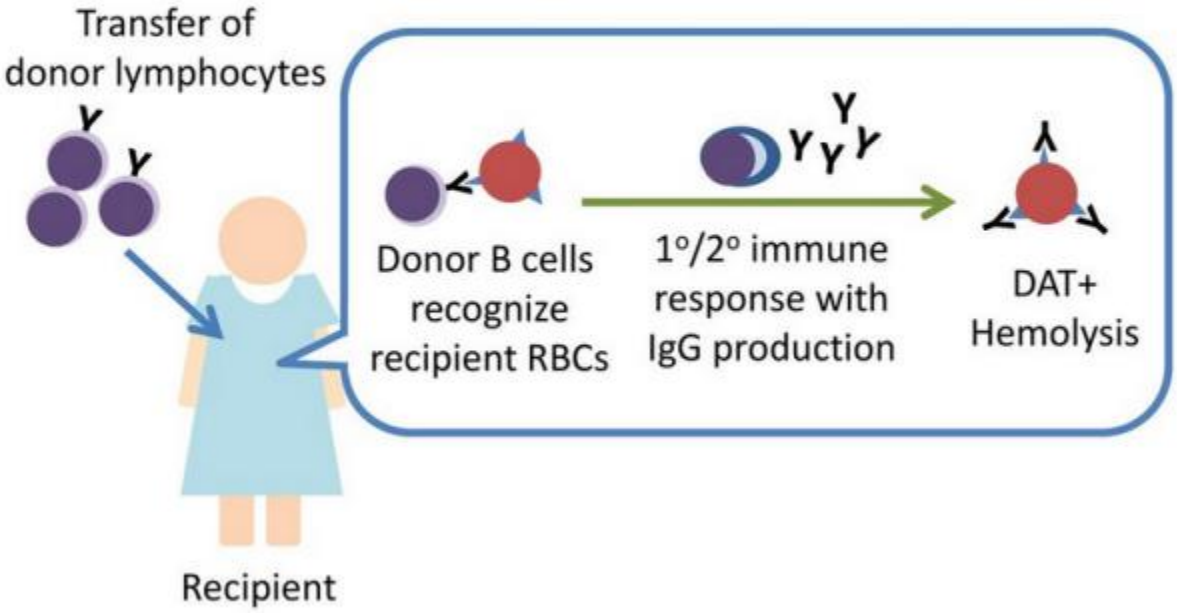
Passenger Lymphocyte Syndrome (PLS)



Critical Care-9 Utilization of Transthoracic Echocardiography Post Cardiac Arrest to Diagnose Left Ventricular Outflow Obstruction Following Surgical Aortic Valve Replacement

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Introduction: The incidence of dynamic left ventricular outflow obstruction (DLVOTO) after surgical aortic valve replacement (AVR) varies widely (1). It has been described to occur intraoperatively following cardiopulmonary bypass (CPB) (2) and may occur post operatively as well (1). DLVOTO may be coupled with systolic anterior motion of the mitral valve or may occur in isolation. Risk factors for this condition to occur include anatomical, physiological, and geometrical causes (1).

Case Report: Our patient was a 65 year old male with past medical history significant for hypertension, coronary artery disease, atrial fibrillation, chronic kidney disease stage 3, and severe bicuspid aortic stenosis who underwent AVR with a 25mm bioprosthetic valve. He was brought to the ICU postoperatively and extubated on postoperative day (POD) #0 without complication. On POD #1 as he was transitioning from bed to chair he suffered an abrupt loss of consciousness with arterial mean blood pressure tracing of 20 mmHG. He underwent cardiopulmonary resuscitation for 1 minute before return of spontaneous circulation. Bedside transthoracic echocardiography showed hyperdynamic left ventricular with DLVOTO. The patient was placed on a phenylephrine infusion and resuscitated with 3 liters of crystalloid with significant improvement in his symptoms. He was treated with beta blockers and slowly weaned off his phenylephrine infusion but continued to have mild LVOTO.

Discussion: Transthoracic echocardiography can be a critical tool in diagnosing complications post cardiac surgery. It can help rule in or rule out key diagnoses and can have a direct effect on management. It's availability and portability make it a key tool for any clinician. Although transthoracic echocardiography might have limitations depending on the clarity of the windows imaged, it can still assist clinicians in bedside decisions to pursue further imaging, return to the operating room, or adjust therapies.

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Critical Care-10 Toxoplasmosis after stem cell transplant complicated by immune reconstitution inflammatory syndrome

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Introduction: This is a medically challenging case submission regarding a patient with a history of CML s/p recent stem cell transplant who presented with headache and fever. The patient underwent an MRI which revealed areas of restricted diffusion in the left parietal and left occipital lobes with evidence of focal subacute hemorrhage in occipital region. There was also evidence of ring-like areas of enhancement in the parenchyma. The patient was admitted to the hospital for further workup. Ultimately the patient was admitted to the ICU for fever, tachycardia, and altered mental status after undergoing lumbar puncture for CSF analysis. CSF testing was consistent with toxoplasmosis infection and he was started on high dose trimethoprim-sulfamethoxazole therapy. He initially demonstrated dramatic improvement, however his mental status fluctuated over the course of his stay, and repeat imaging demonstrated worsening concerning for immune reconstitution inflammatory syndrome. Toxoplasmosis is a rare complication of allogenic stem cell transplant but carries a high mortality rate, estimated between 60-90%. In the United States the incidence after allogenic BMT is less than 0.5%, whereas the incidence in Europe and Latin America range from 1-6%. Post HSCT toxoplasmosis is typically the result of reactivation of a latent infection. There is also wide variation in seroprevalence rates around the world, and this is thought to be due to diet and hygiene. In the US, risk factors include ingestion or exposure to raw meat, mollusks, unpasteurized goat's milk, and being exposed to cats.

Case Report: The patient was a 34-year-old male with history of CML who received an allogenic stem cell transplant 2 months prior to admission. The patient had suffered from headache for one week prior to presentation. He subsequently presented to outpatient neurology for evaluation. An MRI brain was obtained, which demonstrated restricted diffusion in the left parietal and left occipital lobes with evidence of focal subacute hemorrhage in the occipital region. Furthermore, there was a ring-like component of enhancement in the parenchyma. The patient underwent a lumbar puncture which demonstrated elevated protein, low glucose, and lymphocyte predominance. Around the time of his LP the patient became febrile and altered, and a rapid response was called. Upon ICU admission vancomycin, cefepime, and acyclovir were started while awaiting CSF studies. Empiric trimethoprim-sulfamethoxazole was added for toxoplasma coverage, with toxoplasma PCR from the CSF becoming positive shortly thereafter. Antibiotic therapy was de-escalated after clinical improvement, and patient was transferred out of the ICU on the third hospital day. Despite the initial improvement with therapy the patient's mental status deteriorated over the next week. Repeat CSF and imaging studies were performed on the tenth hospital day. Repeat MRI showed new lesions and progressive leptomeningeal enhancement concerning for an inflammatory process. Given the high suspicion for IRIS the patient was started on a three-day course of high dose methylprednisolone therapy, to which he responded and was discharged from the hospital 1 week later.

Discussion: Toxoplasmosis is a rare complication of stem cell transplantation with a high mortality rate, and a significant proportion of diagnoses are made post mortem. When toxoplasmosis does occur, most patients will develop localized CNS disease, however disseminated infection is also possible. Diagnosis of cerebral toxoplasmosis following stem cell transplant is difficult and requires a combination of radiologic findings, PCR, and histology. The mainstay of treatment is pyrimethamine plus sulfadiazine. However, because pyrimethamine was unavailable, the patient was treated with trimethoprim-sulfamethoxazole successfully which is an appropriate alternative. The incidence of immune reconstitution inflammatory syndrome due to toxoplasmic encephalitis post-transplant is exceedingly uncommon, with only case reports present in the literature. This case emphasizes the need to include toxoplasmosis in the differential of post-transplant patients who present with fever and altered mental status, as mortality is high from the disease even when diagnosed and treated early.

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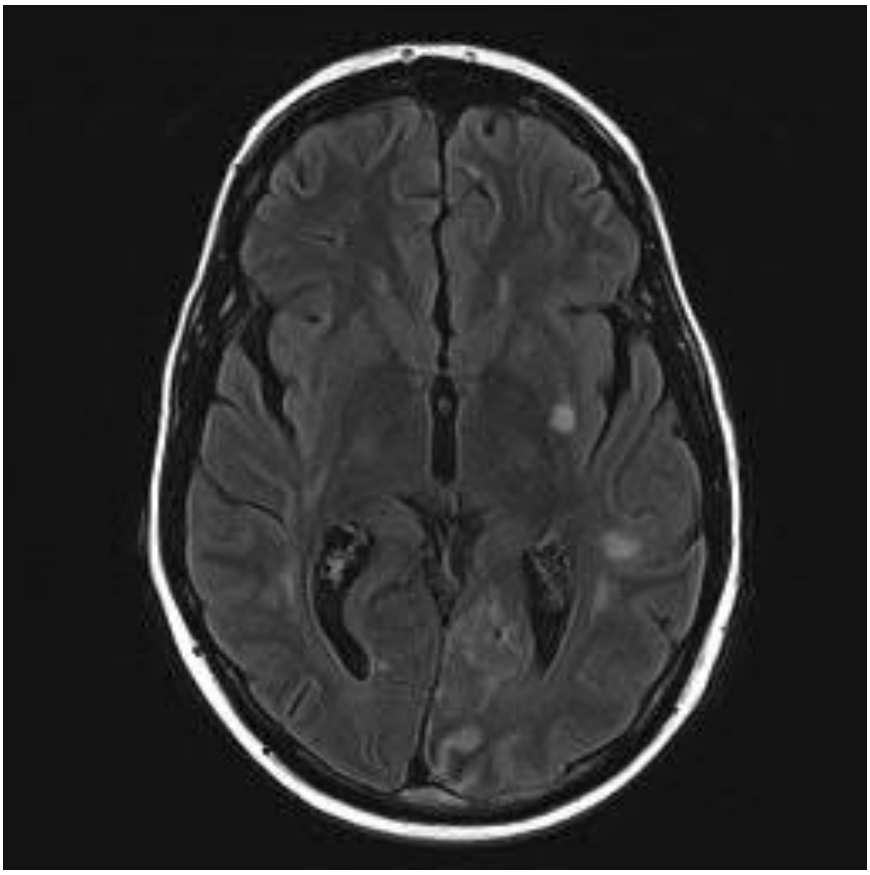

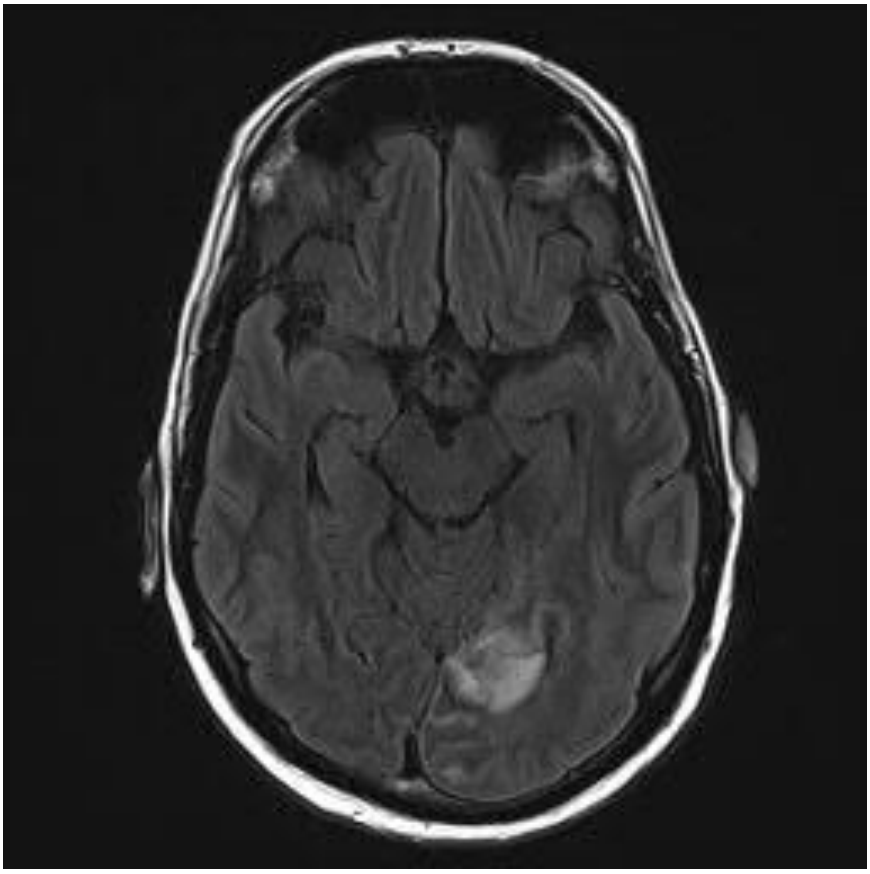

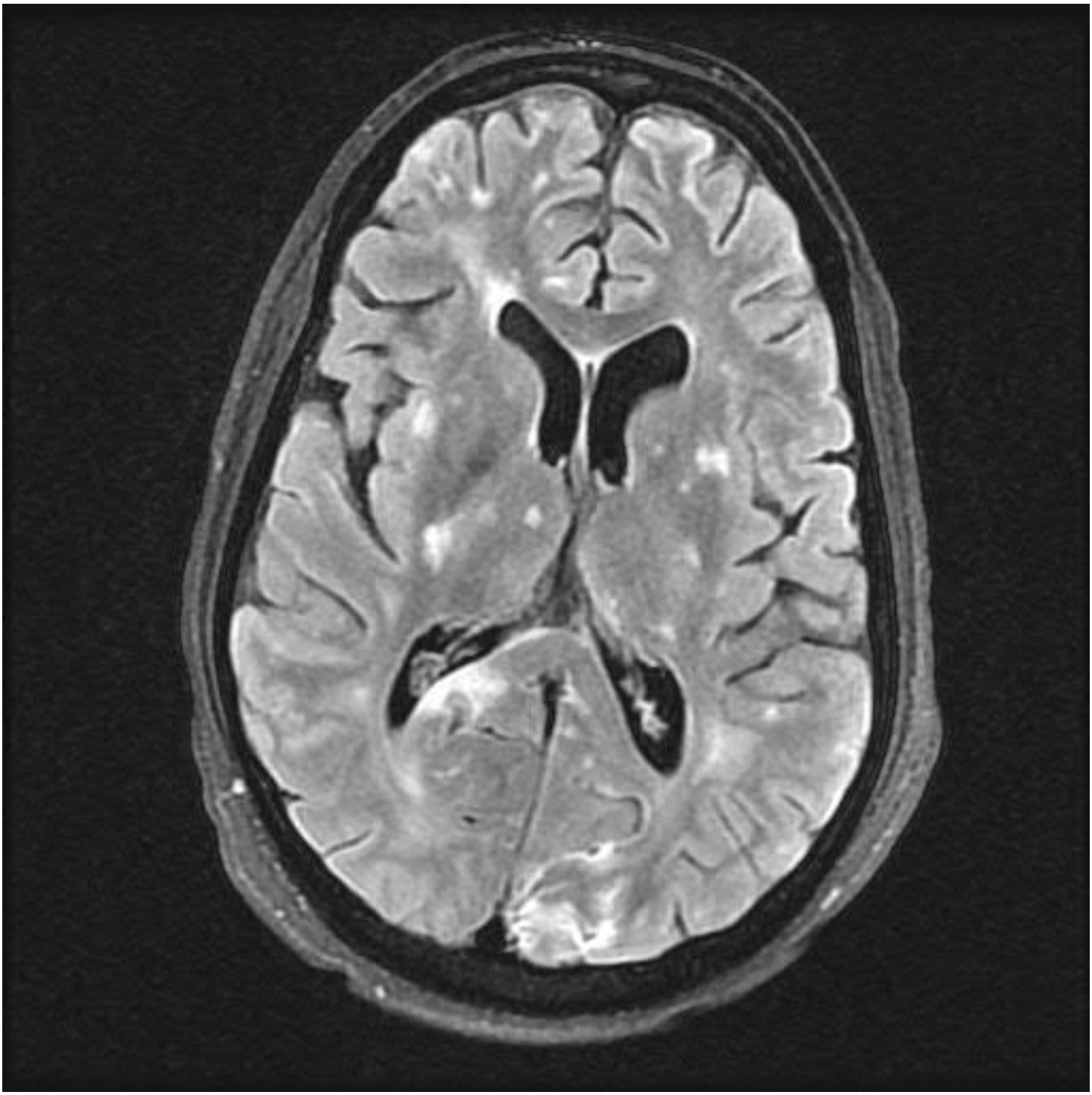

Critical Care-11 Dexmedetomidine-Induced Polyuria in the Surgical ICU.

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Introduction: Demonstration of dexmedetomidine-induced polyuria in the Surgical Intensive Care Unit.

Case Report: Despite its common use in the operating room and the intensive care unit, dexmedetomidine-induced polyuria in humans is rare. Due to its alpha 2 agonist effects, dexmedetomidine was shown to inhibit vasopressin secretion, causing aqueous diuresis. This diuretic effect has been obviously demonstrated in canines (1). Our patient is a 55 year old male with oral squamous cell carcinoma who was admitted to the surgical intensive care unit on his first postoperative day after a PEG tube placement. The patient was admitted to the SICU for acute hypoxic respiratory failure, which required non-invasive positive pressure ventilation for 2 days. During his admission, a dexmedetomidine infusion was initiated for ICU delirium. His urine output began to increase within the first hour of starting the infusion, and remained within a range of 215-500 ml/hour for 10 hours, with an average of 345 ml/hour. Within one hour of stopping the infusion, the patient's urine output returned to baseline levels of 50 to 75 ml/hour for 4 hours, with an average of 61.25 ml/hour. Hypotension did occur with the increased urine output, but responded well to intravascular volume replacement. The patient's heart rate remained normal. Urine osmolality was obtained 5 hours after stopping the dexmedetomidine infusion, it was found to be 319 mmol/L. On literature search, we found very few case reports describing dexmedetomidine-related polyuria, most of which were intraoperative cases and one was a case in the medical ICU (2-7). We present the first description of a surgical ICU patient manifesting polyuria in association with dexmedetomidine infusion.

Discussion: We present the first description of a surgical ICU patient manifesting polyuria in association with dexmedetomidine infusion for ICU delirium.

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Critical Care-12 Management of a massive, persistent hemothorax following CPR in a patient on VA-ECMO and status post PCI

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Introduction: Over one million inpatient percutaneous coronary intervention (PCI) procedures are performed annually in the United States [1]. In-stent restenosis (ISR) is a severe complication following PCI and usually results in death or a large, debilitating MI. To prevent ISR, patients receive dual antiplatelet therapy (DAPT) with aspirin plus a P2Y-12 inhibitor. However, DAPT is a known bleeding risk, with about 5% of patients suffering a major bleed annually [2]. The incidence of hemothorax following standard CPR is about 3.9% [3] and can be the result of damage to the internal mammary arteries, lung parenchyma or the intercostal vessels from resultant rib fractures [4]. Venous Arterial (VA) Extracorporeal Membrane Oxygenation (ECMO) further increases a patient's risk of bleeding due to the need for systemic anticoagulation and temperature management. We present the case of a hemorrhaging patient on VA-ECMO and recent PCI.

Case Report: A 78 year-old male with coronary artery disease and severe aortic valve stenosis presented for transcatheter aortic valve replacement (TAVR) and PCI to the RCA. The patient was loaded with clopidogrel, and one RCA Drug Eluting Stent (DES) was placed followed by TAVR. At the completion of the case, the patient suffered a bradycardic arrest with inferior wall ST segment elevations (STE) requiring 45 minutes of CPR, and he was started on a cangrelor infusion. A repeat PCI was performed with balloon angioplasty, which confirmed a patent RCA. Attempts to transvenously pace the patient were unsuccessful, and the decision was made to cannulate the patient for VA-ECMO and initiate a heparin infusion. Soon after starting VA-ECMO, inferior STE improved, and an intraoperative TEE showed good LV contractility. Shortly after admission to the ICU, the patient was cooled for neurologic protection, and he developed worsening shock with degradation of ECMO venous return and a hemoglobin drop to 6.1 from 14.0. A bedside TTE showed a large left hemothorax. The decision was initially made to refrain from placing a thoracostomy tube, for fear of exsanguination through the chest tube and hope that the expanding hemothorax would tamponade the bleeding. The patient then developed increasing airway pressures with worsening ECMO venous return and loss of pulsatility. The large left hemothorax progressed with significant mediastinal shift, displacing the ECMO cannula. A chest tube was placed with temporary improvements in pulsatility, circuit dynamics, and oxygenation but complicated by continued hemorrhagic shock requiring massive transfusion. The decision was ultimately made by the patient's family to withdraw care.

Discussion: Treatment of a massive, persistent hemothorax is challenging, especially in patients who are receiving necessary antiplatelet and anticoagulation therapy. The differential diagnosis for ECMO 'chugging, ' erratic flow within the system, caused by negative pressure generated within the ECMO system from high pump speed or low volume status [5], in a patient with large volume, persistent hemothorax should include both hypovolemia from hemorrhagic shock, as well as mechanical malpositioning of the ECMO catheter due to mediastinal shift. Furthermore, the decision on whether and how to correct coagulopathy in a hemorrhaging patient when antiplatelet therapy and anticoagulation are necessary presents a challenge to the critical care physician.

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Critical Care-13 Extracorporeal Membrane Oxygenation In A Patient With Toxic Shock Syndrome With Superimposed Cardiogenic Shock

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[1]Rush University Medical Center, Chicago, IL

Introduction: Staphylococcal toxic shock syndrome (TSS) is a rare presentation in adults (1:100,000) but can be detrimental with delayed treatment. TSS is a clinical illness with rapid onset of a rash, fever, hypotension, and multiorgan involvement as result of TSST-1 toxin. Massive T-cell activation and cytokine release can result in sepsis-induced cardiomyopathy which has a mortality rate of greater than 50%. When conventional treatments for septic shock (fluids resuscitation, vasopressors and inotropes) have been exhausted, the initiation of early extracorporeal membrane oxygenation (ECMO) has been shown as a potential lifesaving mechanism.

Case Report: A 40-year-old immunocompetent female with no significant past medical history presented to the ED with fevers, chills, excessive diarrhea, petechial rash on her lower extremity, bilious emesis, altered mental status, and respiratory distress that had progressively worsened over the last five day. Given her altered mental status and inability to protect her airway, she was immediately intubated. Labs showed severe metabolic acidosis (pH 6.9, bicarb 7, CO2 24, and lactic acid 15) and end organ failure (Cr 7, AST 741, and ALT 260). Echo showed an ejection fraction (EF) of 15% with diffuse hypokinesis and regional variations. Her clinical picture was consistent with severe septic shock with superimposed cardiogenic shock with Takotsubo cardiomyopathy resulting in multi organ failure. Patient was resuscitated, vasoactive/inotropes were started, and broad-spectrum antibiotics were initiated. Given her continued metabolic acidosis (pH 7.1, bicarb 10.8, and lactic acid 10) VA-ECMO was initiated early. Blood cultures came back positive for S. Aureus. Augmentin and clindamycin were started along with IVIG for presumed TSS. Over the next five-day, patient had significant improvement. Labs consisted of lactic acid 1.2, AST 121, ALT 93, Cr 1.82 and improvement of ejection fraction to 55%. She was able to be weaned off vasoactive/inotropes and extubated. It took another 10 days for the patient to have significant urine output and not require hemodialysis. Patient was able to be discharged to acute rehab and eventually home with a full recovery.

Discussion: This is the second reported cases of TSS resulting in severe sepsis with significant myocardial depression requiring the use of ECMO in the adult population. Even though ECMO in refractory septic patients is controversial given the mixed data, it may play a role in superimposed cardiogenic shock patients. Ventricular dysfunction secondary to sepsis usually resolves in 7-10 days. The use of ECMO may use to bridge the patient while heart function recovers. This cases report provides an example of that.

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Critical Care-14 Cardiac Arrest Following Intravenous Marijuana: A Case Report

Ryan J Fink[1], David Scheafer[1], Molly Brazil[2], Ryan Ivie[1]

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Introduction: Intravenous (IV) administration of marijuana broth, created by soaking the plant in water, is a rare method for cannabis use associated with a syndrome of hypotension, myalgias and emesis that was first reported in 1968 (1). We present the case of a 34-year-old male who suffered multiple cardiac arrests shortly after IV marijuana injection. This is the first known report of cardiac arrest following this method of use.

Case Report: The patient had a history of IV drug use and was admitted for a lung abscess requiring IV antibiotics. He was stable until day 10 of admission when nursing staff were called for difficulty breathing. He was found dyspneic, pale, and vomiting. His oxygen saturation was 70% despite supplemental oxygen via mask. He became unconscious without a palpable pulse and a Code Blue was activated. Return of spontaneous circulation (ROSC) was achieved after one minute of chest compressions. He regained consciousness and was tachypneic to 30 breaths/min with a heart rate of 150 beats/minute. Venous blood gas showed pH 7.06, pCO2 57, pO2 73, HCO3 16, and a lactate of 10.5. Fluids and norepinephrine were started, and he was transferred to the ICU and intubated. One hour later the patient had a pulseless ventricular tachycardia and received chest compressions for less than one minute before ROSC and return of neurologic status. 12-lead ECG only showed sinus tachycardia. His urine drug screen resulted positive for opioids, which he was receiving for analgesia, and cannabinoids. CT chest/abdomen/pelvis were unremarkable. He was extubated the following day. Renal function, blood counts, and coagulation studies all remained normal. The patient disclosed that, just prior to his initial cardiac arrest, he had poured hot water over marijuana, then collected the broth and injected it directly into his peripheral IV. He recovered and was discharged two days later with oral antibiotics and naloxone.

Discussion: Since the first published case of IV marijuana, multiple reports have shown common symptoms of myalagias, nausea/vomiting, diarrhea, and abdominal pain, along with signs of tachycardia, hypotension, leukocytosis, and renal insufficiency (2). To our knowledge, this is the first report of a cardiac arrest following IV marijuana. While an air embolus may explain the first arrest given the quick onset from the time of injection into an indwelling line, this is unlikely the cause of the second arrest one hour later. Historically, IV marijuana syndrome was characterized by transitive multisystem damage, but this case demonstrates fatal potential. While marijuana can have cardiovascular effects (3), medical-grade delta-9-tetrahydrocannabinol, the main active ingredient in marijuana, appears safe in medical research (4). Thus, the systemic effects of IV marijuana, including cardiac arrest, may be due to impurities/contaminants in the liquid. As more states legalize recreational marijuana, health care providers must be aware of this potentially deadly complication.

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Critical Care-15 ECMO for Salvaging High Risk Liver Transplant with Hepatopulmonary Syndrome

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Introduction: Hepatopulmonary syndrome is a unique sequelae of end-stage liver disease resulting in pulmonary vascular dilatation and subsequent hypoxemia and pulmonary hypertension1. Consequently, special consideration must be given to the intraoperative management of this patient population. Surgical techniques including venovenous bypass and the piggyback approach have been utilized to optimize hemodynamic stability and reduce risk of renal dysfunction in high risk patients2,3. Despite these techniques, liver transplant in the complex patient population has increased morbidity and mortality. The purpose of this report is to demonstrate the utility of extracorporeal membrane oxygenation devices to facilitate recovery in a high-risk surgical transplant patient.

Case Report: A 41 year old male with alcoholic cirrhosis complicated by possible hepatic cellular carcinoma and HPS with baseline oxygen requirement presented for deceased donor liver transplantation. His preoperative evaluation demonstrated rest and exertional hypoxemia as well as right-to-left shunting of venous blood. He received MELD exception points to 32 based on the diagnosis of HPS. During piggyback orthotopic liver transplantation after reperfusion of the hepatic artery, the patient developed mixed hemorrhagic and distributive shock unresponsive to vasopressor support and multiple transfusions as well as refractory hypoxemia. The patient was cannulated for veno-arterial extracorporeal membrane oxygenation (VA ECMO) via femoral arterial and venous cannulation. Due to refractory hypoxemia despite VA ECMO, an additional femoral venous cannula was placed. The patient's ICU admission was complicated by abdominal compartment syndrome with compromised ECMO flow requiring an emergent laparotomy. The graft failed over the first several days and patient was retransplanted with VAV ECMO support without adverse effect. The patient tolerated conversion to VV ECMO for an additional 2 days prior to subsequent decannulation altogether. After an extended ICU admission, the patient recovered well and was discharged home.

Discussion: Patients with HPS have an increased risk of death due to RV dysfunction, and transplantation is the only effective therapy to resolve the condition1. Marked hemodynamic alterations during transplant including increase in cardiac output as high as 15L/min following reperfusion predisposes to circulatory shock4. ECMO may be utilized as a bridge to RV recovery, however special consideration must be made to the unique physiologic changes in HPS. Although ECMO is not electively used as part of surgical planning, it has been instrumental in extending the option of transplant to patients previously thought to have prohibitively high mortality risk due to pulmonary hypertension4. VA ECMO may facilitate decompression of the pulmonary circulation and allow for recovery of the RV. Gradual return of cardiac function however will result in hypoxemia due a hyperdynamic state and transpulmonary shunting. Reconfiguration to VV ECMO ameliorates this effect with eventual normalization of intrapulmonary vasodilation following liver transplantation and eventual liberation from ECMO. Barriers to ECMO following liver transplant include circuit induced coagulopathy, the timing of anticoagulation in the postoperative period and possibility of iatrogenic injury to caval anastomoses. Appropriate utilization of ECMO however may salvage a decompensating patient with cardiopulmonary failure as suggested in this report with the unique feature of intraoperative ECMO used for rescue and subsequent continuation to successful re-transplant.

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Critical Care-16 Oral contraceptive induced hypercoagulability presenting as portal vein thrombosis, complicated by heparin induced thrombocytopenia and alveolar hemorrhage

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Introduction: Estrogen containing oral contraceptive (OCP) use is a known risk factor for thrombosis in reproductive age women. It is less common that the presenting clot specifically affects the portal vein. In this report, we highlight the significant critical care challenges associated with heparin use in an otherwise healthy young patient undergoing systemic anticoagulation for portal vein thrombosis, to include heparin induced thrombocytopenia and alveolar hemorrhage.

Case Report: A 19yo woman presented from an outside hospital for portal vein thrombosis following the initiation of an OCP 2 months prior. She was started on heparin therapy at an outside hospital two days prior to arrival at our facility. Full intensity heparin drip was initiated on arrival. She was taken to interventional radiology for placement of a percutaneous EKOS infusion catheter into the portal vein. tPA was administered through the catheter with significant reduction in clot burden over 24 hours. During this time she developed dyspnea and required HFNC to maintain saturations above 94%. She was taken to the OR for catheter removal and returned to the ICU intubated due to persistent impaired oxygenation during the procedure. Bronchoscopy with sequential bronchoalveolar lavage (BAL) was positive for increasingly bloody washings consistent with diffuse alveolar hemorrhage (DAH). CT chest found diffuse ground glass opacities consistent with alveolar hemorrhage. Lab workup for hypercoagulable states, vasculitis and connective tissue disorders were negative. Heparin drip was paused until her respiratory status improved and she was successfully extubated. Upon reinitiation of the heparin drip, her platelets dropped by >50% and a HIT panel was sent. Results came back negative but due to persistent clinical suspicion, she was switched to an argatroban drip and a repeat HIT panel was positive. She continued the argatroban drip and experienced no further complications throughout her ICU admission.

Discussion: The most common causes of diffuse alveolar hemorrhage include systemic vasculitides, rheumatic and connective tissue disease, infection, and drugs to include anticoagulants. The duration of heparin use made bland alveolar hemorrhage most likely however, given the odd initial presentation and concurrent workup for a genetic clotting disorder, a more thorough investigation was warranted. Treatment of DAH centers on supportive respiratory care and identification of the underlying cause. Prompt cessation of any anticoagulants should be ordered when anticoagulation is the presumptive cause. Continued therapeutic use of anticoagulants must be carefully weighed against the risk of continued alveolar hemorrhage. A multidisciplinary discussion is recommended to evaluate other treatment options. If the underlying cause is due to vasculitis or rheumatic disease, prompt glucocorticoid therapy should be included with general supportive care.

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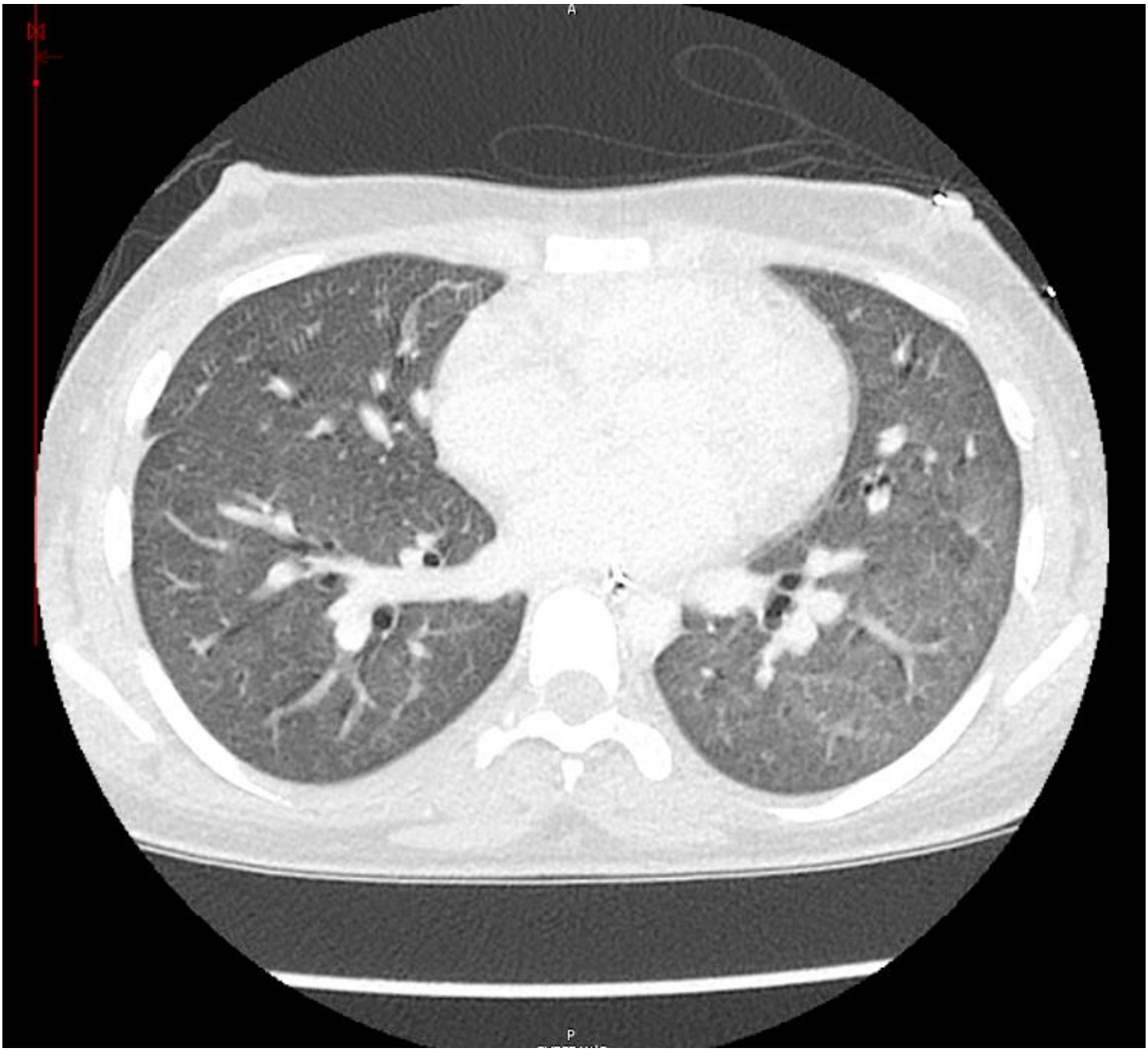
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Critical Care-17 Point of Care Abdominal Ultrasonography in Patients with Postoperative Hypotension

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Introduction: Most data on point of care ultrasound (POCUS) has been acquired in the ED and ICU where this modality has been used for longer than in the perioperative setting (1,2,3). The extended Focused Assessment with Sonography in Trauma (eFAST) was created to rapidly and accurately detect hemoperitoneum in the ED. eFAST requires five minutes to perform and decreases time to OR, radiation exposure, frequency of diagnostic peritoneal lavage, and hospital length of stay (4). eFAST detects intraperitoneal free fluid volumes of 400mL or greater (5). There is a paucity of evidence using POCUS to identify intraperitoneal bleeding in the post anesthesia care unit (PACU).

Case Report: A 79 year old woman presented for Nissen fundoplication. In the PACU, the patient became hypotensive. POCUS showed normal CV function and fluid around the spleen (A&B). The surgery team ordered a formal US redemonstrating fluid around the spleen (C). A hemoglobin (Hgb) returned at 7.9g/dL from 12.7g/dL prompting reexploration. Splenic bleeding was coagulated with an estimated blood loss (EBL) of 1.5L. A 58 year old man presented for right hemicolectomy. In the PACU, the patient was hypotensive. Pressors, naloxone, and glycopyrrolate yielded no improvement. POCUS showed a hyperdynamic LV and fluid in Morrison's pouch. The patient returned to the OR for control of a right gastroepiploic arterial bleed. EBL 1.5L. A 61 year old woman presented for splenectomy. She was hypotensive in the PACU. POCUS showed a hyperdynamic LV and intraperitoneal free fluid. A blood count was ordered returning Hgb 5.7g/dL from 8.9g/dL prompting reexploration. The patient was hemodynamically unstable with ST changes on EKG and required pressor infusions. Bleeding vessels were ligated. EBL 1.5L. A 21 year old man presented for median arcuate ligament release. He was tachycardic in PACU. Fluids, anxiolytics and analgesics were given without resolution. POCUS showed a normal CV exam and no free fluid. Hgb was 9.4 g/dL from 14.3 g/dL after an EBL of 300mL. Repeat Hgb two hours later was 8.4g/dL. Given the normotension and stable hemoglobin, reexploration was deferred.

Discussion: Surgeons often state that intraabdominal fluid is expected after abdominal surgery, though this claim is difficult to substantiate. If intraabdominal fluid is expected (due to irrigation and post-operative changes), the question remains if it should be identifiable by eFAST (> 400mL). Given the sparseness of data on the eFAST exam in the postoperative period, it is unknown if it can expedite clinical decisions or prevent unnecessary reoperations for the decompensating post operative patient. Limitations to the use of the eFAST exam in the postoperative period include appropriate training of PACU staff, equipment availability, confounding from irrigation, and free air obscuring views. We believe prospective studies are needed to investigate the feasibility of postoperative eFAST exams in hemodynamically unstable patients to expedite appropriate management.

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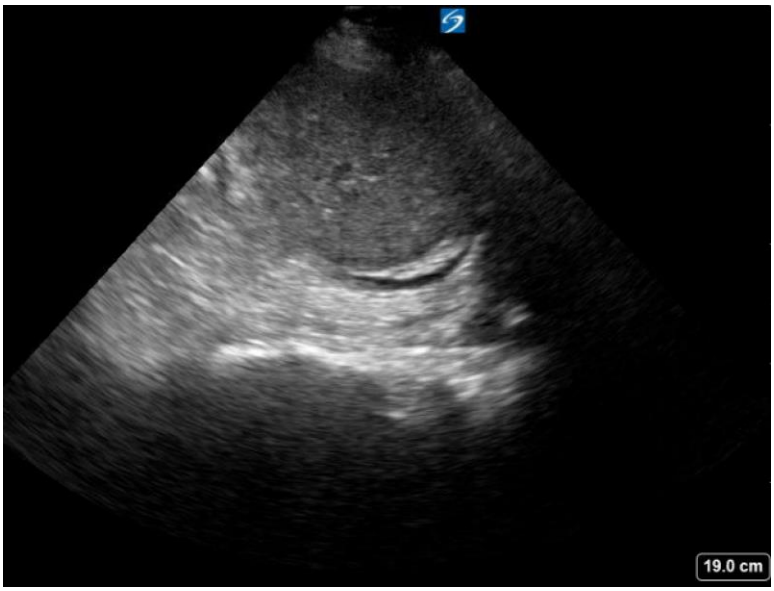
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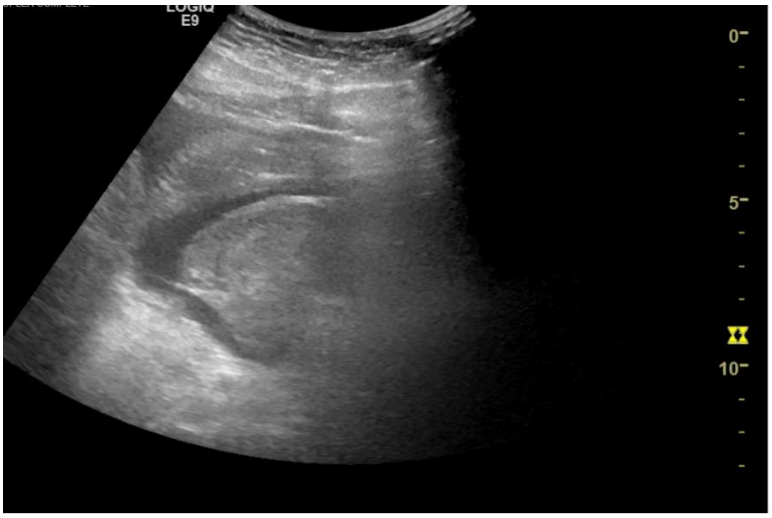
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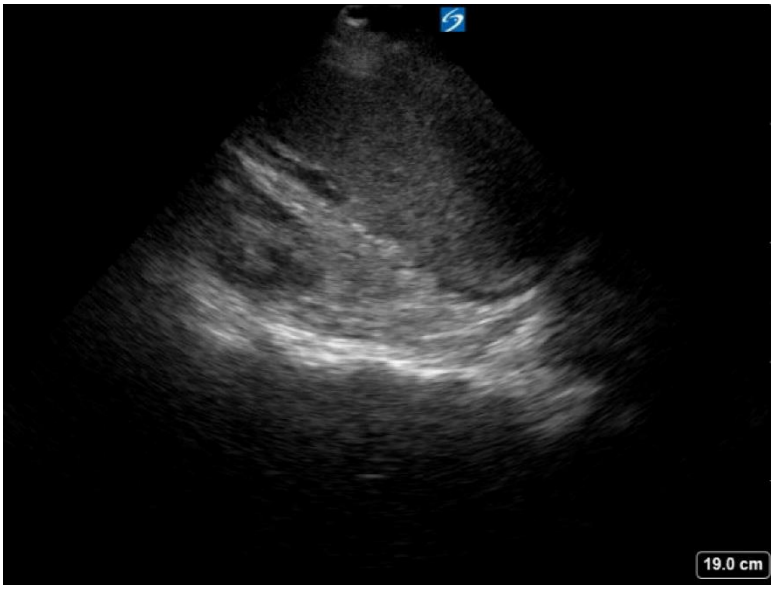
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Critical Care-18 Austrian Syndrome in the CTICU: A Rare Presentation of AIDS Requiring Urgent Surgical Intervention

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Introduction: Invasive pneumococcal disease is rare disease and despite modern day antibiotics still carries a high mortality. The triad of pneumococcal pneumonia, meningitis, and endocarditis was first described in 1956 in a paper by Robert Austrian and hence has been known as Austrian Syndrome. Here we present a case of Austrian Syndrome in a 40 year old male with no known medical history.

Case Report: An otherwise healthy 40 year old male presented to an outside hospital emergency room with 4 days of left arm pain, fever, headache, and vomiting after a recent trip from Los Angeles to New York. He initially attributed these symptoms to heavy lifting and was discharged with a prescription for muscle relaxants. Three days later he again presented to another outside hospital emergency room for fever, continuing headache, and lingering cough. Again he was discharged, this time after administration of IV fluids. 8 days after his initial symptoms he presents to a third emergency room with continued fever, headache, vomiting and new nucchal rigidity. He was admitted and empirically started on vancomycin and ceftriaxone with concern for bacterial meningitis. Spinal fluid was sent for culture and came back positive for strep pneumoniae. His initial blood cultures were negative, he began to have improvement in his clinical symptoms and was being arranged for discharge on hospital day four. However, just prior to being discharged he had sudden respiratory failure requiring BIPAP. He was then transferred to our facility for further workup. Upon arrival, his respiratory status continued to worsen with BIPAP and he was immediately intubated and placed on mechanical ventilation. An echo revealed new severe aortic insufficiency with possible vegetation and a preserved ejection fraction. Further workup revealed an underlying pneumonia with a tracheal culture aspirate positive for strep pneumoniae, blood cultures positive for strep pneumoniae, and a new diagnosis of HIV with a viral load of 21000 along with a reactive RPR suggesting a new diagnosis of syphilis. Despite having this invasive pneumococcal disease, he continued to be fully neurologically intact. He was continued on Ceftriaxone after susceptibilities confirmed sensitivity and cardiothoracic surgery was consulted. On hospital day 4 he underwent an uneventful aortic valve replacement. During his surgery he was noted to have a trileaflet aortic valve with large perforation/destruction of the right coronary cusp with annular involvement. He was successfully extubated postoperative day 0, discharged from the intensive care unit on postoperative day 5, and discharged home without any serious complication on postoperative day 7 with continued IV antibiotics.

Discussion: Austrian Syndrome is a rare disease characterized by the triad of of pneumococcal pneumonia, meningitis, and endocarditis. It was first described in 1956 in a paper by Robert Austrian where he astutely described an association between pneumococcal meningitis and endocarditis of the aortic valve. Since the development of penicillin, strep pneumoniae accounts for less than two percent of all patients with bacterial endocarditis and therefore Austrian syndrome is most commonly seen only in elderly males with a history of alcohol abuse. However, as in our case, it can also be seen in the immunocompromised state. With pneumoccocal endocarditis, the native aortic valve is the most frequent location of vegetation. Despite appropriate antibiotic therapy, the clinical course can often be acute and very aggressive, as in our patient presenting in sudden respiratory failure. Many cases require prompt surgical intervention and are commonly associated with perivalvular abscess or septic emboli [2,3]. One retrospective study on 80 cases of pneumococcal meningitis in an ICU, showed only six patients to develop pneumoccocal endocarditis, and of those one third progressed to cardiogenic shock [4]. In another large cohort of 325 patients with pneumococcal endocarditis, only three presented with the full triad of Austrian Syndrome [5]. Due to its high mortality, early recognition and diagnosis of Austrian Syndrome is key and patients with pneumococcal infections and predisposing risk factors should trigger a high index of suspicion for this rare but life threatening condition.

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Critical Care-19 Streptococcus constellatus Necrotizing Pneumonia

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Introduction: Bacterial pneumonia that progresses to necrotizing pneumonia can be very difficult to manage and treat and has high morbidity and mortality. Identifying the organism, providing supportive management as soon as possible followed by interventions that contain the source is essential. This case report details a Streptococcus constellatus necrotizing pneumonia.

Case Report: The patient is a 50-year old male with suspected alcohol abuse and tobacco use who presented with night sweats, hemoptysis, and left sided flank pain. A CT of the chest demonstrated a large cavitary lesion in the left lower lobe of the lung with air fluid levels and suspected empyema in the left upper lobe and lingula with subcutaneous emphysema in the left chest wall extending up to the neck and down the abdomen. Blood, urine, and respiratory cultures were collected and patient was started on broad spectrum antibiotics which were narrowed once the respiratory and blood cultures were noted to be positive for Streptococcus constellatus. The patient continued to decompensate developing septic shock resulting in metabolic acidosis, intubation and ventilator support, worsening electrolyte derangements requiring dialysis and vasopressor support. The patient was not deemed a surgical candidate due to hemodynamic instability and a pigtail catheter was placed for drainage of the empyema for a possible pneumonectomy. Over a few days, ventilator requirements increased with worsening hypoxia and hypercarbia secondary to worsening lung compliance and development of ARDS. Eventually, the patient was noted to have an agonal rhythm with corresponding acute drop in systolic blood pressure and eventual pulseless electrical activity (PEA) with resuscitation attempts unsuccessful and the patient eventually expired. Streptococcus constellatus is part of the Streptococcus anginosus group that is found in normal flora of the oral cavity and gastrointestinal tract. Predisposing factors of empyema formation include a disturbance in the mucosal layer, a preceding pneumonia, malignancy, or prior surgery. The organism can reach the thoracic cavity via aspiration of oral secretions, hematogenous spread, direct implantation, or extension. 1 It has been noted in prior studies that pulmonary infections from the S. anginosus group have been more commonly associated with males, transaminitis, increased incidence of pneumothorax , and longer hospital stays.2 CT chest findings in patients with S. anginosus infections consisted primarily of ground glass opacities, bronchial wall thickening, cavities and complicated pleural effusions compared to other common pathogens.3 On imaging, patients with necrotizing pneumonia present with more extensive airspaces and often involving multiple lobes compared to lung abscesses. On CT imaging, it can be defined as patchy inflammation with lack of perfusion and microabscesses. Waiting until patients are medically stable allows for better surgical outcomes as highlighted in the largest case series of surgical management of necrotizing pneumonia.

Discussion: Identifying the organism, providing supportive management as soon as possible followed by interventions that contain the source is essential to managing necrotizing pneumonia. Imaging can play a key role in the workup with certain clinical findings notably associated with S. anginosus infections.

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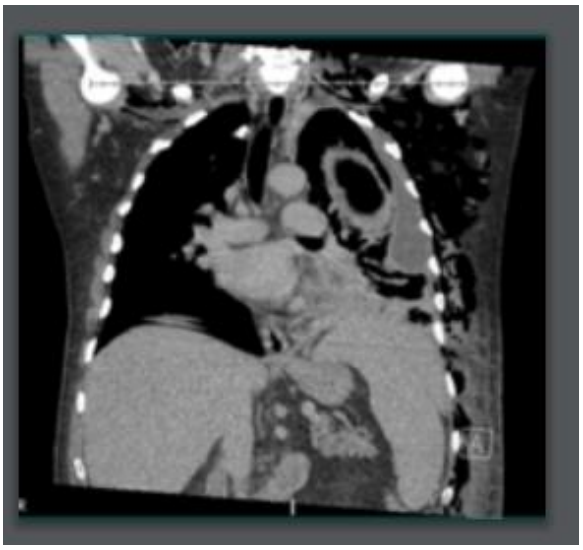

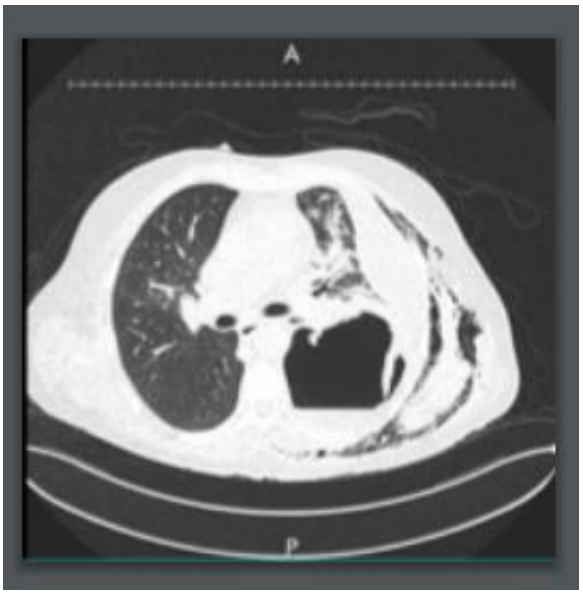
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Critical Care-20 Metabolic acidosis associated with propofol infusion and neuromuscular blockade during targeted temperature management after cardiac arrest

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Introduction: Propofol infusion syndrome (PRIS) remains a rare diagnosis in the intensive care unit. With no specific treatment other than the cessation of propofol administration, and supportive care for involved organ systems, prevention and awareness remain the most helpful interventions to limit development of severe PRIS.

Case Report: A 56-year-old male was brought to the intensive care unit after cardiac arrest. After witnessed collapse, he received first bystander chest compressions, then multiple rounds of compressions, epinephrine, amiodarone, and defibrillation. Return of spontaneous circulation was achieved at twenty five minutes. Initial labs were notable for venous pH 7.07 with lactate 13.9 mmol/L, and base deficit 17 mmol/L. Cardiac catheterization revealed 80-90% LAD stenosis that improved with intracoronary nitroglycerine. He underwent targeted temperature management to 33 degrees Celcius, and was sedated with fentanyl and propofol infusions. Shivering resulted in protocolized treatment with acetaminophen, buspirone, meperidine, and magnesium, and ultimately neuromuscular blockade with cisatracurium. Initial propofol infusion of 20-40 mcg/kg/min was uptitrated to 80 mcg/kg/min, while fentanyl infusion was continued at 75 mcg/hr. Vasopressor support was required with norepinephrine 10 mcg/min and vasopressin 0.02 units/min. During the course of 24 hours of cooling to 33 degrees Celcius, improvements of the initial lactic acidosis led to arterial pH 7.42 with lactate 1.4 mmol/L and base deficit 2 mmol/L. Serum creatinine remained 0.7-0.9 mg/dL. Halfway through cooling, serum triglycerides 366 mg/dL were measured. After 24 hours of cooling, cisatracurium was stopped and rewarming to 36 degrees Celcius was performed, without significant changes in vasopressor requirement or electrolyte abnormalities. After reaching 36 degrees Celcius, he had new increased vasopressor requirement of norepinephrine 20 mcg/min and vasopressin 0.04 units/min, with pH 7.28 and base deficit 11 mmol/L, while lactate remained 1.4 mmol/L. Serum triglycerides reached 596 mg/dL, and serum creatinine kinase was 699 units/L. Aspartate transaminase had increased to 114 from 52 units/L, alanine transaminase to 88 from 58 units/L, and total bilirubin to 4.1 from 3.2 mg/dL. Transthoracic cardiac ultrasound showed unchanged mildly decreased ejection fraction. Propofol infusion was discontinued. Ventilator respiratory rate was increased, and small intermittent boluses of intravenous fluids were continued. After 18 hours of supportive care, pH had returned to 7.34, with base deficit 4 mmol/L. Eventually, creatinine kinase decreased to 307 units/L, and triglycerides to 122 mg/dL. Liver transaminases trended down. Ultimately, he was successfully extubated five days after cardiac arrest, with slow improvement of generalized weakness and mild dysarthria.

Discussion: In this case, consideration of PRIS came with an unexplained metabolic acidosis and concurrent hypotension after a period of relative stability, in the context of a high dose propofol infusion. Laboratory data such as creatinine kinase and liver transaminases were abnormal, and improved after cessation of propofol, along with improvement in the acidosis and hemodynamics. In considering contributing factors, this high dose propofol infusion occurred in the setting of neuromuscular blockade during targeted temperature management. Neuromuscular blockade for that purpose is a common final intervention for severe shivering, and precludes sedation interruptions. High dose infusions in patients receiving paralytics might be a specific population to study further in determining the epidemiology of PRIS, such as in targeted temperature management with severe shivering, or in severe acute respiratory distress syndrome. In considering screening tools that might identify early cases, the rarity of PRIS has made such screening low yield. Protocolized monitoring of creatinine kinase or myoglobin has been suggested, but seems better reserved for when clinical suspicion is elevated. In this case, standard triglyceride monitoring helped identify excessive propofol, and bring PRIS to mind. Early detection, propofol discontinuation, and supportive care were presumably essential in this successful outcome. In severe PRIS, further escalation of supportive care should be available if needed, including extra-corporeal membrane oxygenation in the case of severe cardiovascular collapse.

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Critical Care-21 When Sweet Ain't Sweet Enough: Euglycemic Diabetic Ketoacidosis in a Patient on an SLGT2 Inhibitor with Acute Cholecystitis

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Introduction: This Medically Challenging Case Report describes a case of euglycemic diabetic ketoacidosis associated with SLGT2 inhibitor therapy and discusses the pathogenesis of EDKA as well as the confounding effect of SLGT2 inhibitors in diagnosising this condition.

Case Report: Euglycemic diabetic ketoacidosis (EDKA) is a variant of diabetic ketoacidosis (DKA) that is characterized by a triad of anion-gap metabolic acidosis, ketonemia/ketonuria, and blood glucose <200 mg/ml.1 It typically occurs in insulin-dependent diabetics and can present a diagnostic challenge due to euglycemia masking the underlying DKA. SGLT2 inhibitors such as canagliflozin have been associated with increased risk of EDKA. Here we describe the case of a patient on canagliflozin therapy who developed EDKA after an inciting event. JH is an 81 y.o. male with PMHx significant for T2DM on canafloglizin, paroxysmal Afib, and prostate cancer s/p prostatectomy who presented with abdominal pain and CT findings concerning for new GB mass vs acute cholecystitis secondary to cystic duct obstruction. While in the ED, he developed Afib RVR and was transferred to our ICU for hemodynamic monitoring. A subsequent percutaneous cholecystostomy was performed with improvement in his symptoms. Two days afterwards, he developed sustained Afib RVR as well as new onset anion-gap metabolic acidosis with a nadir ABG of pH 7.25, pCO2 19 and HCO3 8.1. Initial workup was negative for infectious or hemodynamic causes of severe acidosis. Further studies; however, revealed positive urine and serum ketones, despite a blood glucose of 185. EDKA was suspected and he was started on a combination of insulin infusion and dextrose. Over the next several days, his acidosis resolved and he was weaned off the insulin infusion and started on basal-prandial insulin. At time of discharge, the patient was instructed to stop his canagliflozin and continue the prescribed insulin regimen with PCP follow up. EDKA can present a diagnostic challenge due to euglycemia confounding the constellation of symptoms that would otherwise lead to a diagnosis of DKA. Diabetics on SLGT2 inhibitors are known to be at increased risk for EDKA; however, DKA associated with SLGT2 inhibitors is rare, with an incidence rate of 0.52 to 0.76 per 1000 patient-years reported in canagliflozin randomized clinical trials. SLGT2 inhibitors achieve euglycemia by inhibiting the reuptake of glucose in the proximal convoluted tubule.2 The pathophysiology of SLGT2-associated DKA thus is similar to classic DKA, wherein stressors in combination with insulin deficiency and glucagon elevation promote lipolysis and hepatic ketogenesis. However, SLGT2-inhibitor-enhanced glucosuria effectively lowers blood glucose in these patients. Accordingly, a literature review revealed that of 46 cases of SLGT2-associated DKA, 70% were euglycemic.3 We suspect that our patient developed EDKA as a result of his critical illness (acute cholecystisis and Afib w/RVR) in conjunction with SLGT2 inhibitor therapy. While rare, EDKA should be on the differential for patients on SLGT2 inhibitor therapy presenting with metabolic acidosis and high clinical suspicion must be maintained for this patient population to avoid delay of diagnosis and treatment.

Discussion: Euglycemic diabetic ketoacidosis associated with SLGT2 inhibitor therapy can present a diagnostic challenge due to euglycemia confounding the constellation of symptoms that would normally lead to a diagnosis of DKA. High clinical suspicion must be maintained in this patient population when presenting with metabolic acidosis of unknown origin in order to facilitate prompt diagnosis and treatment.

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Critical Care-22 Anesthetic Considerations for CPB Venous Cannula Extraction Debulking of Tricuspid Valve Vegetation and Thrombectomy

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Introduction: Infective endocarditis is a life-threatening diagnosis. The management of IE is largely directed by early recognition, positive blood cultures and evidence of vegetation on echocardiography. Appropriate early and focused antimicrobial therapy is imperative to the treatment of IE (1). For circumstances, where medical management has failed, some patients may require a surgical evaluation for candidacy of cardiac surgery. Patients deemed poor surgical candidates, have limited recourse as there are no clear guidelines for alternative management. With the introduction of the Angiovac, or cardiopulmonary bypass (CPB) venous cannula extraction catheter, patients with right heart thrombi who were deemed prohibitive for surgery may undergo thrombectomy or vegetation debulking (2,3). This case intends to highlight the anesthetic considerations for use of a CPB venous cannula extraction catheter for tricuspid valve vegetation debulking and thrombectomy in the setting of infective endocarditis.

Case Report: A 41 year old female with PMH of IVDA, Crohn's disease s/p multiple bowel resections with colostomy complicated by short bowel syndrome who presented for tricuspid valve vegetation debulking and thrombectomy with a CPB venous cannula extraction catheter. The patient presented from an OSH with complaints of fatigue, malaise and dry cough for several days. On admission to OSH she was in severe septic shock; febrile to 103.5F, hypotensive with blood pressure of 60/40s and tachycardic to 110s. Her labs showed an elevated lactate of 3.7, Creatinine 5.3, BUN 120, ALP 498, SGOT 39 and elevated total bilirubin. She was pan-cultured and broad spectrum antibiotics were initiated. Blood cultures resulted with Methicillin Resistant Staphylococcus aureus. TTE showed a large tricuspid valve vegetation with a mass in the right atrium. CXR and CT revealed evidence of septic emboli. Antibiotics were narrowed to Vancomycin then Daptomycin to treat the MRSA endocarditis, in light of worsening renal function. CT surgery evaluated the patient and deemed her not a candidate for surgical intervention. IR was consulted for debulking/thrombectomy of the tricuspid valve thrombus. Prior to arrival in the IR suite, the patient's vitals were BP 123/86, HR 125, SaO2 97% on 3 L/min supplemental oxygen and RR 40. On arrival to the IR suite the patient was pre-oxygenated and induced with 1 mg midazolam, 50 mcg fentanyl, 100 mg propofol, 30 mg rocuronium, she became profoundly hypotensive with MAPs in the 50s. The patient's blood pressure was subsequently supported with intravenous fluids, phenylephrine and vasopressin infusions. The patient was administered a dose of hydrocortisone for adrenal insufficiency related to sepsis. Pre-intervention intracardiac echocardiography (ICE) demonstrated a large, 30 mm tricuspid valve vegetation. There was evidence of more than 90% of the tricuspid vegetation debulked on post-intervention ICE. At the end of the case the patient remained intubated because of copious purulent secretions thought to be secondary to septic emboli. POD 0 TTE demonstrated no discernible large vegetation yet, POD 5 TTE showed a complex tricuspid valve mass predominantly involving the septal leaflet with moderate regurgitation. Antibiotic management was switched to ceftaroline and the patient remains intubated and off vasopressors.

Discussion: The anesthetic management of a patient with infective endocarditis is challenging. Sepsis and septic shock are familiar morbidities associated with IE. However, with the introduction of the CPB venous cannula extraction catheter and its utility as an alternative treatment strategy for right-sided heart thrombi, Anesthesia providers should be aware of how patients are cannulated for these procedures as well as familiar with the associated morbidities and complications. The CPB venous cannula extraction catheter procedure involves venous access for the target thrombus (i.e. Iliofemoral vein, IVC, SVC, RA) as well as venous access for reinfusion. The extraction catheter is positioned at the site of the thrombus under image guidance. Right-sided IE are most readily seen in intravenous drug abusers. These patients may have severe tricuspid valvular regurgitation or obstruction associated with large vegetations. Isolated right heart failure is rare, but can lead to right atrial dilation, hepatic congestion, coagulopathy and decreased preload.

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Critical Care-23 Dihydropyridine Calcium Channel Blocker Overdose Treated with Veno-Arterial-Venous Extracorporeal Membrane Oxygenation

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Introduction: Dihydropyridine (DHP) calcium channel blockers (CCB), such as amlodipine, preferentially antagonize L-type calcium channels of vascular smooth muscle, resulting in decreased systemic vascular resistance. This selectivity for vascular receptors is lost with higher doses, causing decreased cardiac inotropy and chronotropy via antagonism of myocardial calcium channels (1). High doses can lead to a combination of hypotension and bradycardia refractory to pharmacologic support. Extracorporeal Life Support (ECLS) has been successfully used as a bridge to recovery in many etiologies of cardiovascular collapse. We present a case report which describes the successful use of Veno-Arterial-Venous (V-AV) Extracorporeal Membrane Oxygenation (ECMO) for the treatment of amlodipine overdose.

Case Report: An 18-year-old female with a history of bipolar disorder attempted suicide by ingesting 27 tablets of amlodipine. On admission, she was afebrile with HR 120, BP 75/38, RR 20, and SpO2 100% on room air. Initial chest XR was clear, but abdominal CT scan revealed abdominopelvic ascites. She remained hypotensive after fluid resuscitation, and was admitted to the ICU. In the ICU, the patient was intubated for hypoxemic respiratory failure. Refractory hypotension and bradycardia led to cardiac arrest with ROSC after one round of ACLS. TTE showed severely reduced LV function, and repeat chest XR showed signs of severe pulmonary edema (Figure 1). Hypotension was refractory to high-dosed vasopressors and IV calcium, and she was subsequently transferred to our institution for ECMO support. Bifemoral Veno-Arterial (V-A) ECMO support was initiated, which helped to stabilize hemodynamics. Native cardiac function quickly recovered and all vasopressors were discontinued. As cardiac function improved, the patient's face and upper extremities appeared blue-grey while the lower extremities appeared pink. Right hand pulse oximetry SpO2 was 20-50% and right axially artery PaO2 was <30mmHg. These signs were concerning for differential hypoxia between the upper and lower extremities. Therefore, we elected to place an additional cannula in the right internal jugular (RIJ) vein for V-AV ECMO support. V-AV ECMO removed deoxygenated blood from the femoral vein and delivered oxygenated blood to the femoral artery and RIJ vein. Delivery of oxygenated blood to the RIJ venous cannula immediately resolved the differential hypoxia. A peritoneal drain was placed for intra-abdominal hypertension, and aggressive IV diuresis allowed for a total net -11.2L fluid balance over the next several days (Figure 1). The patient was decannulated from V-AV ECMO on day 4, transferred out of the ICU on day 9, and discharged on day 18.

Discussion: The utilization of ECLS for CCB toxicity is reported in multiple case reports as a rescue treatment for cardiopulmonary collapse refractory to pharmacologic support. The majority of case reports describe V-A ECMO support (2-5), with one case report describing Veno-Venous ECMO support (6). This is the first case description of V-AV ECMO for CCB overdose. Amlodipine has a large volume of distribution and elimination half-life (40-60 hours), which can make the management of cardiac and respiratory failure challenging to treat (7). Although the patient's cardiac function improved within 24 hours, severe fluid overload from systemic capillary leak was evident for nearly 5 days. Persistent pulmonary edema prevented any meaningful gas exchange, and intraabdominal hypertension restricted dynamic pulmonary compliance - contributing to severe hypoxemia from a right to left pulmonary shunt. Deoxygenated blood flow through her heart eventually out-competed the retrograde flow of oxygenated blood from the femoral arterial ECMO cannula. The placement of the RIJ cannula for V-AV ECMO provided antegrade flow of oxygenated blood through the lungs to the coronary arteries and branches of the aortic arch, resolving the differential hypoxia. One explanation for the early resolution of cardiogenic failure may be that as the plasma concentration of DHP CCBs decreased in the subacute phase of recovery, the selectivity for myocardial cells decreased as well. V-AV ECMO should be considered as a viable rescue treatment in cases of DHP CCB overdose, where the duration of systemic fluid overload persists beyond the duration of cardiogenic failure.

Reference(s):

1. European heart journal. 1997;18 Suppl A:A71-9.

2. Perfusion. 2014;29(1):53-56.

3. American Journal of Emergency Medicine. 2017;35(10):1581.e3-1581.e5.

4. Cardiovascular Toxicology. 2018;18(2):192-197.

5. BMJ Case Reports. 2018;2018:bcr-2018-225324-2018-225324. 6. Perfusion. 2019;34(2):167-169. 7. Open Heart. 2016;3(2):e000473.\

Figure 1: Chest X-ray on admission to our institution (left). Chest CT on admission showing total lung opacification with only central airway aeration (middle). Chest X-ray on hospital day 6 (right).

Critical Care-24 Was it the aspergilloma or the immune reconstitution inflammatory syndrome?

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Introduction: This is a medically challenge case submission regarding a patient undergoing chemotherapy for recently diagnosed ALL, complicated by neutropenic fever, invasive pulmonary aspergillosis (IPA) with a fungus ball, followed by immune reconstitution inflammatory syndrome, refractory distributive shock despite lobectomy, prolonged ICU stay and death. Pulmonary aspergillosis is associated with high morbidity and mortality in patients with hematologic malignancies who are undergoing myelosuppressive chemotherapy. Neutropenia from chemotherapy or underlying hematologic disease is an important predisposing host factor for IPA. Sometimes clinical and radiologic deterioration is observed during neutrophil recovery in patients with pulmonary aspergillosis, and its deterioration can be associated with immune reconstitution inflammatory syndrome (IRIS) or with the progression of aspergillosis.

Case Report: A 52 year-old man with a history of recently diagnosed B-cell acute lymphocytic leukemia (ALL) was started on a chemotherapeutic regimen using hyper-CVAD (hyper-fractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone) complicated by pancytopenia and subsequent admission due to neutropenic fever. Workup revealed right upper lobe opacity on chest x-ray that demonstrated to be a cavitary lesion in chest CT. Patient underwent broncheoalveolar lavage and cultures were positive for Aspergillus terreus. Patient was started on Amphotericin B and broad-spectrum triazole antifungal agents, adjusted appropriately to resistance, however had little to no clinical improvement. Diagnosis of Aspergilloma was confirmed with CT guided biopsy. Due to lack of response to medical management, as soon as blood cell counts improved, patient underwent right upper lobectomy. Resection was initially thought to be curative, however in the early postoperative period patient ventilatory and hemodynamic status deteriorated, requiring mechanical ventilation and vasopressor support. Of note, galactomannan (GM) as an Aspergillus-specific polysaccharide was negative after resection, favoring immune reconstitution inflammatory syndrome (IRIS) vs progression of invasive pulmonary aspergillosis (controversy exists surrounding this topic). Clinical status continued to deteriorate with refractory respiratory failure, unable to wean off ventilator, after several weeks of ICU level of care and continuous goals of care discussion with family, artificial measures of life support were withdrawn and patient deceased.

Discussion: Although the exact definition of IRIS in non-HIV patients has not been officially established, by consensus it has been defined as 'a new onset of or worsening clinical and radiologic pulmonary findings consistent with an infectious/inflammatory pulmonary condition temporally related to neutrophil recovery with evidence of microbiologic response'3. IRIS is relatively common among neutropenic patients with invasive pulmonary aspergillosis. It has been found to happen in approximately 25% of patients with pulmonary aspergillosis during neutrophil recovery1. Most of these cases improve with antifungal treatment combined with surgery despite radiological progression of disease. It has been proposed that doing serial measurements of the aspergillus specific - galactomannan antigen (GM) titers, is useful in differenciating antifungal treatment failure vs IRIS.

Reference(s):

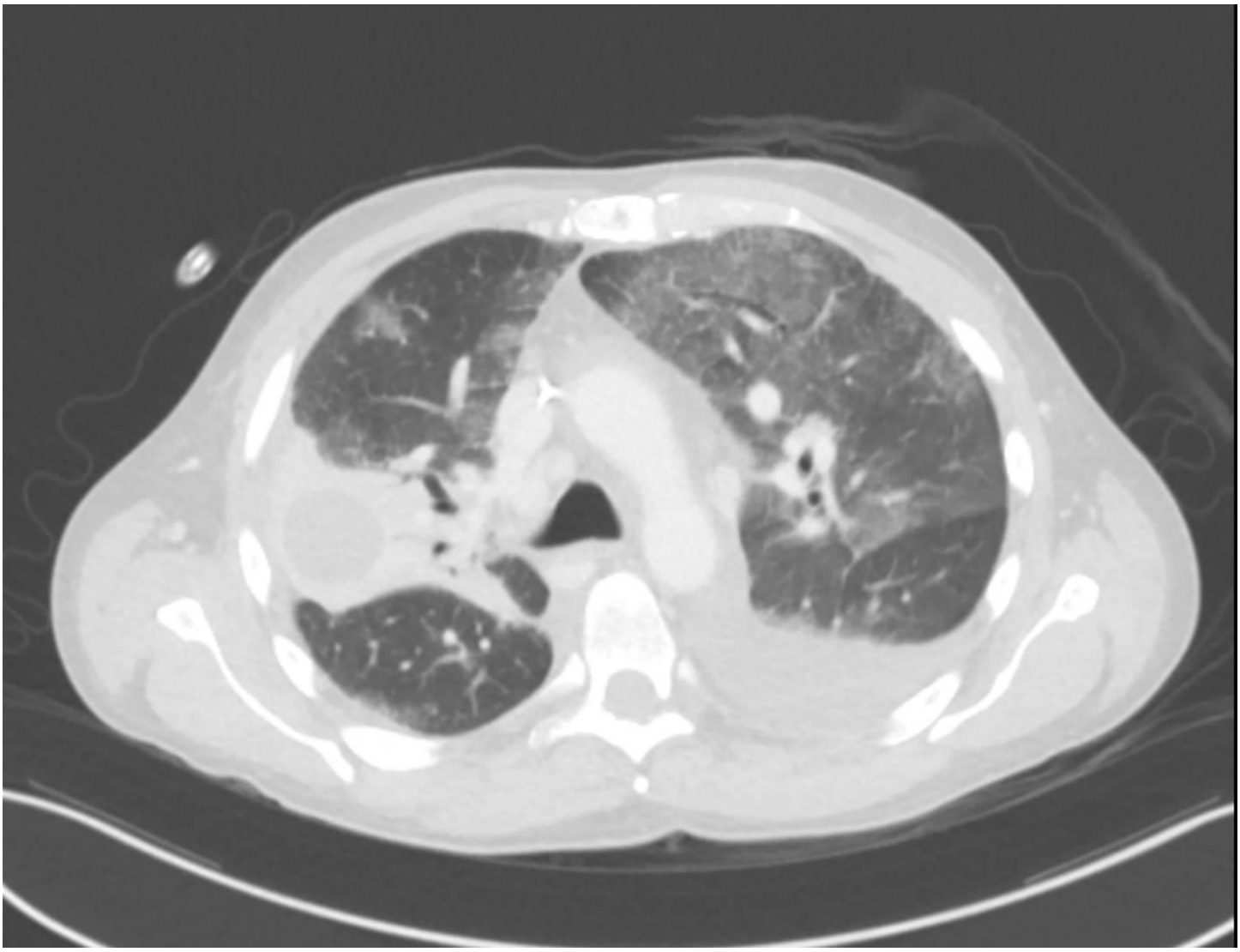
1. Immune reconstitution inflammatory syndrome in neutropenic patients with invasive pulmonary aspergillosis. J Infect. 2015 Jun;70(6):659-67

2. Aspergillosis. N Engl J Med. 2009 Apr; 360:1870-1884

3. Immune reconstitution inflammatory syndrome in cancer patients with pulmonary aspergillosis recovering from neutropenia: Proof of principle, description, and clinical and research implications. Cancer, 110 (2007), pp. 112-120

4. Immune reconstitution inflammatory syndrome associated with Aspergillus terreus pulmonary infection in an autologous stem cell transplant recipient. Transpl Infect Dis, 12 (2010), pp. 64-68

5. Invasive aspergillosis in neutropenic patients: rapid neutrophil recovery is a risk factor for severe pulmonary complications. Eur J Clin Invest, 29 (1999), pp. 453-457



Critical Care-25 A Fatal Foodborne Illness in a Patient with Immune-Active Chronic Hepatitis B Infection

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Introduction: Necrotizing soft tissue infections (NSTI) require rapid diagnosis and often emergent surgical management; however, not every necrotic skin lesion is an NSTI. The following case considers the importance of a thorough exposure history in the setting of rapidly expanding cutaneous lesions with confounding characteristics.

Case Report: A 55-year-old female from SE Asia with a history of untreated chronic Hepatitis B presented with one week of non-bloody diarrhea, N/V, and diffuse lower extremity cramping. Physical exam demonstrated RUQ pain and bilateral lower extremity erythematous patches with central, well-demarcated, raised, violaceous annular lesions concerning for cellulitis (Figure 1). Initial CBC was significant for a mild leukopenia and thrombocytopenia. Transaminases, Alk phos, and T bili were elevated. Hep B serology was consistent with immune-active chronic Hep B infection: HBsAg and Anti-HBe pos; HBeAg neg; and HBV DNA quant 2,530,000 IU/mL. RUQ U/S demonstrated cirrhosis, ascites, and likely portal hypertension. Empiric antibiotics were initiated. She subsequently developed altered mental status, hypotension, and tachycardia and was transferred to the MICU for 'decompensated cirrhosis secondary to chronic Hep B with concern for sepsis.' On arrival her BP was 70's/40's with initial ABG consistent with severe lactic acidosis. She underwent emergent intubation with cardiac arrest on induction. ROSC was achieved in a single cycle of CPR. Lower extremity skin changes progressed to blistering lesions concerning for NSTI (Figure 2). Blood cultures grew Vibrio vulnificus, and empiric antibiotics were modified to cefepime, levofloxacin, metronidazole, and IV Doxycycline. Decompensation continued with rising lactates, worsening acidemia, increasing pressor requirements, DIC, acute liver failure, and increasing oxygen requirements. Despite intensive efforts, the patient passed within 24 hours of first presentation.

Discussion: The CDC estimates 80,000 cases of Vibrio infection annually, but only 1/150 cases require hospitalization, and mortality is less than 1/800 (1,2). Vibrio are aerobic, gram negative rods, typically found in coastal waters. Modes of infection are enteral or cutaneous. Only 10% of reported vibriosis is V. vulnificus, but it has a septicemia mortality rate of nearly 50% (1,2). The initial cutaneous findings were misleading. While V. vulnificus is associated with necrotizing fasciitis, the observed lesions were due to a combination of systemic effects of V. vulnificus and the traditional Chinese medical practices of 'scraping' and 'cupping'. Approximately 80% of cases of V. vulnificus septicemia and 80% of mortality is associated with liver disease (2,3). The patient's family later reported a dinner of Dungeness crab one week prior. Although seven were exposed, the patient was, unfortunately, a susceptible host given her chronic liver disease.

Reference(s):

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Critical Care-26 Not Hot, but Not Cold: A Case of Malignant Hyperthermia in Cardiac Surgery?

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Introduction: This Medically Challenging Case Report describes a case of suspected delayed onset malignant hyperthermia that occurred during an elective cardiac procedure and discusses the differential diagnosis and pathophysiology of malignant hyperthermia.

Case Report: DW is a 53 y.o. male with PMHx significant for CAD, HTN, HLD, alcohol abuse, and depression on paroxetine who presented for elective LIMA-LAD off-pump CABG for coronary-myocardial bridging syndrome. He had previously undergone GA for knee surgery without incident. He underwent smooth induction of general anesthesia using midazolam, fentanyl, propofol, and rocuronium. Isoflurane was used for maintenance anesthesia, and intraoperative pain management included ketamine, hydromorphone, and methadone. At the end of the case, he was noted to have abdominal, upper and lower extremity, and masseter muscle rigidity with severe hypertension at 181/110. ABG showed pH 7.15, pCO2 68, HCO3 19, and lactate 2.4 and core temperature of 35.5C. The patient was breathing spontaneously but unarousable with persistent EtCO2 of ~60 with minute ventilation of 12L/min. At this time, we decided to transport to our ICU for further management, where a critical battery showed pH 7.17, pCO2 66, and HCO3 24 despite a minute ventilation increase to 20L/min. His core temperature had also risen to 37.4C. Malignant hyperthermia (MH) was suspected and the patient was given dantrolene bolus and infusion as well as actively cooled. Within minutes, the patient had resolution of his rigidity, hypercarbia, and acidosis. Notably, in between doses, he had return of rigidity, necessitating 30 hours of dantrolene therapy for complete symptom resolution. He also had a brief rise in CK and K+ with peaks of 233 and 5.6, respectively. Urine output remained stable. He began following commands and was extubated within 24h of arrival. MH is a rare but dangerous complication of anesthesia, arising from a defective ryanodine receptor that leads to uncontrolled calcium release from the sarcoplasmic reticulum culminating in lactic acidosis, muscle rigidity, rhabdomyolysis, and multisystem organ failure. Overall incidence is 1-2 per 100,000 general anesthetics, though susceptibility in the general population may be as high as 1 in 3000.1 Several mutations have been identified as contributing to MH, most notably the RYR1 and CACNA1S genes, which account for 70-80% of genetic MH susceptibilities.2 Dantrolene blocks the mutated ryanodine receptor and prevents further calcium release, which attenuates the downstream symptoms. Previous uneventful anesthesia does not necessarily predict immunity to MH, and MH can present at any time during the anesthetic course, including up to 24h hours afterwards. Though we feel confident in our diagnosis of MH, our case is an interesting one because the initial presentation was not classic, and the patient had risk factors for syndromes with a similar constellation of symptoms. Our differential included NMS, serotonin syndrome, alcohol withdrawal, and seizure. Ultimately, the decision was made to start dantrolene due to the favorable risk/benefit ratio, and resolution of symptoms with treatment confirmed our diagnosis.

Discussion: Malignant Hyperthermia is a rare but devastating complication of anesthesia for which high clinical suspicion must be maintained in order to facilitate prompt diagnosis and treatment.

Reference(s):

1. J. Thorac Cardiovasc Surg. 2011 Jun;141(6):1488-95

2. Semin Cardiothorac Vasc Anesth. 2018 Mar;22(1):95-99

Critical Care-27 Extrapyramidal symptoms masquerading as catatonia secondary to prochlorperazine administration

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Introduction: Although extrapyramidal symptoms (EPS) are a well-known side effect of antipsychotic medications, they are usually easily recognized and treated. However, in rare instances, EPS may present as catatonia, a potentially life-threating psychiatric emergency. Diagnosis and management of this presentation is particularly challenging in the setting of a patient with baseline neuropathology or delirium. Herein we present a case of EPS masquerading as catatonia after giving prochlorperazine.

Case Report: A 24 year old, 33.6kg female with no prior medical history presented after endonasal resection of a sellar mass. Her postoperative course was complicated by CSF leak, hydrocephalus requiring VP shunt placement, meningitis, diabetes insipidus, hyponatremic seizures, cerebral vasospasm, fungemia, and protracted hypoactive delirium. The patient suffered from significant insomnia related to her delirium for which multiple agents were attempted, including a dexmedetomidine infusion, melatonin, trazodone, olanzapine, and mirtazapine. Additionally, she received dronabinol and intermittent doses of ondansetron, haloperidol, and promethazine for nausea. Three days after VP shunt placement, the patient complained of nausea and headache for which two doses of prochlorperazine were given. Over approximately 8 hours, the patient had declining alertness, decreased speech, and only intermittently followed commands. CT imaging of the head was obtained, which revealed unchanged vasospasm and stable hydrocephalus with potentially misplaced shunt hardware. Shortly thereafter, the patient demonstrated complete mutism, negativism, and catatonic posturing, including neck extension, tongue protrusion, and waxy flexibility. Psychiatry was emergently consulted and the patient was taken emergently for shunt exploration by neurosurgery. Postoperatively, the patient had improved but persistent catatonia with brief response to caffeine sodium benzoate,1 but no response to lorazepam. She had begun to slowly follow commands, but exhibited a new tremor of her upper extremities, akathisia, and cogwheel rigidity concerning for EPS. CT imaging continued to show unchanged hydrocephalus. Diphenhydramine was administered and the patient improved to baseline over the following two hours.

Discussion: Because of their known side effects, including EPS, the use of prochlorperazine and other phenothiazine derivatives has declined since the emergence of atypical antipsychotics and other antiemetic medications with a better safety profile. Moreover, EPS presenting as catatonia due to phenothiazine derivatives has only rarely been reported, with our patient possibly marking the third such case and the first in nearly two decades.2,3 Given the rarity of this presentation and the potential for permanent tardive dyskinesia with continuation of such medications, it is important to have a high index of suspicion for this reaction. Our case represents a particularly interesting diagnostic challenge in light of the patient's delirium and neuropathology.

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Critical Care-28 Bilateral hemothoraces complicating total en bloc spondylectomy for recurrent thoracic chondrosarcoma: a case report

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[1]Massachusetts General Hospital, Boston, MA

Introduction: Total en bloc spondylectomy provides superior oncologic outcomes for malignant spinal tumors and involves removal of involved vertebrae through laminectomy and vertebrectomy as well as circumferential reconstruction of the spinal segment through a staged posterior-anterior approach. However, there is considerable morbidity and mortality associated with this procedure due to critical neighboring anatomy, particularly in lesions of the thoracic spine juxtaposed to the vessels and organs of the mediastinum.1-4 Here we describe the case of a patient with recurrent T10 thoracic chondrosarcoma who experienced refractory hypotension during the Stage I procedure. We explore the differentiation of potential etiologies of intraoperative shock and the successful use of intraoperative rescue transesophageal echocardiography to identify hypovolemic shock and hemothorax.

Case Report: A 27-year-old man with recurrent T10 chondrosarcoma presented for two-stage total en-bloc spondylectomy. Past medical history was significant for two prior resection procedures and local radiation therapy with a third recurrence producing severe spinal stenosis leading to significant lower extremity weakness. The patient received preoperative spinal angiography to evaluate normal spinal vasculature and embolize arterial supply to the tumor. The Stage I procedure involved revision laminectomy, revision instrumentation, and passage of Tomita saws with removal of ribs T8-T12 bilaterally. The patient was placed in a prone position with neuromonitoring, central and invasive arterial monitoring, and large-bore intravenous access. Intraoperative course was notable for loss of lower extremity motor evoked potentials in the setting of surgical decompression for which relative hypertension was induced without change. The incision was closed and the patient was returned to a supine position, at which point he became hemodynamically unstable despite massive resuscitation via a Belmont rapid infuser and vasopressor support. Rescue transesophageal echocardiography (TEE) revealed a hyperdynamic left ventricle and significant right pleural effusion. Emergency right thoracotomy was performed with evacuation of right hemothorax and clipping of a segmental artery. Chest x-ray to confirm thoracostomy tube placement revealed interim whiteout of the left hemithorax, at which point the patient again became hemodynamically unstable. Bronchoscopy was unrevealing. Emergent left thoracotomy was performed with identification of a massive left hemothorax in the setting of segmental intercostal bleeding. The patient was stabilized and transferred to the intensive care unit for further monitoring and resuscitation. The estimated blood loss was approximately 10500 milliliters. The patient remained intubated in the intensive care unit for 48 hours before undergoing the Stage II procedure for en bloc resection of tumor and reconstruction with vascularized allografts and completion of instrumentation. He had a prolonged recovery in the intensive care unit complicated by lower extremity paraplegia, respiratory failure requiring tracheostomy, mediastinitis and ventilator-associated pneumonia requiring antibiotic therapy, and malnutrition requiring percutaneous gastrostomy tube placement. However, he eventually discharged to acute rehabilitation and eventually home.

Discussion: This case illustrates the complexity of anesthetic management in patients undergoing total en bloc spondylectomy. A notable potential complication is damage to the great vessels or segmental intercostal arteries during bilateral rib resection. Prompt diagnosis and definitive management of hemothorax is essential to prevent cardiac arrest from hypovolemic and obstructive shock. Intraoperative TEE can rapidly identify the presence of pleural effusions by rotating the probe counterclockwise (left) or clockwise (right) from the midesopageal 4-chamber view.[5] Total en bloc spondylectomy should only be attempted by a multidisciplinary team including, but not limited to, cardiac anesthesiology, orthopedic surgery, neurosurgery, and thoracic surgery after careful consideration of the surgical risks. In addition to invasive monitoring and central access, we recommend availability of TEE, bronchoscopy and equipment for lung isolation, and a rapid infuser device with anticipation of massive resuscitation for this procedure.

Reference(s):

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2. J Orthop Sci, Vol 11, p3-12, 2006.

3. J Spine Surg, Vol 5, p296-299, 2019.

4. Neurosurgery, Vol 69, e248-256, 2011.

5. BJA, Vol 98, p442-446, 2007. Figures adapted from references 4 and 5.

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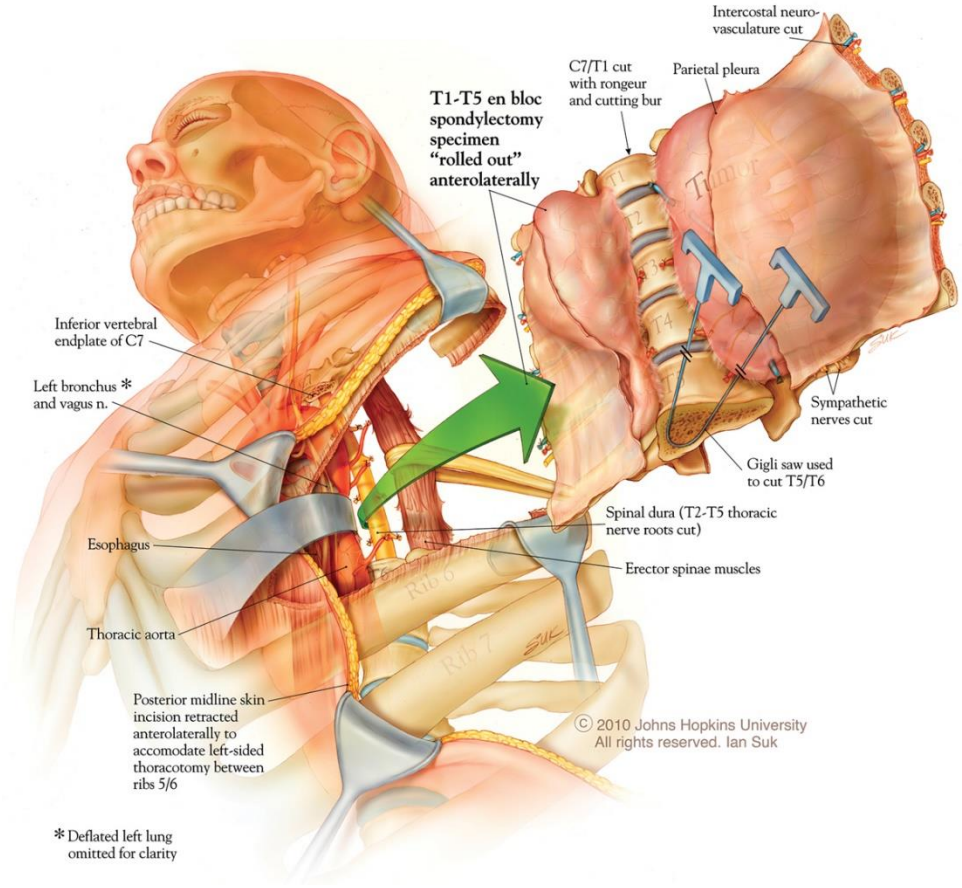
Intercostal neuro-vasculature cut
C7/T1 cut with rongeur and cutting bur
Parietal pleura
T1-T5 en bloc spondylectomy specimen "rolled out" anterolaterally
Inferior vertebral endplate of C7
Left bronchus * and vagus n.
Sympathetic nerves cut
Gigli saw used to cut T5/T6
Spinal dura (T2-T5 thoracic nerve roots cut)
Esophagus
Erector spinae muscles
Thoracic aorta
Posterior midline skin incision retracted anterolaterally to accomodate left-sided thoracotomy between ribs 5/6
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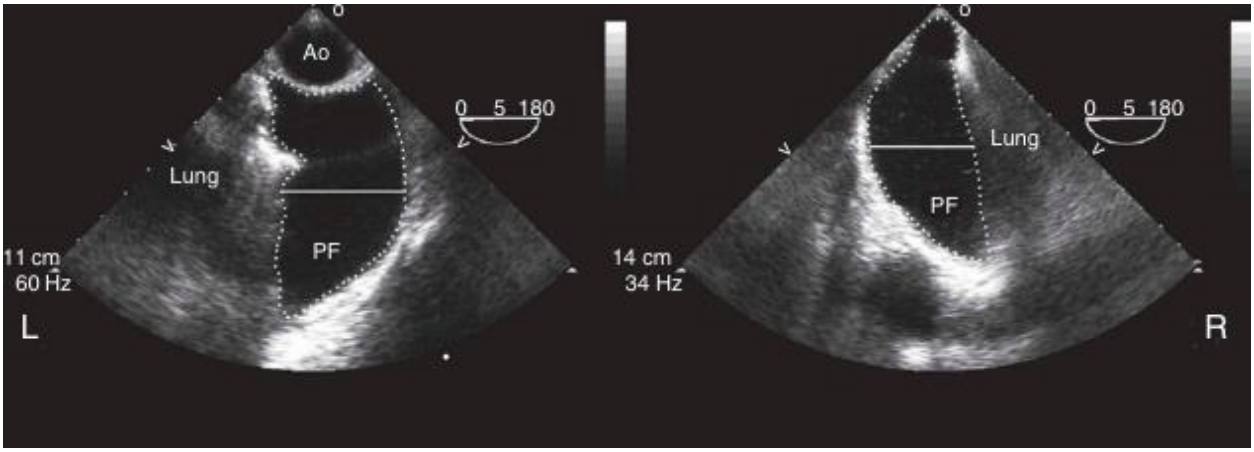
* Deflated left lung omitted for clarity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Critical Care-29 A Case of Prolonged Acidosis from Metformin Associated Lactic Acidosis

Dallas Joiner[1], Miguel Cobas[2], Alexander C Fort[3], Ivet T Cordoba Torres[4], Juan Kusnir[5]

[1]Jackson Memorial Hospital, Miami, FL, [2]Jackson Health Systems, Miami, FL, [3]University of Miami Miller School of Medicine, Miami, FL, [4]Jackson Health Systems/University of Miami Health System, Miami, FL, [5]Nephrology Associates of South Miami, Miami, United States of America

Introduction: Metformin associated lactic acidosis (MALA) is a rare condition seen with metformin exposure in association with renal failure leading to a severe lactic acidosis with mortality rates ranging from 30-50%(1,2,3). Here we present a case of MALA with severe acidemia requiring prolonged hemodialysis (HD) combined with continuous renal replacement therapy (CRRT) for 8 days with extremely high bicarbonate requirements.

Case Report: The patient is a 61 year old female with history of uncontrolled diabetes mellitus who presented with severe lactic acidosis, acute renal failure, and altered mental status requiring intubation, high dose vasopressors, and chest compressions for a brief cardiac arrest after intubation. She had a pH of 6.54, base deficit (BD) of -35, bicarbonate < 5, lactate > 24, anion gap > 27, creatinine of 8, and prothrombin time of 26.7. Remaining labs showed trace ketones, elevated lipase, osmolar gap of 30, ammonia 134, normal glucose, and negative toxicology. CT abdomen was normal, making acute pancreatitis unlikely. Initial exam showed dilated and non-reactive pupils, no cough, and no gag. Per family, she was self medicating with 3g of metformin and 6-8 tabs of ibuprofen daily. Patient was admitted to the intensive care unit (ICU) with the working diagnosis of MALA. One dose of fomepizole was given for possible toxic alcohol ingestion. She received IV fluids, bicarbonate drip, and CRRT at a blood flow rate (BFR) of 250 mL/hr and dialysate rate of 5L/hr. However, her pH remained 6.7 with BD -30. She was then changed to HD for 3.5 hours with improvement in neuro status and pH, but requiring high doses of vasopressors. However, after converting back to CRRT, her acidosis and base deficit worsened. The patient continued to require almost daily HD in addition to CRRT to keep up with her acidosis. Dialysate baths contained 35mEq/L of bicarbonate for CRRT and 37 mEq/L for HD. For HD, her BFR was set at 400 mL/min for 2-3 hour sessions running dialysate at 800mL/min. By day 8, the patient's base deficit normalized and she was off vasopressors. She was extubated day 10, achieved renal recovery by day 14, and transferred out of ICU on day 19 neurologically intact.

Discussion: Due to metformin's lipophilic properties and the extremely large volume of distribution (Vd), it is slow to be dialyzed off as there is a rebound effect (4). However, other cases of severe lactic acidosis and low pH from MALA have been reported, yet their acidosis resolved rapidly with CRRT or HD in just 1-2 days (2,3,5,6). For this patient, her calculated bicarbonate deficit using Vd of 0.88L/kg and ideal body weight was 830 mEq of bicarbonate, which would have taken 4.7 hours to correct on CRRT. Yet, she required 58,642 mEq of bicarbonate over a period of 17.5 hours of HD and 157 hours of CRRT to correct her deficit, which speaks to her significant acid production. In conclusion, we present a complicated case of severe and prolonged acidosis from MALA secondary to lack of patient education about metformin use and risks

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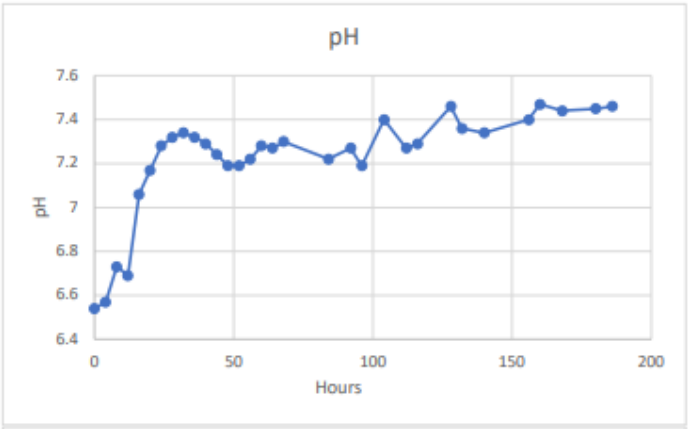
3. Metformin-associated lactic acidosis in an intensive care unit. Crit Care 2008;12(6):R149

4. Metformin-associated lactic acidosis. Am J Med 1996;101(1):109–110.

5. Metformin induced lactic acidosis: a case series. Journal of Medical Case Reports 2007; 1:126

6. A Unique Case of Metformin-Associated Lactic Acidosis. Case Reports in Nephrology 2018; 2018.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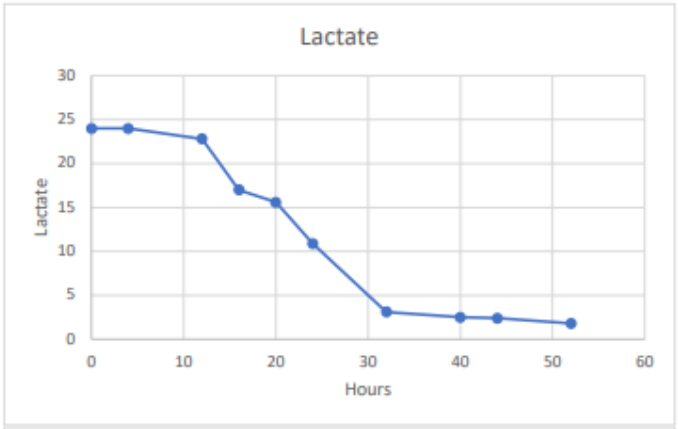
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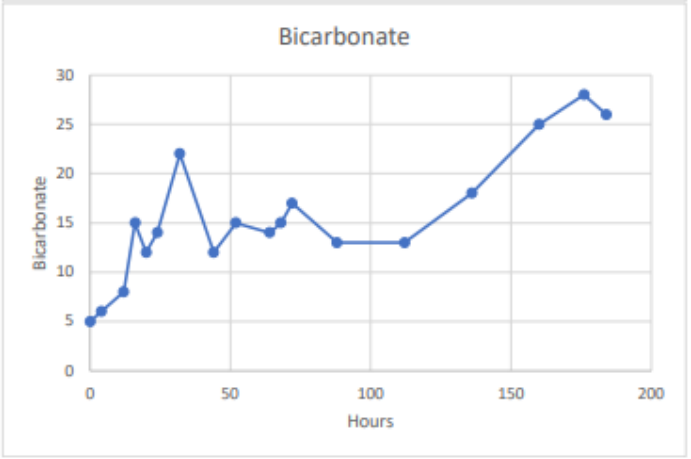
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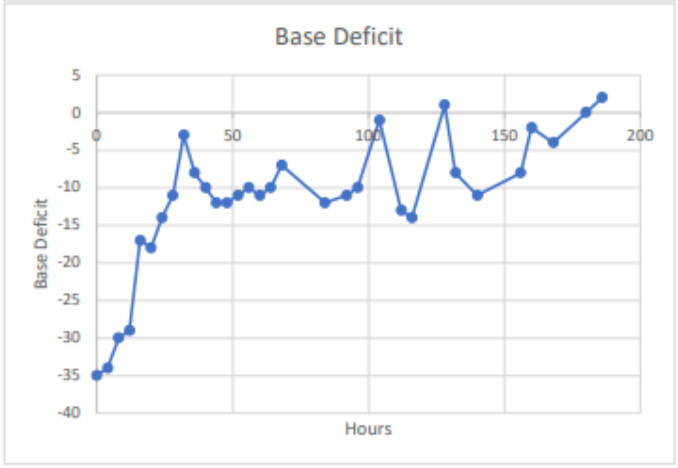
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Critical Care-30 Inotropic Support, Too Much of a Good Thing?

Miguel T Teixeira[1], David Finkel[1], Carlos Puig[2], Jonathan Charnin[1]

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Introduction: Dynamic left ventricular outflow tract (LVOT) obstruction with systolic anterior motion (SAM) may be seen beyond patients with hypertrophic cardiomyopathy or mitral valve repair and is a common cause of unexplained or refractory hypotension in the perioperative setting. Our case highlights the importance of recognizing those at risk, identifying subtle clinical signs, confirming the diagnosis with echocardiography and initiating prompt therapy.

Case Report: A 68-year-old man with severe calcific aortic stenosis and ascending aortic aneurysm underwent an elective aortic valve and hemiarch replacement, and Cox-Maze IV. Transesophageal echocardiography (TEE) after valve placement noted a well-seated bioprosthetic aortic valve with a gradient of 4mmHg, normal left ventricular function and no LVOT obstruction. While separating from cardiopulmonary bypass, the patient sustained acute right heart failure from a right coronary air embolus. Epinephrine, milrinone, nitric oxide, and ventricular pacing were used for successful separation from bypass. The patient presented to the ICU in a stable condition (epinephrine 0.08mcg/kg/min, milrinone 0.25mcg/kg/min, vasopressin 0.04mcg/kg/min, norepinephrine 0.03mcg/kg/min), but developed acute kidney injury and needed continuous renal replacement. Hemodynamic support was weaned by postoperative day one (epinephrine 0.05mcg/kg/min, milrinone 0.125mcg/kg/min, vasopressin 0.02mcg/kg/min; nitric oxide/norepinephrine were discontinued). His course was further complicated by seizures treated with benzodiazepines necessitating reintubation to protect his airway and prevent worsening right ventricular function from hypercarbia. Gas exchange normalized with mechanical ventilation, but the patient developed progressive hypotension (BP 72/44, CI 1.6L/min/m2 and SVRI of 2021dynes.sec/cm5/m2) despite escalation of support (epinephrine 0.08mcg/kg/min, milrinone 0.25mcg/kg/min, vasopressin 0.04mcg/kg/min, norepinephrine 0.1mcg/kg/min). A prominent V–wave and a systolic murmur prompted a transthoracic echocardiogram which showed an under-filled hyperdynamic left ventricle with a maximal LVOT instantaneous gradient of 117 mmHg and severe SAM. Right ventricular function was normal. A followup TEE was obtained. Between the studies, ventricular pacing was slowed from 90 to 60 beats per minute, milrinone was stopped and catecholamine vasopressors were reduced (epinephrine 0.03mcg/kg/min and norepinephrine 0.04mcg/kg/min, vasopressin 0.04mcg/kg/min). The TEE showed persistent but improved left ventricular outflow tract obstruction with a bright echo density thought to be redundant tissue in the base of anterior mitral leaflet folding over on itself and resulting in posteriorly directed mitral regurgitation. The changes were felt to be secondary to the resection of calcified subaortic membranes along the aorto-mitral continuity. With medical optimization, including weaning of inotropes, hemodynamics drastically improved (BP 106/59, CI 2.2L/min/m2 and SVRI of 2122dynes.sec/cm5/m2). Two weeks after surgery, the patient was neurologically normal without seizures on phenytoin. He experienced renal recovery and renal replacement therapy was discontinued. A permanent pacemaker was placed for ongoing heart block. Prior to discharge the patient had a successful surgical outcome with normal biventricular function, and mild mitral valve regurgitation without chordal systolic anterior motion.

Discussion: Dynamic LVOT obstruction and SAM are well described in the literature resulting from various cardiac risk factors including aortic valve replacement and RCA infarct, but they may be easily missed. A new holosystolic murmur, a bifid carotid upstroke or the presence of a V wave in the setting of worsening hemodynamics despite escalating doses of inotropes and catecholamine vasopressors are consistent with an LVOT obstruction with SAM. The diagnosis is confirmed by echocardiography with continuous wave Doppler. Dynamic LVOT obstruction is hastened by a high catecholamine state, including tachycardia and increased cardiac contractility, vasodilation, increased intrathoracic pressure, and hypovolemia. It should be treated with preload augmentation, increasing SVR with non-catecholamine vasopressors and paradoxically decreasing both inotropy and chronotropy.

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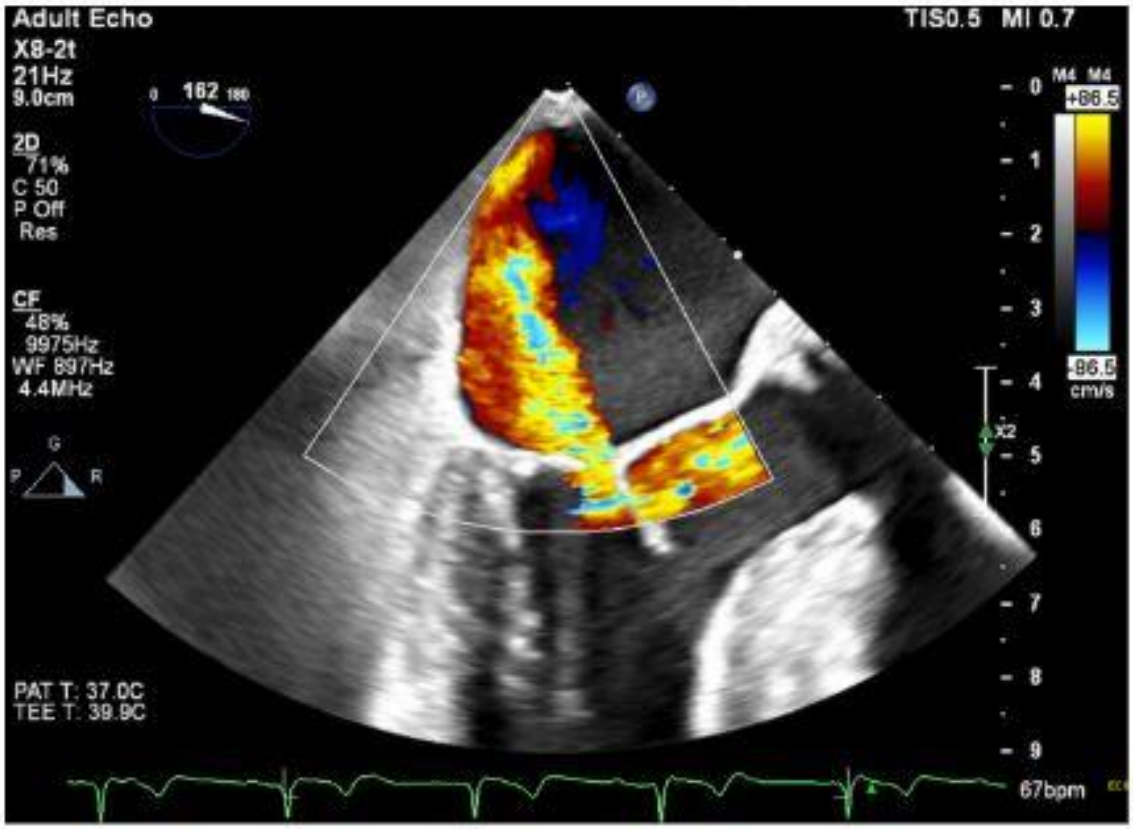

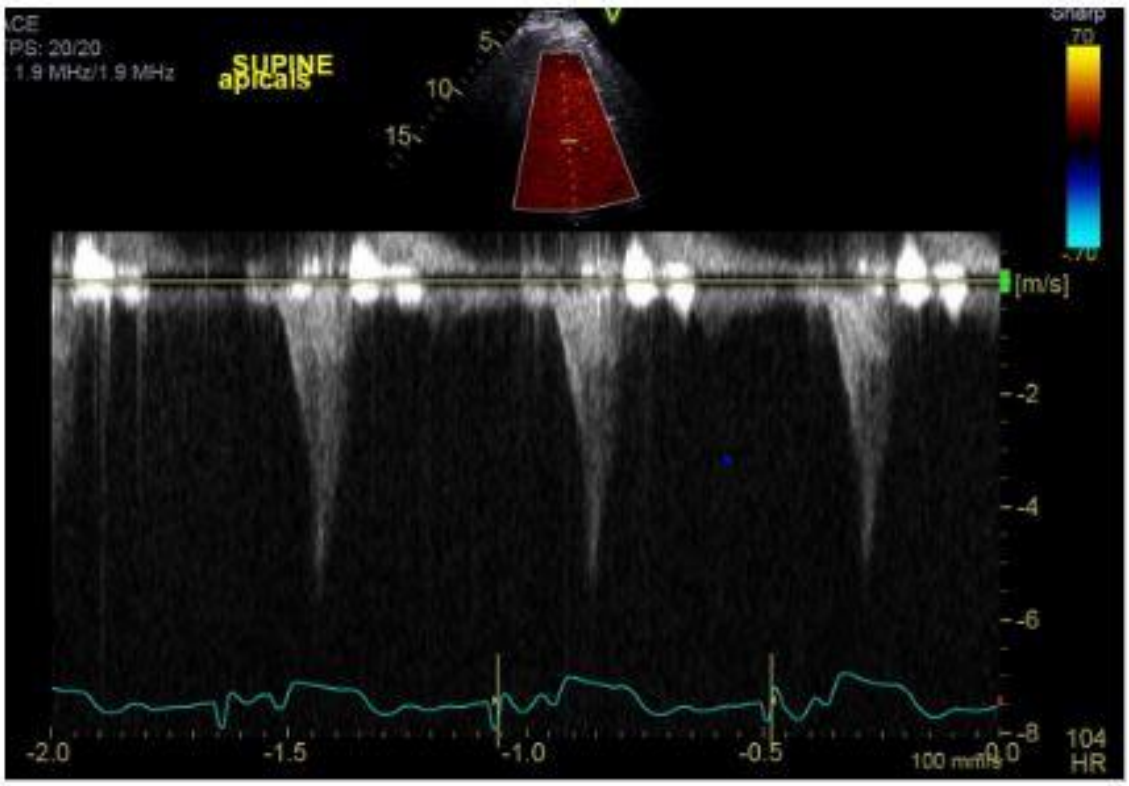

a) TEE midesophageal long axis: Bright echo density noted in LV outflow tract on TTE appears to be redundant tissue in base of anterior mitral leaflet, which folds over on itself. The posteriorly directed mitral regurgitation and elevated consistent with systolic anterior motion (SAM) of the mitral valve with dynamic LVOT obstruction.

b) TTE supine apical continuous wave doppler: Dynamic left ventricular mid cavity and/or outflow tract obstruction; maximal instant gradient 117 mm Hg calculated by the Bernoulli equation.

Critical Care-31 Conservative Positional Management of a Posterior Tracheal Perforation after Intubation

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Introduction: Tracheal perforation after instrumentation of the airway is infrequent but carries the risk for high morbidity. The incidence of this serious complication after an endotracheal intubation is estimated to be less than 0.037%. We present the case of a posterior tracheal perforation after orotracheal intubation for routine surgery, promptly recognized in the post-anesthesia care unit and successfully managed conservatively. The striking feature of the presented case is the positional nature of a tracheal defect and the role of supine positioning in successful conservative management.

Case Report: A 60-year-old woman with prior medical history of gastroesophageal reflux disease, asthma, hypothyroidism and urinary incontinence, was scheduled for urethral sling procedure under general anesthesia. Her past anesthetic history was uncomplicated. During induction and direct laryngoscopy at the time of general anesthesia for the genitourinary procedure, the initial attempt at intubation was complicated by a recognized atraumatic esophageal intubation, immediately after which the trachea was successfully intubated with a 7.0 endotracheal tube. After an uneventful surgical procedure, the trachea was extubated successfully, and the patient was sent for further recovery in the post-anesthesia care unit. Over the course of the next few hours, the patient developed the sensation of a 'swollen neck', accompanied by a facial swelling and subjective neck and tongue fullness on observation by the nursing staff. Upon evaluation by the anesthesia team, she was noted to have bilateral face and neck swelling, accompanied by mild tongue swelling. The decision was made to transfer the patient to the intensive care unit. Over the next hour, she developed progressive subcutaneous emphysema of her face, neck and upper thorax. A Computed Tomography (CT) scan of the chest demonstrated severe subcutaneous and mediastinal emphysema as well as a posterior tracheal defect (Figure 1). The patient was managed expectantly but the subcutaneous emphysema worsened over the course of a few days. We noticed that the subcutaneous air extended to her eyelids when walking but improved when recumbent. A fiberoptic naso-laryngoscopy was performed, revealing no abnormalities. A rigid bronchoscopy was performed to further define the pathology and a 2-cm linear defect was seen posteriorly, in the membranous trachea, about 2 cm proximal to the carina. Immediately following the bronchoscopy, the subcutaneous emphysema was considerably worse. This was confirmed on a new CT-scan (Figure 2). Given the lack of evidence of infection and concerns over worsening the injury with reintubation for a surgical repair, the decision was made to continue with expectant management. As we noted that the subcutaneous emphysema worsened with upright position, patient was kept in supine position for 1 week. After completing the course of bedrest, she was allowed to sit upright at first, then to stand and walk. She did not develop any worsening of the subcutaneous emphysema after ambulating and thus was discharged.

Discussion: Symptoms of tracheobronchial injuries include dyspnea, hemoptysis, soft tissue or mediastinal emphysema, pneumothorax and if unrecognized it may progress to mediastinitis and tracheal strictures. The diagnosis can be delayed because of these lesions are not always readily apparent and this delay may lead to worse outcomes. In the case presented, positional changes of the patient were associated with worsening or improvement of the subcutaneous emphysema. We hypothesize that when the patient was in the supine position the weight of the trachea itself and the mediastinal structures, provided an occlusion of the tracheal tear, limiting air leak from the trachea and leading to improvement of the subcutaneous emphysema. This may explain the lack of subcutaneous emphysema in the initial clinical approach. As soon as the patient raised up, the subcutaneous emphysema frankly worsened. Meticulous prevention, prompt recognition and treatment are the cornerstone of the clinical approach of these patients to assure positive clinical outcomes.

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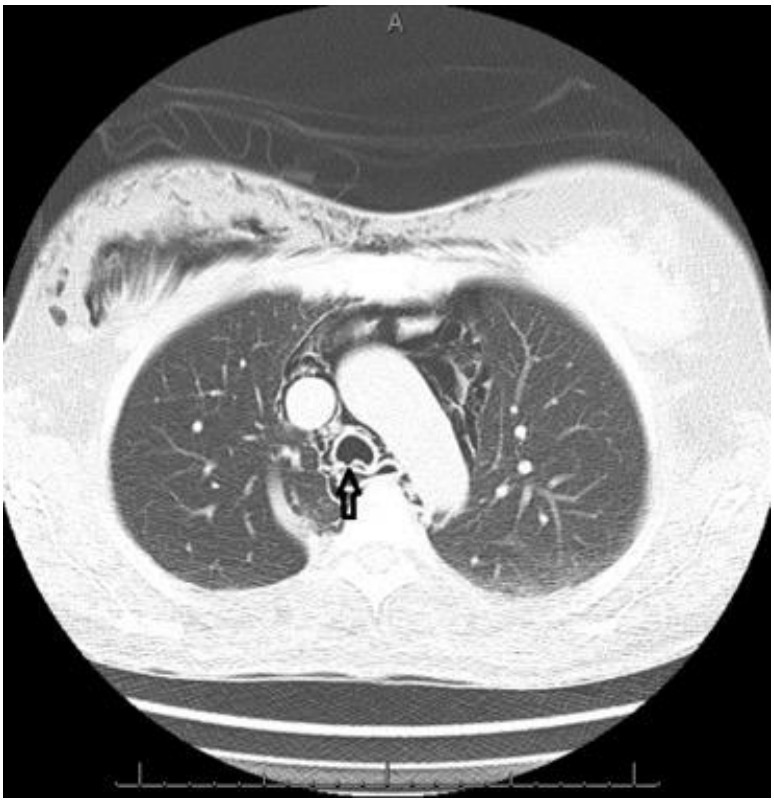
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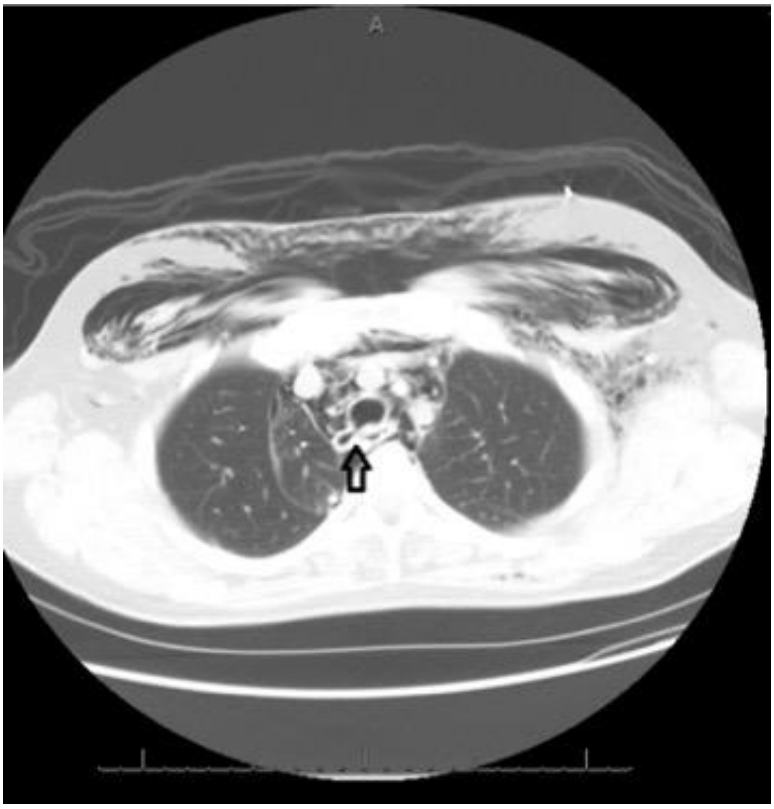
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Critical Care-32 Epidemiology and Outcomes of Acute Respiratory Distress Syndrome Following Isolated Severe Traumatic Brain Injury

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Introduction: Patients with traumatic brain injury (TBI) are at risk for extra-cranial complications, such as the acute respiratory distress syndrome (ARDS) [1,2]. We conducted an analysis of the incidence, risk factors, mortality, and healthcare utilization associated with ARDS following isolated severe TBI.

Case Report: The National Trauma Data Bank (NTDB) dataset files from 2007-2014 were used to identify adult patients who suffered isolated [other body region-specific Abbreviated Injury Scale (AIS) <3] severe TBI [admission total Glasgow Coma Scale (GCS) from 3 to 8 and head region-specific AIS >3] [3,4,5]. We excluded patients who were not admitted to the hospital and those who died within 48 hours of admission. In-hospital mortality was compared between patients who developed ARDS and those who did not. Utilization of healthcare resources (ICU length of stay, hospital length of stay, duration of mechanical ventilation, and frequency of tracheostomy and gastrostomy tube placement) was also examined.

Discussion: The study included 38,213 patients with an overall ARDS incidence of 7.5%. Younger age, admission tachycardia, pre-existing vascular and respiratory diseases, and pneumonia were associated with the development of ARDS. Compared to patients without ARDS, patients that developed ARDS experienced increased in-hospital mortality (OR 1.13, 95%CI 1.01 - 1.26), length of stay (p = <0.001), duration of mechanical ventilation (p = <0.001), and placement of tracheostomy (OR 2.70, 95% CI 2.34 - 3.13) and gastrostomy (OR 2.42, 95% CI 2.06 - 2.84). After isolated severe TBI, ARDS is common and associated with increased mortality and healthcare utilization. Future studies should focus on both prevention and management strategies specific to TBI-assoicated ARDS

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Critical Care-33 When Standard Treatment Isn't Standard: Azithromycin Induced Myasthenic Crisis

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Introduction: Myasthenia gravis is relatively rare, affecting 5−15 people per 100,000. It is an acquired, autoimmune disorder caused by an antibody-mediated blockade of neuromuscular transmission resulting in skeletal muscle weakness. While myasthenic crisis is rare, it is a true emergency. Although infection is a known cause of decompensation in myasthenia gravis, antibiotics have been implicated in precipitating myasthenic crisis.

Case Report: A 28-year-old male with no past medical history presented in January with fever, cough, dyspnea and myalgia for four days. He tested positive for influenza B and chest radiograph revealed bilateral infiltrates. He was commenced on oseltamivir, ceftriaxone and azithromycin and admitted. Shortly after receiving azithromycin, he complained of difficulty breathing. Oxygen saturation was 70%, arterial blood gas with pH of 7.04, pCO2 105 and pO2 of 97. Diphenhydramine and methylprednisolone given and patient emergently intubated. Presumed diagnosis was respiratory failure secondary to influenza and pneumonia, with possible allergic reaction. Antibiotics were switched to vancomycin, doxycycline, and aztreonam. Successfully extubated on day 2. Later that day, Patient noted to have progressively poor respiratory effort and weak cough. Physical examination at that time was notable for ptosis, diminished gag, dysphonia and proximal muscle weakness. A NIF was performed and was -40 which was normal. Fexofenadine, diphenhydramine, famotidine and a slow taper of steroids were started for management of presumed allergic reaction. He improved marginally. During rounds on day 3, the patient showed a picture of a medication he uses that, 'helps me breathe': pyridostigmine! He was commenced on a five-day course of IVIG with marked improvement in strength and transferred out of the ICU.

Discussion: Respiratory failure due to myasthenic weakness occurs in about 20% of patients, usually within the first year of illness. Crisis is a life-threatening condition defined as weakness that most of the time requires intubation. Several triggers have been identified, including infection, stress, medication non-compliance and medications including certain antibiotics. Choice of antibiotic therapy in a patient with myasthenia can be challenging. Fluoroquinolones, aminoglycosides, macrolides, and β-lactams are associated with precipitating myasthenic crisis. We will discuss azithromycin here since it is presumed to have been the instigating agent in this patient. Azithromycin is a macrolide antibiotic commonly used in the treatment of community-acquired respiratory tract infections. The mechanism thought to be involved in deterioration of neuromuscular junction synaptic transmission involves competitively inhibiting the release of acetylcholine from presynaptic membrane, impairing depolarization of the postsynaptic membrane, ultimately leading to the blockade of neuromuscular junction. We argue that the transient improvement observed on day 1 was most likely related to the treatment with steroids following his initial reaction to azithromycin. The delay in the return of strength to baseline was most likely due to the 68-hour half-life of Azithromycin, which outlasts the duration of the effects of the steroid. Ultimately, the patient was started on IVIG given his fluctuating weakness. It is our opinion that the crisis was triggered by azithromycin in this patient who did not provide his past medical history, in conjunction with underlying acute illness. Clinicians should be familiar with these precipitants of myasthenic crisis in treating the myasthenic patient and there should be a low threshold for intubation and admission to the ICU. This is especially important since tests for vital capacity and blood gases are of limited value as deterioration can be rapid. Most importantly, astute clinicians should always look for alternative explanations for worsening clinical status, and seek to gain more history from patients as well as completing thorough physical examinations which more often than not yield the most valuable information.

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Critical Care-34 Successful AngioVac Extraction of a SVC/RA Septic Thrombus in an Unstable Burn Patient

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Introduction: Right heart thrombi present an imminent risk and are associated with high rates of pulmonary embolism, cardiac arrest and high mortality (1). Unfortunately, there is no consensus regarding the management of right heart thrombus. Surgical embolectomy and thrombolytic therapy are two well-known approaches for the treatment of large intravenous or right heart thrombi. However, both of these approaches are of limited utility in the critically ill (1,2). We present the challenging case of an unstable burn patient with a mobile septic thrombus at the superior vena cava/right atrial junction. After consultation with cardiothoracic surgery(CT), the patient underwent a thrombectomy with an AngioVac aspiration device since it was determined that she was not a good candidate for surgical thrombectomy.

Case Report: A 39-year-old female with no prior PMH presented to the ER with severe burn injuries after her boyfriend allegedly doused her with gasoline and lit her on fire with a blow torch. She suffered approximately 75% TBSA burns, both partial and full thickness, to the face, BUE, BLE, and torso. She was intubated in the ED, received burn resuscitation and was admitted to the Burn ICU for management. Her several months-long hospital course was complicated by recurrent MDR Pseudomonas bacteremia, and Candida fungemia. Despite prolonged antimicrobial therapy, she remained in septic shock requiring vasopressor support for many weeks. Along with the clinical findings of skin changes, CT imaging revealed bilateral opacities in a random distribution in the lungs, as well as new focal splenic infarcts concerning for septic emboli. A TEE was obtained which showed a well-defined echo density seen extending from the distal SVC to the junction of the RA and SVC. The diagnosis of a septic thrombus was made and CT surgery was consulted for source control with surgical thrombectomy. She was deemed a poor candidate for sternotomy due to her critically ill state with various issues including septic shock with pressor requirements, renal failure requiring CRRT, and adrenal insufficiency. After a multidisciplinary discussion that involved the burn surgery team, cardiology, infectious diseases and CT surgery, the decision was made to start anticoagulation with a heparin infusion and attempt evacuation of the thrombus with a percutaneous AngioVac system. The patient was taken to the OR by the CT surgery team and underwent near-complete extraction of the thrombus with no further thrombus visible on intra-operative or a follow-up TEE performed 2 weeks later. Follow-up blood cultures 48 hours post-operatively and 2 weeks post-operatively both showed no growth. She continued to receive antibiotic therapy for many weeks per ID recs as well as anticoagulation therapy for her other DVTs (bilateral IJ).

Discussion: The AngioVac device is a catheter based system designed primarily for the extraction of intravascular material in the venous system and the right-sided heart chambers. It can be inserted via the right common femoral vein or internal jugular vein. The AngioVac cannula is then connected to a veno-venous pump circuit with a percutaneously placed reinfusion cannula in the left common femoral vein. This pump creates a negative pressure vacuum that can remove blood and debris around the AngioVac cannula. The pump circulates the blood through a filter, and then returns the blood to the patient through the reinfusion cannula (1,2). Originally approved by the United States Food and Drug Administration in 2009 for removal of unwanted intravascular materials, the AngioVac system is now in its 3rd generation. While the previous generations were more restricted in utility due to their large size and rigidity, the newer generation cannula offers a flexible 20-degree or a 180-degree angled tip that allows for more manipulation around curves (1,3). This expands its potential application to extraction of venous thromboses, extraction/debulking of infectious vegetation on cardiac leads or native/artificial valves, pulmonary embolisms, and even cardiac tumors (3,4). This case illustrates the use of an alternative treatment device to surgical and medical therapy for thrombus removal in a patient with limited therapeutic options.

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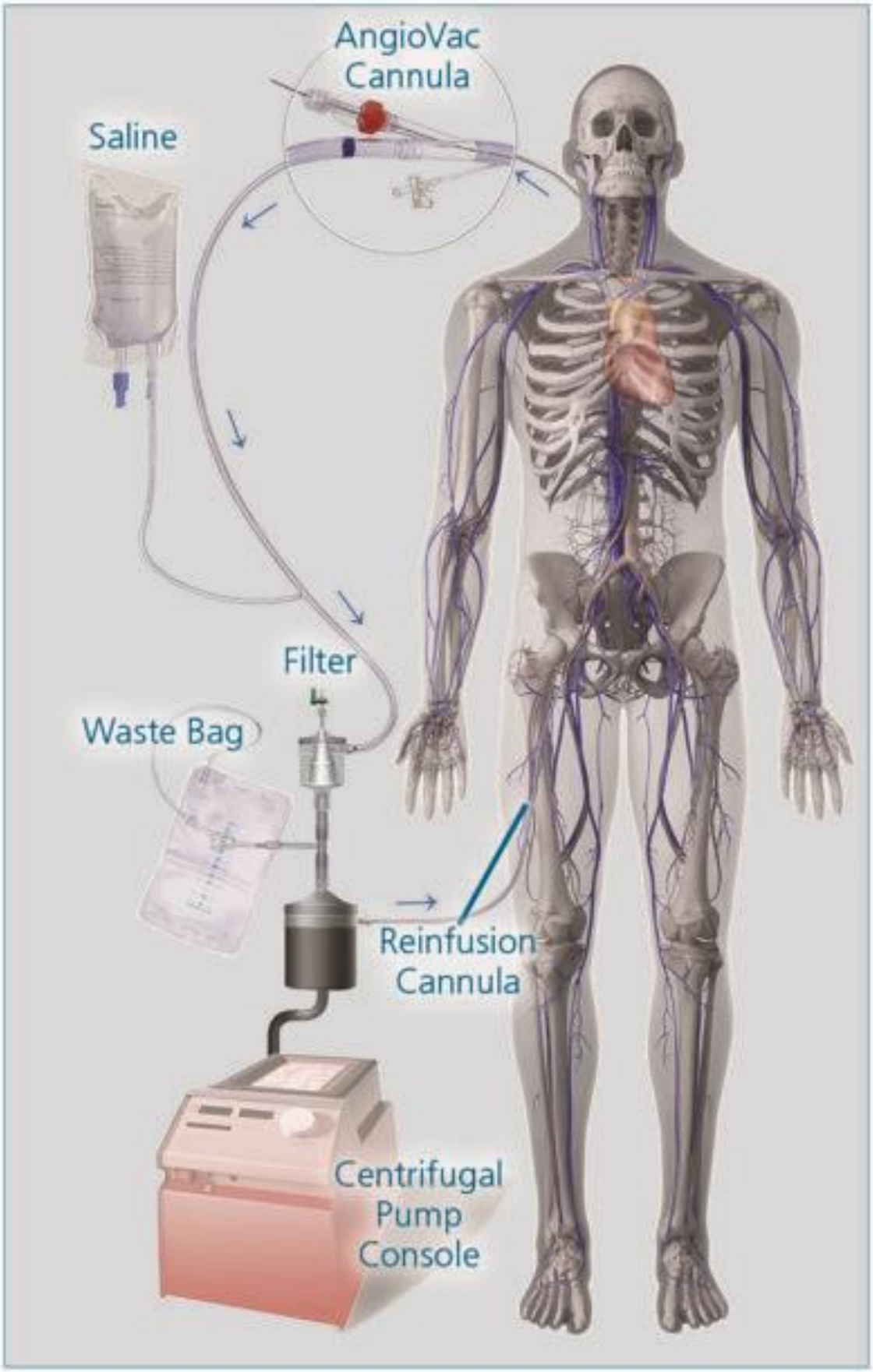
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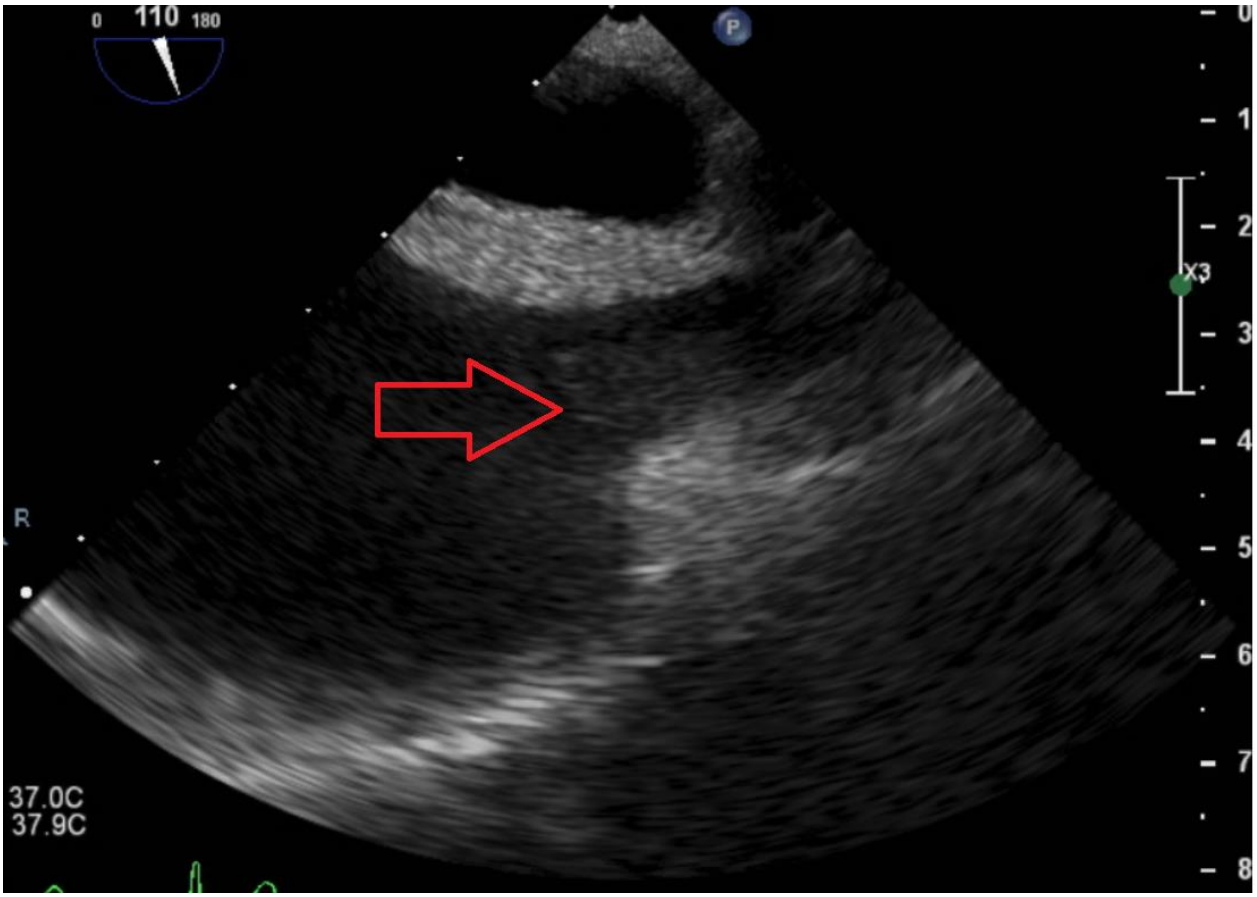
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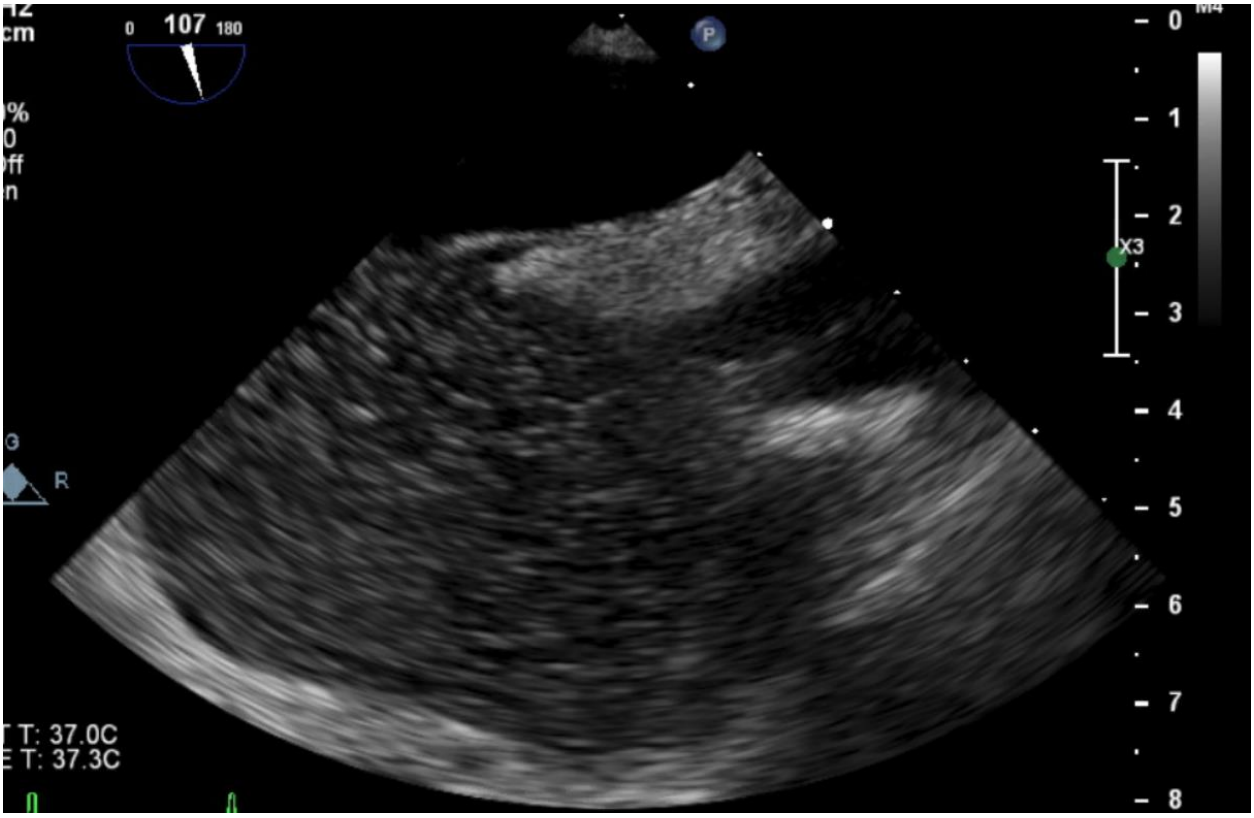
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Critical Care-35 Angiotensin II for the Treatment of Refractory Vasoplegia in a Patient Supported with Veno-Arterial ECMO, Mechanical Ventilation and Renal Replacement Therapy

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Introduction: Vasoplegic shock is a major contributor to morbidity in critically ill patients.(1) The mainstay therapy are catecholamines and vasopressin, which have toxic effects at high doses.(1,2) A recent trial in hypotensive patients refractory to standard therapy showed that angiotensin II (AT II) increased blood pressure and allowed reduction in catecholamine dose.(3) In the subgroup requiring renal replacement therapy (RRT), both increased survival and recovery of kidney function were achieved.(4) Vasoplegia is common in patients after surgery with cardiopulmonary bypass (CPB), and in patients requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO).(2) Published data on AT II use in post-CPB or VA-ECMO patients is limited to small case series.(5,6) More reports and studies on AT II in patients requiring mechanical circulatory support are needed to identify those who would preferentially benefit from the therapy. In this report we present a case where a post-cardiac surgery patient supported with VA-ECMO, mechanical ventilation and RRT was treated with AT II for severe refractory hypotension.

Case Report: A 46 year old woman with medical history significant for breast cancer, Hodgkin lymphoma and chronic myelomonocytic leukemia (CMML) with associated anemia, thrombocytopenia and hyperleukocytosis, presented with severe mitral and tricuspid valve regurgitation. As a treatment option for CMML, bone marrow transplant (BMT) was advised, but subsequently declined due to severe valvular disease. She underwent mitral valve replacement with a bioprosthesis and a tricuspid repair. Eighteen days after the surgery she suffered a cardiac arrest secondary to ventricular tachycardia, and was intubated and resuscitated with return of spontaneous circulation. Upon admission to the intensive care unit VA-ECMO and RRT were initiated. Subsequently her cardiac function recovered, but remained supported with VA-ECMO due to a bioprosthetic valve clot causing severe mitral stenosis. On the fifth day of admission she became septic and hypotensive with mean arterial pressure (MAP) 30-40 mmHg, elevated serum lactate, and remained somnolent but easily arousable. During the hypotensive period ECMO flow rates and cardiac index remained unchanged (4 L/min and >2.2 L/min/m2, respectively). When the norepinephrine-equivalent dose reached 0.7 mcg/kg/min (epinephrine 0.2 mcg/kg/min, norepinephrine 0.2 mcg/kg/min, phenylephrine 2 mcg/kg/min, vasopressin 0.04 unit/min), AT II was started at 20 and up-titrated to 80 ng/kg/min. Within 3 hours MAP increased to >65 mmHg. AT II was stopped after 15h, and the other vasoactive drugs reduced to a norepinephrine-equivalent dose of 0.35 mcg/kg/min within 24h, with improvement in mental status and serum lactate.

Discussion: AT II significantly improved hemodynamics in a vasoplegic patient supported with VA-ECMO, mechanical ventilation and RRT. More data is needed to identify patients on mechanical circulatory support who would benefit most from AT II therapy.

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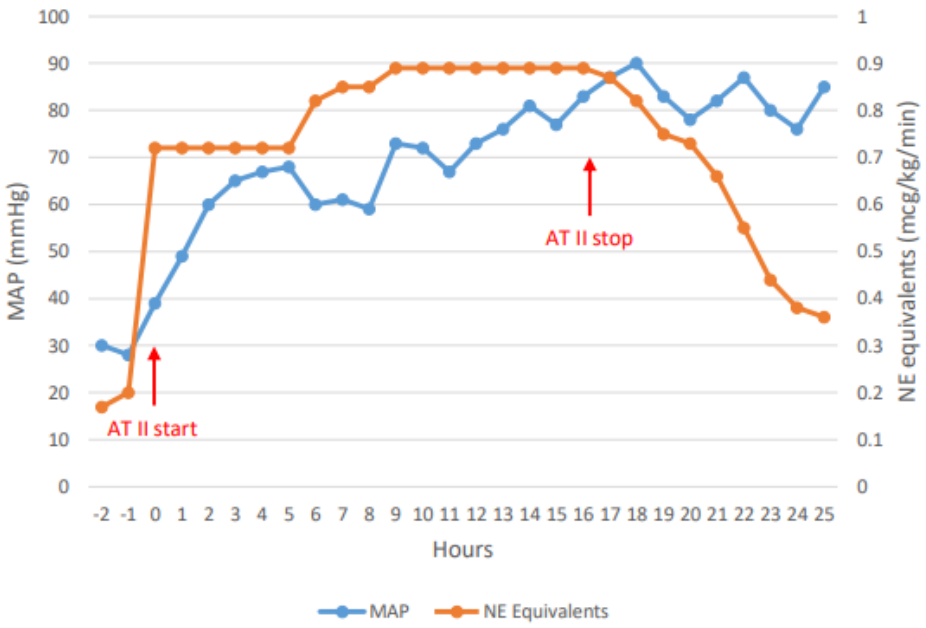
Drug	Dose	NE equivalent
Norepinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Epinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Vasopressin	0.04 units/min	0.1 mcg/kg/min
Phenylephrine	1.0 mcg/kg/min	0.1 mcg/kg/min

NOREPINEPHRINE - EQUIVALENT DOSES OF DIFFERENT VASOACTIVE MEDICATIONS. Table used to calculate NE equivalent doses. NE, norepinephrine



EFFECTS OF ANGIOTENSIN II ON BLOOD PRESSURE AND VASOPRESSOR REQUIREMENTS. Angiotensin infusion was started at "hour 0" at 20 ng/kg/min and gradually up-titrated to 80 ng/kg/min by "hour 1". Weaning started at "hour 4", and the infusion was stopped at "hour 16". AT II, angiotensin II; NE, norepinephrine; MAP, mean arterial pressure

Critical Care-36 A case of crashing pulmonary hypertension with echocardiographic evidence of right heart failure in response to norepinephrine administration and subsequent recovery with vasopressin.

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Introduction: This case report demonstrates the potential harm of norepinephrine in pulmonary hypertension with decompensated right heart failure and the utility of vasopressin in resuscitating these patient. This case provides further evidence that vasopressin may be the vasopressor of choice in shock due to right heart failure.

Case Report: This is a case of a 47 yo F with a PMH of hepatitis B cirrhosis who was POD#7 from a DCD liver transplant. Intra-operatively she suffered a PEA arrest necessitating placement onto VA ECMO. The etiology of her arrest was unclear but we suspect she had occult pulmonary hypertension pre-operatively and developed decompensated right heart failure intraop. On POD#6 she was weaned from VA ECMO and on POD#7 was transferred from the CTICU to the SICU where we assumed care of the patient. On arrival she was hemodynamically unstable with BPs 80s/40s on multiple vasoactive medications including norepinephrine (0.04 mcg/kg/min), epinephrine (0.05 mcg/kg/min), vasopressin (0.06 units/min) and dobutamine (7.5 mcg/kg/min). She was intubated and undergoing BVM ventilation with in-line inhaled epoprostenol. We performed a bedside echo which revealed a severely dilated RV with intact systolic function with a TAPSE of 2.1 cm (IMG 1). In response to her hypotension we titrated up her norepinephrine gradually from a rate of 0.04 mcg/kg/min to a rate of 0.4 mcg/kg/min, however paradoxically her hemodynamics worsened in response to this until she was peri-arrest with a BP of 50s/20s. We repeated her echo (IMG 2) and found that her RV systolic function was now severely depressed with a TAPSE of 0.6 cm (IMG 3). Her RVSP was moderately elevated at 56 mmHg. At this point we decreased the rate of her norepinephrine back down to 0.04 mcg/kg/min and bolused 1 unit of vasopressin. Her hemodynamics responded favorably to this with her BP improving to the 110s/50s. We repeated her echo again (IMG 4) and found that her RV systolic function had recovered back to a TAPSE of 1.6 cm (IMG 5) and her RVSP had increased to 101 mmHg. We placed a pulmonary arterial catheter which revealed supra-systemic PAPs in the 120s/50s. Her BP was maintained on vasopressin at a rate of 0.12 units/min and she stabilized for the next several hours. IV sildenafil was administered for her elevated PA pressures. Unfortunately she decompensated again, requiring multiple boluses of vasopressin, and ultimately had to be placed back on VA ECMO and transferred back to the CTICU. Her workup included a CT pulmonary angiogram which was negative. She remained in the ICU for several more weeks, eventually being weaned from VA ECMO and transferred to the floor. She spent several more weeks in the hospital with severe pulmonary hypertension that was refractory to medical management. Eventually she was transferred to a hospice facility where she passed several days later.

Discussion: In this case we provide echocardiographic evidence of progressive shock due to decompensated right heart failure which correlated to the rapid up titration of a norepinephrine infusion. We also provide echocardiographic evidence of the resolution of this shock state and recovery of right heart systolic function which correlated with weaning of the norepinephrine in lieu of vasopressin boluses and infusion. This case adds to the emerging body of evidence^1-2 that vasopressin may be the vasopressor of choice in decompensated right heart failure. A recent in-vitro study^3 showed that vasopressin worked exclusively on the systemic vasculature and spared the pulmonary circulation. This sparing of the pulmonary vasculature we suspect makes it superior to norepinephrine in supporting the MAP in patients with right heart failure where any increase in the pulmonary vascular resistance may worsen right heart function. We propose that providers consider utilizing vasopressin in cases of right heart failure who fail to respond to norepinephrine. If further data accumulates supporting our conclusion then societal guidelines should recommend vasopressin as the first line agent in pulmonary hypertension with right heart failure.

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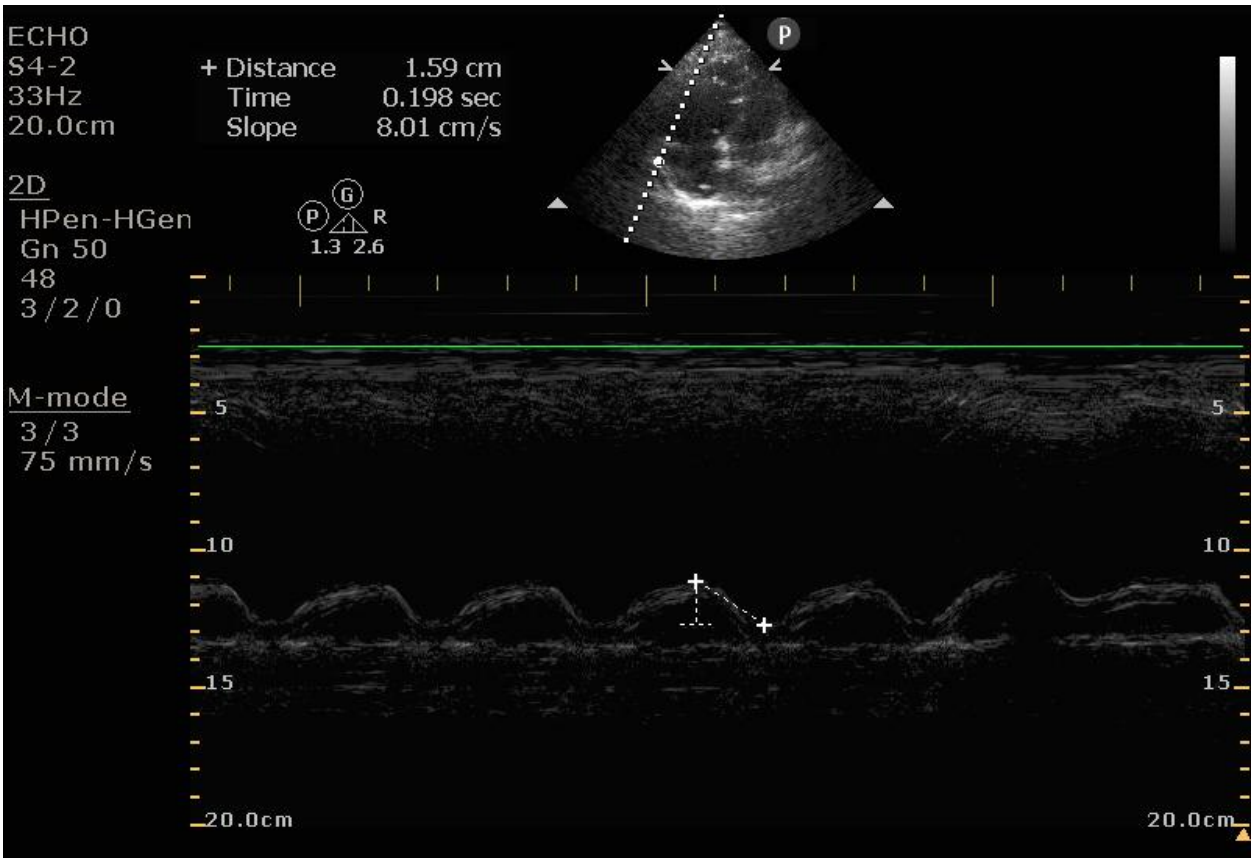
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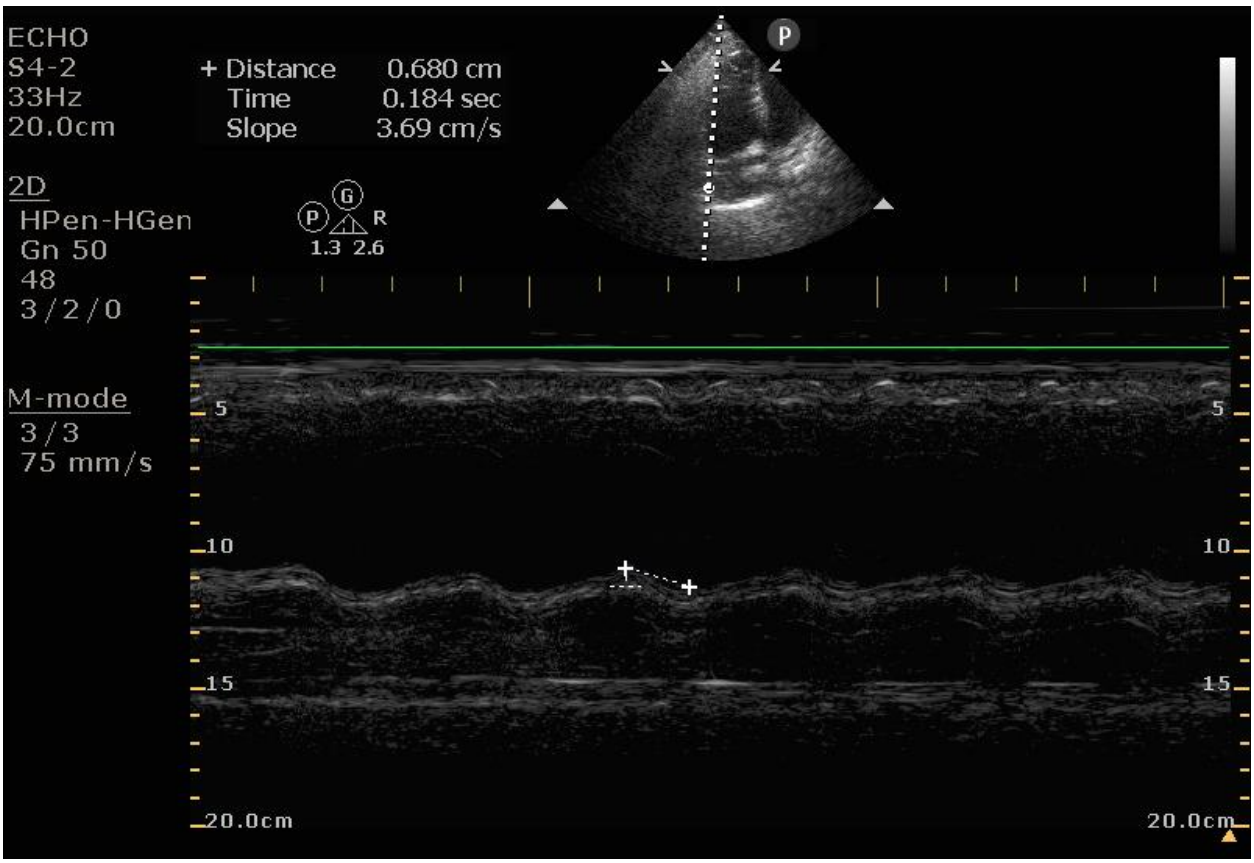
33Hz
20.0cm
+ Distance 1.59 cm
Time 0.198 sec
Slope 8.01 cm/s
2D
HPen-HGen
Gn 50
48
3/2/0
M-mode
3/3
75 mm/s
1.3 2.6
5
10
15
20.0cm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2D
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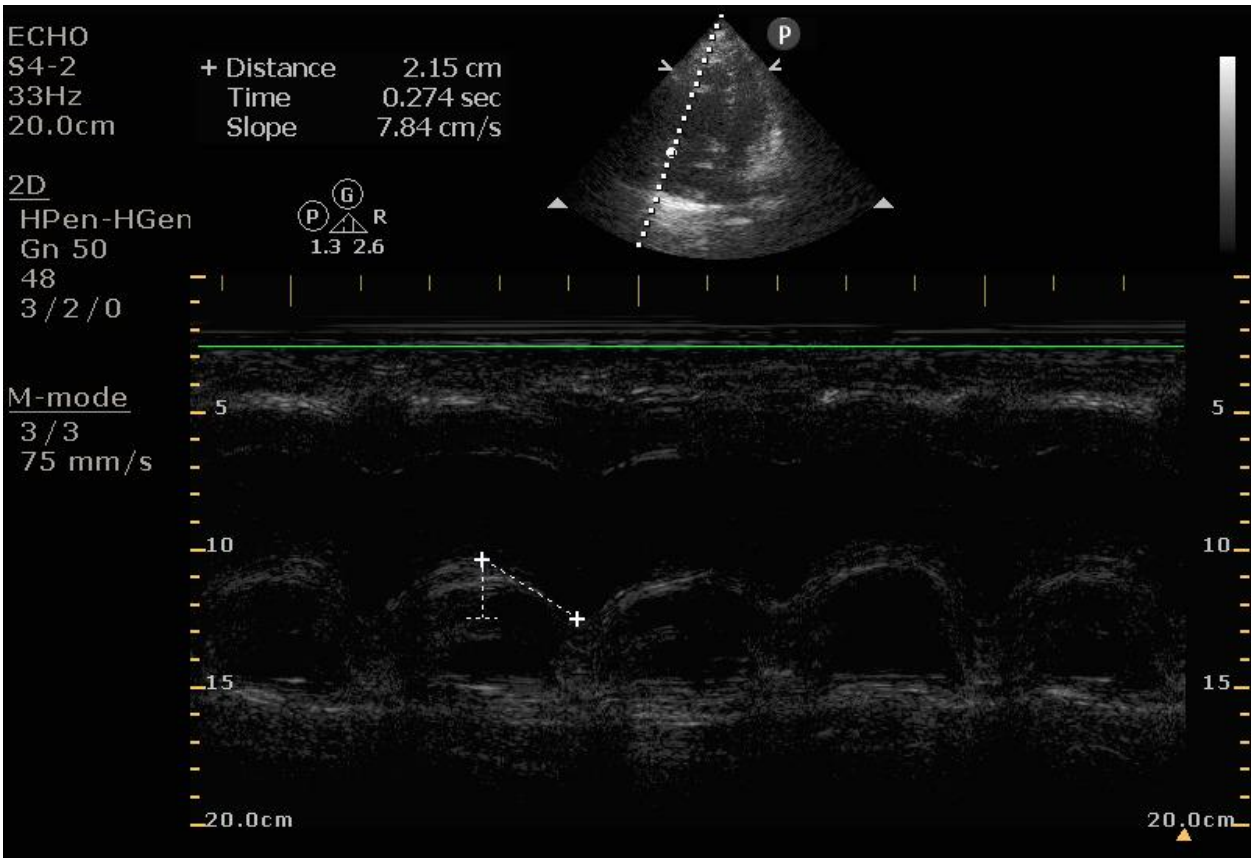
5
10
15
20.0cm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20.0cm
+ Distance 2.15 cm
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Slope 7.84 cm/s
2D
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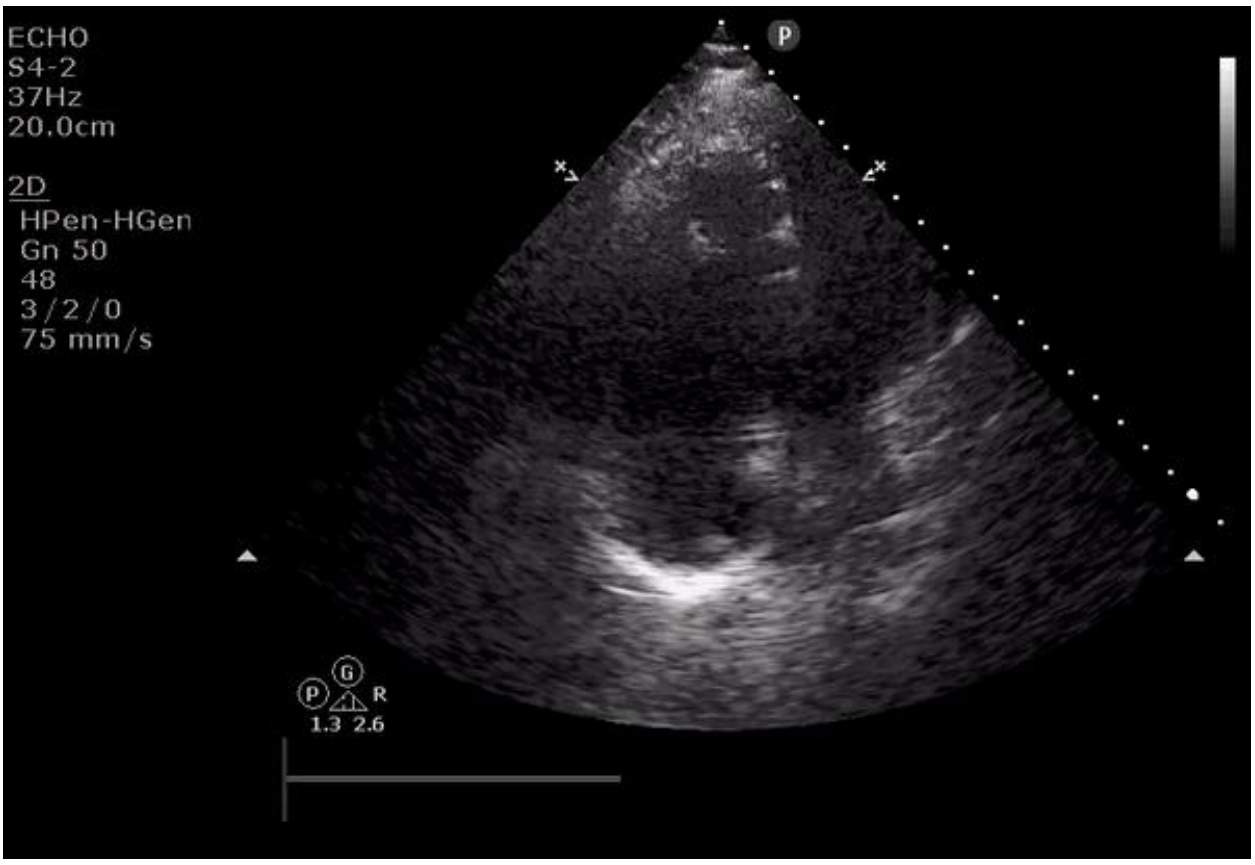
48
3/2/0
M-mode
3/3
75 mm/s
1.3 2.6
5
10
15
20.0cm


ECHO
S4-2
37Hz
20.0cm
2D
HPen-HGen
Gn 50
48
3/2/0
75 mm/s
1.3 2.6

Critical Care-37 Tension Hydrothorax and Cardiopulmonary Arrest Due to Peripherally-Inserted Central Catheter Migration into Pleura

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Introduction: Spontaneous migration is a known complication of peripherally-inserted central catheter (PICC) insertion1, 2. Consequent PICC extravasation secondary to such migration is rarely reported3, 4, 5. We present a case of hemodynamically-significant hydrothorax secondary to PICC migration and consequent extravasation into the pleural space occurring over a matter of hours.

Case Report: A 61-year-old woman with history of complex abdominal surgeries requiring total parenteral nutrition (TPN) via PICC was admitted to the intensive care unit (ICU) for septic shock in the setting of a new abdominal fluid collection. A chest x-ray performed one week prior showed her PICC terminating at the cavoatrial junction. Over the first 24 hours after ICU admission, she improved with vasopressors, fluid resuscitation, and intraabdominal fluid drainage. On ICU day 2, an afternoon chest x-ray showed that the tip of her PICC now projected superiorly, overlying the right brachiocephalic vein. Approximately ten hours later, she became acutely tachycardic and tachypneic. A repeat chest x-ray showed complete opacification of the right hemithorax with associated leftward mediastinal displacement, with persistent superior projection of her PICC. Point of care ultrasound showed a large, simple right pleural effusion. The patient underwent emergent endotracheal intubation given her rapid pulmonary deterioration. After intubation, she became pulseless requiring multiple rounds of cardiopulmonary resuscitation. Placement of a pleural drain with immediate evacuation of three liters of serous fluid during resuscitation was followed by immediate return of spontaneous circulation. Four separate analyses of the evacuated pleural fluid showed >1,100 mg/dl of glucose and a protein level less than assay.

Discussion: Extravasation of PICC contents leading to pleural effusion is a rarely reported complication. In our patient, rapid development of unilateral effusion was the etiology for cardiopulmonary arrest. Diagnostic studies of pleural fluid were consistent with TPN, suggesting the PICC contents had extravasated into the pleural space. Several prior case reports of extravasation of PICC contents report that measurement of pleural fluid glucose can be a useful diagnostic tool for this condition 4, 5. In our case, drainage of the pleural effusion via chest tube and removal of the PICC led to clinical improvement in hemodynamics and oxygenation.

Reference(s):

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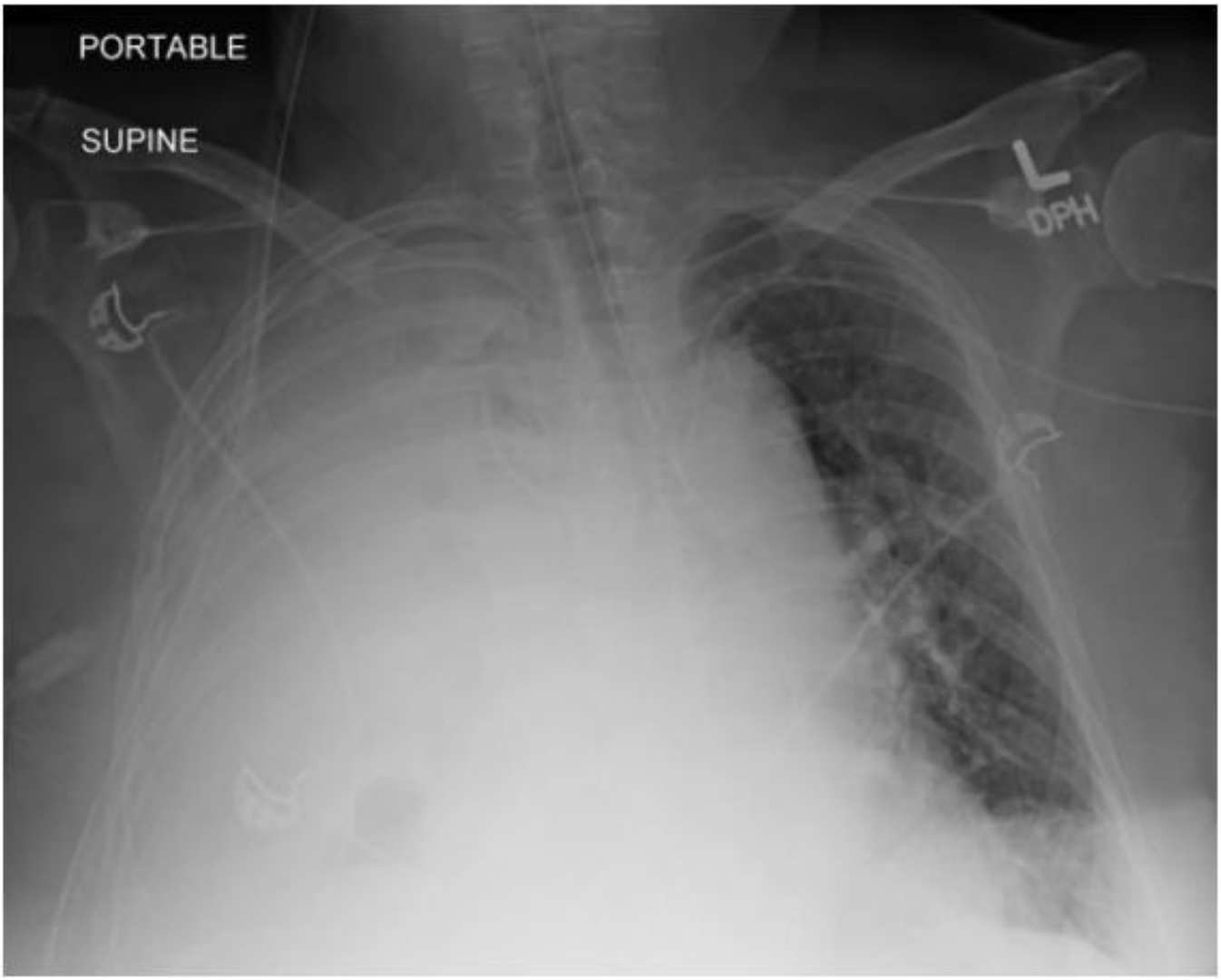

Image 1: Anteroposterior chest xray demonstrating complete opacification of the right hemithorax with leftward mediastinal shift, and peripherally inserted central catheter with tip overlying the right brachiocephalic vein.

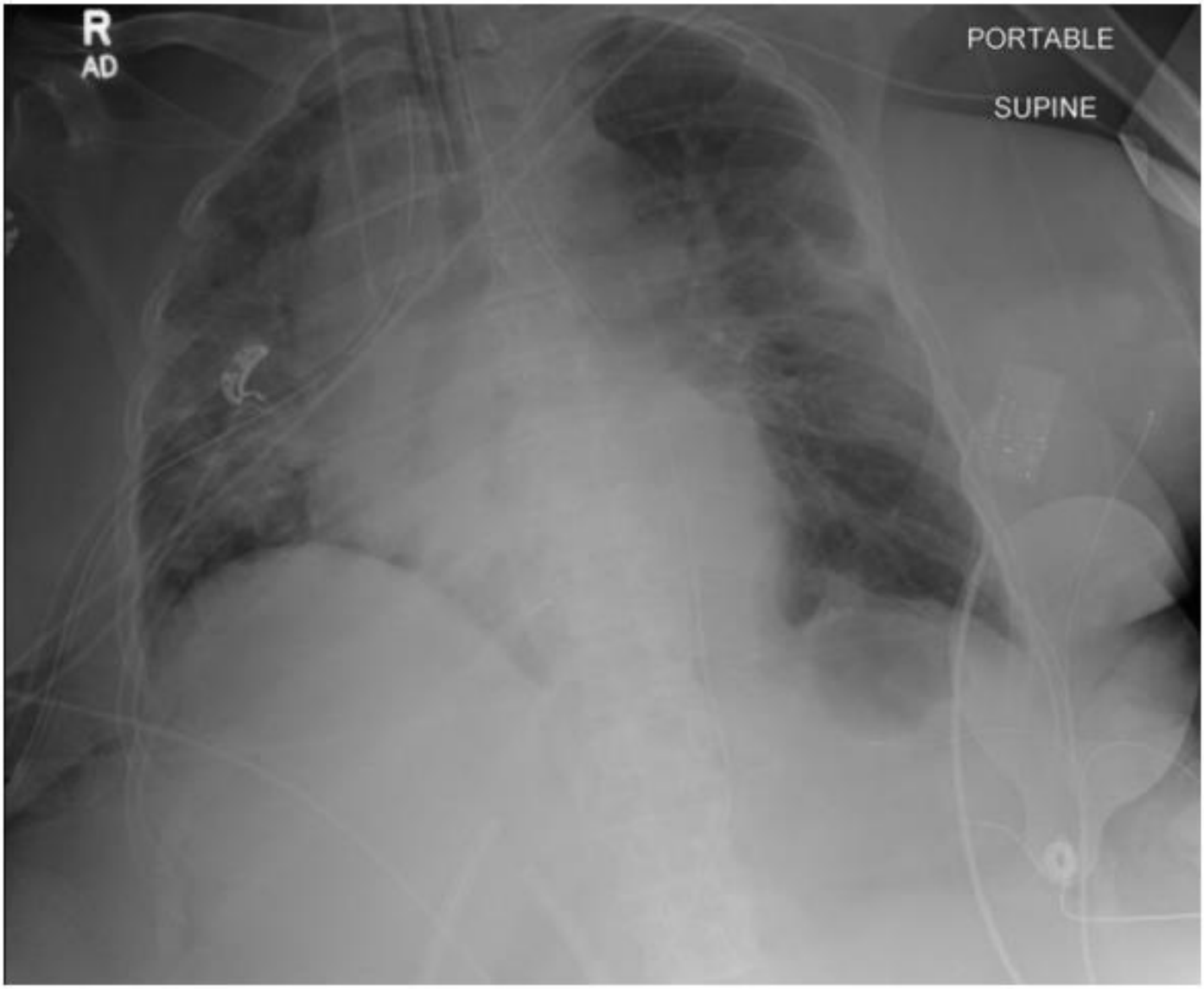

Image 2: Anteroposterior chest xray performed 3 hours after the xray in Image 1. Interval changes include placement of apically terminating right chest tube, placement of right internal jugular central venous catheter, retraction of peripherally inserted central catheter (PICC) now projecting over the confluence of the brachiocephalic veins, and improvement in right pleural effusion. Fluids were no longer running through the PICC at the time of this image.

Critical Care-38 Development of Angioedema Requiring Intubation Following tPA Administration for Acute Ischemic Stroke

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Introduction: Angioedema (AE) is a rare, condition that results from localized swelling of the subcutaneous and submucosal tissues of the face, oral cavity, and neck, and is a well-documented complication of tissue plasminogen activator (tPA), angiotensin converting enzyme inhibitor (ACEI) therapy, and contrast media. Patients who present with an acute ischemic stroke (AIS) are often taking an ACEI (most commonly lisinopril), and are subsequently exposed to tPA and/or contrast media. The mechanism underlying tPA and ACEI-induced AE is due to the production of bradykinin, while that of contrast media exposure is typically due to an allergic reaction associated with mast cell degranulation. While angioedema can occur in both scenarios, the differing pathogenesis of the two forms AE require very different treatment to expedite resolution, but both forms will resolve with time. In both types of AE, maintenance of the airway is paramount as airway compromise can occur.

Case Report: A 46-year old female with a past medical history significant for breast cancer and hypertension treated with lisinopril presented with left-sided hemiparesis and a NIH Stroke Scale score of 10. She was treated with tPA, and shortly thereafter developed angioedema. Diphenhydramine, famotidine, and dexamethasone were given, but the angioedema continued to worsen with associated increased work of breathing and concern for airway collapse. The patient was intubated with a glidescope. Dexamethasone was continued following intubation, and the patient was extubated without event approximately 48 hours later. She was discharged to an acute rehabilitation facility on hospital day five with the diagnosis of tPA aborted stroke and conversion disorder as no acute intracranial abnormalities were seen on neurologic imaging.

Discussion: In bradykinin-mediated angioedema (BMAE), the oropharyngeal swelling can develop rapidly and typically resolves in approximately 48-72 hours after tPA administration. Those patients concurrently being treated with an ACEI are at increased risk of developing BMAE following tPA therapy with an incidence of approximately 16%, significantly higher than the risk associated with the administration of tPA (0.1-0.7%) or lisinopril (1.3-5.1%) alone. tPA converts plasminogen to plasmin which contributes in the activation of the kallikrein-kinin pathway and the generation of bradykinin. Angiotensin converting enzyme (ACE) contributes to the break down bradykinin, but is inhibited by lisinopril. Thus, this combination increases bradykinin levels by both increasing production and preventing breakdown. In cases of life-threatening BMAE, two medical therapies may be efficacious. Icatabant, a bradykinin B2-receptor antagonist and complement-1 inhibitor concentrate can be administered, but these medications are typically given to patients with hereditary AE and have not been extensively studied in BMAE due to tPA and/or ACEI. Further, these medications are expensive and may not be readily available in many hospitals. FFP contains angiotensin II that degrades bradykinin, and may also be effective. BMAE is typically unresponsive to conventional treatments such as epinephrine, antihistamines, and glucocorticoids, which are more appropriate for treatment of mast cell degranulation derived AE, yet these interventions are often the treatments utilized by physicians. As such, the treatment for BMAE is often supportive. If BMAE results during the infusion of tPA, the medication should be immediately stopped. The patient should be serially evaluated approximately every 15 minutes for worsening facial, oral and airway edema as respiratory distress and life-threatening hypoxemia can result. If this occurs, securing the airway is paramount. In situations of BMAE after tPA, we recommend strong consideration to early airway intervention to help ensure first pass success. Worsening of airway edema due to multiple failed intubation attempts in a patient with worsening hypoxemia and an increased bleeding risk could be catastrophic. A consult for an emergent surgical airway should performed and the surgical team should be on standby at the time intubation is performed.

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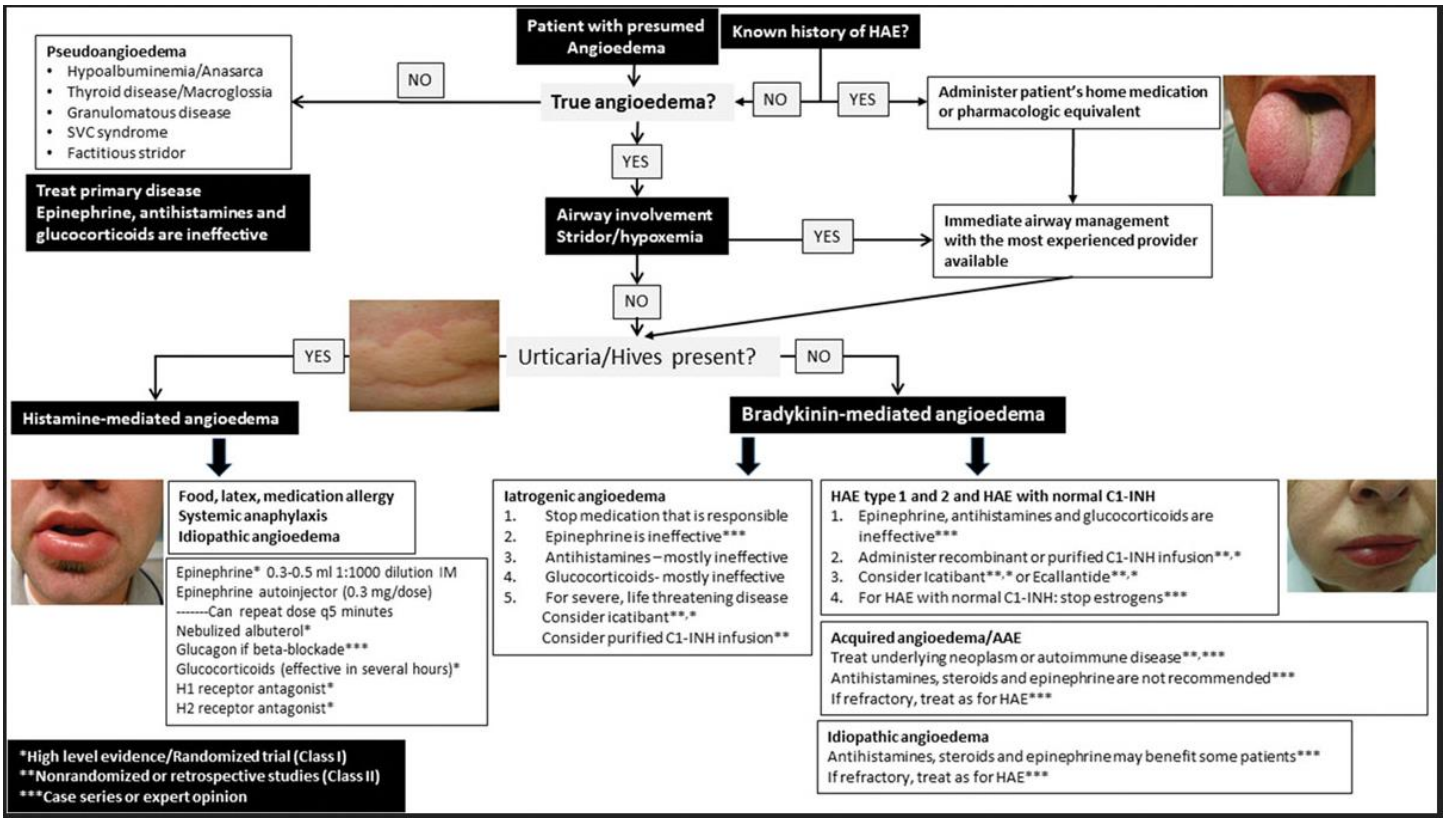
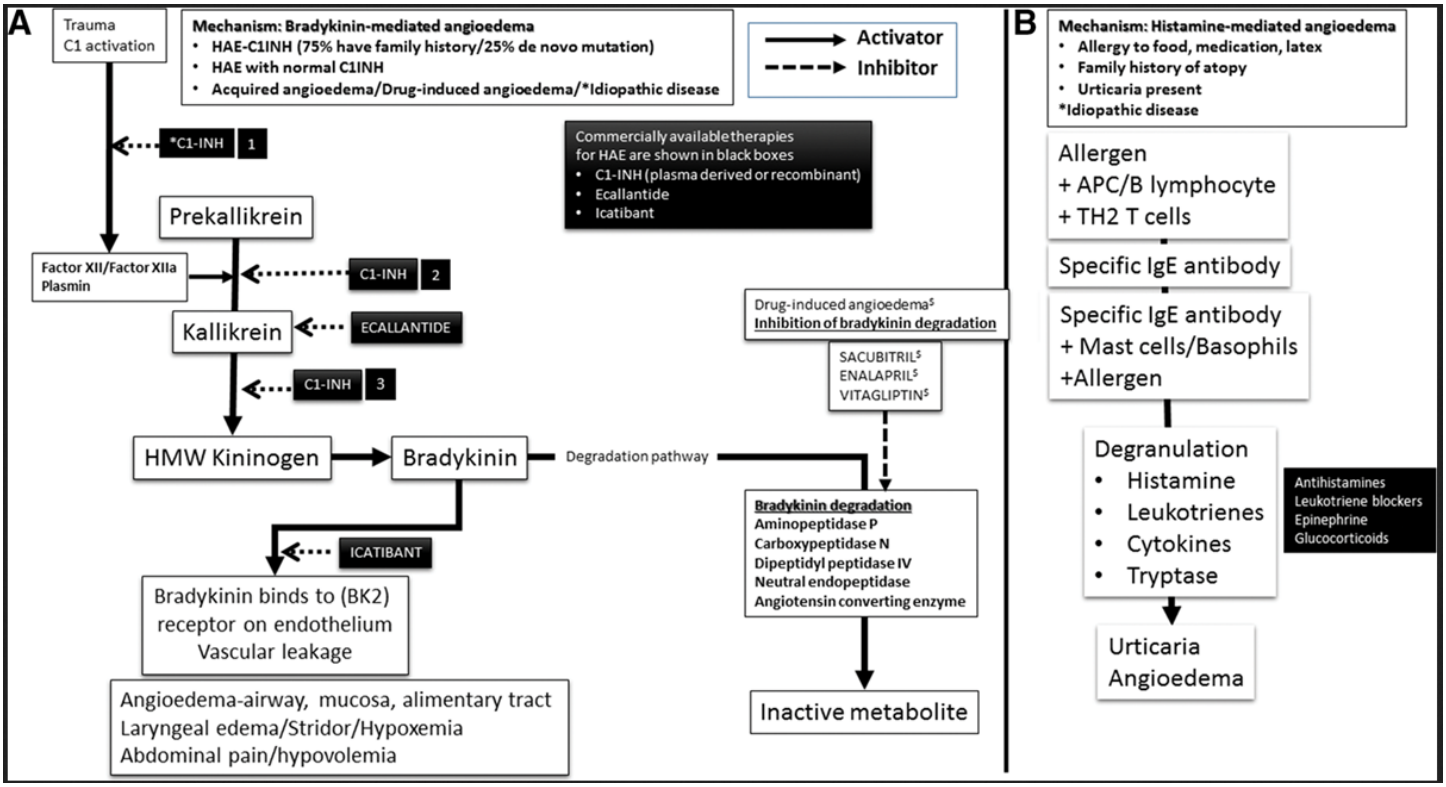

Patient with presumed Angioedema
Known history of HAE?
Pseudoangioedema
• Hypoalbuminemia/Anasarca
• Thyroid disease/Macroglossia
• Granulomatous disease
• SVC syndrome
• Factitious stridor
NO
True angioedema?
NO
YES
Administer patient's home medication or pharmacologic equivalent
YES
Treat primary disease
Epinephrine, antihistamines and glucocorticoids are ineffective
Airway involvement Stridor/hypoxemia
YES
Immediate airway management with the most experienced provider available
NO
YES
Urticaria/Hives present?
NO
Histamine-mediated angioedema
Bradykinin-mediated angioedema
Food, latex, medication allergy
Systemic anaphylaxis
Idiopathic angioedema
Epinephrine* 0.3-0.5 ml 1:1000 dilution IM
Epinephrine autoinjector (0.3 mg/dose)
-------Can repeat dose q5 minutes
Nebulized albuterol*
Glucagon if beta-blockade***
Glucocorticoids (effective in several hours)*
H1 receptor antagonist*
H2 receptor antagonist*
Iatrogenic angioedema
1. Stop medication that is responsible
2. Epinephrine is ineffective***
3. Antihistamines – mostly ineffective
4. Glucocorticoids- mostly ineffective
5. For severe, life threatening disease
Consider icatibant**,*
Consider purified C1-INH infusion**
HAE type 1 and 2 and HAE with normal C1-INH
1. Epinephrine, antihistamines and glucocorticoids are ineffective***
2. Administer recombinant or purified C1-INH infusion**,*
3. Consider Icatibant**,* or Ecallantide**,*
4. For HAE with normal C1-INH: stop estrogens***
Acquired angioedema/AAE
Treat underlying neoplasm or autoimmune disease**,***
Antihistamines, steroids and epinephrine are not recommended***
If refractory, treat as for HAE***
Idiopathic angioedema
Antihistamines, steroids and epinephrine may benefit some patients***
If refractory, treat as for HAE***
*High level evidence/Randomized trial (Class I)
**Nonrandomized or retrospective studies (Class II)
***Case series or expert opinion


A
Trauma
C1 activation
Mechanism: Bradykinin-mediated angioedema
• HAE-C1INH (75% have family history/25% de novo mutation)
• HAE with normal C1INH
• Acquired angioedema/Drug-induced angioedema/*Idiopathic disease
Activator
Inhibitor
*C1-INH 1
Commercially available therapies for HAE are shown in black boxes
• C1-INH (plasma derived or recombinant)
• Ecallantide
• Icatibant
Prekallikrein
Factor XII/Factor XIIa
Plasmin
C1-INH 2
Kallikrein
ECALLANTIDE
C1-INH 3
HMW Kininogen
Bradykinin
Degradation pathway
ICATIBANT
Bradykinin binds to (BK2) receptor on endothelium
Vascular leakage
Angioedema-airway, mucosa, alimentary tract
Laryngeal edema/Stridor/Hypoxemia
Abdominal pain/hypovolemia
Drug-induced angioedema§
Inhibition of bradykinin degradation
SACUBITRIL§
ENALAPRIL§
VITAGLIPTIN§
Bradykinin degradation
Aminopeptidase P
Carboxypeptidase N
Dipeptidyl peptidase IV
Neutral endopeptidase
Angiotensin converting enzyme
Inactive metabolite
B
Mechanism: Histamine-mediated angioedema
• Allergy to food, medication, latex
• Family history of atopy
• Urticaria present
*Idiopathic disease
Allergen
+ APC/B lymphocyte
+ TH2 T cells
Specific IgE antibody
Specific IgE antibody
+ Mast cells/Basophils
+Allergen
Degranulation
• Histamine
• Leukotrienes
• Cytokines
• Tryptase
Antihistamines
Leukotriene blockers
Epinephrine
Glucocorticoids
Urticaria
Angioedema

Critical Care-39 Chylous Pericardial Tamponade - A Life Threatening Complication After Esophagectomy

Laua Phelan[1], Sui An Lie[1], Caroline Gross[1], Jeff Swanson[2], George Frendl[3]

[1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Womens Hospital, Boston, MA, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Introduction: Chylopericardium (or chylous pericardial effusion) occurs when chylous fluid accumulates in the pericardial space. It is a rare condition that is most commonly idiopathic in etiology. Secondary causes include congenital lymphatic malformations (lymphangiomas), mediastinal neoplasms, iatrogenic after cardiac or thoracic surgery, blunt chest trauma, thrombosis of subclavian vein and superior vena cava, Gorham syndrome and tuberculosis[1]. The pathogenesis of chylopericardium can be explained by possible congenital communication between the lymphatic trunk and pericardial space, elevated pressure in the thoracic duct causing chylous reflux, operative injury or disruption to the tributaries of lymphatic ducts in the pericardium and mediastinal pleura, or traumatic injury to the thoracic duct [2-5]. In severe cases, chylopericardium may progress to pericardial tamponade that can be rapidly fatal if not identified and treated promptly [5]. Chylous pericardial tamponade after esophagectomy is distinctly rare, with only a few cases described in the literature [6-7]. We report a case of massive chylous pericardial tamponade leading to cardiovascular collapse in a 54-year-old man on day 6 after minimally invasive esophagectomy.

Case Report: A 54 year old male with a remote history of gun shot wound to the chest and recent diagnosis of squamous cell carcinoma (SCC) of the esophagus status post chemotherapy and radiation with local recurrence and evidence of PET avid left cervical lymph nodes presented for scheduled esophagectomy and left radical neck dissection. Surgical dissection was difficult due to scarring of tissues in the chest in the setting of prior radiation and projectile injury to the chest. Within the first 24 hours after surgery, the patient was noted to be tachycardic and hypotensive with evidence of hemoperitoneum on abdominal ultrasound. He was taken to the operative room for emergent exploratory laparotomy where he was found to have bleeding from gastric vessels near the conduit. The bleeding was surgically controlled and the patient was admitted to the ICU. On post operative days (POD) 1 and 2 his chest tube output was noted to be 460 and 550 ml respectively. It was clear in color and the volume of chest tube output decreased to 80-160 ml per day in the following days. He was successfully extubated on POD 3. PEA arrest occurred on POD 6. Point of care ultrasound during arrest was concerning for cardiac tamponade. Return of spontaneous circulation was obtained and transthoracic echocardiography demonstrated tamponade physiology. The patient underwent emergent pericardial drain placement and subsequent pericardial window. Pericardial fluid studies demonstrated exudative effusion with a high lymphocyte count and normal triglycerides. These findings were highly concerning for chyle leak although the triglycerides were normal as the patient was NPO. He subsequently underwent IR guided thoracic duct embolization and lymphangiogram at that time demonstrate leak high in the chest at the level of the sternoclavicular joint. He ultimately recovered without further evidence of chyle leak and was discharged to rehab.

Discussion: Pericardial tamponade is a rare complication after esophagectomy and can result from either extrinsic cardiomediastinal compression or accumulation of intra-pericardial fluid. Although chylous pericardial tamponade is a rare complication of esophagectomy, cases have been described in the literature [6]. The patient in this case was noted to have a difficult surgical dissection due to changes from radiation and prior injury, which may have led to inadvertent injury of the thoracic duct or its tributaries. This case demonstrates that chyle leak after esophagectomy may lead to cardiac tamponade and cardiovascular collapse. Drained pericardial fluid is often clear with a normal triglyceride count as these patients are often NPO and not consuming the dietary triglycerides that give chyle its characteristic milky appearance. Management of these patients should include appropriate ACLS care, drainage of the pericardial effusion, and intervention to stop the ongoing chyle leak.

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Critical Care-40 An Unusual Presentation and Management of Hypercortisolism

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Introduction: This case report aims to communicate the potential utility of Etomidate in the medical management of hypercortisolism.

Case Report: Case Report A 51-year old male with a history of tobacco use presented to the emergency department for evaluation of diarrhea with occasional hematochezia that had been ongoing for a month. During the evaluation he was diagnosed with hypokalemia (Potassium- 2.4 meq/L) and hypertensive urgency (systolic blood pressure > 180mmHg). The differential diagnosis included hyperaldesteronism and infectious diarrhea. Work-up for infectious diarrhea was negative. Tests for hyperaldosteronism were still being processed, and concurrent computed tomography (CT) imaging of the abdomen was positive for a pancreatic body mass, as well as multiple liver masses. The patient was taken to the procedure room on hospital day (HOD) 4 where he had a hepatic biopsy. While biopsy results were being processed, other laboratory tests returned on HOD 9 with abnormal ACTH, aldosterone, and renin levels; this prompted concern for Cushing's disease. Metyrapone and ketoconazole were promptly initiated. The biopsy results were positive for neuroendocrine tumor. Despite management with ketoconazole and metyrapone, cortisol levels increased and he developed symptoms of hypercortisolism including retinal damage. Thus he was started on etomidate infusion for management of excessive adrenal function pending surgical adrenalectomy. Discussion Hypercortisolism or Cushing's syndrome is relatively uncommon. Given its paucity of presentation, it is important for the intensivist to have a great degree of suspicion when a patient presents with electrolyte abnormalities that are too severe to be explained by mundane causes. The next step after suspicion is to manage the electrolyte derangements and order laboratory tests including ACTH level, and dexamethasone suppression test to ascertain the diagnosis. Imaging should also be done, as it can frequently be a paraneoplastic syndrome. Finally, biopsy should be obtained to guide oncologic treatment. Ketoconazole and metyrapone are well-known pharmaceutical therapies for adrenal hyperactivity. Interestingly, our patient's condition was poorly responsive to these first-line treatments prompting the use of etomidate. Etomidate is an anesthetic induction agent well known for its cardiac stability. However its use has been limited by its side effect profile including significant post-operative nausea and vomiting, platelet inhibition, and adrenal suppression via inhibition of 11-β hydroxylase. The concept of utilization of etomidate as an adjunct for management of hypercortisolism is a testament to the severity of adrenal suppression that can occur with its use.

Discussion: Etomidate can be utilized to manage hypercortisolism when a patient's condition is poorly responsive to first line medical treatments.

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Critical Care-41 Acute Narcolepsy-Catapexy due to Desvenlafaxine Withdrawal after Cardiac Surgery

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Introduction: Desvenlafaxine is a selective serotonin- and norepinephrine-reuptake inhibitor (SNRI) approved for the treatment of major depressive disorder (MDD). We present a postoperative patient who displayed symptoms of narcolepsy-catapexy after abrupt discontinuation of this medication. Symptoms resolved following resumption of therapy, suggestive of a withdrawal effect.

Case Report: A 69-year-old woman with a history of HTN, HLD, carotid artery stenosis, multiple strokes and MDD was admitted to the ICU following a four-vessel CABG. The OR course was uncomplicated and the early postoperative period was notable for hypertension refractory to multiple therapies. Desvenlafaxine, the patient's antidepressant, was not resumed due to its potential to further increase blood pressure. On POD4, the patient developed a GI bleed leading to ICU readmission and a protracted hospital stay. Although the patient's hypertension was adequately controlled at this time, desvenlafaxine was not available from the hospital pharmacy and was not resumed.

On POD12, the patient appeared to have two near-syncopal events while on the commode. Both were associated with several minutes of observed lethargy, and the second event with documented hypotension (90s/50s mmHg). These events were attributed to symptomatic anemia (Hgb 7g/dL) for which the patient was transfused 1 unit of PRBCs. On POD14, the patient become acutely stuporous and was noted to have new anisocoria with reactive pupils in the setting of normotension. Emergent head CT, serum electrolytes and infectious workup were unremarkable. The patient's mental status returned to baseline within several hours. Over the following three days, the patient experienced multiple similar episodes of somnolence and decreased responsiveness in the setting of stable hemodynamics and a non-focal neurologic exam. The patient had no prior history of similar lethargic events, which were sudden-onset and self-limited. Between events, the patient was alert and oriented, with intact memory and abstract reasoning capacities. Video EEG was negative for seizure but captured bitemporal slowing indicative of nonspecific or multifocal cerebral dysfunction during a single lethargic episode. Empiric vasopressor therapy to increase cerebral perfusion pressure did not prevent further episodes. Desvenlafaxine withdrawal was suspected, and the medication was resumed on POD18. The patient experienced no further lethargic events.

Discussion: Desvenlafaxine is the active metabolite of a venlafaxine, another common SNRI.1 Due to increased levels of norepinephrine, desvenlafaxine has been associated with increased risk of new-onset hypertension.2 Due to a relatively short half-life of 11 hours, desvenlafaxine may be associated with increased risk of withdrawal symptoms.1, 3 There are limited descriptions of SNRI 'discontinuation syndrome' in the literature. The condition may include by anxiety, dysphoria, disequilibrium, gastrointestinal symptoms, flu-like symptoms, sensory disturbances, and sleep disturbances.3 The most common adverse effects associated with desvenlafaxine withdrawal include headache, nausea and dizziness.1 More severe venlafaxine withdrawal symptoms have been described, including severe headaches and auditory hallucinations.4 Most notably, new-onset narcolepsy-catapexy was described in two patients following cessation of venlafaxine therapy.5 The case presented here suggests that a similar withdrawal phenomenon may occur after abrupt discontinuation of desvenlafaxine, and highlights the importance of prompt resumption of SNRI therapy when not otherwise contraindicated in post-operative patients.

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Critical Care-42 Impediments to Nutrition and Maintenance of Body Weight in a Patient on VA ECMO Awaiting Heart-Lung Transplantation, and Strategies to Overcome Them

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Introduction: Patients awaiting heart and lung transplantation may be malnourished and deconditioned due to their underlying chronic disease and acute exacerbations. Both malnutrition and physiologic limitations in physical activity play a significant role in reducing candidates' functional status, compromising recovery and survival post transplantation.[1-3] We present the case of a patient awaiting heart-lung transplantation, who faced multiple challenges to nutrition and mobility, and the strategies utilized to overcome those obstacles.

Case Report: A 33-year-old woman with a 10-year history of idiopathic pulmonary arterial hypertension requiring intravenous pulmonary vasodilators presented with worsening dyspnea on exertion, dependent edema, and ascites. Her body mass index (BMI) was 17.8 kg/m2, indicative of chronic malnutrition. During her 3-week stay at an outside hospital, her condition deteriorated despite maximal medical therapy, and she required femoral venoarterial extracorporeal membrane oxygenation (VA ECMO). In this setting, total parenteral nutrition (TPN) was initiated, and she was transferred to our hospital for expedited heart-lung transplantation evaluation. Upon arrival at our institution, her weight was 55 kg in the setting of significant volume overload (Fig. 1). Her Johns Hopkins Highest Level of Mobility (JH-HLM) scale score was 2 (bed activity).[4] TPN was discontinued due to evidence of refeeding syndrome, and nutrition was interrupted for a day to allow electrolyte stabilization. She was extubated on hospital day 2, and a functional endoscopic evaluation of swallowing demonstrated hypomobile vocal cords and frank aspiration. A nasoduodenal feeding tube was placed and enteral feeds were initiated with several overnight interruptions for ECMO cannulation site revisions. Following aggressive diuresis, she achieved a weight of 34 kg (BMI of 15 kg/m2), a serum albumin of 2.0 g/dL (Fig. 2), and developed an unstageable sacral decubitus wound. Her JH-HLM scale score remained 2, and proximal muscle strength was anti-gravity in each limb. Listing for en bloc heart-lung transplantation was deferred pending improvement in her nutrition and physical conditioning. Tracheostomy and percutaneous endoscopic gastrostomy were performed to help optimize her nutritional status and facilitate an aggressive mobility strategy. Enteral feeding was continued with strict avoidance of interruptions. Due to her sacral wound, she was not a candidate for the use of a tilting bed, and given small axillary artery caliber, she remained on bifemoral VA ECMO. A multidisciplinary team consisting of the patient, her family, physical and occupational therapy, perfusionists, and members of the ICU care team was assembled to ensure daily mobility. Her BMI remained stable and her physical conditioning gradually improved. She was listed for and successfully underwent en bloc heart-lung transplantation 6 weeks after arrival at our institution. Her post-operative recovery was notable for a 5-day delayed chest closure. She remained on an aggressive enteral feeding and multidisciplinary physical therapy regimen. By post-transplant day 25, her weight re-stabilized at 30 kg (BMI 13.3 kg/m2) with a serum albumin concentration of 4.0 g/dL. By 6 weeks post-transplant, she was able to stand unassisted, walk 25 feet (JH-HLM score of 7), and continues to make progress in her recovery.

Discussion: Optimizing pre-transplant nutritional status and physical strength and mobility may be challenging in patients awaiting transplantation, including those supported on ECMO, but are essential given the increase in mortality associated with lower functional status, BMI, and serum albumin. [1-3] While albumin is known to be a negative acute phase reactant, transplant literature shows up to a 35% increased odds of mortality in the first year after transplantation when pre-transplant albumin is < 3.0 g/dL.[2] However, a pre-planned, appropriately aggressive multidisciplinary effort that includes the expertise of dieticians and physical therapists can combat many of the challenges associated with pre-existing physical weakness, physiologic limitation, and the presence of medical devices (Table 3) and may mitigate the impact of malnutrition and deconditioning.[5,6] Both the barriers to mobility and nutrition and the corrective strategies discussed are applicable to many critically ill patients in the intensive care unit.

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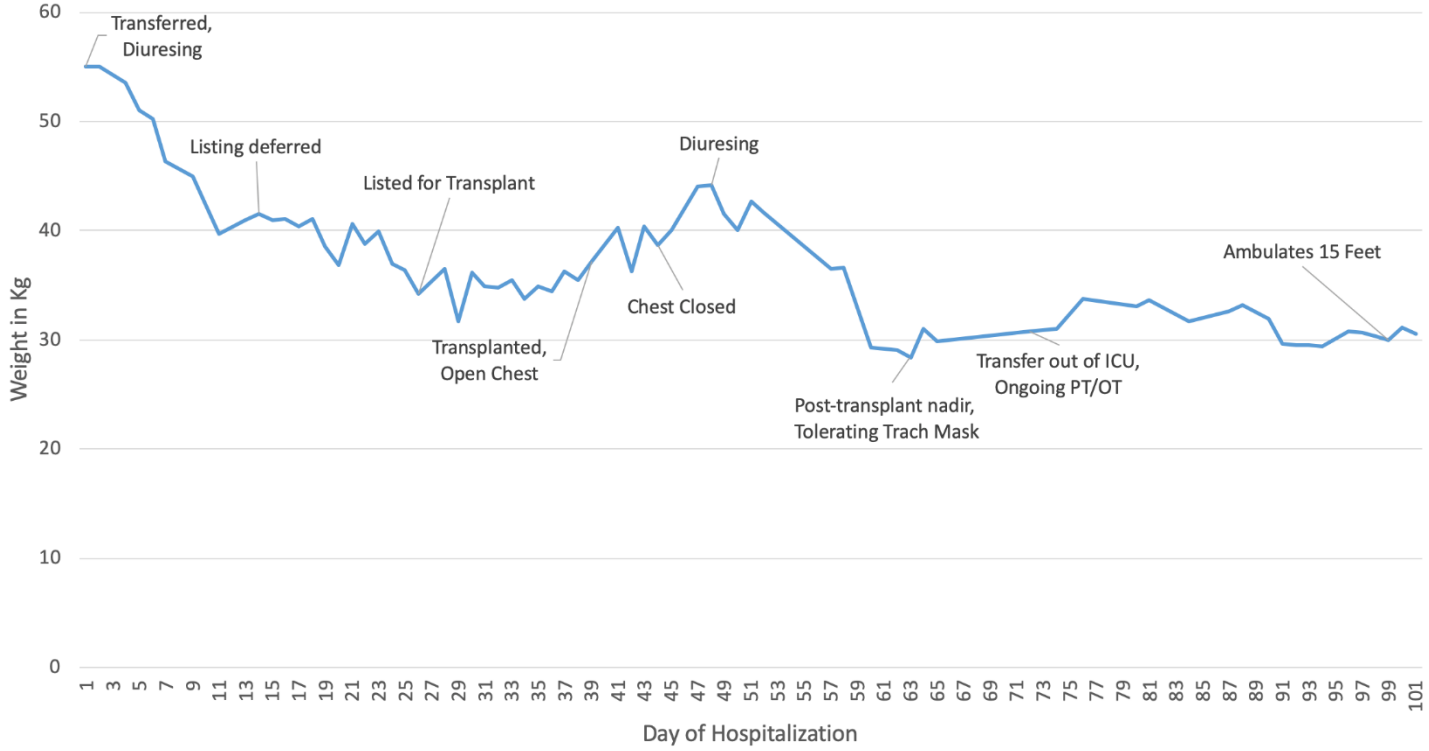
Body Weight over Time



Serum Albumin over Time

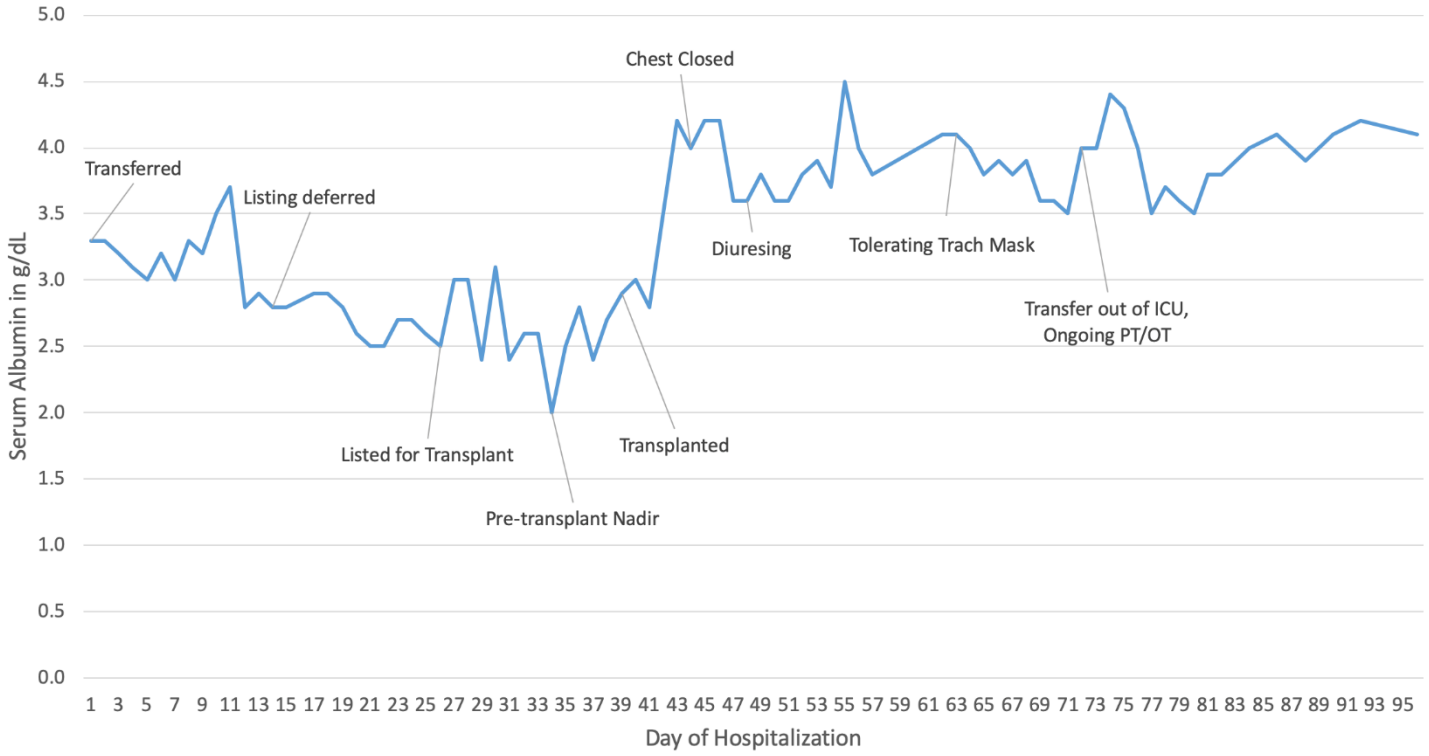


Table 1. Impediments to Nutrition and Maintenance of Body Weight

Category	***Impediments***	***Interventions***
Threatened Enteral Access	Concern for aspiration	Speech therapy consult, FEES
	Pharyngeal muscle weakness	
	Vocal cord injury or paralysis	ENT consult, Vocal cord injections
	Tracheostomy tube *in situ*	Swallowing exercises
	Endotracheal tube *in situ*	Nasal or percutaneous feeding tube placement
	Altered mental status and ICU delirium	
	Difficult post-pyloric feeding tube placement	Endoscopically place tube vs percutaneous approach
		Consider total parenteral nutrition
Disruptions to Feeding	Ileus	Provide at least trickle feeds (e.g. 10 mL/hr) whenever possible
	High-dose splanchnic vasoconstrictors (e.g. epinephrine infusion)	
	Refeed syndrome	Closely monitor and correct electrolytes, restart feeding as soon as safe
	Frequent planned trips to the operating or procedure room	Continue full tube feeds for select procedures in patient with a secured airway, trickle feeds for others
	Loss off access (dislodged feeding tube, migration of post-pyloric feeding tube into stomach) or long-term access needed	Surgical placement of percutaneous gastric or jejunal feeding tube
Reduced Physical Activity	Deconditioning and muscle wasting	Early consult to physical and occupational health service
		Adjustment of ECMO Sweep to reduce dyspnea during activity
	Withdrawn or depressed affect	Early psychiatric consultation
	Delirium	Family in-room
	Femoral ECMO cannulation sites	Avoid or revise away from groin cannulation for ECMO
	Sacral wounds limiting time in a chair	PM&R and Wound ostomy nurse consults
		Appropriate hospital bed and equipment
		Use system to ensure proper patient rotation / rolling
	Physical and Occupational Therapy resources limited	Family and bedside team may assist with prescribed exercises

Critical Care-43 Management of Acute Coronary Syndrome in a patient following open ruptured abdominal aortic aneurysm (AAA) repair

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Introduction: Ruptured abdominal aortic aneurysms (rAAA) effect almost 5000 patients per year with an overall mortality of 80-90% and postoperative mortality of 40-50%.[1] Risk factors for rAAA including hypertension, coronary artery disease, COPD, and smoking further contribute to perioperative morbidity and mortality. [2] Specifically, postoperative cardiac complications occur in up to 42% of patients. [3] We present a medically challenging case involving the management of acute coronary syndrome and ultimate revascularization by CABG in a patient on POD#3 status post open AAA repair.

Case Report: A 69-year-old male with history of tobacco use was emergently transferred from a network hospital after presenting with a ruptured abdominal aortic aneurysm (rAAA). The patient underwent open AAA repair with intraoperative course notable for transient ST depressions and tachycardia with improvement after fluid resuscitation. On POD#1, hypotension continued and bedside echocardiogram demonstrated anterior wall hypokinesis with reduced LVEF=40% as well as a dynamic troponin. He was presumed to have had a myocardial infarction and was started on norepinephrine for cardiogenic shock. Vascular surgery team initially requested avoidance of left heart catheterization for 5 days postoperatively for concern of bleeding if dual antiplatelet therapy were to be required. He was weaned from vasopressor support and extubated on POD#2. On POD#3 the patient experienced chest pain and dizziness followed by an acute cardiac arrest with ventricular fibrillation. ROSC was achieved after two rounds of CPR with 2 defibrillations, epinephrine, and amiodarone boluses. Bedside echocardiogram was significant for new regional wall motion abnormalities (RWMA) with troponin elevation to 8.33. After discussion with cardiology and surgical team, heparin infusion was started and he underwent cardiac catheterization. Patient was found to have multi-vessel disease with severe calcification and tortuous vessels preventing stent placement. Cardiothoracic Surgery was consulted and the patient immediately underwent emergent coronary artery bypass grafting (CABG) x2 with sternal plating. On POD#4 following open rAAA repair and POD#1 following CABGx2, the patient was weaned from vasopressor support and required one unit blood transfusion. He remained hemodynamically stable and was extubated POD#3. He was discharged home, independently, POD#21s/p open repair rAAA and POD#18 s/p CABGx2.

Discussion: Conclusion (Discussion) With the prevalence of CAD greater than 50% in patients with rAAA, cardiac morbidity and mortality is frequently encountered postoperatively. [4,5] This patient could have benefitted from ischemic workup of his RWMA and troponinemia on POD#1 s/p rAAA repair. However, the risk of bleeding seemed too great so soon after open rAAA repair. On POD#3, the acute coronary syndrome and cardiac arrest prioritized the benefits of revascularization despite potential bleeding from the necessary anticoagulation. When PCI was not possible due to patient disease, revascularization was achieved with CABGx2 on cardiopulmonary bypass without significant bleeding at the site of his ruptured AAA. To our knowledge, this is the first case report of a patient undergoing emergent CABG so quickly following open AAA repair for ruptured AAA. Furthermore, the patient recovered to discharge home independently three weeks after presentation.

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Critical Care-44 Cardiac arrest in a 30-year-old female from pulmonary embolism after dilation and evacuation for intrauterine fetal demise

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Introduction: Intrauterine fetal demise may be associated with coagulopathy and bleeding, but also disseminated intravascular coagulation (DIC) (1). Concurrent venous thromboembolism, leading to acute cor pulmonale and cardiac arrest, is challenging to manage. We present a case to illustrate the clinical considerations and options for addressing such a scenario.

Case Report: A previously healthy 30 year-old-female, G6P2032 had intrauterine fetal demise. She was scheduled for an elective, outpatient dilation and evacuation. Moderate sedation was administered by an anesthesiologist with a combination of midazolam, fentanyl, and propofol, with maintenance of spontaneous ventilation. The surgical procedure took 35 minutes. As the team prepared to move the patient from the operative table to a stretcher, it was noted that the patient was cyanotic. The blood pressure reading was <40mmHg, and her pulse was not palpable. Advanced cardiac life support was initiated, including approximately 100 chest compressions and a bolus of epinephrine. Return of spontaneous circulation was then achieved. The airway was intubated, and an arterial and central catheter were placed emergently. Rescue transthoracic echocardiography revealed dilation of the right ventricle, with a larger size compared to that of the left ventricle, interventricular septal flattening, and echodensities in the right atrium (Figures 1-3). An epinephrine infusion was started and the patient was transported to the intensive care unit. Vaginal bleeding was noted to be persistent, despite completion of the D&E, with no residual material in the uterus evident by ultrasound. A balloon was used to tamponade the uterus. Computed tomography with contrast of the chest confirmed the presence of segmental pulmonary emboli in both lungs. A rotational thromboelastometry (ROTEM) assay revealed severe coagulopathy, including evidence of fibrinolysis, extremely low clotting factor activity, and extremely low fibrinogen activity (Figures 4). Bleeding improved with transfusion of 30 units of cryoprecipitate, 1 unit of platelets, and 1 unit of red cells. Repeat ROTEM showed resolution of fibrinolysis and improvement in intrinsic clotting and fibrinogen activity. After taking down the intrauterine balloon and verification that the bleeding was minimal, a heparin infusion was started. Her right ventricular failure and pressure overload was treated with inhaled epoprostenol (50ng/kg/min) and milrinone. Echocardiography revealed improvement in the right ventricular function over the course of the day. Epoprostenol was tapered and then milrinone, and repeat echocardiography was reassuring that there was right ventricular recovery. The patient was extubated on the same day as her cardiac arrest, and transferred out of the intensive care unit on post-operative day 1. She was discharged to home on apixaban on post-operative day 2. Testing for hypercoagulable state (including Factor V Leiden, Lupus anticoagulant, Prothrombin G20210A, and Antiphospholipid antibodies) was negative. At outpatient follow up with a thrombosis specialist, she was deemed to have an ongoing intermediate risk of recurrent venous thromboembolism, and the plan was to continue abixaban, but to eventually lower the dose from 5mg twice daily to 2.5mg twice daily.

Discussion: Fetal death is associated with an increased risk of maternal hemorrhage and DIC (1) and bleeding may be more common when fetal demise duration is >=4 weeks (2). Echo after cardiac arrest may guide resuscitation (3). Considerations for anticoagulating surgical patients with bleeding who also have thromboembolism should be multidisciplinary. Specific interventions to consider to treat acute right ventricular failure include milrinone and inhaled epoprostenol (4). DIC may lead to hemorrhage AND thromboembolism. After correction of coagulopathy, heparin was started. In cases of massive clot burden, consideration should be given to thrombolytics and thrombectomy. The degree of right heart failure was surprising, given that only a few segmental emboli were present. We speculate that the coagulopathy triggered by the D&E included mediators of pulmonary vascular constriction, such as thromboxane, which increased resistance in pulmonary vessels which were free from emboli. Considerations for treating different categories of acute right heart failure are presented in the table.

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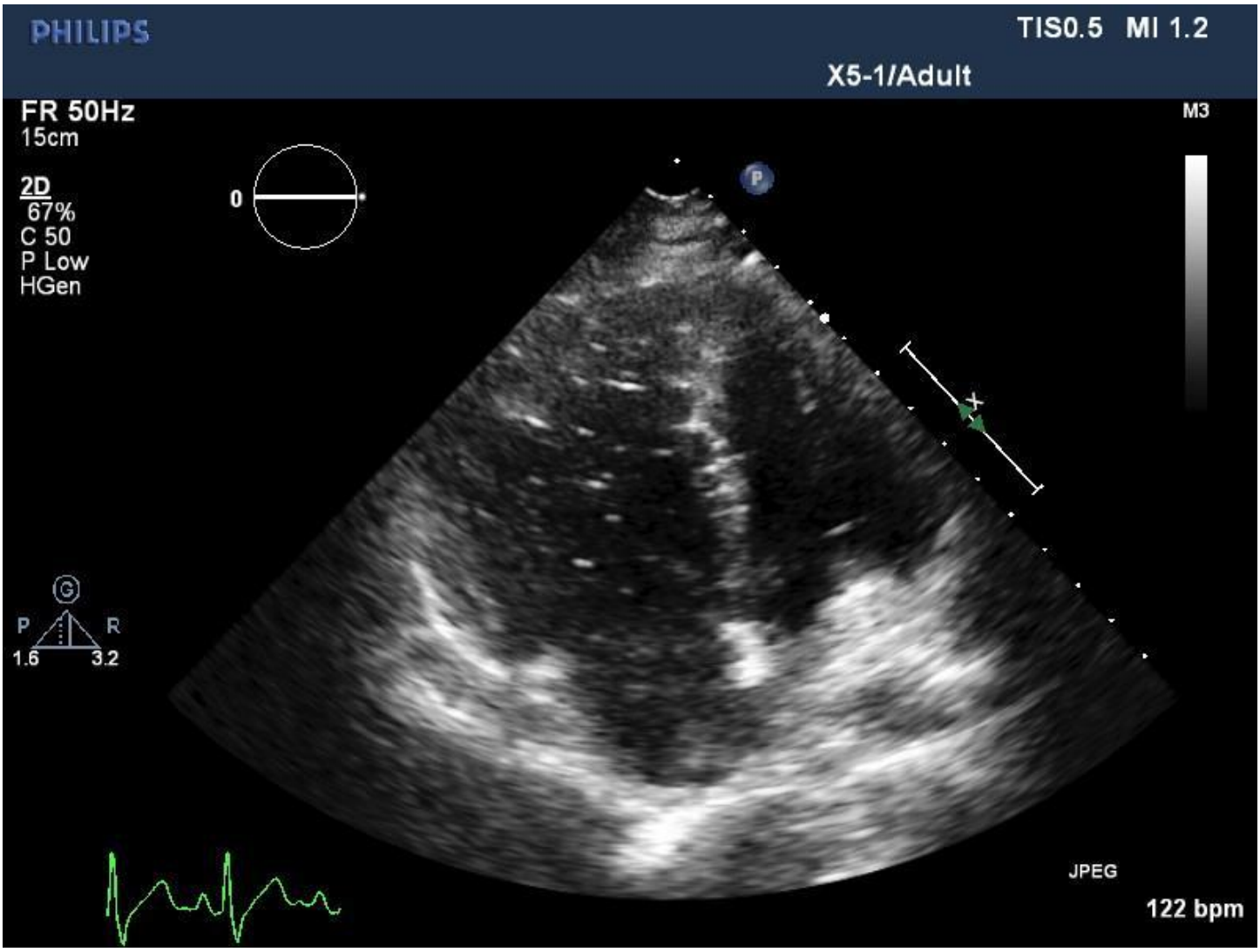
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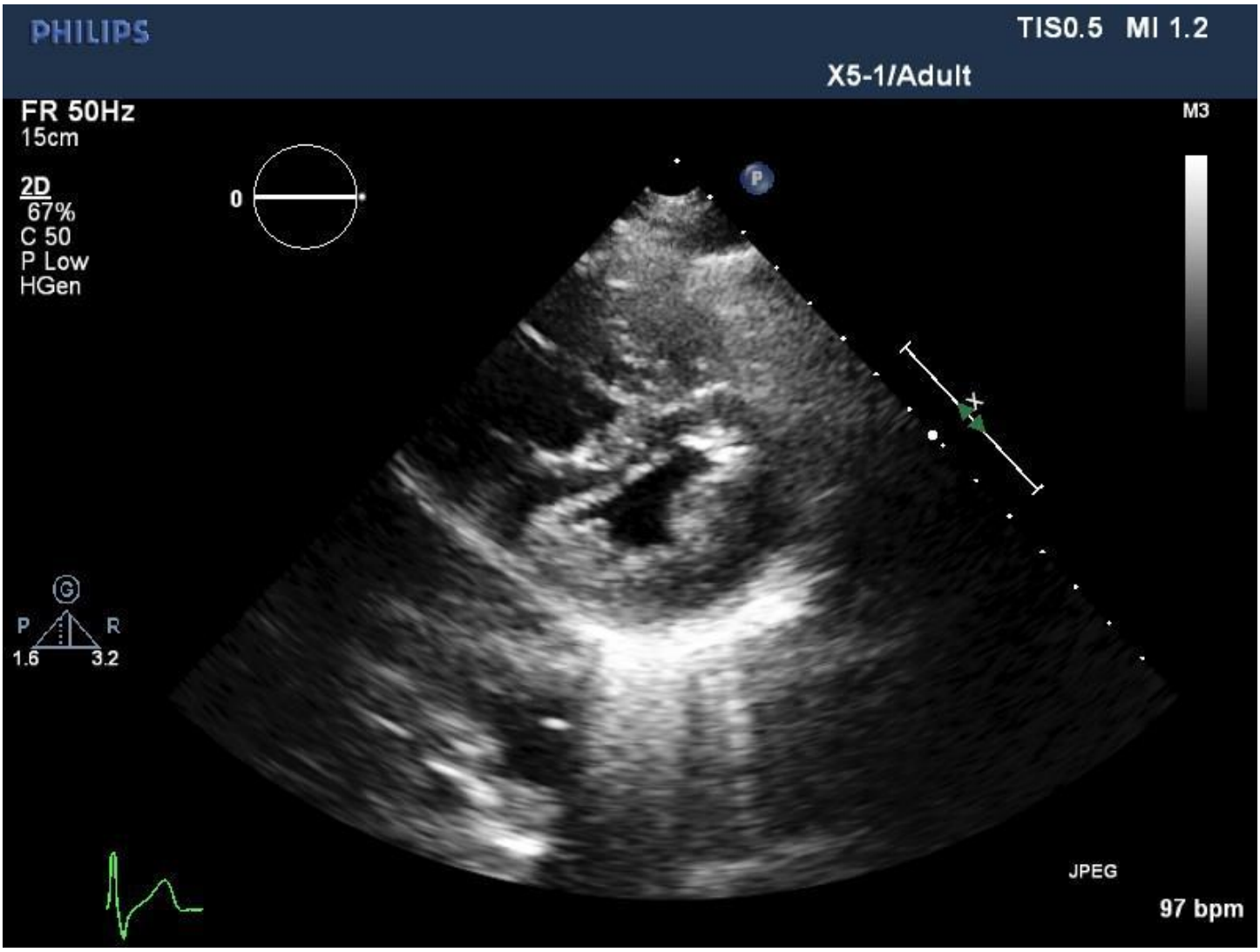
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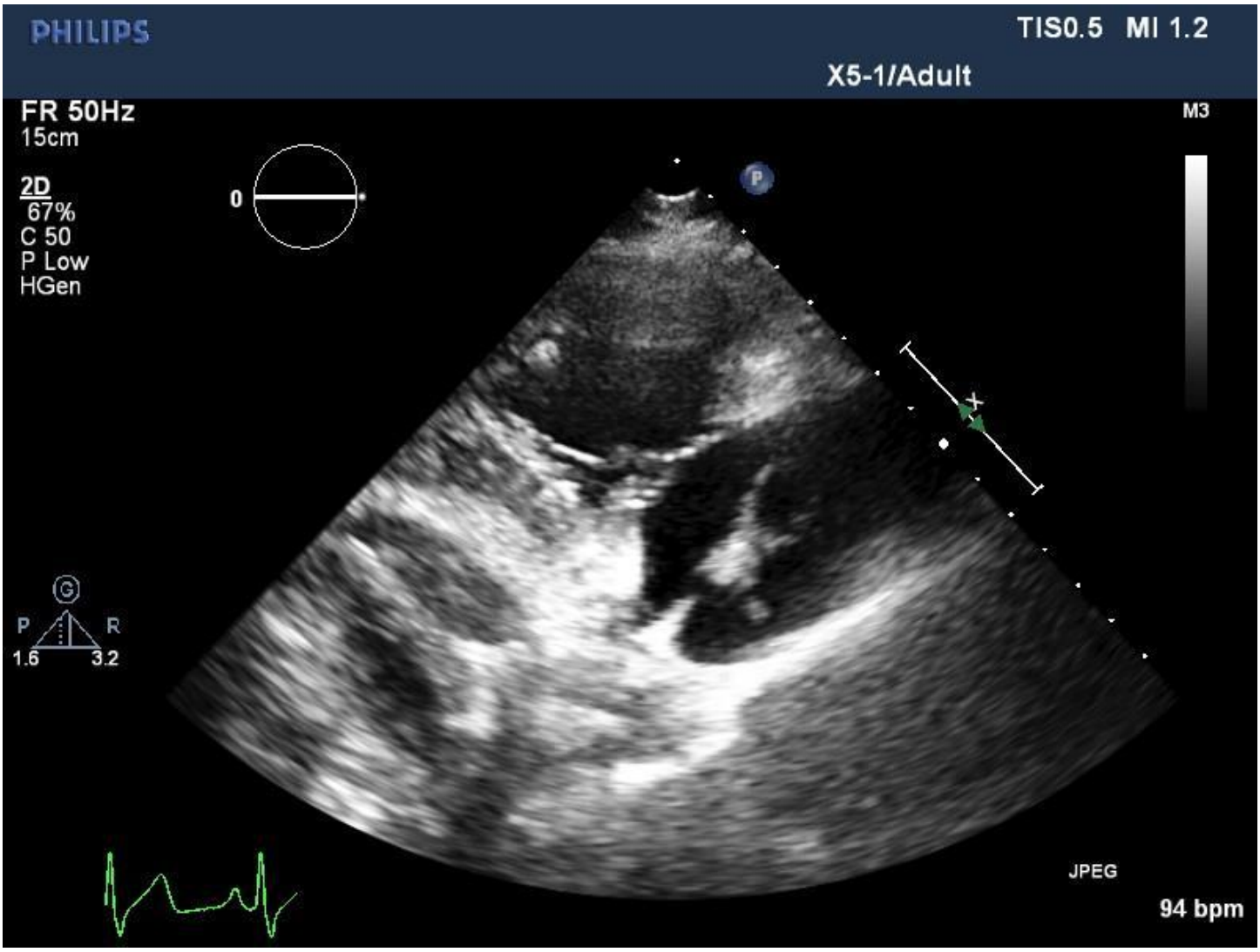
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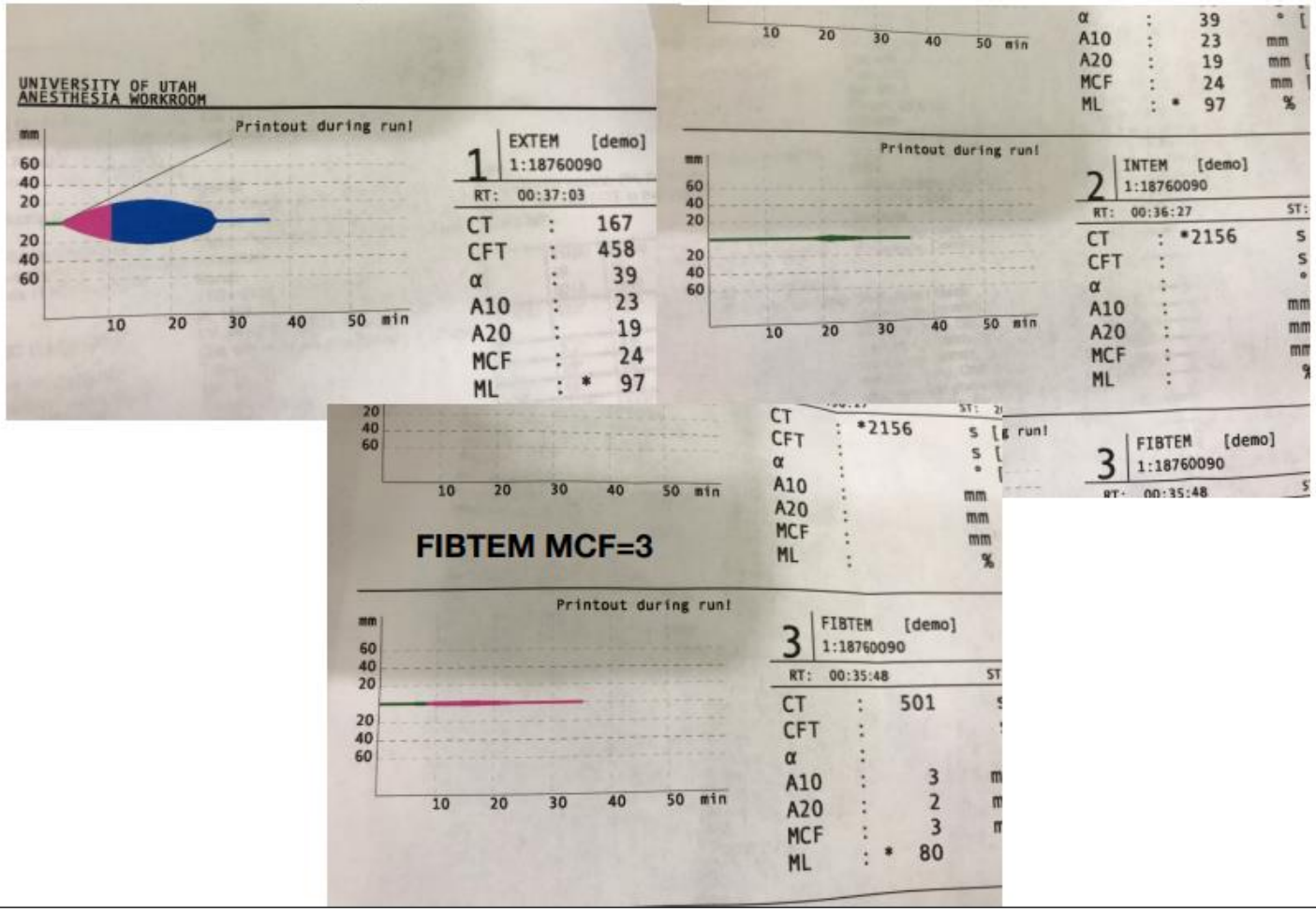

Category of P.E.	Catastrophic- persistent, acute threat to life	Submassive - Recovery of cardiac output with First Aid for P.E.
First Aid for Acute P.E.	• Supplementary Oxygen • Initiation of heparin • Evaluation of clot burden and oxygen supply/demand • Heparin bolus and infusion	
Criteria for Category	• Persistent hypoxemia • Ongoing shock • Large Clot Burden	• Oxygenation Adequate • Perfusion Intact • Modest Clot Burden
Options for Supporting RV	• Epinephrine • Milrinone • Epoprostenol • ECMO	• Milrinone • Epoprostenol
Options for Treating Clot and preventing additional embolism	• tPA • Thrombectomy • Catheter Lysis • IVC Filter	• Heparin and warfarin

Critical Care-45 Esophagopleural fistula after multi-heart valve surgery and coronary artery bypass grafting

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Introduction: Esophageal perforation is an uncommon complication that carries significant morbidity and mortality (as high as 67.7% and 19.9%, respectively)[1]. It is commonly associated with advanced esophageal carcinoma, chemical injury after ingestion, radiation therapy, iatrogenic injury 55% , spontaneous perforation , foreign body and traumatic penetrating injury.[2]

Case Report: We present the case of a 67-year-old female with history of coronary artery disease, aortic stenosis, mitral and tricuspid insufficiency who underwent a 2-vessel CABG, tricuspid valve repair, aortic and mitral valve replacements. The patient's micrognathia prevented intraoperative transesophageal echocardiography. On postoperative day 14, the patient developed a fever with a right sided pleural effusion requiring a chest tube. Over a period of 24 hours chest tube drainage turned milky white from straw colored. Fluid cultures grew multi-drug resistant pseudomonas, and the patient was started on appropriate antibiotics. On day 24, pink fluid resembling the patient's strawberry supplement shakes was present in the chest tube drain. CT esophagram found contrast in the dependent portion of the right subpleural space, consistent with an esophagopleural fistula (figure 1). EGD showed a 5 cm esophageal opening starting approximately 30 cm from the incisors. This was treated with an esophageal stent, J-tube feedings and antibiotics. Figure 1. collection demonstrated by arrow

Discussion: The etiology of the esophageal injury remains unclear in a patient with no significant risk factors for esophageal perforation, such as prior esophageal surgery, radiation, or cirrhosis. The patient also had no transesophageal echocardiogram performed or intra-operative trauma to the esophagus. No gastric tubes were placed near the time the injury was discovered. The very late presentation, along with no pneumomediastinum or pneumothorax is also uncommon. An esophagopleural fistula is a rare complication that can present after cardiothoracic surgery. As in this case, it can present as late as 4 weeks postoperatively. CT esophagram is the diagnostic method of choice and treatment requires prompt intervention with either a GI or thoracic specialist.[3]

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Critical Care-46 Hepatic Mucormycosis in a Patient with Diffuse Large B Cell Lymphoma

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Introduction: Mucormycosis is any fungal infection caused by the order Mucorales. Species generally identified include Mucor, Rhizopus, Cunninghamella, and Absidia. Mucoralean fungi are fast-growing saprophytes with wide, aseptate hyphae, growing on organic substrates. The major predisposing risk factor for disease development is immunosuppression, with a variety of etiologies including uncontrolled diabetes, HIV/AIDS, long-term corticosteroid therapy, and certain cancers - in this case, Diffuse Large B Cell Lymphoma. Hepatic involvement has been encountered very seldom.

Case Report: A 65 year old male with history of relapsed Diffuse Large B Cell Lymphoma, status post CD19 Chimeric Antigen Receptor (CAR) T-cell therapy, presented to the emergency department with shortness of breath, hemoptysis, and pleuritic chest pain. His CAR T Cell therapy was initially complicated by cytokine release syndrome, neurotoxicity, and pancytopenia, for which he was maintained on dexamethasone, levetiracetam, anakinra, and siltuximab. His workup included two sets of blood cultures positive for pansensitive Pseudomonas and CMV antigenemia, and sputum culture positive for Acinetobacter. He was intubated and mechanically ventilated and treated with broad spectrum antibiotics. He remained intubated and on pressor support for one week, and was extubated and downgraded to a regular nursing floor. He continued to have lab abnormalities, at this point including transaminitis with AST/ALT levels as high as 728/1431, respectively, with complaints of right upper quadrant pain. He continued to have intermittent, unexplained neutropenic fevers. CT of the abdomen and pelvis revealed hepatosplenomegaly with interval development of numerous hepatic bilobal hypodense lesions, some which demonstrated more peripheral geographic hypoenhancement concerning for abscesses (Fig 1). He was started on Micafungin and Meropenem for presumed hepatocandidiasis. He was planned for an IR-guided biopsy of his liver lesions, however shortly before the scheduled procedure the decision was made to transition to inpatient hospice, and the patient expired. Limited post-mortem autopsy of the liver revealed hepatosplenomegaly with multiple ill-defined tan-gray hepatic nodules, occupying 30-40% of the hepatic volume (Fig 2). There was extensive involvement of the portal venous system and hepatic parenchyma by fungal organisms. The fungus consisted of aseptate, variable-width, medium-to-large hyphae branching at acute and right angles (Fig 3), consistent with Mucormycosis.

Discussion: Mucormycosis is an opportunistic, invasive fungal infection with infections predominantly affecting severely immunocompromised patients. The vast majority of reported cases have been rhinocerebral, pulmonary, or gastrointestinal in nature. Hepatic involvement is rare, and presents as part of a disseminated disease with. Reported immunocompromised populations include those with severe, uncontrolled diabetes, transplant history, chronic steroid usage, and history of malignancy, particularly leukemia or lymphoma [2]. These patients may present with neutropenic fever refractory to broad-spectrum antibiotics, jaundice, and right-sided abdominal pain. Laboratory workup reveals hyperbilirubinemia, transaminitis, and elevated alkaline phosphatase. Imaging reveals hypodense hepatic lesions [2], however definitive diagnosis can on be made only with biopsy specimens. Histologic examination will show irregularly shaped, aseptate hyphae with right angulation. These lesions are commonly perivascular in location and may present with thrombosis or clinical signs of necrosis [2]. Therapy for disseminated Mucormycosis includes a prompt and prolonged course of high-dose Amphoteracin B. Cases have been reported of a combined medical-surgical therapeutic approach. Roden et al. reviewed 929 cases of zygomycosis, which revealed 96% of patients with disseminated disease expired; limited spread to the gastrointestinal tract had an 85% mortality, and limited pulmonary involvement had 76% mortality [3]. Survival rate was 3% without any treatment, 61% for cases treated with Amphoteracin B alone, 57% for cases treated with surgery alone, and 70% for cases treated with combined medical and surgical approach. Khan et al. reported a case of a 21-year-old male with Acute Lymphocytic Leukemia and subsequent hepatic mucormycosis who was successfully treated with Amphoteracin B and limited hepatic resection [4].

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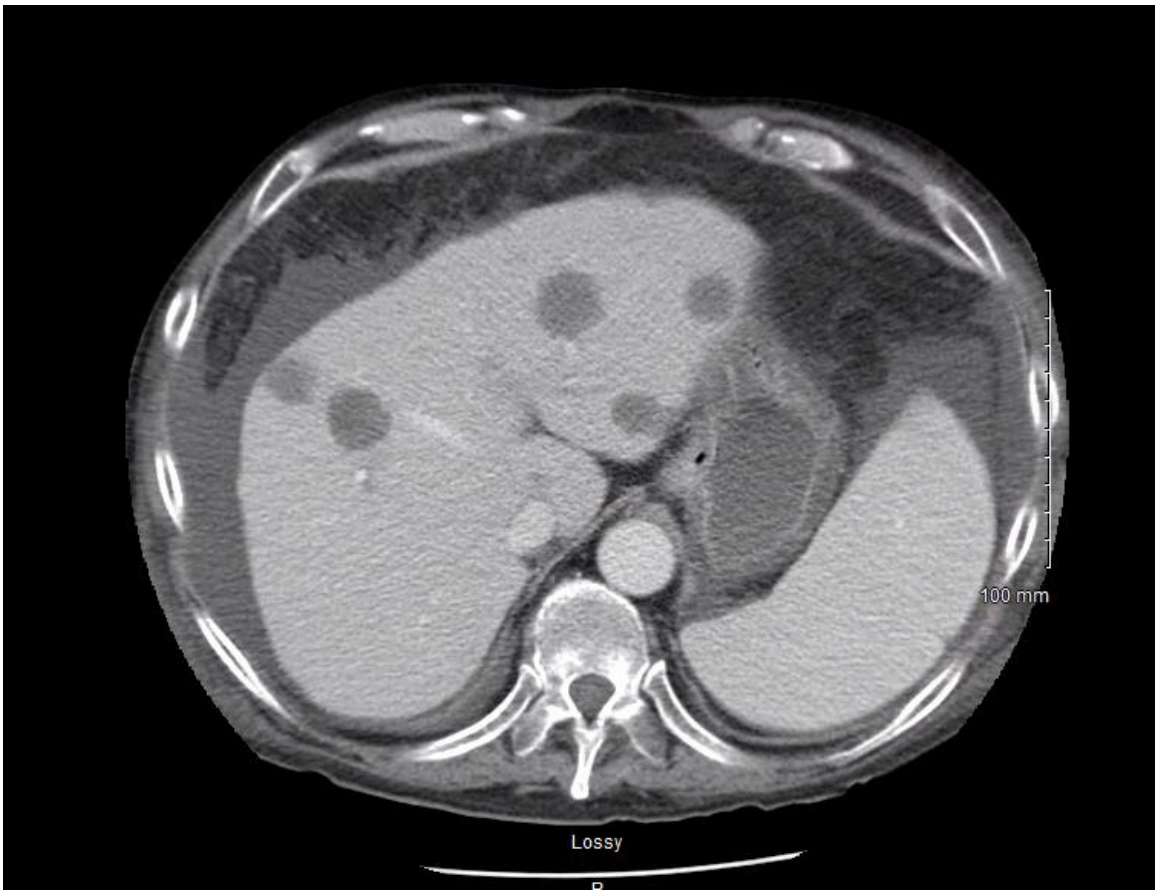
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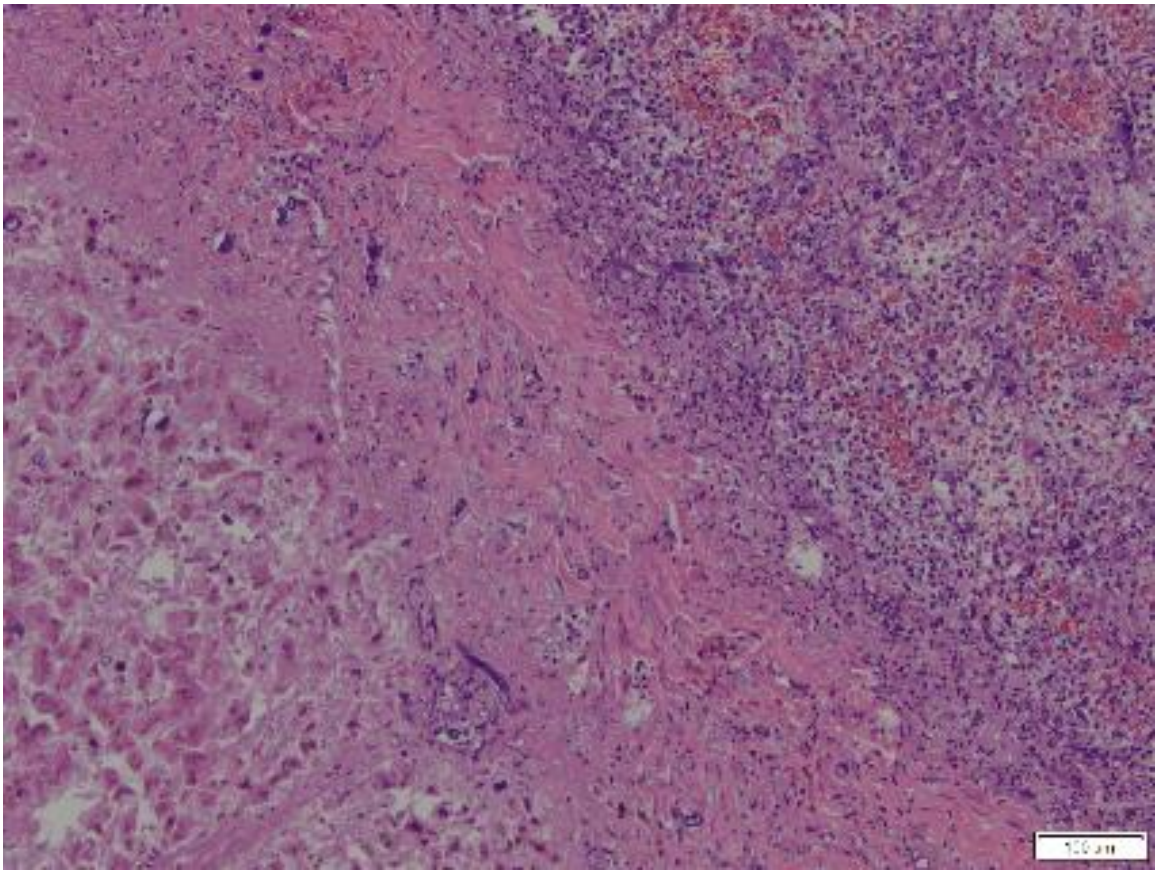

Critical Care-47 Pseudo-Hypoxic Brain Swelling, A Rare Complication of Spinal Surgery

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Introduction: Pseudohypoxic brain swelling (PHBS), also known as postoperative intracranial hypotension associated venous congestion, is a rare complication of spine and brain surgeries. First described in 2003 in brain(1) and 2011 in spine(2) surgeries, PHBS manifests as slower than expected return of mental status and imaging findings characteristic of cerebral hypoxia(3). The mechanism is believed to be a rapid loss of CSF volume, leading to venous cerebral congestion, with subsequent brain edema, and is often seen in the setting of sub-fascial or sub-galeal drains(4). PHBS has only been described by a small number of case reports, but is a diagnosis that anesthesiologists, surgeons, and intensivists should consider when patients are slow to awaken following otherwise uneventful brain and spine surgeries.

Case Report: The case describes a 57 year old man with ankylosing spondylitis who had previously underwent an uncomplicated posterior segmental spinal instrumentation and fusion (PSSIF) one year prior, who was returning for further PSSIF to correct cervicothoracic junctional kyphosis. The surgery was complex, extending from cervical to sacral levels and complicated by dural tears, with estimated blood loss of 4 liters, and requiring placement of a subfascial hemovac drain. Surgical time was 14.5 hours and anesthetic time was nearly 18 hours. After surgery was completed and anesthetic agents stopped, the patient was slow to awaken and unresponsive to commands, despite breathing spontaneously, and demonstrated seizure like activity. The patient was kept intubated and a computed tomography (CT) scan showed diffuse cerebral, cerebellar, and brainstem edema consistent with hypoxic brain injury. Hyperosmotic agents and anti-epileptics were initiated. As this patient had no intraoperative hypoxic events, the intensive care unit team made the diagnosis of 'cerebral edema secondary to significant intraoperative fluid shifts'. Fortunately, the patient made rapid improvements and interval CT scans showed decreased cerebral edema within 24 hours. The patient was extubated on post-operative day (POD) #1 and was fully following commands by POD#2. This author proposes an alternative diagnosis of pseudohypoxic brain swelling as the cause for the patient's clinical presentation.

Discussion: Pseudohypoxic brain swelling is a rare complication of otherwise uneventful brain and spinal surgeries. It manifests as delayed awakening and cerebral edema, and is believed to be caused by acute decreases in CSF volume following brain and spine surgeries. Although rare, practitioners caring for neurosurgical patients should be mindful of this diagnosis when intracranial hypotension, such as from CSF leaks and suction drains, are a possibility. In addition to treating the resultant cerebral edema, techniques such as intraoperative valsava maneuvers to check for CSF leaks and testing drain output for CSF components, such as beta-2-transferrin, are important for its prevention and identification.

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2.Pseudohypoxic brain swelling (postoperative intracranial hypotension-associated venous congestion) after spinal surgery: report of 2 cases. Parpaley Y, Urbach H, Kovacs A, et al. Neurosurgery. 2011;68:0–83

3.Postsurgical intracranial hypotension: diagnostic and prognostic imaging findings. Hadizadeh DR, Kovács A, Tschampa H, et al. AJNR Am J Neuroradiol. 2010;31:100–105

4.Postoperative intracranial hypotension-associated venous congestion: case report and literature review. Evins AI, Boeris D, Burrell JC, Ducati A. Clin Neurol Neurosurg. 2013;115:2243–2246

Critical Care-48 Veno-venous ECMO for necrotizing pancreatitis complicated by abdominal compartment syndrome

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Introduction: Veno-venous extra-corporeal membrane oxygenation (ECMO) is intended to be used to support primary respiratory failure, as a bridge to pulmonary recovery or pulmonary transplant. For patients in primary severe refractory hypoxic respiratory failure such as ARDS or Influenza, V-V ECMO can be a life-saving therapy. Treatment for non-pulmonary disease states, such as pancreatitis, can result in secondary respiratory failure. We present a case report of secondary severe hypoxic respiratory failure partially as a sequela of treatment to necrotizing pancreatitis, where V-V ECMO was utilized as a bridge to allow for aggressive treatment of the primary disease process.

Case Report: A 46 year old male with a history of recurrent hypertriglyceridemic pancreatitis presented with clinical, laboratory, and imaging data suggestive of necrotic vs hemorrhagic pancreatitis. He subsequently decompensated with shock requiring vasopressors and intravenous fluid (IVF) resuscitation, tachypnea, AKI and metabolic acidosis requiring mechanical ventilation and continuous hemodialysis. Aggressive intravenous fluid resuscitation resulted in abdominal compartment syndrome requiring decompressive laparotomy. Although peak airway pressures subsequently improved, severe ARDS ensued with pulmonary edema, massive bibasilar atelectasis and a p:f ratio <100. Attempts to correct hypoxia with increases in PEEP as small as 2cmH2O resulted in profound hypotension despite maximal 4 agent vasopressor therapy due to ongoing hypovolemia. Chemical paralysis provided little improvement in oxygenation and an open abdomen prohibited proning. Given his need for continued aggressive IVF resuscitation and the inability to tolerate rescue ARDS therapies including high PEEP and proning, preemptive support with venovenous (VV) ECMO was initiated. Once on ECMO, treatment was continued for his mixed vasodilatory and septic shock with aggressive volume replacement, broad spectrum antibiotics and vasopressors. Once volume resuscitation was complete and his shock resolved, he was decannulated after 6 days on VV ECMO (Figure 1). His post-ECMO course included renal failure requiring dialysis, multiple abdominal washouts with eventual abdominal closure and tracheostomy. There were no embolic or hemorrhagic complications from VV ECMO. Although his pulmonary pathology resolved and he was eventually weaned from ventilator assistance, he ultimately developed refractory bacteremia and progressive liver failure. The decision was made to switch to comfort-focused care and he expired on hospital day 51.

Discussion: Hypertriglyceridemia is a well-documented cause of acute pancreatitis, often treated supportively1. When severe, pancreatitis causes vasodilatory shock and volume replacement can cause compartment syndrome and pulmonary edema. Our patient highlights the challenges when treatment for the primary condition will cause significant injury to other organ systems. In this case, the need for intravascular fluid resuscitation resulted in abdominal compartment syndrome and severe hypoxia. Although decompressive laparotomy provided relief for the viscera, options were limited to provide pulmonary relief. Given his need for continued volume replacement, the decision to provide early VV ECMO allowed volume replacement therapy to continue without resulting in continued failure of oxygenation and ventilation (Image 1). Prior reports of VV ECMO have established a role in the setting of pancreatitis-induced ARDS, however in our patient, V-V ECMO was used not primarily as lung rescue, but to maintain oxygenation in light of ongoing intravascular depletion, and expected worsening pulmonary edema2,3. Even though our patient ultimately succumbed to multi-system organ failure, it is notable that his shock and ARDS resolved during his short course of VV ECMO with aggressive treatment and lung rest. This experience highlights the use of early VV ECMO for non-pulmonary critical illness where treatment of the primary pathology will cause significant pulmonary challenges.

Reference(s):

1: Clin Gastroenterol Hepatol, 2008 Oct; 6(10): 1070-6

2: Annals of Surgery 1998 ; 227(4) 572-4

3: JAMA. 2012;307(23):2526-2533

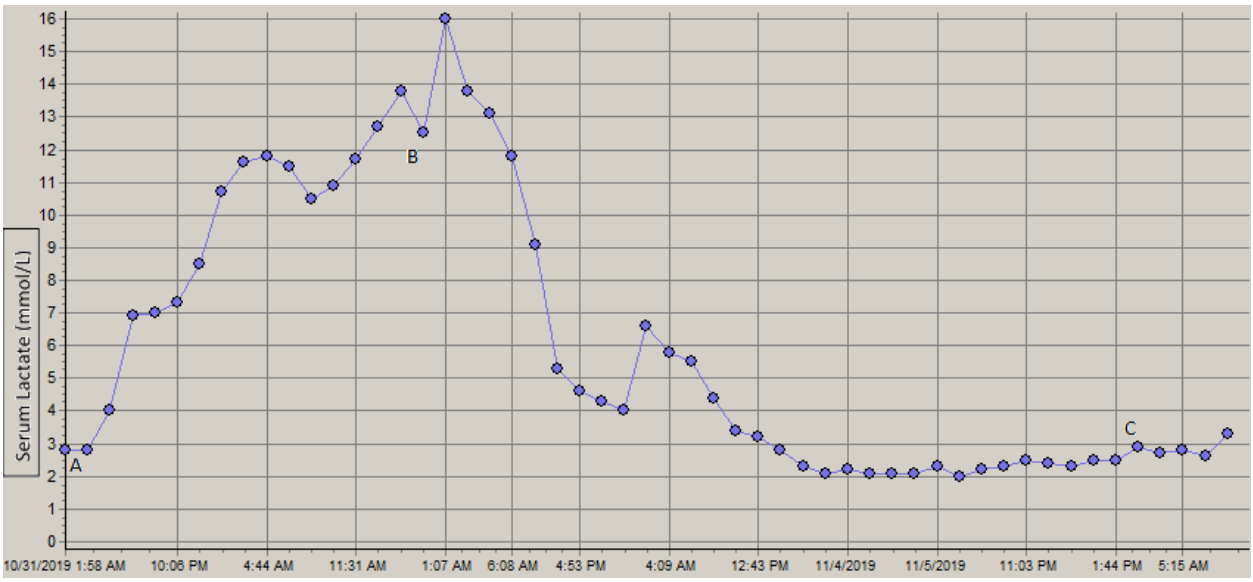

Figure 1: Lactate trend; A: Admission (2.8mmol/L) B: Time of ECMO Cannulation (12.7mmol/L) C: ECMO decannulation (2.9mmol/L)

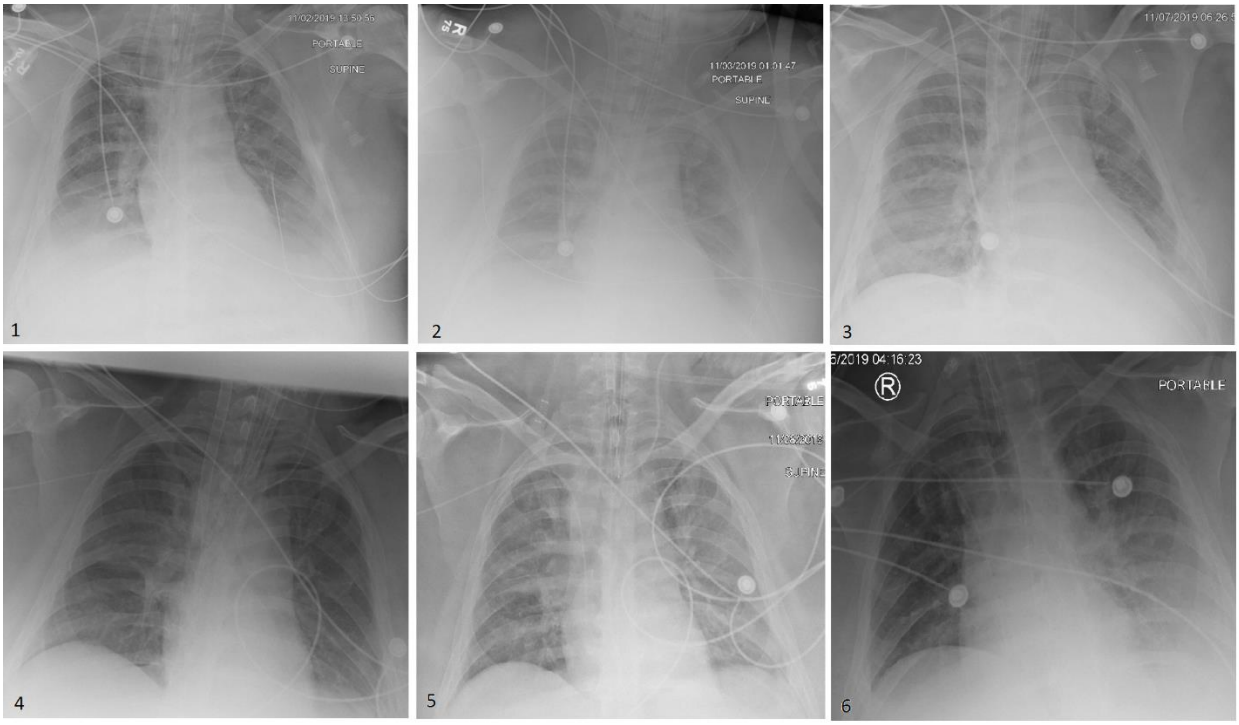

Image 1: Serial chest radiographs during his hospital course illustrating development of, and recovery from pulmonary edema/ARDS. 1: 12 hours prior to V-V ECMO cannulation. 2: Immediately after cannulation (note return cannula in right IJ/RA) 3: Day 4 of V-V ECMO 4: Immediately prior to V-V ECMO decannulation on ECMO day 6 5: First day off of V-V ECMO 6: 7 days after decannulation

Critical Care-49 ACE Inhibitor-Induced Angioedema Managed with Icatibant in a Postpartum Patient

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Introduction: Angioedema is a rare disorder that can be caused by ACE inhibitors directly interfering with the degradation of bradykinin. We describe the management of angioedema in a young postpartum woman taking ACE inhibitors.

Case Report: A 32-year-old African American female with a past medical history of hypertension, preeclampsia, and a recent cesarean section presented to the emergency department with progressively increasing anasarca, episodic facial swelling, headache, nausea, and vomiting. She had been taking enalapril 5 mg daily for approximately 10 weeks. When she was admitted to the family medicine ward, her enalapril was discontinued. Overnight, she developed worsening of her facial swelling. The next morning, she had also developed dyspnea. ENT was consulted and noted airway swelling on flexible laryngoscopic exam. She was treated with racemic epinephrine and steroids and was transferred to the MICU. One hour later, her airway exam was unchanged. She was offered, but ultimately declined, elective intubation for airway protection. Based on clinical and medication history, icatibant was administered. On repeat exam two hours later, there was marked reduction in airway swelling and resolution of dyspnea. After one day of observation, she was transferred back to the family medicine ward for further management.

Discussion: ACE inhibitor-induced angioedema is most often seen within the first 3 months of therapy; however, it can occur at any time. Symptoms peak within hours and can resolve spontaneously 24-72 hours after the onset of swelling. Icatibant is a bradykinin B2 receptor antagonist. Only small trials and case reports have been published on the use of icatibant for ACE inhibitor-induced angioedema. Some of this data suggests decreased duration of symptoms in patients treated with icatibant, although quality data is lacking. As our patient was still within the timeframe for potential worsening angioedema, icatibant was ordered on transfer to the MICU. This case highlights an example of successful use of icatibant for ACE inhibitor-induced angioedema in a patient in whom there was a concern for impending airway compromise. Because early treatment of airway swelling is critical, the use of agents such as icatibant that target the bradykinin system should be considered in suspected ACE inhibitor-induced angioedema with similar concern for airway compromise.

Reference(s): Arch Intern Med. 172(20):1582-9, 2012. Ann Otol Rhinol Laryngol. 110(9):834-40, 2001. Expert Opin Pharmacother. 13(15):2233-47, 2012. J Emerg Med. 53(5):662-679, 2017. Curr Treat Options Allergy. (6):18–26, 2019.

Critical Care-50 Erector Spinae Plane Block: An Important Role in the Management of Rib Fractures

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Introduction: Rib fractures are common in trauma patients. In addition to managing simultaneous injury to abdominal organs, other skeletal fractures (e.g., spine and pelvis), underlying acute and chronic disease states and medications, and anatomic and physiologic changes are targeted. The management of rib fractures mandates effective analgesia to prevent subsequent respiratory complications. An analgesic plan should minimize opioid pain medication, prevent cognitive dysfunction, and as much as possible maintain patient mobility. We present 2 patients in whom the erector spinae plane block (ESPB) played an important role in achieving these therapeutic goals. For some patients the EPSB is preferred to paravertebral blocks or epidural analgesia.

Case Report: The ESPB is a deep tissue planar block that penetrates the trapezius, rhomboid, erector spinous muscle, and separates the latter muscle from the transverse process (Fig. 1). The positioning for administration of the block is usually sitting but it can also be performed in the lateral or prone position. It is an ultrasound-guided block. The majority of blocks can be performed using a high frequency (10 -15 MHz) linear spectral array transducer which provides an image with a higher resolution. A low frequency curvilinear transducer (2 - 5 MHz) is useful for obese patients in whom the transverse processes are image at a depth greater than 4cm. The transducer is placed in a parasagittal position approximated 3cm right or left of the spinous process. Best position for needle entry is ascertained by moving the transducer right and left in the sagittal plane, i.e. medial vs. lateral. If the transducer is too lateral the ribs will come into view, if too medial the hyperechoic lines of the thoracic laminae will be in view. Best position is further confirmed by identifying the transverse process. In general this examination focuses on the injured rib, although significant cranial-caudal spread of the local anesthetic impacts a large area. With monitors in place and baseline data recorded, the back is prepped and draped in standard fashion for regional anesthetic blocks. Needle selection is a matter of preference with either a catheter over the needle kit, or a through the needle (Tuohy) for catheter placement; an 18 gauge needle is most often selected. A stiffer catheter aides in positioning as there are no bends or catheter curls with successful placement. An in-plane cranial to caudal approach is used with needle advancement under direct vision to gently contact the bony surface of the transverse process. A small test dose of normal saline results in linear spread of fluid and a lifting of the erector spinae muscle from the transverse process surface. The catheter is threaded into place and secured then tested again, an infusion of ropivacaine 0.2% at 8 - 10 ml/hr is begun and adjusted for optimal pain relief.

Discussion: Case 1: See image 1 Case 2: See image 2 The ESPB is ideally suited for analgesic management of a patient with rib fractures. It achieves 3 goals: opioid-sparing, optimizing respiratory function, and preventing cognitive dysfunction. The sonoanatomy is recognizable and the insertion of a planar indwelling catheter is relatively easy. There are no anatomic structures in the vicinity of catheter placement. Sympatholysis or hypotension seldom results from an epidural block. No vascular puncture that can complicate an epidural or paravertebral block. No risk of pneumothorax compared to intercostal nerve block. The effect of the block is measurable. Prior to intervention, supervised incentive spirometry is performed, a numerical pain score is assigned, and O2 requirement to maintain O2 sat > 94% is noted. Signs of a successful block are based on all 3 of these parameters and supervised incentive spirometry performed on hourly bases and maintained > 50% predicted. Progressive and/or persistent deterioration in these parameters requires intervention up to and including tracheal intubation and mechanical ventilation. Neither patient was mechanically ventilated during the hospital stay, and both demonstrated a nuance that deserves further investigation in future studies i.e., an octogenarian who more than doubled the IS inspired volume with an opioid-sparing analgesic technique and a patient who was discharged with the catheter in place (subsequently removing it himself). Rib fracture protocols should be re-examined to move the ESPB to first-line therapy soon after admission in appropriate patients.

Reference(s): Brit J Anaesth. 2017; 118(3):474-475. Anaesthesia. 2017; 72:427-438. Scand J Trauma Resusc Emerg Med. 2018; 26:67-72. Korean J Anesthesiol. 2019 Jun; 72(3): 209–220

Case 1

A 78 y/o woman was admitted to ER following MVC. She had a past history of heart failure, controlled with a regimen of spironolactone, carvedilol, losartan. She sustained left-sided rib fractures ribs 6/7, pelvic fractures, a tibia-fibula fracture, non-displaced femur fracture. CXR showed small left pneumothorax. When evaluated for block, she was in respiratory distress, hyperventilating, pain with deep breathing

	FIO2	RR	SaO2	Coached IS
On HFNC 45 L/min	.75	24/min	.88	<400cc
After ESPB	.50	22/min	.92	=700cc
At D/C SICU (24hr)	.21	28/min	.93	=750cc

Other fracture pain was managed without opioids and went to OR for fracture fixation under opioid free anesthesia.

Case 2

A 39 y/o man who owns a tree service fell from a tree while chain sawing at an estimated 20 feet above ground. He landed on a pile of cut wood, landing on his left chest. There was no LOC, and on presentation to ED no other fractures. CXR = no hemo or pneumothorax, Fractured left ribs 4/5/6. He is found to be in obvious respiratory distress, hyperventilating RR =28/min, FIO2 =.90 on nasal cannula @ 2 L/min. Bent over with hand on left chest, splinting respiration.

	FIO2	RR	SaO2	Coached IS
Initial Exam	~.28	28/min	.90	Unable to complete due to pain
After ESPB	~.28	20/min	.94	=500cc
After 2hr infusion	RA	18/min	>.95	>1000cc

Patient was mobilized six hours after infusion begun, pain free, wants discharge, he is caretaker for his elderly mother. Sent home 2nd day post ESPB with On Q pump, managed at home by phone for 3 days, discontinued catheter on 4th day himself.

Critical Care-51 Capnocytophaga: A Rare Infection with an Unusual Presentation

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Introduction: Capnocytophaga is a family of gram-negative rod bacteria present in the oral cavities of humans (ochracea, gingivalis, haemolytica, sputigena, granulosa), dogs and cats (canimorsus, cynodegmi). Both human and zoonotic species have been isolated in cases of sepsis, mengingitis, osteomyelitis, peritonitis, pneumonia, septic arthritis, and endocarditis. Risk factors for Capnocytophaga infection include states of immunocompromised and excess iron, with described cases occurring in patients with asplenia, cirrhosis, alcohol abuse, corticosteroid use, advanced age, neutropenia, chronic pneumonia, hematopoietic neoplasms, hemochromatosis, beta-thalassemia major and cigarette smoking. The success of isolation of this organism depends in large part to the sample source. While blood and cerebrospinal fluid may readily reveal positive Capnocytophaga growth, wound cultures are rarely positive for Capnocytophaga due to the overgrowth of skin flora and favorable response to prophylactic broad-spectrum antibiotics.

Case Report: A 74 year old male with IDDM2, prostate adenocarcinoma s/p prostatectomy, squamous cell carcinoma of the esophagus with metastases to the liver s/p chemoradiation, Hodgkin's lymphoma s/p curative chemotherapy, alcoholic liver cirrhosis and CKD stage III presented to CCF for recurrent left posterior periscapular hematoma/abscess. He had 6 weeks prior received intraarticular steroid injection for left shoulder pain. Worsening of pain and fullness of shoulder musculature on physical exam prompted CT of the extremity which revealed a cystic fluid-containing mass replacing the entire infraspinatus muscle (Fig. 1, 2). Aspiration of 120cc of chocolate-milk colored fluid provided pain relief, and cytology was significant for necrotic inflammation without evidence of malignant cells. When fluid reaccumulated within one week the patient underwent surgical decompression (Fig. 3) and wound vac placement, 2 of 2 cultures from which grew Capnocytophaga on day 3 of incubation at which point Infectious Disease was consulted and recommended ampicillin-sulbactam. His course was complicated by bleeding around the wound vac for which he eventually underwent embolization of a branch of the thoracoacromial artery. When oozing continued, wound vac was discontinued and TXA applied to site. Hemoglobin subsequently stabilized and he was discharged to SNF on POD#42.

Discussion: With approximately 484 reported cases of infection with Capnocytophaga in the literature and a fatality rate of 26%, this organism may be more clinically significant than is currently recognized. Different strains exhibit different degrees of virulence, but of particular importance in human infection is C. canimorsus. Factors contributing to virulence of C. canimorsus include evasion of complement killing, elicitation of only low-grade cytokine and nitric oxide responses, catalase-mediated degradation of hydrogen peroxide within phagocytic vacuoles, possess sialidase, an enzyme that allows it to obtain nutrients from the amino-sugars present on host cell membranes, possesses a lipopolysaccharide (LPS) that does not interact with toll-like receptor 4 (TLR-4), resulting in lack of cytokine production and failure to activate the innate immune system.The insidious nature of Capnocytophaga infection also contributes to its potential danger, as presenting symptoms are often mild, nonspecific, and localized. When care is sought, cultures are often negative for this fastidious organism due to its specific growth requirements, long incubation times, and use of polyanethole-sulfonate anticoagulant in automated blood culturing systems as it inhibits growth of C. canimorsus. PCR is the gold standard for identifying Capnocytophaga infections.

Reference(s): Butler T. Capnocytophaga canimorsus: an emerging cause of sepsis, meningitis, and post-splenectomy infection after dog bites. European Journal of Clinical Microbiology & Infectious Diseases. 2015;34(7):1271-1280. doi:10.1007/s10096-015-2360-7. Gaastra W, Lipman LJA. Capnocytophaga canimorsus. Veterinary Microbiology. 2010;140(3-4):339-346. doi: 10.1016/j.vetmic.2009.01.040 Zajkowska J, Krol M, Falkowski D, Syed N, Kamienska A. Capnocytophaga canimorsus - an underestimated danger after dog or cat bite - review of the literature. Przegl Epidemiol . 2016; 70(2): 289-295.

Critical Care-52 Successful Use of the Impella Device in Giant Cell Myocarditis as a Bridge to Heart Transplant

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Introduction: Idiopathic giant cell myocarditis (GCM), a rapidly progressive inflammation of the myocardium, predominantly affecting younger people is associated with conduction system abnormalities, fulminant heart failure, and refractory ventricular arrhythmias. We report a patient who presented with features of acute heart failure due to GCM that was successfully managed with a left ventricular assisted device (LVAD) bridging to heart transplant.

Case Report: The patient is a 24-year-old athletic male with no prior medical history whose prodrome was two weeks of intermittent palpitations. The symptoms were not related to exertion, were associated with mild dizziness, usually self-resolved in seconds, and were attributed to stress from a new job. He also noted being more fatigued with workouts. He was a lifelong non-smoker who only drank socially. The patient reported recreational marijuana use less than once per month and denied use of any other illicit substances. He had no pertinent family history of cardiac disease. On the day of the actual event, he was working a shift as a medical scribe when he experienced sudden palpitations, lightheadedness, dizziness, and felt pre-syncopal. He was evaluated by a colleague and noted to be tachycardic, with ECG showing monomorphic ventricular tachycardia (VT) with a rate of 230bpm. He had a TTE done showing normal Left ventricular (LV) size with reduced function and estimated EF of 25-30%, global hypokinesis with mild regional variation, severe diastolic dysfunction (grade 3), normal right ventricular (RV) size with reduced systolic function, prolapse of the anterior mitral valve leaflet, moderate eccentric mitral regurgitation and RV systolic pressure estimated to be 33mmHg. His laboratory findings included a WBC 14000, troponin of 39, and BNP of 1078. He was admitted and started on an esmolol drip which was switched to an amiodarone infusion with subsequent conversion to normal sinus rhythm. He underwent cardiac catheterization which demonstrated low cardiac index without obstructive disease. An endocardial biopsy showed GCM. He was then transferred to our center for higher level care. On admission, he had multiple episodes of VT and chest pain. Emergent right axillary LVAD Impella 5.0 was inserted for hemodynamic support, LV unloading and life-threatening arrhythmias. 10 days later, he received a heart offer and underwent impella removal and transplantation. He was discharged in good health and currently is doing well.

Discussion: Giant cell myocarditis is an incompletely understood, rare cause of myocarditis. Patients present predominately with heart failure and dysrhythmia. Diagnosis is confirmed by histopathology. In the absence of treatment, prognosis is poor with a median survival of three months. Our case necessitated quick recognition and treatment with mechanical support making this the first known case of GCM with successful placement of impella and ultimately heart transplantation.

Reference(s): Case Rep Cardiol. 2019 Jun 19; 2019:7276516. Cardiovasc Pathol. 2019 Dec 2; 45:107190. J Am Coll Cardiol. 2019 Jul 23;74(3):299-311. Clin Case Rep. 2018 Feb 14;6(4):617-620. ESC Heart Fail. 2017 Aug;4(3):371-375. BMJ Case Rep. 2017 May 22;2017.

Critical Care-53 Postpartum Type A Dissection in Patient with Familial Pulmonary Hypertension

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Introduction: Aortic dissection is a rare complication of pregnancy with a majority of cases occurring during the third trimester. However, many women are diagnosed within the first 7 days post-partum. Dissections during pregnancy are often associated with preeclampsia-related hypertension or underlying connective tissues disorders such as Marfan's syndrome. Here, we describe the case of a woman without preeclampsia or connective tissue disorders but familial pulmonary hypertension who developed a Type A dissection during the post-partum period.

Case Report: A 27-year-old woman with a past medical history of patent ductus arteriosus and asthma presented to an outside hospital 7 days post-partum from spontaneous vaginal delivery with chest pain and shortness of breath. Computed tomography demonstrated a type A dissection with an aneurysmal ascending aorta. She was transferred to our institution for emergent surgical intervention. Insertion of a pulmonary artery catheter revealed elevated pulmonary artery pressures. Intraoperative transesophageal echocardiography demonstrated moderate aortic insufficiency despite normal aortic root size. The patient subsequently underwent a mechanical aortic valve-, ascending aorta- and hemiarch-replacement. The patient was then transferred to the cardiothoracic intensive care unit (CTICU) while intubated and sedated on inotropic and vasopressor support. Several hours after her procedure, she was extubated. Repeat transthoracic echocardiography on post-operative day one demonstrated severely reduced right ventricular (RV) function, a thickened right ventricle at 6mm, and an estimated RV systolic pressure of 56mmHg. She required extended inotrope wean and diuresis over the next three days but was eventually discharged from the CTICU and subsequently from the hospital. Her family history revealed a diagnosis of pulmonary hypertension in her mother, who is treated with two pulmonary vasodilators, and maternal aunt. Her maternal grandmother suffered from unspecified aortic valve disease. A genetic work-up is ongoing.

Discussion: Aortic dissection is rare complication of pregnancy especially without associated connective tissue disorders or pre-eclampsia. WHO group 1 pulmonary hypertension represents a diverse compilation of diseases that account for 9% of all cases of pulmonary hypertension. Of this group, familial or inheritable pulmonary hypertension represents only a small fraction. Over 75% of cases with familial pulmonary hypertension are related to BMPR2 lesions. In the case above, the patient presented seven days post-partum for emergent aortic surgery prior to diagnosis of her pulmonary hypertension.

Reference(s): Circulation Research 2014 111 189-202 European Respiratory Review 2106 25: 431-437 Netherlands Heart Journal 2011 19: 504508 International Journal of Surgery Case Reports 2019 56:101-106

Critical Care-54 Residual Neuromuscular Blockade In Myasthenic Crisis, Successfully Reversed With Sugammadex

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Introduction: Myasthenia Gravis (MG) is an autoimmune disease where IgG antibodies directed against nicotinic acetylcholine receptors in the postsynaptic myoneural junction results in an overall reduction in the number of available receptors causing fatigable muscle weakness.[1] In myasthenic crisis there is acute airway compromise due to respiratory failure and/or inability to tolerate oral secretions and requires ICU admission. 15-20% of patients with MG experience a crisis at some point in their disease course[2] often early after the initial diagnosis.[3]

Case Report: An 81 year old female with a past medical history of HTN, thyroid disease and recent diagnosis of MG presented to the ED for a 2 day history of progressively worsening shortness of breath and dysphagia. She arrived via EMS on 2L NC and shortly after arrival developed acute respiratory failure eventually progressing to successful RSI. IVIG therapy was started without complication. She met weaning parameters for extubation on day 3 and was extubated to 40% Venturi mask. Respiratory distress developed over the next 2 hours and eventually necessitated re-intubation overnight. Intubation required 40 mg IV rocuronium for difficulty passing the ET tube through the vocal cords. The following morning she was persistently weak, had no cough, and was unable to open her eyes. 200 mg Sugammadex was administered with rapid improvement in strength. The rest of her ICU course was uneventful and she was extubated on day 6.

Discussion: MG patients are particularly susceptible to post-operative residual curarization (PORC). In cases where neuromuscular blockade (NMB) is used to facilitate intubation, it is important to reverse the paralytic effect to prevent residual paralysis, downstream respiratory complications and myopathies even while the patient remains intubated in the ICU. Traditional reversal of non-depolarizing paralytics requires acetylcholinesterase inhibitors. The resultant increase in acetylcholine levels affects not only nicotinic receptor binding sites in the skeletal muscles, but also the muscarinic receptors in the cardiovascular, respiratory and gastrointestinal systems.[4] The muscarinic action can precipitate a cholinergic crisis with bradycardia, hypotension, arrhythmias, bronchoconstriction, increased secretions and diarrhea. In MG patients who are on chronic anticholinesterase therapy, the potential for drug-drug reactions makes reversal of NMB with these agents even less favorable. Sugammadex selectively encapsulates the NMB agent in a permanent inclusion complex which prevents further binding at the nicotinic acetylcholine receptors.[4] This occurs in a 1:1 ratio which creates a concentration gradient that draws even more NMB molecules from the motor junction into the plasma where they are bound in the inclusion complex. The advantages over anti-acetylcholinesterase medications include rapid skeletal muscle recovery as well as a lack of the muscarinic side effects thereby minimizing the risk for a cholinergic crisis.

Reference(s): Clin Immunol. January 2019:879-890.e1 Fortschritte der Neurol Psychiatr. 2018;86(5):301-307 J Emerg Med. 2017;53(6):843-853 JBI Database Syst Rev Implement Reports. 2018;16(10):1922-1928

Critical Care-55 Cytokine Release Syndrome: Clinical Manifestation in patient on Ipilimumab & Nivolumab

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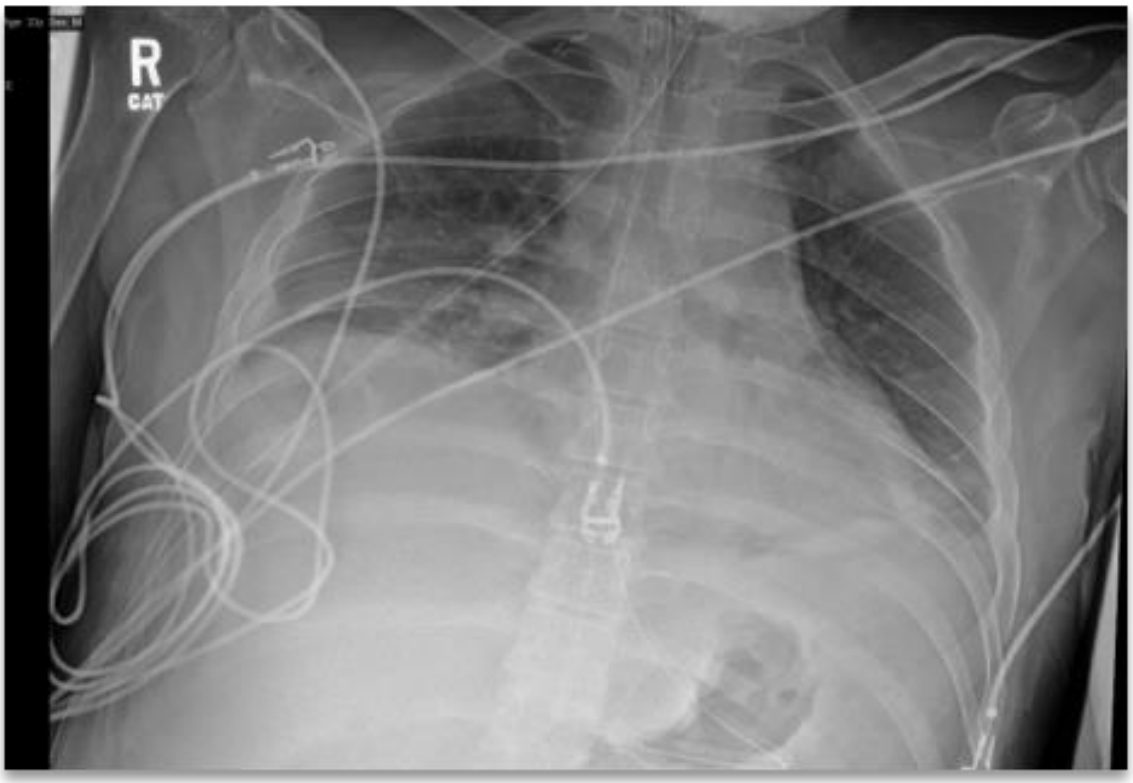
Introduction: Pt JM is a 32 yo M with a pmhx malignant melanoma with metastasis to brain and liver s/p multiple craniotomies and XRT who was given C1D1 Ipilimumab and Nivolumab on 10/29/19. Arrived on 11/11/19 at 1300 c/o severe abdominal pain after eating dinner with associated nausea and non-bloody, non-bilious emesis x 1-day. In ED, underwent CT C/A/P which showed moderate volume pneumoperitoneum, likely due to small bowel perforation. Within 6-hours of arrival underwent ex-lap and SBR for perforation. Uneventful intraoperative course, successfully extubated in the OR and transferred to floor for continued management. Uneventful initial recovery POD #0 through POD #2, patient was ambulating and stable while managed on a surgical floor bed. Overnight on POD #2, pt developed a new oxygen requirement overnight with desaturations to the upper 80s on room air. Needed 4 L for >94%. A CXR at that time showed new R effusion w/ R middle lobe consolidation, concerning for aspiration (no observed aspiration event). His antibiotic regimen was broadened to include Vancomycin. His potassium was 3 and was supplemented. His lactate was 1.3. ABG 7.46/31/69/22 with A-a gradient >100. He was bolused 500 cc NS. Throughout the morning on POD #3, he continued to have an oxygen requirement, and was tachypneic to the 30's-40s, but remained on 6L NC. An ABG at 1100 demonstrated 7.45/28/72/20. Morning labs showed HCT stable (32 from 27), increased WBC to 12.8 from 10.1, potassium 3.7, and creatinine stable at 0.58. An additional IV was obtained and he was bolused an additional 500NS. In the evening, POD #4 a rapid response was called because the pt acutely desaturated to the mid-70'S on 6L NC. He was placed on on-rebreather and the ICU team was called to assess the patient.

Case Report: Transferred to the SICU and dx with severe ARDs (P:F ratio 70) on FiO2 100% and PEEP 18-20, chemically paralyzed, inhaled epoprostenol. No significant recovery and appeared to be clinically decompensating over course of ICU admission during initial 28-hrs. A family meeting was called POD#4 with patients oncologist present. Concern for Cytokine Release Syndrome given absence of apparent alternative toxic metabolic etiology or infection to explain source that potentiated ARDs. On POD #4, pt was placed on hydrocortisone 100 mg q8hrs for 3 days with a dramatic decrease in ventilatory requirements. In fact, oxygenation requirements dramatically improved as is radiologic appearance of infiltrates. Pt was weaned off of both inhaled epoprostenol and paralysis POD #5 while maintaining FiO2 at 0.5.

Discussion: Work-up failed to demonstrate any bacterial or viral source of underlying infection with repeat imaging studies failing to demonstrate evidence of anastomotic leak, concern for perforation, or evidence of mesenteric ischemia with benign abdominal exams. Etiology appeared to an an exaggerated T-cell response directed against normal tissues resulting in high levels of proinflammatory cytokines following first dose administartion of Ipilimumab & Nivolumab in the 7-14 day window often seen in Cytokine Release Syndrome. The rapid improvement strongly supports the hypothesis that his pulmonary injury was due to the immunotherapy instituted for his malignancy. Most likely immunotherapy mediated ARDS, or Cytokine Release Syndrome, without any evidence of infectious etiology to explain onset ARDs.

Reference(s): Critical Care Medicine: Volume 48 - Issue 1 - p 10-21, January 2020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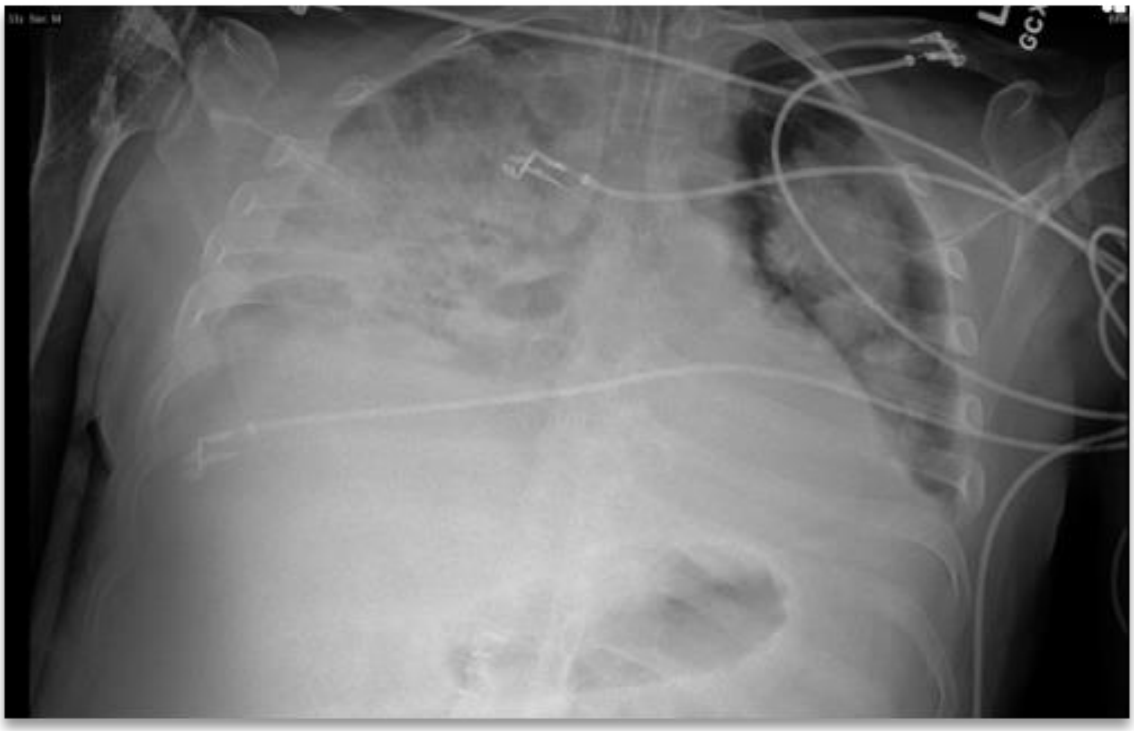

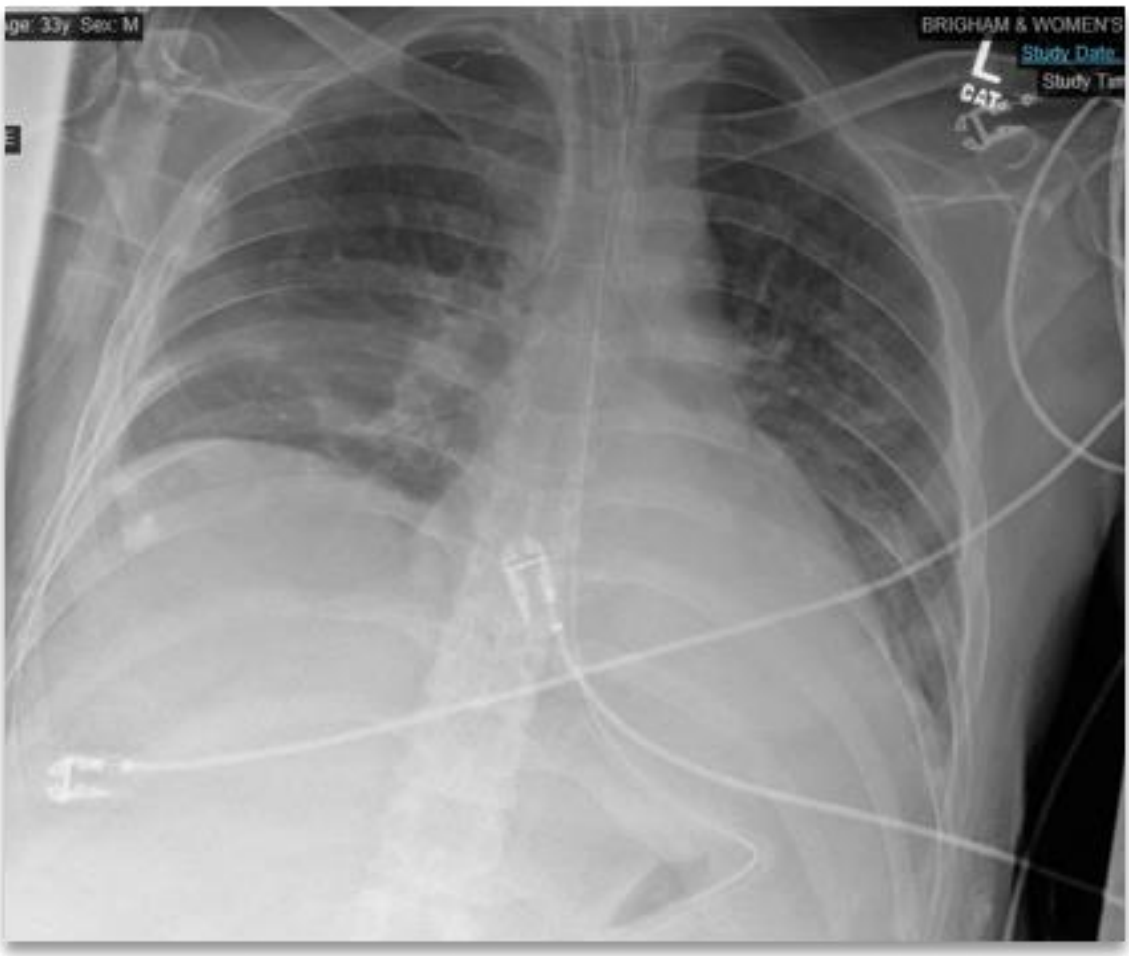
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Critical Care-56 A case of aspergillus flavi meningitis in a pregnant patient

Jocelyn Y Wang[1], Tichaendepi Mundangepfupfu[2]

[1]University of Washington, Seattle, WA, [2]University of Rochester, Rochester, NY

Introduction: Invasive CNS aspergillosis is poorly understood, with only 13% due to A. flavus . It also has a fatality rate of 72%, partly due to poor detection with PCR (only 30%) but also the varying lengths of antifungal treatments, which are not without toxicities.

Case Report: A 31yo female G2P1 at 27 weeks gestational age was transferred from another hospital for evaluation/management of persistent headache, fevers, and neurologic changes. Medical history was notable for possible tuberculosis (TB) a decade prior, which was treated and resolved. Prior to transfer, an MRI showed a pontine lesion; but broad autoimmune and infectious work up was only notable for an elevated ESR, lumbar puncture (LP) showing neutrophilic pleocytosis, and mild prominence of the right hilar region on chest imaging. She was started on steroids prior to transfer. On arrival, repeat LP was unremarkable and amniocentesis was negative for chorioamnionitis. Steroids were held due to concern of infection and broad-spectrum empirical antibacterial and antiviral therapies were started. Repeat MRI was notable for an evolution of the known pontine lesion with new infarcts concerning for central embolic etiology; transthoracic echo was negative for bacterial endocarditis. CT Chest showed multiple lung nodules, which were biopsied but unremarkable. Screening for Takayasu arteritis and bronchoalveolar lavage cultures were also negative. She was started on treatment for TB and dexamethasone. Her neurologic deficits acutely worsened, she was intubated and transferred to the medical ICU. MRI showed new multifocal acute infarcts involving the anterior, middle, and posterior circulations (Img 1a/b). MRI also noted abnormal flow voids concerning for thrombosis/occlusion of the left MCA and PCA. Due to concerning fetal tracings, cesarean section was performed at 28 weeks. Post-operatively, CT head revealed a large hemisphere infarct with subfalcine and uncal herniation (Img 1c). She lost brainstem reflexes by hospital day 8 and transitioned to comfort care the next day, at which time she expired. Final autopsy report showed aspergillus flavi meningitis.

Discussion: CNS aspergillosis risk factors are severe neutropenia, high doses of glucocorticoids, or impaired cellular immune responses. While there was a case of fungal fibrosing mediastinitis in pregnancy in India, this is the second known CNS aspergillosis case in pregnancy (the last from 1979). Aspergillosis brain imaging typically shows ring-enhancing lesions, infarction with superimposed hematomas, and mucosal thickening of paranasal sinuses with dural enhancement. However, our case only showed infarction, a non-specific finding. In our case, aspergillus CSF PCR was negative. PCR has a high false negative rate and galactomannan antigen testing may have a higher sensitivity/lower specificity, but aspergillus is a rare cause of meningitis, so we still know very little about the pathogenesis and diagnosis. It is important to keep CNS aspergillosis in the differential and repeated testing may be necessary to make a diagnosis.

Reference(s): Epidemiology and outcome of mould infections in hematopoietic stem cell transplant recipients.' Clinical Infectious Diseases 34.7 (2002): 909-917. 'Aspergillus meningitis: a rare clinical manifestation of central nervous system aspergillosis. Case report and review of 92 cases.' Journal of Infection 66.3 (2013): 218-238. 'Diagnosis and management of Aspergillus diseases: Executive summary of the 2017 ESCMID-ECMM-ERS guideline.' Clin. Microbiol. Infect. 2018, 24 (Suppl. 1), e1–e38 'Leptomeningeal aspergillosis causing internal carotid artery stenosis.' The British journal of radiology 52.616 (1979): 328-329. Aspergillosis of the brain and paranasal sinuses in immunocompromised patients: CT and MR imaging findings.' AJR. American journal of roentgenology 162.1 (1994): 155-159.

Appendix:

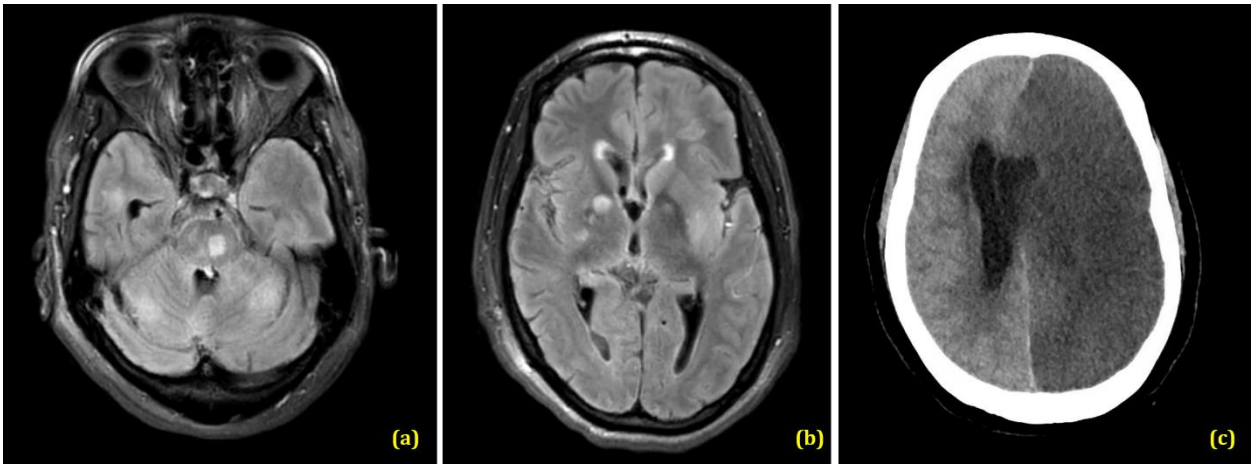

Image 1 (a) Brain MRI demonstrating pontine infarct from hospital day 5 (b) Brain MRI demonstrating basal ganglia and parietal infarctions from hospital day 5 (c) Brain CT notable for massive infarct and herniation from hospital day 7

Critical Care-57 Acquired Hemophilia A in the setting of Antiphospholipid antibody and Bleeding Gastric Ulcers

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Introduction: Acquired hemophilia (AH) is a rare disorder resulting from autoantibodies against clotting factors. It presents as severe bleeding in patients with a negative past medical and negative family history for hemorrhages. AH typically occurs in the elderly with half of patients having no identifiable trigger, while the other half have evidence of co-existing autoimmune disease, solid tumor, or certain medications.

Case Report: We present the case of a 68 year old female with past medical history significant for ulcerative colitis, aortic stenosis, renal insufficiency, and resection of a right retroperitoneal (RP) liposarcoma. She was admitted with tumor recurrence after surveillance CT imaging showed an enlarging heterogenous soft tissue mass in the RP space. She underwent an exploratory-laparotomy, right RP sarcoma resection, transverse colectomy, small bowel resection and inferior vena cava resection and reconstruction. She required a return to the operating room (OR) for evacuation of a 2L hematoma with no identified bleeding source. She continued to have continuous hemoglobin drop requiring multiple units of packed red blood cells (PRBC's) and bloody nasogastric tube (NGT) output. The Hematology and Gastroenterology services were consulted for persistently elevated PTT and bloody NGT output. Esophagogastroduodenoscopy (EGD) revealed stomach ulcerations. Hematologic workup was revealing for positive lupus anticoagulant and a diagnosis was made of antiphospholipid syndrome with concurrent upper gastric bleed.

Discussion: We present a post-surgical case of a patient with acquired hemophilia A in the setting of other potential causes of significant bleeding. The patient had a solid tumor which required resection and reconstruction of a central vein. She had known ulcerative colitis and EGD-confirmed gastric ulcers with positive anticardiolipin antibodies as an explanation for her elevated PTT. In this patient a diagnosis was only made after procedural control of bleeding was obtained and she developed cutaneous bleeding, inconsistent with lupus antibody. We believe this case illustrates the need for increased vigilance in patients with ongoing bleeding.

Reference(s): https://rarediseases.org/rare-diseases/acquired-hemophilia/ Exp Hematol Oncol; 6: 8. (2017)

Critical Care-58 Mycotic common iliac artery aneurysm with a communicating iliocaval fistula presenting with multi-organ system failure & septic shock

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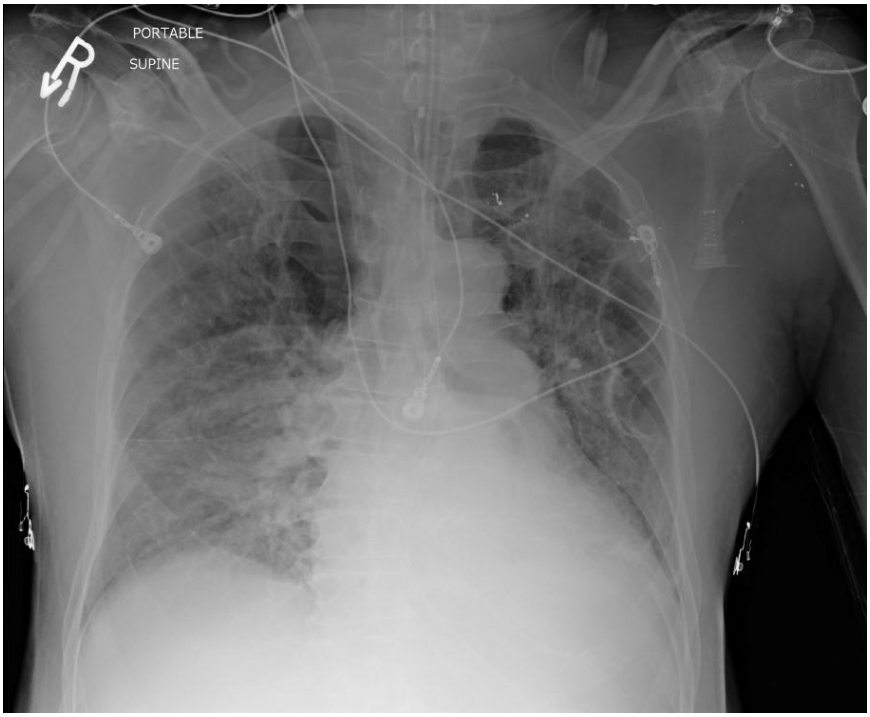
Introduction: Pathological communication between the common iliac artery and the vena cava account for approximately <1% of reported AV fistulous communications. Their formation results from ruptured aneurysms, blunt and penetrating abdominal trauma, genetic connective tissue disease or iatrogenic. Rapid diagnosis and definitive treatment of such fistulas is mandatory due to their high mortality. Therefore, we are presenting the diagnostic, surgical intervention and critical care management of an iliocaval fistula presenting with septic shock and multi-organ system failure.

Case Report: 71 year-old male with PMH of CKD, HTN and hypothyroidism presented to the ED with com-plaints of SOB and right-sided abdominal pain for one week. He exhibited AMS, respiratory distress requiring emergent intubation, severe hypotension with widened pulse pressure and electrolyte derangements. Examination revealed scleral icterus, diffuse non-peritoneal abdominal tenderness, abdominal bruit, unilateral lower extremity swelling and weak bilateral lower extremity pulses. Objective findings demonstrated signs of septic shock, heart failure with hepatic congestion, renal failure, and encephalopathy due to a fistula between a mycotic aneurysm in the right common iliac artery and the inferior vena cava. The patient underwent endovascular repair with aortobiiliac endoprosthesis grafts. In the intensive care unit, E. Coli induced septic shock was treated with systemic antibiotics, balanced fluid resuscitation, vasopressors and continuous renal replacement therapy. Resuscitation was guided by bedside TTE. Eventually, the patient was liberated from the ventilator, returned to baseline mental status, hepatic and renal function improved and was able to stop dialysis. He developed a type Ib endoleak adjacent to the left aortobiiliac graft limb which was repaired with graft extension into the external iliac artery and coil embolization of the internal iliac artery. Definite repair require open intervention which patient refused and elected for hospice care.

Discussion: Early diagnosis of large AV fistulas is important since prompt treatment increase the survival rate from 25% to 50%. The presentation of major vessel AV fistulas comprise a triad of signs: hypotension, pulsatile mass and heart failure. Heart failure is due to increased venous pressure and venous return yielding cardiac overload. Multi-organ failure can result from arterial insufficiency and passive congestion. Measures to manage the physiological consequences of these fistulas are ineffective without definitive repair of the shunt. Surgical intervention aims to repair arterial injury and obliteration of communication with the venous system. Traditionally, large vessel fistulas and aneurysms were repaired by open surgery with the known risk of profound blood loss, longer hospitalization and more frequent complications. Endovascular repair has demonstrated equivalently high success rates, but exposes the patient to an increased risk to reintervention.

Reference(s): Iliocaval arteriovenous fistula presenting with multiple organ failure. Australasian Radiology, 2006;50(4):381–5. Emergency endovascular repair of aortocaval fistula-a single center experience. Vascular and Endovascular Surgery, 2011; 45: 442-6. Endovascular stent-graft repair of major abdominal arteriovenous fistula: a systematic review. Journal Endovascular Therapy. 2009;16:514–523. Aortocaval and iliac arteriovenous fistulas: Recognition and treatment. Journal of Vascular Surgery. 1991, 13(2):253-64. Common iliac artery aneurysm: Expansion rate and results of open surgical and endovascular repair. Journal of Vascular Surgery. 2008; 47(6): 1203-1211.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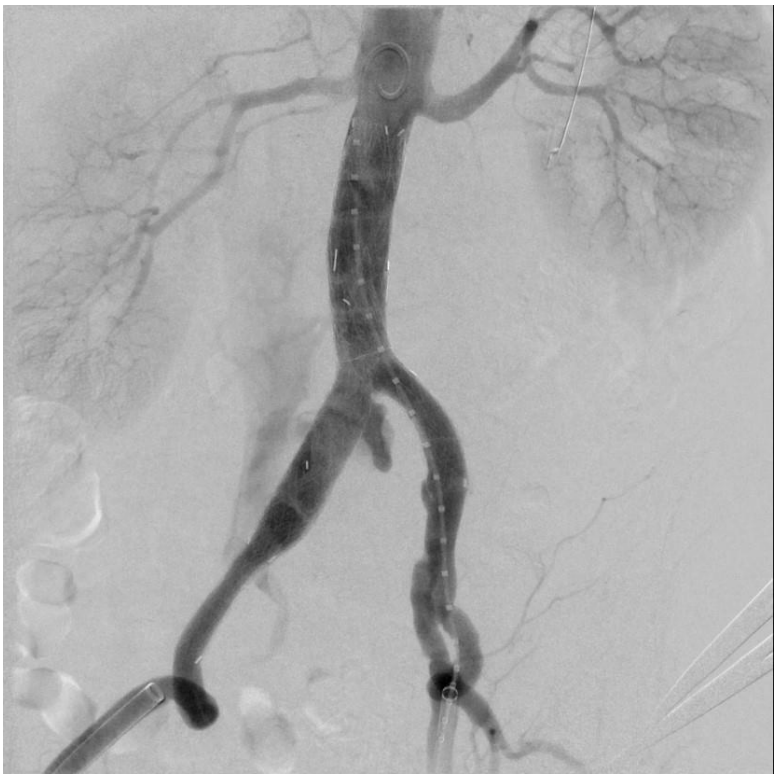

Critical Care-59 Empagliflozin-Induced Euglycemic Diabetic Ketoacidosis After Esophagectomy

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Introduction: Sodium-glucose cotransporter-2 (SGLT2) inhibitors, recently approved by FDA in 2013, have been widely prescribed to patients with type 2 diabetes. SGLT2 inhibitors disrupt renal glucose resorption, shifting body glucose homeostasis toward a starvation-like state [1], and therefore have been reported to induce severe ketoacidosis [2]. In contrast to classical diabetic ketoacidosis (DKA), prompt diagnosis can be challenging as patients typically remain euglycemic [3]. Here, we report a patient developing euglycemic DKA after esophagectomy due to preoperative empagliflozin exposure. The combination of widespread use of SGLT2 inhibitors and the risk of prolonged enteral nutrition interruption during the perioperative period makes euglycemic DKA an important differential diagnosis for anesthesiologists.

Case Report: A 72-year-old male with type 2 diabetes taking metformin and empagliflozin underwent an elective transhiatal esophagectomy due to his newly diagnosed esophageal adenocarcinoma. As per surgical protocol, the patient was kept strictly nil per os (NPO) for 2 days after surgery. On postoperative day (POD) 2, the patient became progressively hyperpneic. Arterial blood gas analysis revealed pH 7.32, PaCO2 16 mmHg, and bicarbonate 8.2 mmol/L. Serum biochemistry demonstrated Na 141 mEq/L and Cl 105 mEq/L revealing a high anion gap metabolic acidosis with respiratory compensation. Further workup revealed lactate 0.42 mmol/L, urine ketones 20 mg/dL, serum beta hydroxybutyric acid > 4.5 mmol/L, and a puzzlingly low serum glucose level of 76 mg/dL. Empagliflozin-induced euglycemic DKA was suspected; therefore, intravenous glucose infusion with insulin drip was started. Within 12 hours of treatment initiation, serum glucose increased to 180 mg/dL and metabolic acidosis resolved - pH 7.49, PaCO2 36 mmHg, and bicarbonate 27.8 mmol/L. Enteral nutrition was reestablished on POD 4 and patient was transitioned to an insulin sliding scale. The patient was discharged on POD 13 without any recurrence of ketoacidosis or residual acid-base disorders.

Discussion: Patients taking long-acting SGLT2 inhibitors are predisposed to euglycemic DKA during the perioperative period. Treatment with an insulin infusion with glucose supplementation is required to restore acid-base and glucose homeostasis along with discontinuation of the drug for appropriate management. Clinical vigilance in high risk patients is required for early diagnosis and treatment, as euglycemic status does not exclude the diagnosis of SGLT2-inhibitor-induced ketoacidosis.

Reference(s): Int J Endocrinol, 2018. 2018: p. 7074868. Diabetologia, 2017. 60(8): p. 1385-1389. Diabetes Care, 2015. 38(9): p. 1638-42.

Critical Care-60 Central Retinal Artery Occlusion Post-Cardiac Surgery

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[1]University Hospitals Cleveland Medical Center, Cleveland, OH, [2]University Hospitals Cleveland Medical Center, Cleveland , OH

Introduction: The ophthalmic artery (OA) is the first intracranial branch of internal carotid artery (ICA). It arises soon after ICA emerges from cavernous sinus, follows a short intracranial course, transverses the optic canal, and enters the orbit. There it ramifies in a complex pattern and vascularizes the eyeball and periophthalmic tissues. Most critical branch of OA is central retinal artery (CRA) that vascularizes retina and is of critical importance for vision (Michalinos, et al 2015). Central retinal artery occlusion (CRAO) is an ocular emergency that frequently leads to devastating monocular vision loss. The estimated incidence of CRAO following cardiac surgery is .077% (Calway, et al 2016). Patients undergoing coronary artery bypass grafting are at highest risk (Calway, et al). Acute interventions in non-arteritic CRAO have shown no benefit and minimizing stroke risk factors remains mainstay of therapy. Risk factors include diabetes, hyperlipidemia, hypercoagulable state, carotid artery stenosis, hypertension, anemia, smoking, coronary artery disease, and atrial fibrillation. It occurs most frequently in white males aged 61-70. We present a 66 year old male undergoing coronary artery bypass grafting who experienced CRAO.

Case Report: A 66 year old white male with past medical history of hypertension, hyperlipidemia, smoker (>20 pack year), and remote myocardial infarction presented with exertional chest pain and underwent urgent, on-pump coronary artery bypass grafting x 3 with left anterior descending endarterectomy. The operative course was significant for cardiopulmonary bypass time of 177 minutes, aortic cross clamp time of 152 minutes, and 500ml estimated blood loss. Intra-operative echo showed normal biventricular and valve function. The postoperative course was complicated by hypotension requiring vasopressor support and a notable 20-30mmHG difference in blood pressure (Left arm < Right arm) concerning for left subclavian stenosis. An angiogram was performed and revealed severe atherosclerotic disease with 90% subclavian stenosis with complete resolution following endovascular stent. He was extubated on his initial day of surgery and reported left eye blindness without any other neurological deficits. He denied floaters, photopsia, or seeing a black curtain. Ophthalmology was consulted and performed a comprehensive exam. The fundus exam had a cherry spot on the macula, with whitening of the central artery, completely white optic nerve and 'boxcarring' along the arterioles of the left eye. There were no signs of emboli on the retina exam, however likely presence of emboli proximal to the vessels branching out of the optic nerve. Other imaging performed included CT/MRI of brain that was negative and a carotid ultrasound showing 70% occlusion of left carotid artery.

Discussion: Our case demonstrates many of the known risk factors for CRAO including coronary artery bypass surgery, carotid artery disease, hypertension, hyperlipidemia, and age. We further show the typical course for CRAO, that is, the initial presenting visual loss, which is typically profound, is the end long-term result. In 15% of patients the inner retina and optic nerve may be supplied by the cilioretinal artery, which allows for preservation of some vision. Treatment is essentially supportive and includes risk factor modification. In a small portion of patients with CRAO due to arteritis, steroids may be indicated acutely. Regardless, given the infrequent occurrence and devastating prognosis, consultation with ophthalmology is clearly indicated.

Reference(s): Michalinos, Adamantios, et al. “Anatomy of the Ophthalmic Artery: A Review Concerning Its Modern Surgical and Clinical Applications.” Anatomy Research International, vol. 2015, Sept. 2015, pp. 1–8., doi:10.1155/2015/591961.
Calway, Tyler, et al. “Perioperative Retinal Artery Occlusion.” Ophthalmology, vol. 124, no. 2, 2017, pp. 189–196., doi:10.1016/j.ophtha.2016.10.025.

Critical Care-61 A Case of Diabetes Insipidus induced by Vasopressin-withdrawal and Dexmedetomidine leading to Torsades de Pointes in the Surgical Intensive Care Unit

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Introduction: Dexmedetomidine is a central acting alpha-2 agonist which is commonly used as a sedative during surgery and in the intensive care unit. There is growing evidence that the use of dexmedetomidine as a sedative agent is associated, albeit rarely, with the development of polyuria. Infusions of vasopressin for the management of hypotension are similarly commonplace, and the abrupt withdrawal of this medication is also linked to the development of polyuria. We present a case of polyuria consistent with central diabetes insipidus induced by the combination of dexmedetomidine infusion and vasopressin-withdrawal resulting in profound electrolyte disturbances and subsequent ventricular arrhythmia.

Case Report: This patient is a 32 year old male with no significant past medical history who was transferred from an outside hospital to our Surgical ICU with extensive burns from ignited alcohol. The patient sustained over 50% TBSA superficial and deep 2nd degree burns with scattered 3rd degree involvement. The patient required intubation and mechanical ventilation to facilitate adequate analgosedation for routine burn care, which was maintained initially by infusions of propofol and fentanyl. Several days after admission, the patient developed septic shock secondary to pseudomonas infection which was isolated from both blood and wound cultures. After volume resuscitation, blood pressure support targeting a MAP >65 was initiated via infusions of norepinephrine, epinephrine, and vasopressin. With antibiotic therapy, the patient recovered from his septic shock and vasopressors were able to be weaned in a stepwise fashion, eventually to vasopressin only at 0.02 u/minute. As the patient recovered, he was noted to develop hypertriglyceridemia which was attributed to propofol. In this setting, a dexmedetomidine infusion was initiated, and propofol was discontinued. Immediately after the transition from propofol to dexmedetomidine, the patient's blood pressure increased to the point that vasopressin could be discontinued. Within an hour, the patient's urine output began to steadily rise from 100mL/hr to a maximum of 1300mL/hr (6.2L of urine output was recorded over a period of 6 hours). Serum sodium was noted to increase from 135 to 146 mmol/L and serum potassium trended from 3.4 to 2.6 mmol/L. Further urine and serum studies were sent to characterize the patient's increasing diuresis. 12 hours after onset of polyuria, the patient developed polymorphic ventricular tachycardia with a twisting QRS morphology consistent with Torsades de points. The patient had a detectable pulse at this time. An intravenous bolus of magnesium was given with return of a sinus rhythm. 12 lead ECG revealed multiple abnormalities including prolonged QT interval, diffuse ST depressions, and U-Waves consistent with hypokalemia. Repeat metabolic panel was obtained which revealed serum sodium had risen to 154 mmol/L and serum potassium was below the limit of detection. Serum osmolality resulted at 318 mOsm/kg and urine osmolality at 278 mOsm/kg, consistent with a diagnosis of diabetes insipidus. Dexmedetomidine infusion was discontinued and midazolam used for sedation subsequently. Desmopressin (DDAVP) was administered intravenously, along with D5W and aggressive replacement of potassium and magnesium. Over the next 24 hours the patient's urine output downtrended to 100 mL/hr and serum sodium and potassium returned to the normal range. 12 lead ECG demonstrated resolution of previous abnormalities. Desmopressin was discontinued after 48 hours and the patient had no further episodes of polyuria.

Discussion: The discontinuation of a continuous infusion of vasopressin, and the use of dexmedetomidine, have both been associated with the development of marked polyuria. Dexmedetomidine is theorized to inhibit the endogenous release of ADH, which may be masked by an infusion of vasopressin when used simultaneously. Clinicians should be aware of these rare adverse effects and remain vigilant for changes in urine output and serum electrolytes when utilizing these medications.

Reference(s): Pratt A, Aboudara M, Lung L. Polyuria Related to Dexmedetomidine, Anesthesia & Analgesia: 2013 - Volume 117 p 150–152 Peskey, Candy S. et al. Vasopressin withdrawal associated with massive polyuria: The Journal of Thoracic and Cardiovascular Surgery, Volume 138, p 491 - 492

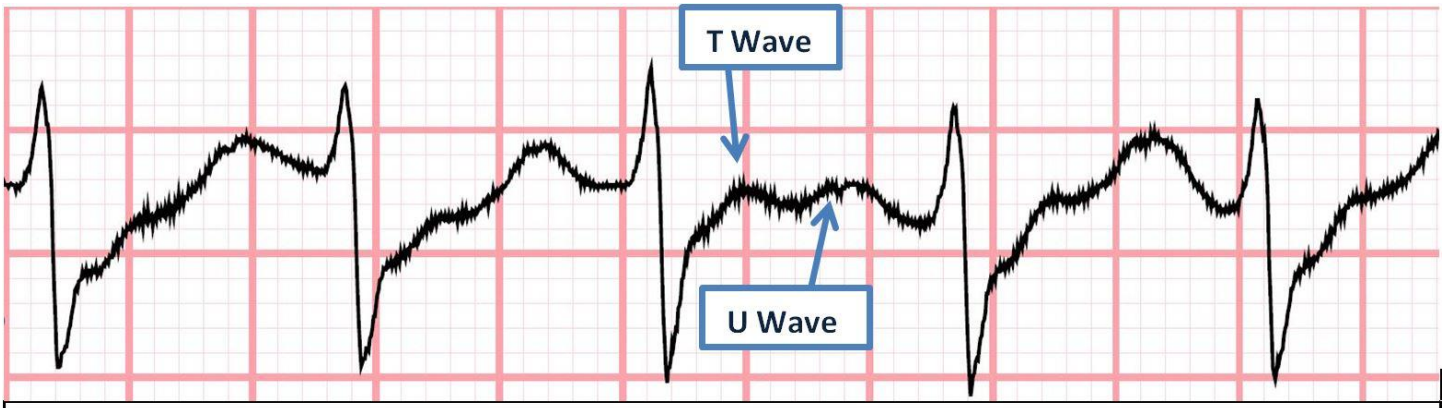
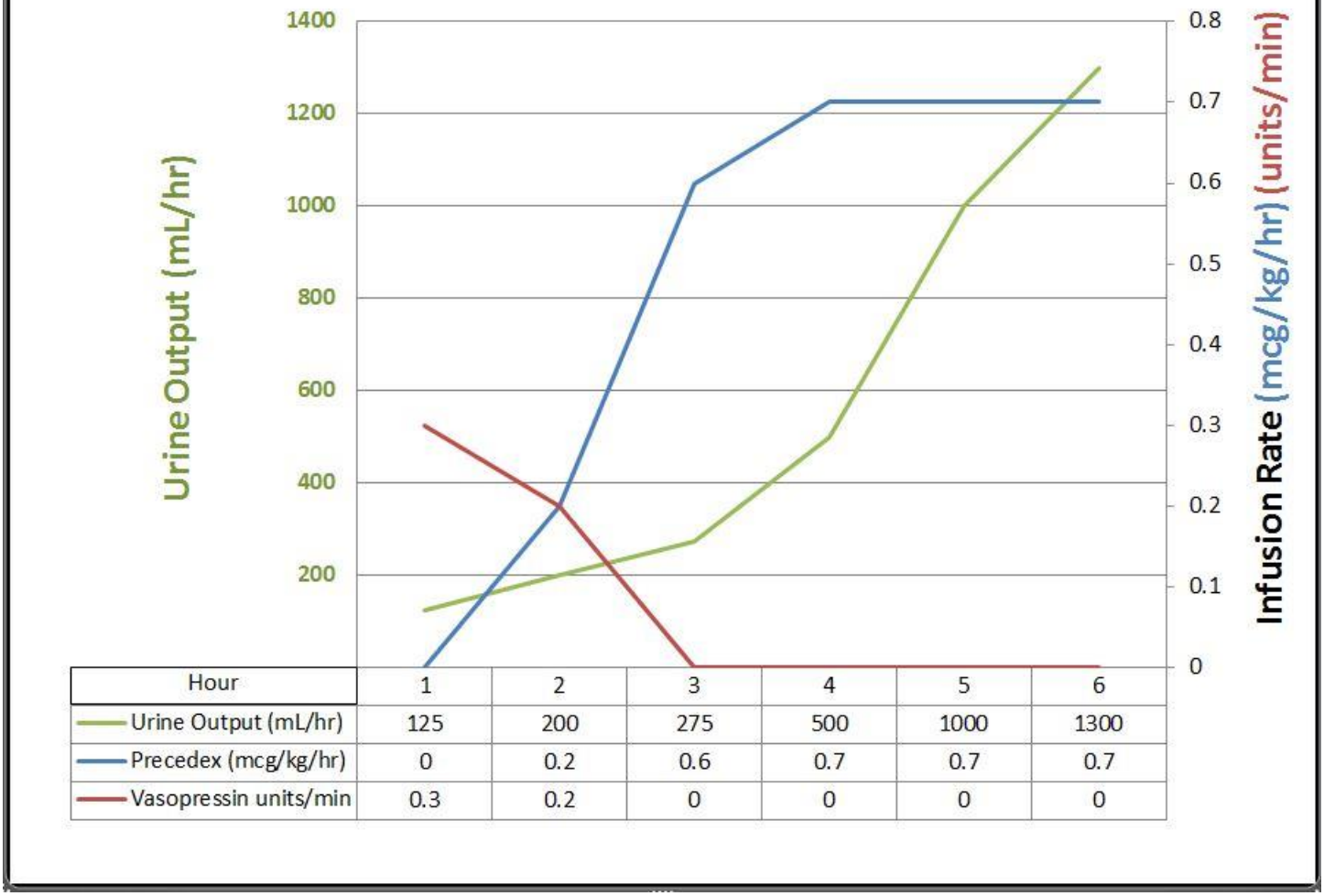


Image 1. Patient's ECG after recovery from Torsades de pointes

Figure 1. Hourly Urine Output Over Infusion Rates



Hour	1	2	3	4	5	6
Urine Output (mL/hr)	125	200	275	500	1000	1300
Precedex (mcg/kg/hr)	0	0.2	0.6	0.7	0.7	0.7
Vasopressin units/min	0.3	0.2	0	0	0	0

Critical Care-62 Use of Angiotensin II for Treatment of Acute Vasoplegia in the Setting of Angiotensin Converting Enzyme Inhibition - 3548

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Introduction: Current cost and risks of intravenous angiotensin II in many settings limits its use to primarily a last-line vasopressor for distributive shock, despite initial and primary studies using it as a second-line agent. Furthermore, our institutional experience has demonstrated significantly higher mortality correlated with the use of intravenous angiotensin II than quoted in the primary literature. The following case suggests that a subset of the our patient population, those on angiotensin converting enzyme inhibitors, may have a dramatically more appropriate response to this medication and thereby an improved outcome, and that patients with chronic exposure to ACE-Is may have a increased vasopressor requirement in the setting of acute distributive shock.

Case Report: This is a report of a 68 year-old male with a history of COPD on chronic steroid therapy, multivessel coronary artery disease, diabetes, and heart failure with reduced ejection fraction (EF 46%), who developed profound vasoplegia following a single dose of lisinopril, a previously but rarely described complication of ACE inhibitor therapy. The patient initially presented to an outside hospital with COPD exacerbation. His hospital course was complicated by NSTEMI and the patient was transferred to our facility for evaluation for CABG. He was deemed not a surgical candidate and was thereby being considered for percutaneous coronary intervention. As part of the treatment for the COPD exacerbation and possible superimposed pneumonia, he was converted from levofloxacin to cefepime and vancomycin on hospital day 0. On hospital day 8, the patient had increasing tachypnea, and mental status alteration prompting eventual intubation and admission to the ICU. Chest xray at the time of admission to the ICU lacked focal consolidation and respiratory and blood cultures were negative. Four hours following admission to the ICU, the patient became abruptly hypotensive with mottling of the upper extremities, despite increasing doses of norepinephrine, vasopressin, and epinephrine. During this time, the patient remained non acidemic, had no lactatemia, and exhibited only a mild increase in procalcitonin. Clinical evidence suggested that this was due to distributive shock. Stress dose glucocorticoids were administered and cefepime was escalated to meropenem, with no immediate response. Four hours after the initial onset of hypotension, angiotensin II infusion was administered. Within 30 minutes, norepinephrine was weaned off and all other vasopressors and inotropes were weaned off over the next 16 hours, extubated ICU day 3, and discharged following successful PCI. Upon chart review after the event, the only new medication change was a single dose of lisinopril given 6 hour prior to the event, raising concern for precipitation a profound angiotensin II deficiency, remedied by the administration of intravenous angiotensin II, suggesting a potential novel use of angiotensin II in patients with pharmacologic modification of the renin-angiotensin-aldosterone pathway.

Discussion: In this case, the patient appears to have developed a severe distributive shock state, initiated by a single dose of lisinopril in a naive patient. The same appears to have happened a patient in France as reported by Desachy et al. in 2000. This type of reaction appears to be fundamentally different that the well-known angioedema complication, and based on the lack of case reports and available data in the literature, significantly more rare. As a result, data to direct treatment of this complication is limited, but based on a case report by carpenter et al. in 2019, and the case in this example, even modest doses of intravenous angiotensin II may provide significant improvements in patient hemodynamics. This certainly questions the mechanism of such a reaction and its relation to angioedema, and the contribution of chronic ACE-I therapy to vasoplegia and vasopressor requirements in patient with distributive shock. Though this requires significantly more study, this may provide an important predictive tool for determining the likelyhood that a patient will respond well to the initiation of angiotensin II. This may significantly help to better utilize this medication at the current price-point and minimize risk generation with the side-effect profile.

Reference(s): Presse Medicale. 2000, 29(13):696-698
Journal of Emergency Medicine. 2019 Sep;57(3):339-344

Critical Care-63 Amiodarone Induced Fulminant Hepatic Failure: A Case Report

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Introduction: Introduction: Amiodarone is an anti-arrhythmic agent frequently used in the critical care setting despite its many known toxicities including hepatotoxicity. We present a case report describing a serious adverse event associated with the use of amiodarone for the treatment of atrial fibrillation which resulted in fulminant hepatic failure and the patient's demise.

Case Report: Medically challenging Case: A patient with a history of paroxysmal atrial fibrillation and grade 2 diastolic dysfunction presented with septic shock due to ischemic colitis and C. difficile colitis, status post total abdominal colectomy. During this episode of septic shock, the patient required norepinephrine, vasopressin, epinephrine, angiotensin II, and phenylephrine infusions to maintain her mean arterial pressure at 60 mmHg. After achieving source control, she was quickly weaned to norepinephrine and vasopressin on post-operative day 0. In the intensive care unit on post-operative day 2, she continued to be hemodynamically unstable requiring norepinephrine and vasopressin infusions, and she was in atrial fibrillation with rapid ventricular response. Liver enzymes were trended post-operatively revealing a mild ischemic hepatic insult thought to be due to relative hypo-perfusion during the episode of septic shock. Therefore, on post-operative day 2 the patient was given an amiodarone bolus of 150mg and an amiodarone infusion at 1mg/hour was initiated to attempt to restore sinus rhythm. This amiodarone bolus resulted in weaning of both norepinephrine and vasopressin and immediate return to sinus rhythm. The following morning, the patient's liver enzymes were noted to rise precipitously, and amiodarone was discontinued. The patient received a total of 170mg over a period of approximately 20 hours. This toxicity was classified as an acute hepatocellular injury [1]. A right upper quadrant ultrasound performed after discontinuation of amiodarone revealed hepatic parenchymal disease with a patent portal vein and without cholelithiasis or acute cholecystitis. The patient received N-acetylcysteine. Despite discontinuation of amiodarone, the patient's liver enzymes continued to uptrend and she developed a severe lactic acidosis and fulminant liver failure which resulted in her death on post-operative day 4.

Discussion: Amiodarone is known to have hepatotoxic side-effects. While asymptomatic transaminase elevations occur in 25% of patients, symptomatic hepatitis is rare and thought to occur in 1-3% of patients receiving amiodarone and generally associated with high dose or chronic therapy [2]. We describe a case in which a relatively low dose of intravenous amiodarone resulted in acute fulminant hepatic failure and death despite prompt discontinuation of the drug. Acute liver damage associated with amiodarone exposure has been hypothesized to occur due to multiple mechanisms: hypersensitivity, increased hepatic susceptibility to toxicity due to pre-existing liver impairment, immune mediated centrilobular necrosis, or polysorbate 80, a carrier in the IV formulation. Discontinuation of amiodarone after discovery of elevated liver enzymes have been reported in multiple studies to result in recovery [3,4]. In this case, despite discontinuation within 20 hours after administration and treatment with N-Acetyl-cysteine, the hepatic toxicity was irreversible. We suggest that this case of fulminant hepatic failure after amiodarone treatment could be due to any of the above mechanisms and encourage close monitoring of transaminases and lactate especially in patients with pre-existing hepatic impairment.

Reference(s):

1. Benichou, C. (1990). 'Criteria of drug-induced liver disorders. Report of an international consensus meeting.' Journal of hepatology 11(2): 272-276.

2. Lewis, J. H., et al. (1989). 'Amiodarone hepatotoxicity: prevalence and clinicopathologic correlations among 104 patients.' Hepatology 9(5): 679-685.

3. Tsuda, T., Tada, H., Tanaka, Y. et al. Amiodarone-induced reversible and irreversible hepatotoxicity: two case reports. J Med Case Reports 12, 95 (2018)

4. Paudel, R., et al. (2016). 'Acute liver and renal failure: a rare adverse effect exclusive to intravenous form of amiodarone.' Case reports in critical care 2016.

Table 1: Trend of Liver Enzymes, Total Bilirubin, and Lactate

	POD0	POD1	POD2	POD3	POD4
AST	343	602	517	4311	10930
ALT	148	251	322	1909	4532
Total Bilirubin	1.1	2.9	2.1	2.9	3.9
Lactate	13.4	1.8	1.5	13.7	14.5

Critical Care-64 NO ECMO, NO PROBLEM! IMPELLA RP FOR RIGHT-SIDED HEART FAILURE IN THE SETTING OF MASSIVE PULMONARY EMBOLISM

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Introduction: This is a case of an elderly patient who suffered a provoked massive pulmonary embolism with acute right sided heart failure that underwent Impella RP placement for right ventricular (RV) support.

Case Report: An 82 year old female with past medical history of type 2 diabetes mellitus, hypertension, and chronic kidney disease stage 3 underwent left total knee arthroplasty 14 days prior to admission. She presented with an episode of syncope and collapse. She was found to be hypotensive in the emergency department which improved after intravenous fluid resuscitation. Her lab work demonstrated acute kidney injury, acute liver injury, lactic acidosis, thrombocytopenia, and elevated troponins. CT pulmonary angiography demonstrated large bilateral pulmonary emboli (PE) originating in the distal main pulmonary arteries, extending into segmental branches, with evidence of right heart strain. The PE was considered submassive at the time given lack of hemodynamic instability. She underwent bilateral ultrasound-assisted catheter-directed thrombolysis and was admitted to the intensive care unit. The next morning she became acutely hypotensive and developed a worsening acidosis. Bedside echocardiography showed worsening RV dilation. She was started on vasopressors, inotropes, and inhaled epoprostenol to treat cardiogenic shock secondary to RV failure. Despite optimal medical therapies she developed refractory cardiogenic shock. The patient was deemed to be a poor candidate for extracorporeal life support given her advanced age and multiorgan dysfunction. The decision was made to place an Impella RP, after which there was rapid hemodynamic improvement and significant decrease in vasopressor support. Impella RP support was weaned and removed on hospital day 4. Inotropic support and inhaled epoprostenol were gradually weaned over the next few days. Her hospital course was complicated by acute renal failure requiring hemodialysis, atrial fibrillation treated with amiodarone, clostridium difficile infection, and anemia requiring transfusion. She was discharged home on hospital day 15 on warfarin.

Discussion: Right heart failure resulting from massive and submassive PE is associated with significant morbidity and mortality. Management of severe right heart failure involves medical therapy and mechanical circulatory support (MCS). Impella RP is a percutaneous technique that provides temporary MCS to the right heart. The approved indications of Impella RP include right heart failure following LVAD implantation, myocardial infarction, heart transplant, and open cardiac surgery. The use of Impella RP for massive PE-associated RV failure is seldom reported in the literature. In this case, we used an Impella RP in conjunction with catheter-directed thrombolysis for a patient with a massive PE, which resulted in significant improvement of hemodynamic compromise related to RV failure. This case illustrates that the Impella RP is a viable alternative for patients who are not candidates for ECLS in the treatment of massive PE with associated right heart failure.

Reference(s): Shokr, M., Rashed, A., Mostafa, A., Mohamad, T., Schreiber, T., Elder, M., & Kaki, A. (2018). Impella RP Support and Catheter-Directed Thrombolysis to Treat Right Ventricular Failure Caused by Pulmonary Embolism in 2 Patients. Texas Heart Institute Journal, 45(3), 182-185. Youssef, A., Selle, A., Ende, G., & Ibrahim, K. (2018). The successful use of the Impella RP after a long cardiopulmonary resuscitation and systemic thrombolytic therapy in a patient with a fulminant pulmonary embolism: the first case report. European Heart Journal-Case Reports, 2(1), ytx023. Kumar Bhatia, N., Dickert, N. W., Samady, H., & Babaliaros, V. (2017). The use of hemodynamic support in massive pulmonary embolism. Catheterization and Cardiovascular Interventions, 90(3), 516-520.

Critical Care-65 Delayed Presentation of Toxoplasmic Encephalitis in a Renal Transplant Patient

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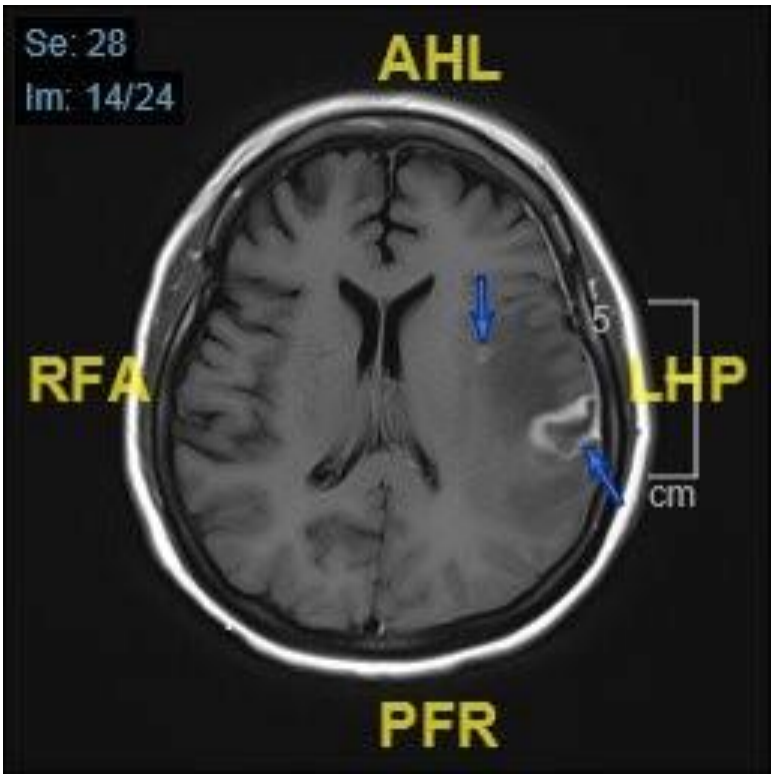
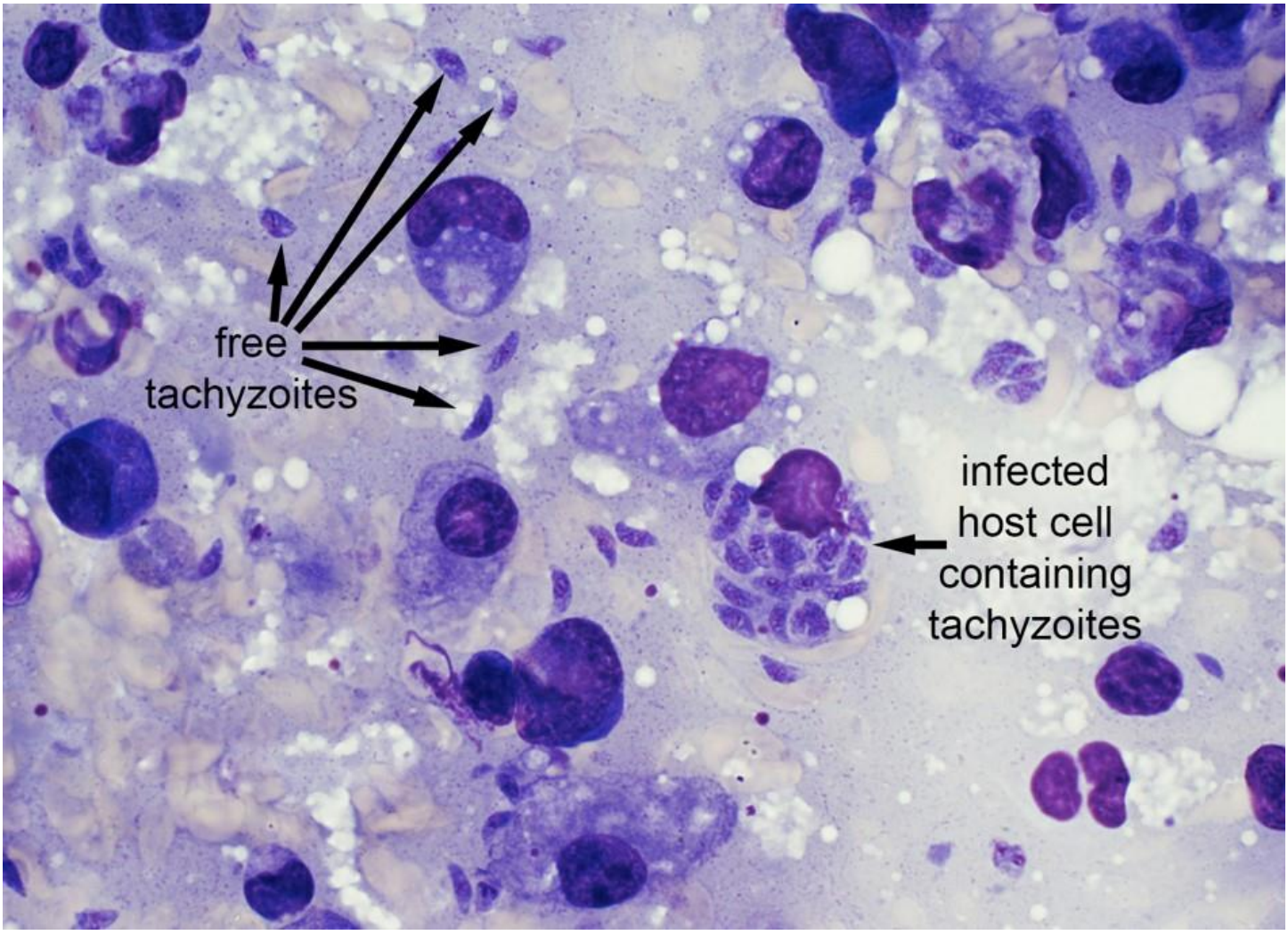
Introduction: Toxoplasmosis, an infection caused by the intracellular parasite Toxoplasmosa gondii, is widely prevalent in the US with 11% of persons aged 6 to 49 reportedly seropositive. Clinical manifestations are variable with immunocompetent hosts remaining asymptomatic with primary infection. However, immunocompromised individuals may develop a reactivation syndrome commonly involving the CNS. As transplant individuals' post-operative lifespan continues to lengthen, the current case study seeks to provide novel insight for the timeline for Toxoplasmosis encephalitis in this vulnerable group.

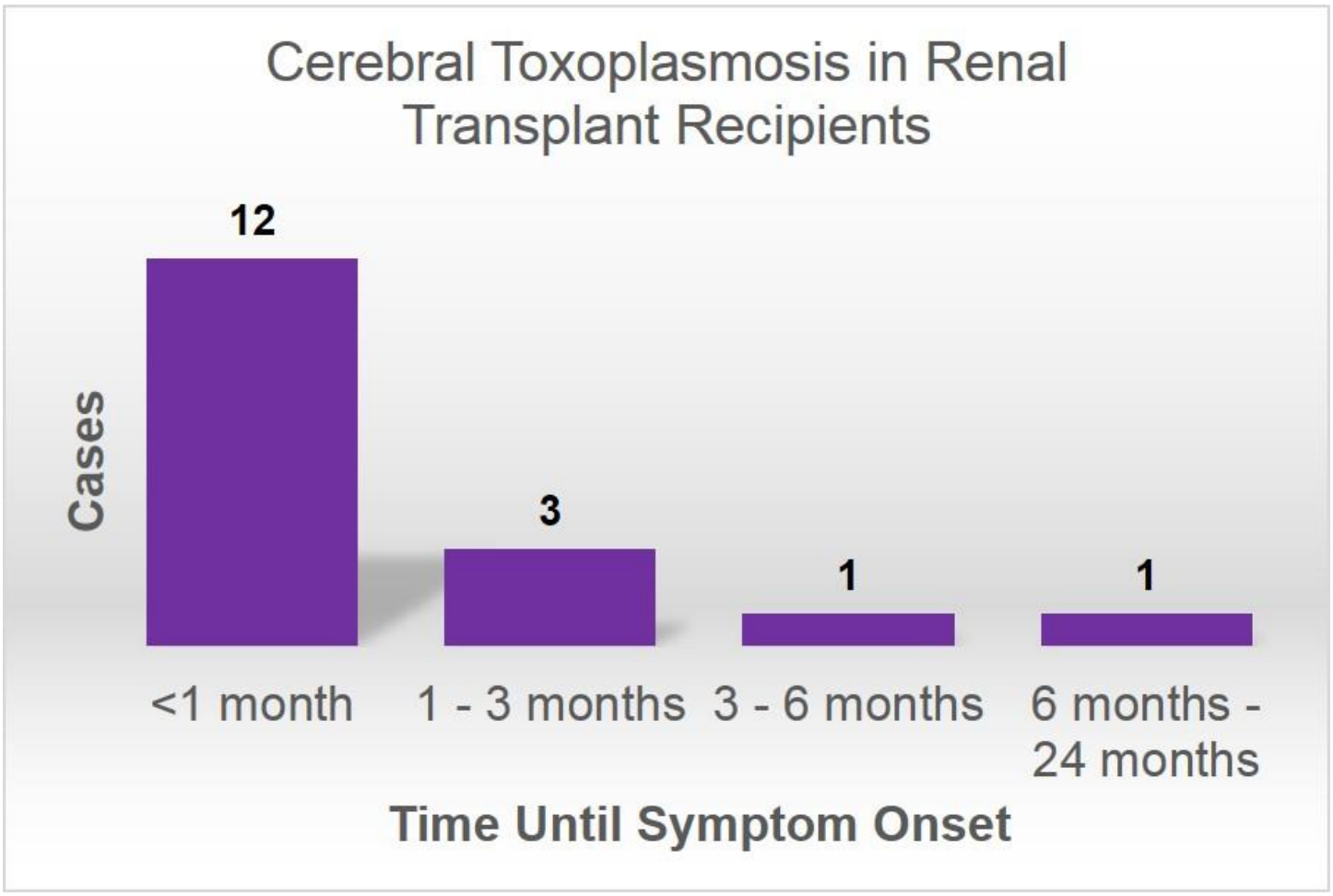
Case Report: A 62 year old female with a past medical history of end-stage renal disease status-post right kidney transplant in 2010 on immunosuppressive therapy presented in 2019 with a course of intermittent word-finding difficulty and right facial droop of one month duration. A CT Head showed left frontal cerebral edema concerning for a mass, and physical exam demonstrated expressive aphasia, right sided facial droop, and right upper extremity weakness. An MRI Brain revealed enhancing lesions in the left frontal and bilateral parietal lobes with surrounding vasogenic edema, raising concern for metastases. The patient's home immunosuppressants were discontinued, and dexamethasone was initiated for cerebral edema. After discussion with the patient, consent was granted for brain biopsy and resection of the left frontal lesion. Pathology demonstrated structures consistent with Toxoplasmosis tachyzoites, and the diagnosis was later confirmed with immunostaining. A treatment regimen of Sulfadiazine and Pyrimethamine was initiated with marked improvement of patient's aphasia, facial droop, and pronator drift within 48 hours.

Discussion: Disseminated Toxoplasmosis in immunocompromised patients oftentimes presents with non-specific signs and symptoms, requiring a high degree of clinical suspicion for diagnosis. Symptoms include fever, neurological deficits, and pneumonia. Timely diagnosis is essential, as mortality in renal transplant recipients reaches 65% when left untreated. In renal transplant recipients, the current literature reports that 70% of cases presented within 3 months of transplant with the latest case presenting 21 months after transplant, correlating to the highest levels of immunosuppression. Our patient's presentation of Toxoplasmic Encephalitis 9 years after transplantation and immunosuppresive therapy offers an important nuance that disseminated toxoplasmosis with CNS involvement can occur over a much longer timeframe than previously reported, and should be included in the differential diagnosis of post-transplant patients with CNS lesions.

Reference(s): Transplant International, Volume 24, Pages e6-12, 2011. Clinical Infectious Diseases, Volume 24, Pages 676–683, 1997.


Se: 28
Im: 14/24
AHL
RFA
LHP
PFR
5
cm


free
tachyzoites
infected
host cell
containing
tachyzoites


Cerebral Toxoplasmosis in Renal Transplant Recipients
Cases
12
3
1
1
<1 month
1 - 3 months
3 - 6 months
6 months - 24 months
Time Until Symptom Onset

Critical Care-66 Stroke Secondary to Retrograde Cerebral Venous Air Embolism from Continuous Renal Replacement Hemodialysis Catheter

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[1]University of Michigan, Ann Arbor, MI

Introduction: We describe a unique case of ischemic stroke from retrograde central venous air embolism (CVAE) in the context of hemodialysis (HD) catheter malfunction while undergoing continuous renal replacement therapy (CRRT).

Case Report: A 69-year-old male with history of hypertension, hepatitis C, and former smoking was admitted for surgical repair of abdominal aortic aneurysm. His immediate postoperative course was complicated by colonic ischemia requiring partial colectomy, sepsis, and renal failure requiring CRRT. On hospital day 24, patient became acutely tachypneic, tachycardic, and hypotensive with altered mental status. Air was noted to be in the access limb of the HD catheter, but not in return limb. The HD line was clamped and vital signs improved with hemodynamic support and supplemental oxygen. Patient exhibited neurologic deficits concerning for right middle cerebral artery (MCA) syndrome with right sided gaze preference and both sensory and motor deficits in left arm. Non-contrast head computed tomography (NCCT) was significant for hypoattenuation overlying the cortical sulci in the right hemisphere concerning for intracranial air (see image). CT angiography (CTA) showed bilateral saccular aneurysms of internal carotid arteries and non-occlusive thrombus in bilateral carotid bulbs and non-occlusive thrombus in left cervical internal jugular vein. No air was seen in arterial circulation and no overt occlusion was seen in distal ICA or proximal MCA. Further studies indicated absence of right-to-left shunt: chest CTA showed no arterio-venous malformation or evidence of air embolism and TTE bubble study was negative for any structural abnormalities. Positioning of HD catheter in RIJ was confirmed with imaging and blood gas analysis. Repeat NCCT of head several hours later showed further ischemic evolution in initial distribution without evidence of air. The patient was supported conservatively for remainder of hospitalization and experienced marginal neurologic improvement prior to discharge to long term care facility. With regards to the etiology of our patient's CVAE, it is clear the HD line malfunctioned to allow air into circuit. The source of air is uncertain, but could include an iatrogenic cause such as direct introduction or CRRT machine malfunction. CVAEs occur by retrograde ascension or paradoxical embolism from right to left shunts or by large introduction of air overwhelming pulmonary filter (1). In our case paradoxical embolism is unlikely given imaging showed no evidence of right-to-left shunt and no air was seen arterial circulation. The cerebral air was isolated to right anterior cerebral artery and MCA territories and aligns with the theory of retrograde venous air embolism introduced from RIJ HD catheter. Cerebral CVAEs related to HD catheters although uncommon have been described (2,3). However, to the best of our knowledge a stroke secondary to retrograde CVAE has not been described in the setting of CRRT.

Discussion: This was a medically challenging case of critically ill patient who suffered the rare event of a stroke caused by CVAE from HD catheter while on CRRT.

Reference(s): Wong, S., Kwaan, H., and T. Ing. 2017. 'Venous air embolism related to the use of central catheters revisited: with emphasis on dialysis catheters.' Clinical Kidney Journal 10 (6): 797–803. Hysell, Matthew K. 2015. “Cerebral Air Embolism After Hemodialysis.” The Journal of Emergency Medicine 49 (1): 27–28. Pellisé, A., X. Ustrell, V. Ruiz, and A. Guedea. 2012. “Retrograde Venous Cerebral Air Embolism as a Cause of Stroke.” Neurología 27 (2): 119–21.

Brain CT demonstrating air density in right frontal and parietal areas (white arrows).

Critical Care-67 A Curious Case of Complications from a Cough

Jessica Nelson[1]

[1]*Washington University School of Medicine in, St. Louis, WA*

Introduction: A 48-year-old female presented to the emergency department (ED) with a complaint of sore throat, cough, and fever. She was febrile at that time and noted to have tonsillar exudates. She was discharged home with antibiotics for presumed bacterial pharyngitis. Later the same day, her family called an ambulance to bring the patient in after she had been coughing and vomiting for several hours and had worsening fatigue and malaise. On ED arrival, the patient was poorly responsive and hypotensive. She was given 4 liters of IV fluids and started on a norepinephrine infusion. She received vancomycin and cefepime for antibiotic coverage. Her mental status significantly improved, her lactic acidosis cleared, and she was weaned off the norepinephrine. Suddenly, the patient started complaining of shortness of breath and her blood pressure again dropped. The norepinephrine infusion was restarted and she was given pushes of phenylephrine and epinephrine to maintain her blood pressure and facilitate emergent intubation. She received additional fluids and a vasopressin infusion was added. Bedside transthoracic echo showed poor cardiac filling but normal right and left ventricular function. Abdominal ultrasound showed possible free fluid in the left upper quadrant. The patient was given emergency blood products via a rapid infuser and the massive transfusion protocol was activated. The patient was brought emergently to CT scan. Shortly after this, repeat labs resulted that showed a hemoglobin drop from 8.9 g/dL to 3.9 g/dL. CT scan showed large-volume hemoperitoneum with active extravasation over the pancreatic head, likely secondary to a ruptured pseudoaneurysm possibly arising from the superior or inferior pancreaticoduodenal branches. The patient was taken emergently to the operating room (OR). She was also noted to be developing abdominal compartment syndrome with a tense abdomen and worsening acidemia.

Case Report: In the OR, branches of the gastroduodenal artery (GDA) and the right gastroepiploic artery were ligated. The patient was taken to the intensive care unit (ICU) with an open abdomen for further resuscitation. In the ICU, the patient had continued intra-abdominal bleeding with ongoing transfusion requirements. She was taken to interventional radiology and had a coil embolization of a branch vessel off the superior mesenteric artery (SMA) and proximal GDA in an attempt to exclude a pseudoaneurysm arising off the branch vessel of the SMA with likely collateral flow through the inferior pancreatoduodenal artery and GDA. The patient returned to the OR the same day for an exploratory laparotomy with abdominal washout. No active bleeding was noted at that time. Three days later, she was again taken to the OR for another exploratory laparotomy with mesenteric bleeding identified and controlled. Her abdomen was closed at that time and the patient did not have any further bleeding events. She was extubated shortly afterwards, though noted to have critical illness myopathy. The patient's ICU course was also complicated by acute kidney injury requiring renal replacement therapy, but her renal function recovered over the next few weeks. The etiology of the patient's pseudoaneurysm was unclear. However, the pseudoaneurysm likely ruptured in the setting of her upper respiratory illness due to coughing and retching. Vasculitis workup was negative. She was discharged to inpatient rehabilitation after a twenty-day hospital stay. Approximately four months after her initial ED presentation, the patient returned to work.

Discussion: Visceral arterial pseudoaneurysm are rare. They can be associated with trauma, recent surgery, infection, or inflammatory disease. These pseudoaneurysms also carry a high risk of rupture and thus a similarly elevated chance of mortality. This case represents the complexity of diagnosing and caring for these patients.

Critical Care-68 Acute liver injury precipitated by impending cardiac tamponade.

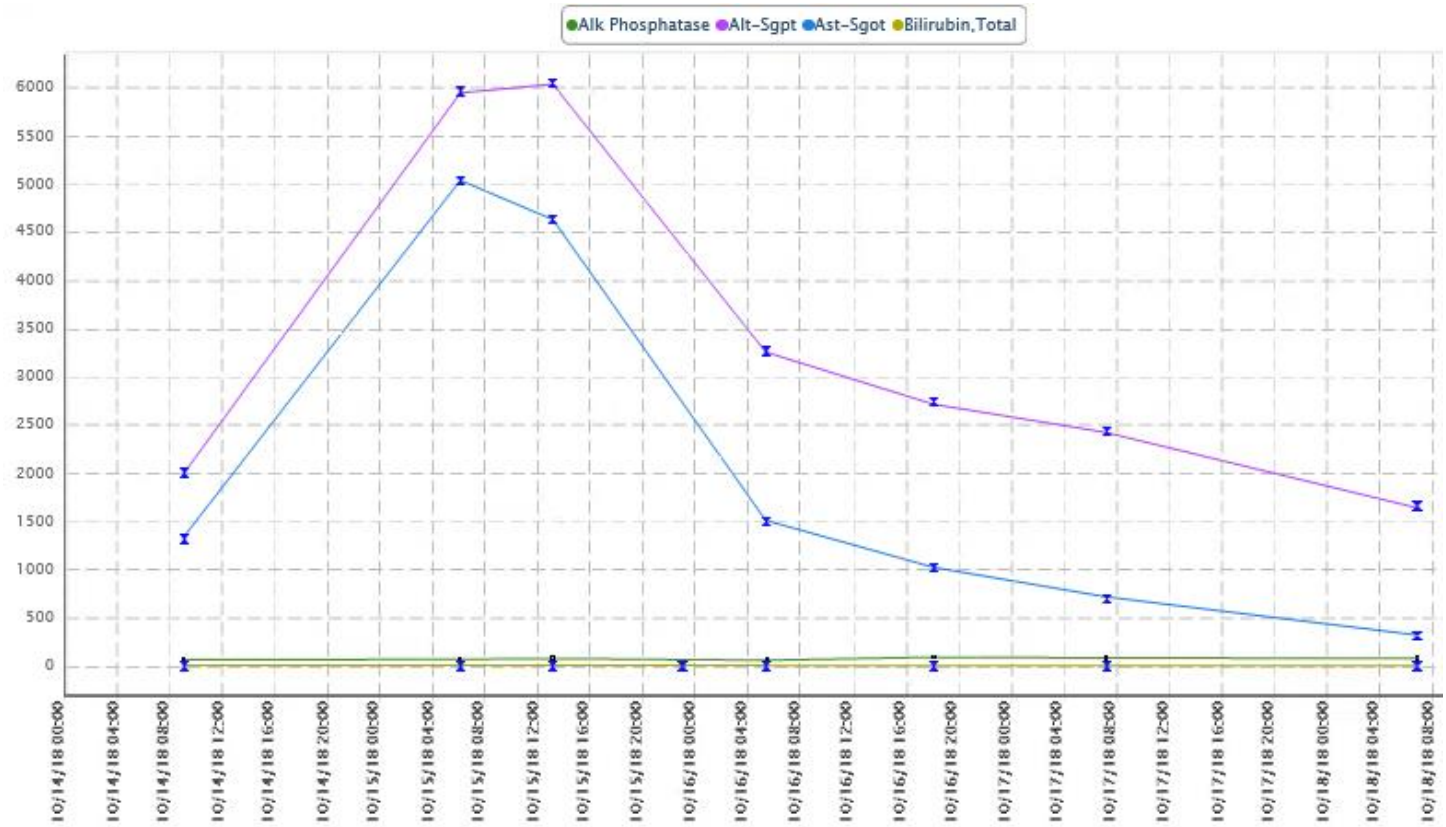
Max Masgudov[1], Abdalhai Alshoubi[1]

[1]Lewis Katz School of Medicine at Temple University, Philadelphia, PA

Introduction: The known etiologies of acute liver failure are viral (hepatitis A, B, C, CMV, Paramyxovirus, Dengue, Epstein Bar, HSV), ischemic (thrombosis), trauma related, drug related (Acetaminophen toxicity), acute fatty liver of pregnancy, HELLP syndrome, Toxin related hepatotoxicity (Amanita phalloides mushroom, Bacillus cereus, Cyanobacterium), and Organic solvents (Carbon tetrachloride). We are presenting a rare cause of ALI precipitated by impending cardiac tamponade. This type of failure typically occurring after a period of hypotension, however, cases may also occur without a hypotensive episode. In fact, up to half of the cases of 'hypoxic hepatitis' have been noted to occur in patients without shock. Serum transaminases during initial insult will climb up into thousands but typically will return to baseline level within 8-12 days after treating the source. Patients may present with symptoms suggestive of acute hepatitis, including nausea, vomiting, epigastric pain, and fatigue. In our patient the source of acute liver injury was identified and following definitive treatment resulted in completed resolution.

Case Report: 72 y/o F w/hx CAD, NIDDM, paroxysmal A-Fib on rivaroxaban, hypothyroidism presented to ED with pre-syncopal episodes associated with nausea, vomiting and generalized weakness and fatigue. Her vital signs were BP 123/75 mmHg, HR 65 beats/min, RR 20 cycles/min, oxygen saturation was 96% on 2 L nasal cannula, Temp 98.6 F. On the day of admission, she was noted to have acute liver failure where ALT 2013 and AST 1331, INR was 4.0, PT 38.8. The Ultrasonographic findings were suggestive of acute cholecystitis, however, HIDA scan and MRCP were negative. The MRCP accidentally picked up pericardial effusion. Follow with 2D echo confirmed large pericardial fluid collection with RA and RV diastolic collapse consisting with impending cardiac tamponade. Liver transaminases peaked at ALT 6059 and AST 4633, INR 5.1, PT 46.6. Emergent pericardiocentesis was performed. The pericardial fluid was bloody and found to have malignant cells of adenocarcinoma. The next day, LFTs started to trend downward. Follow-up CT scan of the chest revealed 2.3 mm right upper pulmonary nodule. The patient made full recovery and was discharged from the hospital. Later the patient was diagnosed with stage IV Non-small cell lung cancer, and was started on immunotherapy.

Discussion: This interesting case stresses the need for appropriate workup when patients present with acute liver injury. As the literature outlines, the most common causes of elevated aminotransferases to the thousands including trauma, acute viral hepatitis, toxins, and ischemic hepatitis which will often times be cardiac in origin due to myocardial infarction, heart failure, or tamponade as in this patient. Though this patient did not reveal the signs and symptoms of pericardial tamponade, it nonetheless was the cause of the presenting acute hepatic injury. Furthermore, as the review of the literature demonstrates, ischemic hepatitis is prevalent and associated with high mortality. overlooking the necessity for broad differential and early recognition can result in increased morbidity and mortality.


Alk Phosphatase
Alt-Sgpt
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Bilirubin,Total
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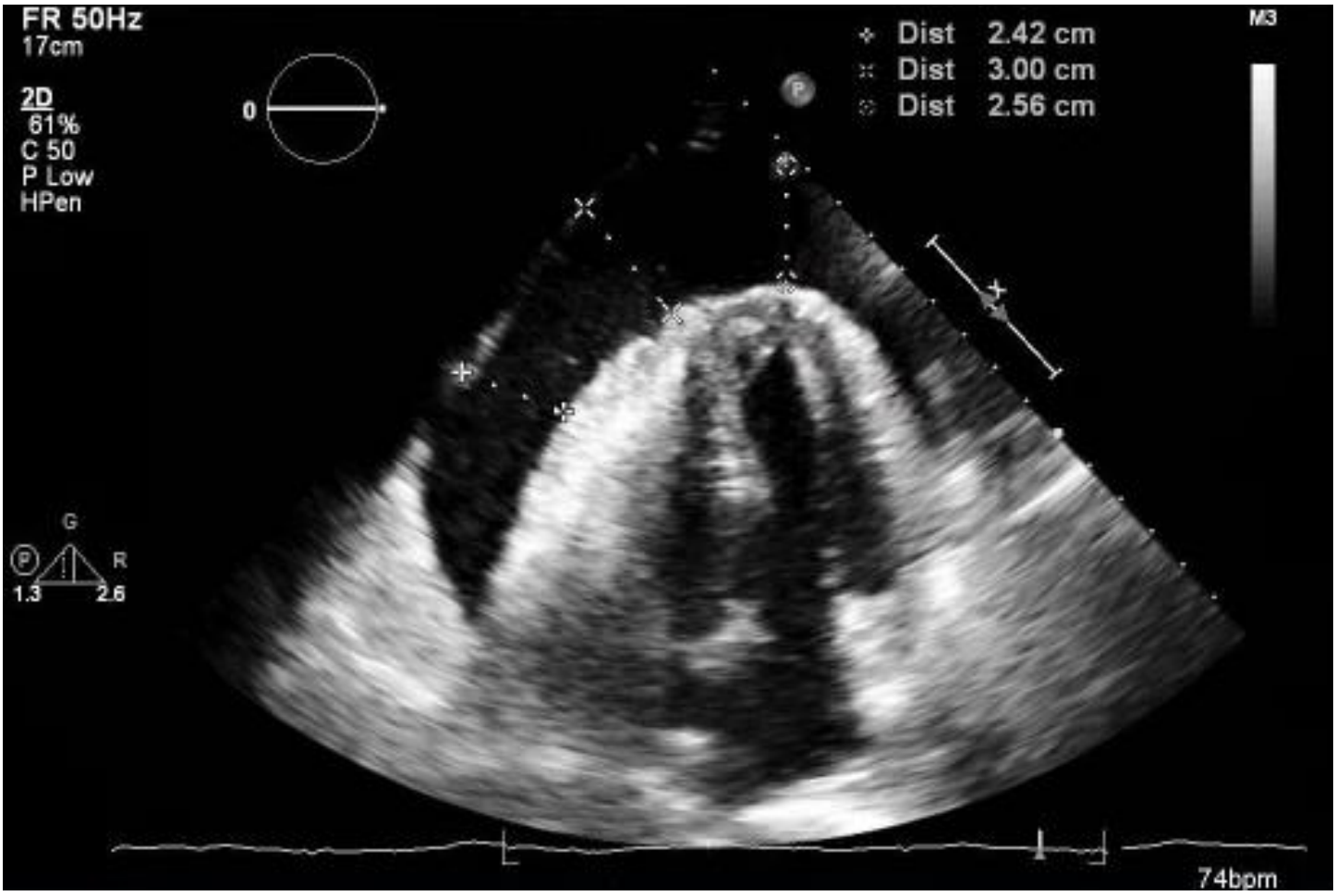

FR 50Hz
17cm
2D
61%
C 50
P Low
HPen
Dist 2.42 cm
Dist 3.00 cm
Dist 2.56 cm
M3
G
R
1.3
2.6
74bpm

Critical Care-69 Intraoperative transhepatic focused cardiac ultrasound: a novel rescue method to guide hemodynamic management.

Jennifer Cha[1], Aliaksei Pustavoitau[2], Nibras Bughrara[3]

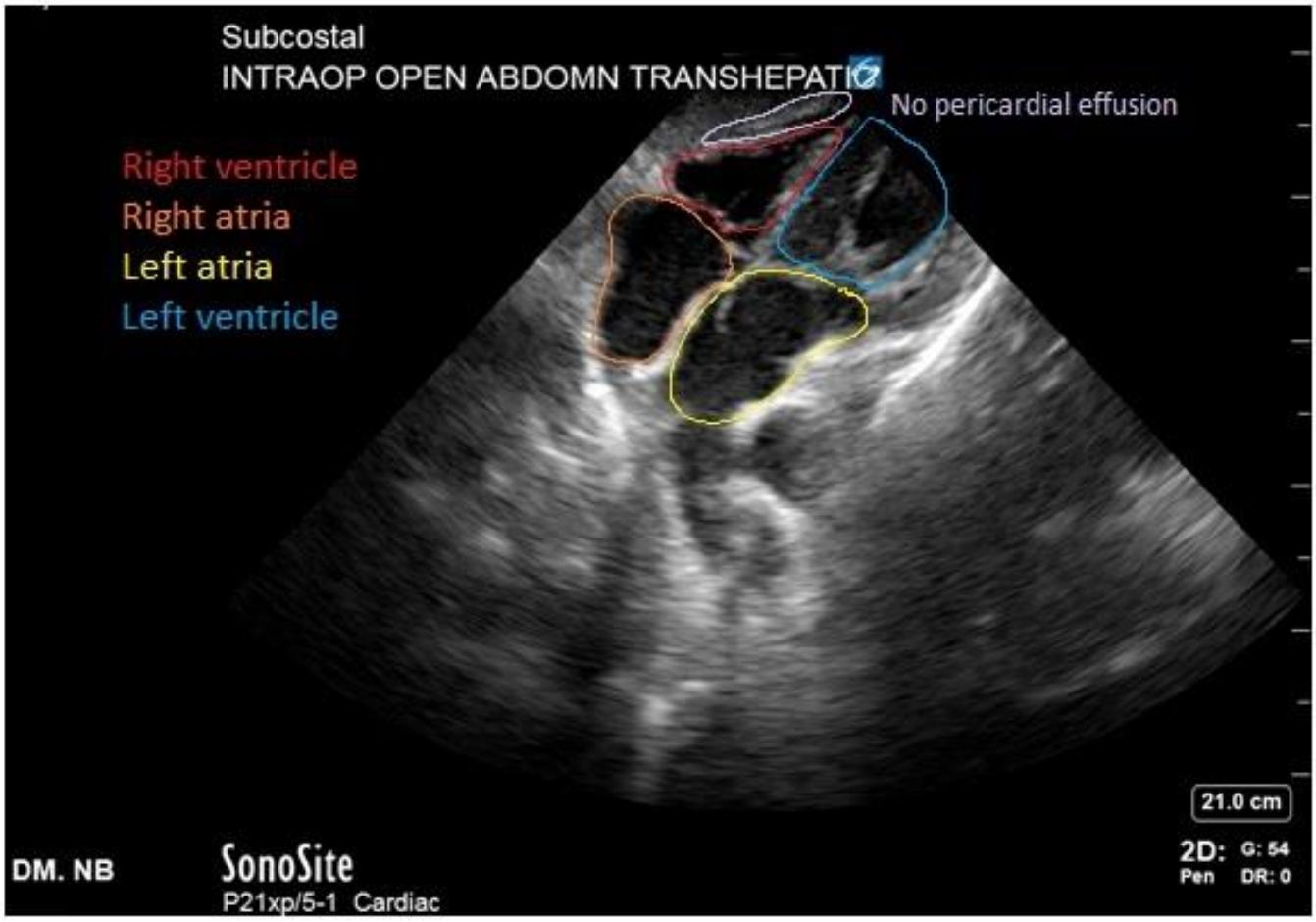
[1]Albany Medical College, Albany, United States of America, [2]Johns Hopkins University, Baltimore, MD, [3]Albany Medical College, Albany, NY

Introduction: Transthoracic echocardiography (TTE) is considered the standard in point-of-care assessment of various cardiac measures, though transesophageal echocardiography (TEE) can also be used to obtain cardiac images. Intraoperatively, it may not be feasible to obtain either a TTE or a TEE due to time, potential barriers or contraindications to such imaging (e.g. esophageal surgery). Under those circumstances, a single intraoperative transhepatic view (THV) obtained through the upper abdominal wound can be an option to provide with relevant information. We describe the successful use of the THV in two patients to rule out potential causes of intraoperative hypotension when a TTE or TEE was contraindicated.

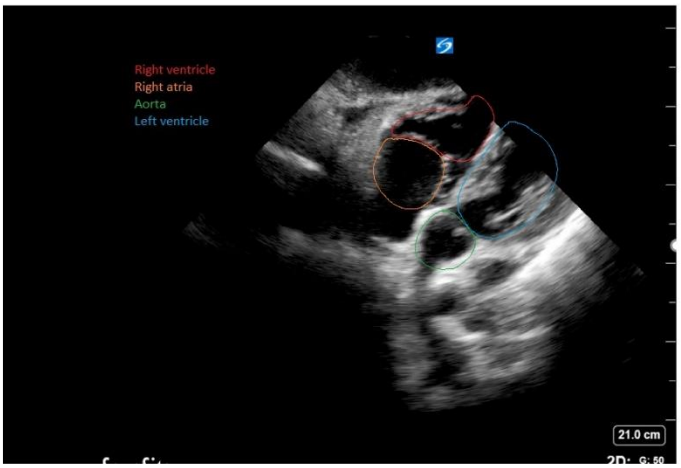
Case Report: Case 1: A 28-year old Caucasian male with a history of pancreatitis, cirrhosis, polysubstance abuse, suicide, and type II diabetes mellitus presented to the operating room with a reopening of a recent laparotomy. The preoperative diagnosis was transverse colon perforation status post partial colectomy, open abdomen, and hemorrhagic shock. At the time of assessment, his intraoperative vital signs were 100% SpO2, BP 80/40, and HR 80 despite infusions of phenylephrine, ephedrine, and vasopressin. A TTE could not be performed due to lack of access to the patient's chest. In addition, TEE could not be accomplished due to the possible risk of esophageal rupture . The surgeon, at the instruction of the anesthesiologist, placed the transducer inside the abdomen to acquire THV of the heart. Trace pericardial fluid was present without tamponade physiology, and both ventricles were small and hyperdynamic. The time to image acquisition was 2 minutes and the image quality was good. The patient was transfused with blood emergently with improvement in blood pressure. Case 2: A 21-year old African-American male presented to the emergency department with multiple gunshot wounds. There was apparent arterial bleeding in the left upper extremity. The patient was preoperatively diagnosed with intra-abdominal sepsis secondary to gunshot wound. The patient's peak inspiratory pressures at the start of operation ranged from 32 to 35 cmH2O. Upon abdominal closure, the peak inspiratory pressures increased. An ultrasound was indicated by arterial hypotension; the surgeon performed the ultrasound intraoperatively via the THV at the instruction of the anesthesiologist which demonstrated bilateral pleural effusions. The chest was prepped, and two chest tubes were placed bilaterally to the 5th intercostal space in order to drain the effusions to alleviate ventilatory efforts. Inferior vena cava (IVC) was then visualized and found flat indicating hypovolemia prompting IVF resuscitation. The patient tolerated the procedure well.

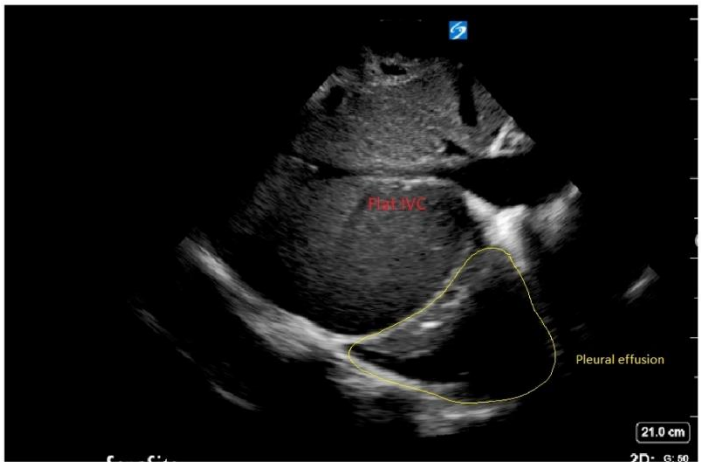
Discussion: In both cases, a single intraoperative THV proved to be necessary and sufficient for ruling out cardiac causes of intraoperative hypotension. Furthermore, the time to achieve images was short at an average of 2 minutes which can be vital in critical care scenarios when rapid clinical decision-making is required. An echocardiography-trained anesthesiologist can coach a surgeon with no training in cardiac ultrasound in obtaining diagnostic images. THV is a rescue imaging option when TTE and TEE cannot be performed.

Case 1.


Subcostal
INTRAOP OPEN ABDOMN TRANSHEPATIC
No pericardial effusion
Right ventricle
Right atria
Left atria
Left ventricle
21.0 cm
2D: G: 54
Pen DR: 0
DM. NB
SonoSite
P21xp/5-1 Cardiac

Case 2.


Right ventricle
Right atria
Aorta
Left ventricle
21.0 cm


Flat IVC
Pleural effusion
21.0 cm

Critical Care-70 Meropenem-Induced Encephalopathy Causing a Comatose State in Patient Treated for Bacteremia: A Case Report

Simona I Lupu[1], Michael Maile[1], Reed Kamyszek[1]

[1]University of Michigan, Ann Arbor, MI

Introduction: Carbapenem antibiotics, such as meropenem, are frequently used to treat multidrug-resistant bacterial infections, which are commonly encountered in critically ill patients. Neurologic side-effects of this antibiotic class are not commonly reported. Seizures, reported in less than 1% of patients, are the most common neurologic adverse event of this class of drugs. Others include psychosis and delirium. However, these medication-related adverse events may go unnoticed due to the numerous comorbidities that often exist in patients receiving this class of drug. Here, we report a case of meropenem-induced encephalopathy that produced what appeared to be a comatose state.

Case Report: A 66-year-old female was being treated with meropenem for extended-spectrum beta-lactamase producing Enterobacter infection of a vascular graft. The patient had presented from an outside hospital two weeks prior with an infected vascular graft and osteomyelitis, and with blood cultures growing multiple bacteria. After one week of treatment with meropenem, she was transferred to the intensive care unit for an acutely altered mental status. She was intubated for airway protection, and underwent a battery of diagnostic tests to investigate her condition. After ruling out other causes of altered mental status, including seizures, metabolic, and infectious causes, the etiology of the patient's comatose state was thought to be secondary to meropenem. This was supported by a recent increase in the dose in response to the severity of her infection. The dose was decreased back to the initial dose after discussion with the infectious disease specialists, and the patient's mental status returned to baseline. After extubation, she reported experiencing a paralyzed state in which she was aware of what was happening around her, but could not move or communicate purposefully.

Discussion: In conclusion, in patients with new onset encephalopathy after treatment with meropenem or a recent dose increase, we recommend consideration of meropenem as a potential causative factor. While the case described may be extreme in its presentation, less severe presentations of meropenem-induced encephalopathy may go unrecognized given that patients receiving this medication often have other potential causes for their condition. It is important for providers to keep meropenem-induced encephalopathy as part of their differential diagnosis in their workup of patients who develop acutely altered mental status, as dose reduction or discontinuation of the drug could make a significant difference in the patient's condition.

Critical Care-71 Middle cerebral artery occlusion due to paradoxical emboli in a patient with severe ARDS supported with venovenous ECMO, requiring innovative approach to PFO closure.

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Introduction: MCA syndrome is a rare but potentially fatal complication of VV ECMO. We present a complex case of severe ARDS supported with ECMO, complicated by MCA syndrome due to paradoxical emboli requiring an innovative approach to PFO closure.

Case Report: A previously healthy 29 year old female presented to an outside hospital with severe ARDS from H1N1 pneumonia and rapidly developed refractory hypoxemic respiratory failure. Pregnancy and spontaneous abortion was incidentally noted. Our mobile ECMO team cannulated the patient using a standard bifemoral venovenous approach. Sedation interruptions to assess mental status were initially limited due to ventilator dyssynchrony and hemodynamic instability. On ECMO day 1, the patient was noted to have right hemiparesis. Head CT showed a left MCA ischemic CVA with 3mm of midline shift (Figure 1). Systemic anticoagulation was immediately discontinued and sedation minimized to permit serial examinations. TEE confirmed a moderately sized PFO with right to left shunt. Lower extremity ultrasound revealed extensive bilateral femoral DVTs. The patient remained awake, while ICP measured 8-11mmHg by subdural bolt. Due to the patient's stable neuro exam and neuroimaging, neurosurgery advised against immediate craniectomy; ICP was managed with hyperosmolar therapy and CO2 control. However, the need for early decompressive craniectomy in the case of neurologic deterioration was constantly under consideration. Due to the threat of recurrent emboli in the setting of high DVT burden and ongoing VV ECMO support, urgent PFO closure was undertaken. Typical femoral venous access was not possible in the presence of large ECMO cannulae and distal DVT. Initial attempt at PFO closure via right internal jugular approach was aborted after the patient's ICPs were prohibitively elevated (above 30mmHg) during supine positioning. Repeat approach for PFO closure was performed with head of bed at 30 degrees using the ECMO circuit for access. Prior to the procedure, bench testing of the cannula-based approach was performed to refine the technique for PFO access through the long circuit. To minimize the risk of dislodging clots, an initial angiogram ruled out the presence of thrombus in the inflow cannula. The 21 Fr ECMO outflow cannula was withdrawn to the RA-IVC junction, and a specialized 8Fr Shuttle-type sheath was inserted into the ECMO circuit using a Seldinger technique. The Amplatzer occlude device was deployed, the sheath removed, and the ECMO circuit was spliced back together. The patient remained stable on uninterrupted VV-ECMO support throughout entire procedure. On day 6, tracheostomy was performed and on day 8, ECMO was decannulated with simultaneous IVC filter placement. Patient was transferred to a rehabilitation facility 5 days later tolerating aspirin and systemic anticoagulation.

Discussion: This case presents a complex multidisciplinary management and innovative approach for PFO closure via the ECMO system in patients with severe ARDS complicated by life-threatening MCA syndrome.

Critical Care-72 Post-operative status epilepticus in a patient on peritoneal dialysis

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Introduction: Antiepileptic drugs (AEDs) are well-known for their complex pharmacokinetics and drug interactions. In comparison to continuous renal replacement therapy or intermittent hemodialysis, clearance of AEDs is highly unpredictable in patients who receive peritoneal dialysis. Here, we report a patient with peri-operative ischemic stroke complicated by status epilepticus requiring treatment of multiple AEDs, while concurrently receiving peritoneal dialysis for end-stage renal disease (ESRD). A multidisciplinary team was assembled and the treatment principles were discussed.

Case Report: A 69-year-old patient with ESRD on home peritoneal dialysis and repetitive venous thrombosis secondary to lupus and Sjogren's syndrome underwent elective aortic valve replacement and mitral valve repair due to severe aortic stenosis and mitral regurgitation. On postoperative day 1, the patient developed status epilepticus secondary to a cerebral embolic event. Seizure activity was initially treated with lorazepam but subsequently required concomitant use of propofol, phenytoin, levetiracetam, and lacosamide added in successive order. The patient received home peritoneal dialysis at baseline as both of her prior arteriovenous fistulas had failed. Venous access remained technically challenging. The patient remained unarousable on postoperative day 3 even though all electrographic seizure activity had stopped. Supratherapeutic AED accumulation were concerned. A team of neurologists, nephrologists, and clinical pharmacologists, lead by our intensivists, was assembled and reached the following consensus. Propofol was first titrated off under real-time video electroencephalogram surveillance. Corrected serum phenytoin level was closely monitored and levetiracetam was adjusted according to her peritoneal dialysis status. Lacosamide was aimed to be tapered off the first due to lack of dosing guideline. Due to technical difficulty and the patient's hypercoagulable status, continuous renal replacement therapy was deferred as a rescue therapy in case if the patient's consciousness status inadequately recovered. The patient's consciousness state improved afterwards and was extubated on postoperative day 7. Lacosamide was stopped on day 9.

Discussion: In peritoneally dialyzed patients with status epilepticus, continuous renal replacement therapy should be considered for concerns of AED pharmacokinetics. In situations which options other than peritoneal dialysis were not available, a multidisciplinary approach should be adopted. Frequent drug level monitoring and close monitoring of their therapeutic effects are advised.

Critical Care-73 Use of Bedside Ultrasound to Diagnose Free Intra-abdominal Fluid in a Critically Ill Post-Arrest ECMO Patient

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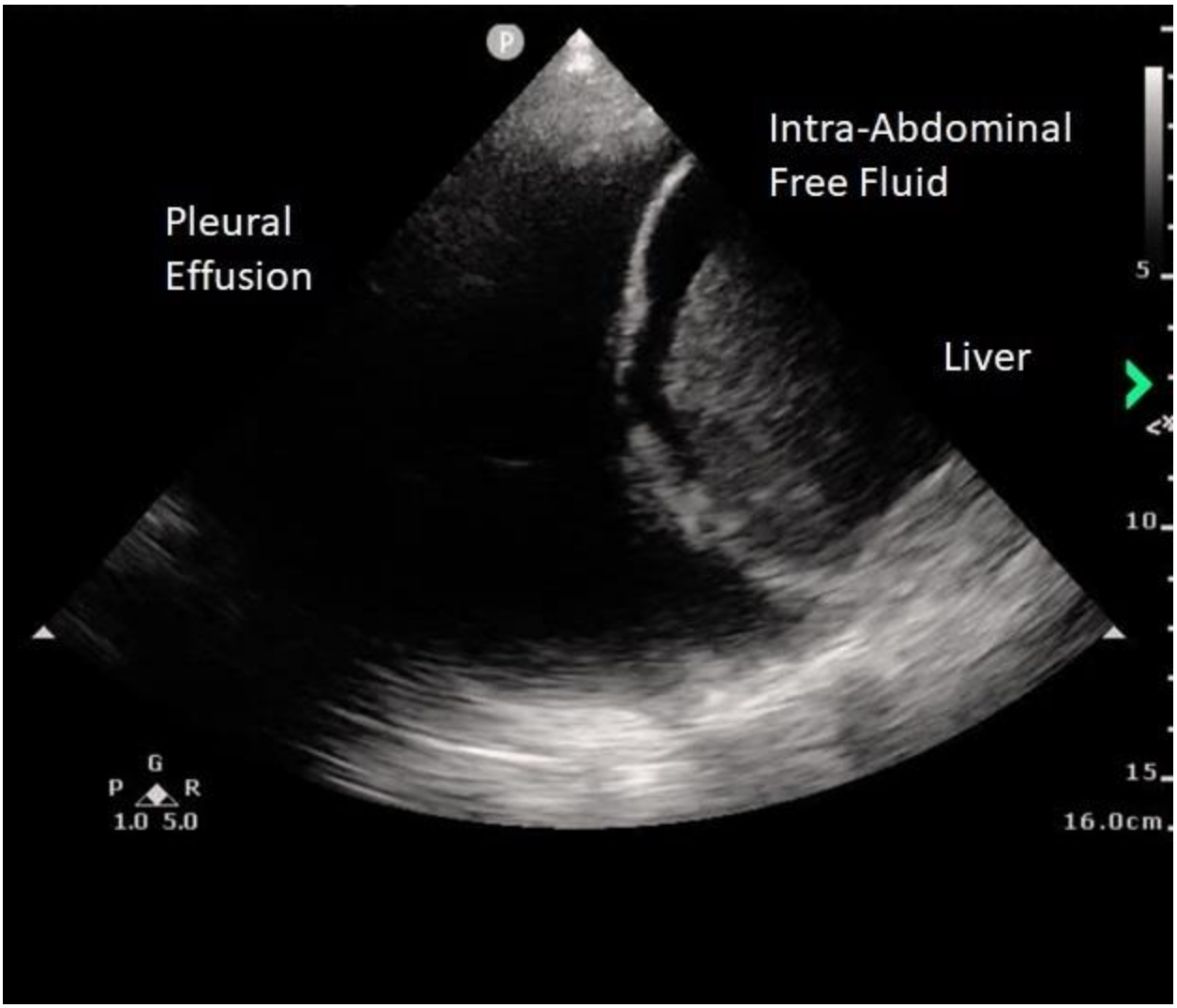
Introduction: We describe the diagnostic impact of bedside ultrasound in a critically ill post-arrest patient on veno-arterial ECMO (VA-ECMO) who developed compartment syndrome secondary to significant intra-abdominal fluid.

Case Report: Case Report: The patient is a 45-year-old with a medical history of cardiac sarcoidosis and heart transplant, stage-3 chronic kidney disease and hypertension that was admitted for acute decompensated heart failure due to anti-body mediated transplant rejection. On hospital day 6, the patient underwent a right heart catheterization that was complicated by cardiac arrest. The patient received 96 minutes of ACLS, during which he was successfully cannulated for left femoral VA-ECMO. En route to the cardiovascular intensive care unit the patient developed disseminated intravascular coagulation and a massive upper gastrointestinal bleed. High dose vasopressors (vasopressin, norepinephrine, angiotensin II) and inotropes (epinephrine and milrinone) were required to maintain hemodynamics. Massive transfusion was also required - 16 units of packed red blood cells, 3 units of cryoprecipitate, 3 five-packs of platelets, and 12 units of fresh frozen plasma (8.8L of product). A bedside upper endoscopy was notable for friable duodenal mucosa without areas of active hemorrhage. Three hours after endoscopy, the patient became hypotensive with a mean arterial pressure (MAP) of 65 (prior MAPs were in the mid 70s), heart rate 80s, central venous pressure 17 mmHg and elevating lactate. His ECMO flows decreased from a baseline of 3.0-3.1 LPM (RPMs 3500, Pvenous -65 mmHg) to flows of 1.6 and 2.6 LPM with pVenous < -100. His abdomen became more distended and his intraabdominal pressure was approximated via bladder pressure, measuring 17 mmHg. An eFAST exam using a phased array probe revealed an appropriate location of the venous VA-ECMO cannula, a moderate sized right pleural effusion, and significant free fluid in the right and left paracolic gutters with free floating bowel (images attached). A 32 French chest tube was placed and 650 cc of serosanguinous fluid was removed. Given his hypotension, decreased ECMO flows, coagulopathy and intra-abdominal free fluid, there was concern for abdominal compartment syndrome secondary to an intraperitoneal vs retroperitoneal hemorrhage vs third-spacing from resuscitation. The patient received a bedside exploratory laparotomy where more than 1L of serous yellow fluid was evacuated. A partial thickness ischemic-reperfusion injury of the distal small bowel and extensive cecal bruising were also noted. His abdomen was left open and a wound vac was placed. After the procedure the patient's status improved: decreased lactate, intra-abdominal pressure 9 mmHg, MAP 78-80 and improved ECMO flows. The patient was eventually de-cannulated from ECMO and is currently neurologically intact in the cardiac intensive care unit.

Discussion: Bedside point of care ultrasound is a useful adjunct to physical exam when patients on VA-ECMO become unstable.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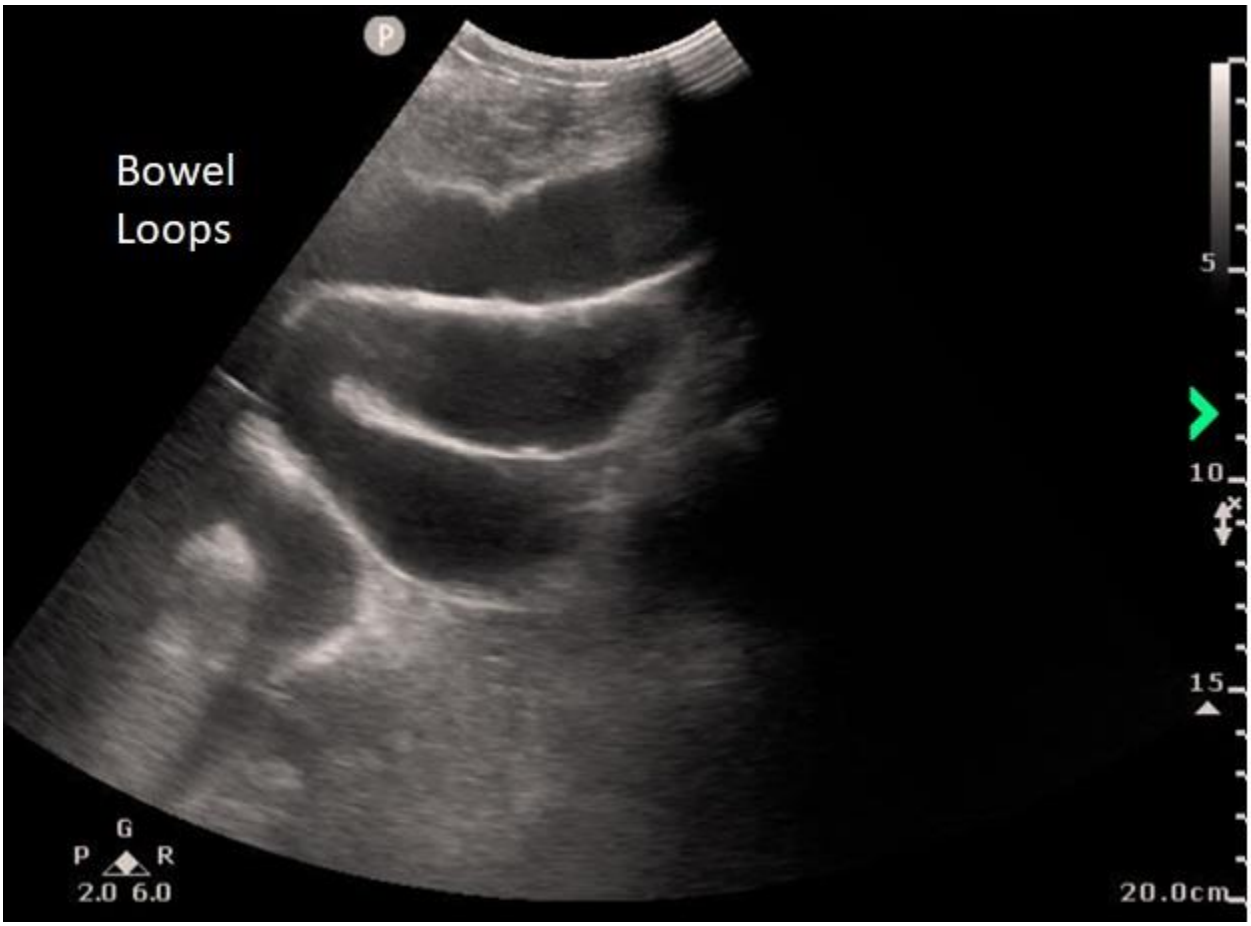
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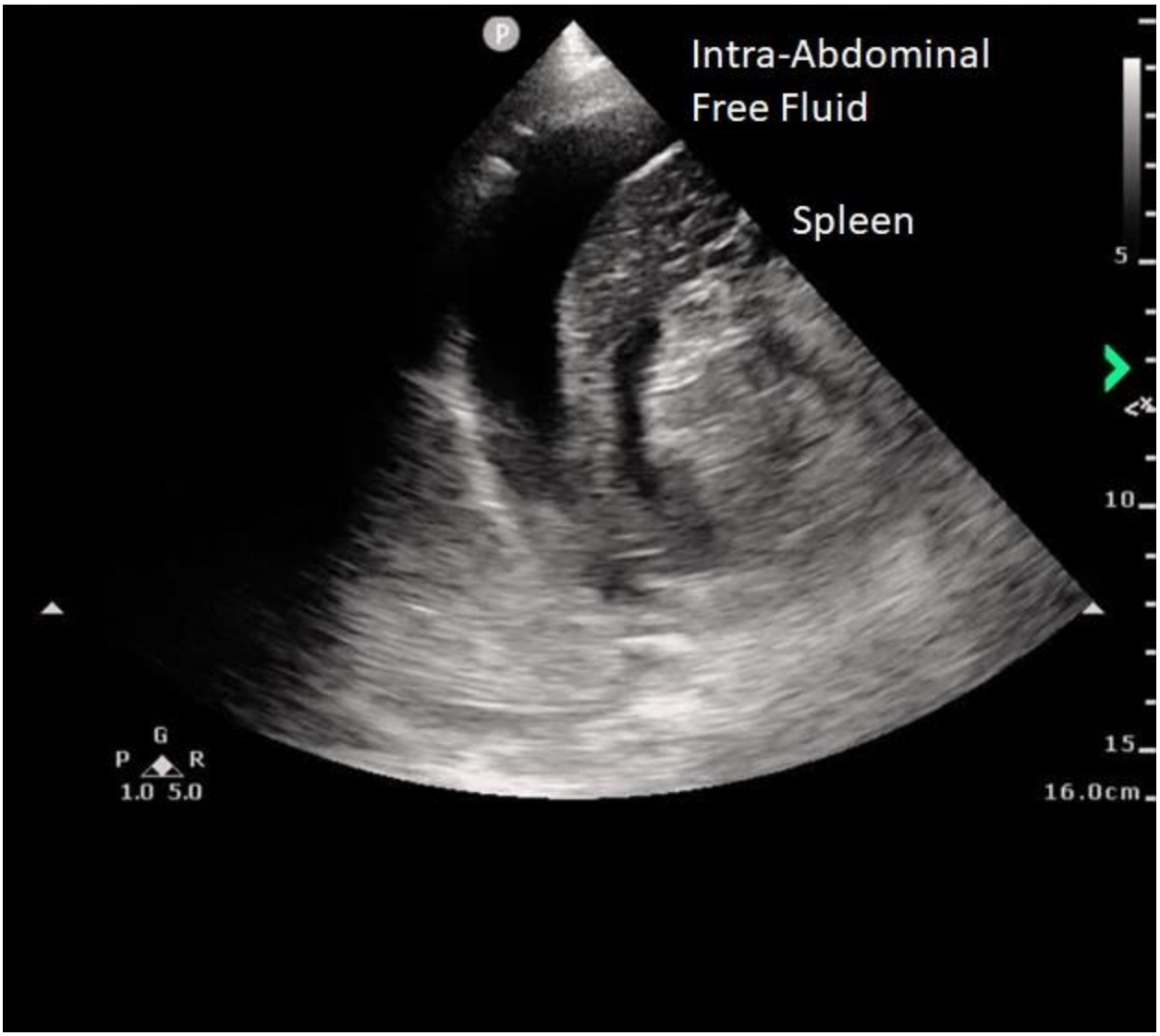
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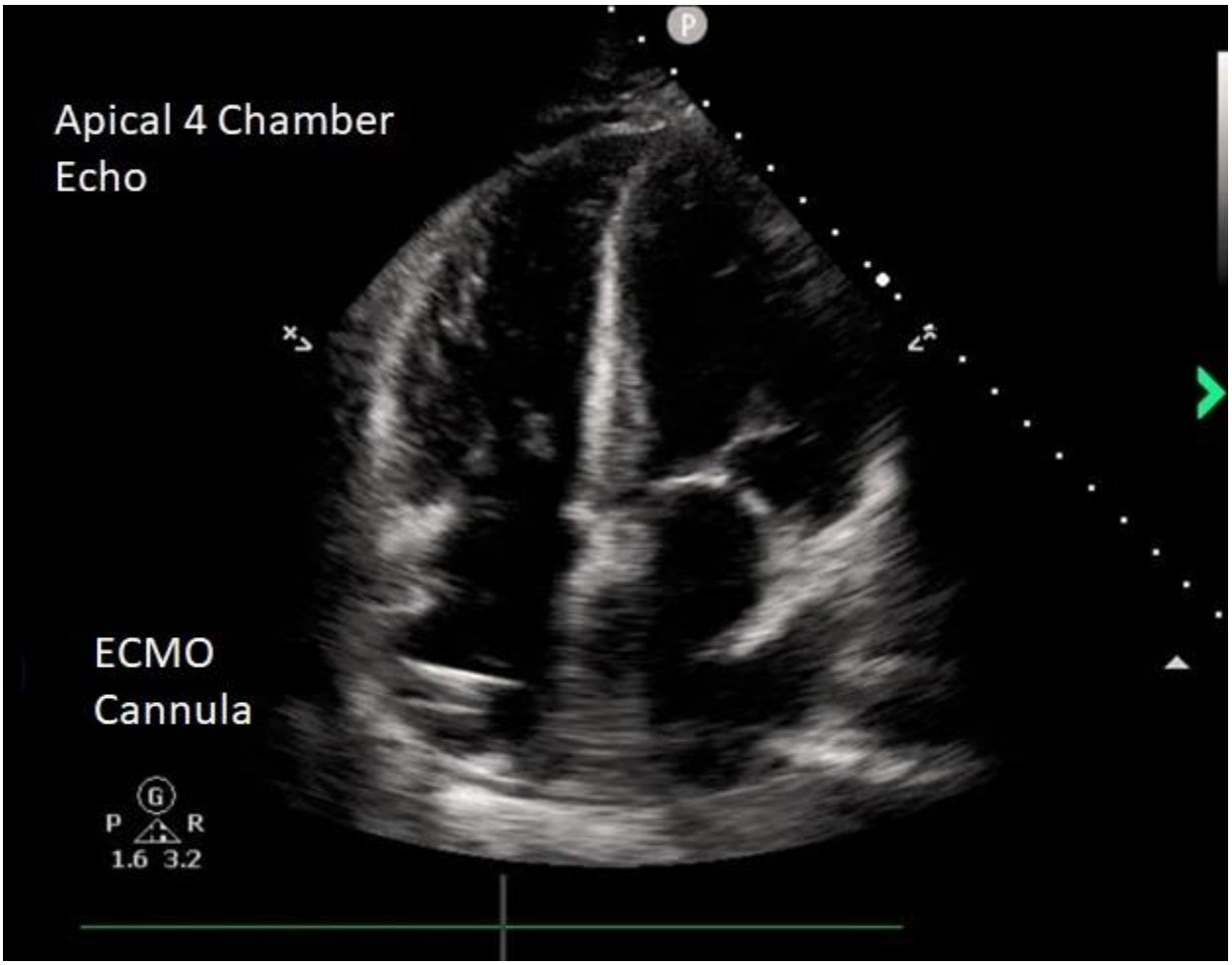
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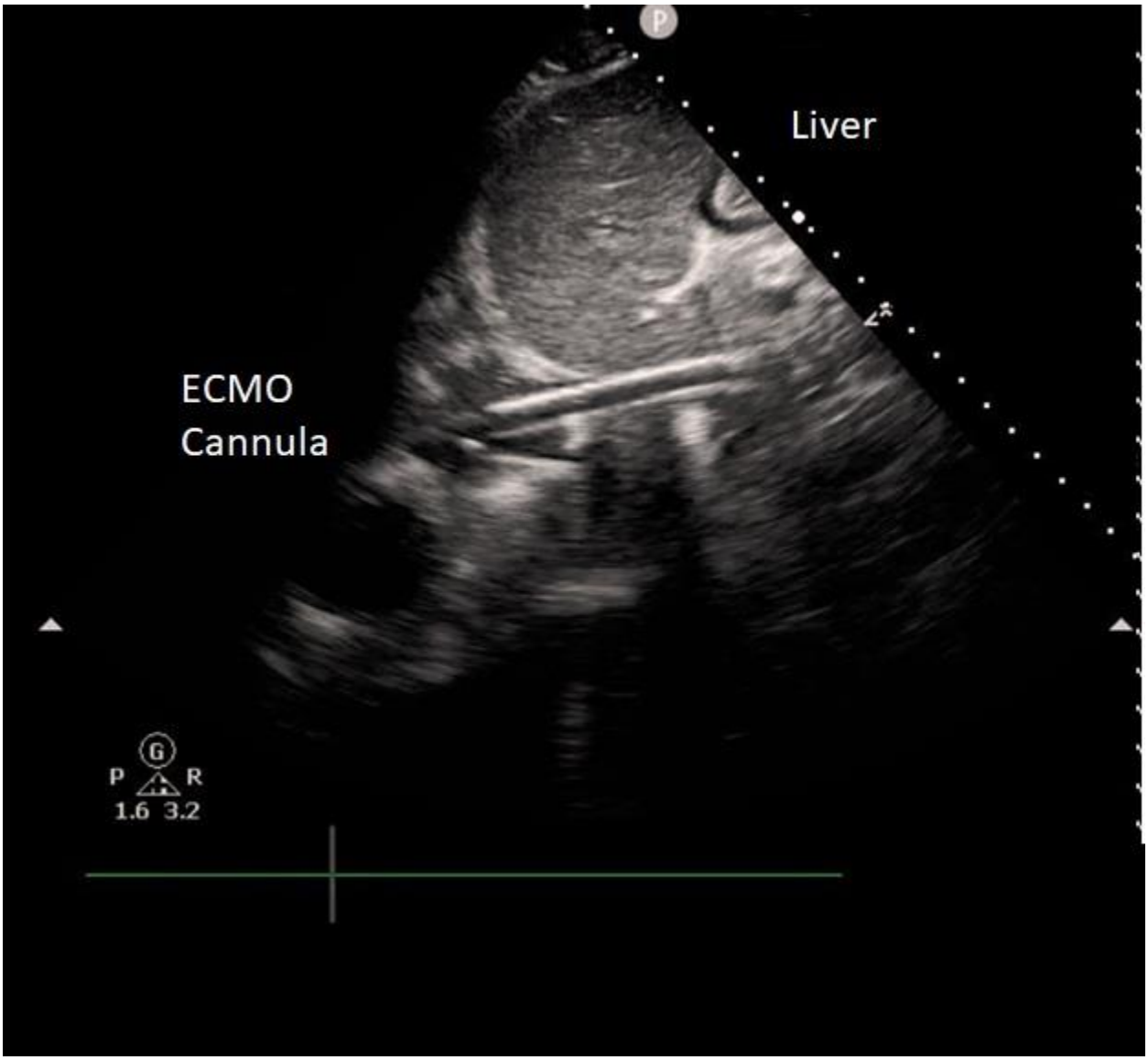
Liver
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Critical Care-74 Robotically assisted Transcranial Doppler with Artificial Intelligence for Assessment of Cerebral Vasospasm after Subarachnoid Hemorrhage

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Introduction: Transcranial Doppler Ultrasound (TCD) is an important tool for detection of cerebral vasospasm after subarachnoid hemorrhage (SAH), but is limited by availability of skilled operators. We examined the clinical feasibility and concordance of a robotically assisted TCD system with artificial intelligence with routine handheld TCD after SAH.

Case Report: We evaluated TCD velocities in the anterior (ACA) and middle cerebral arteries (MCA) of two patients with high-grade SAH and angiographic evidence of vasospasm. A single channel TCD device with a handheld diagnostic probe as well as a robotically assisted TCD device were used, the relationship of the two tests was evaluated using the Concordance correlation coefficient paired with a Pearson's correlation analysis, followed by a Bland-Altman plot.

Discussion: Patient 1 developed angiographic and TCD evidence of vasospasm in the proximal right MCA, but except for periods of disorientation remained neurologically intact. Angiographic, TCD and clinical evidence of ACA spasm occurred six days after ictus in patient 2. Robotically measured mean flow velocities were comparable to manual TCDs in the MCAs (concordance correlation coefficient = 0.83 (95% COI = 0.52 - 0.95), P = 0.001) but not in the ACAs (concordance correlation coefficient = 0.32 (95% COI = -0.15 - 0.68), P = 0.15). Robotically assisted TCD system with artificial intelligence provides an alternative to manual TCD for assessment of MCA velocities in patients with SAH, expanding the availability of TCD to settings in which specialized clinicians are not available. Further studies for validation of this technology are warranted.

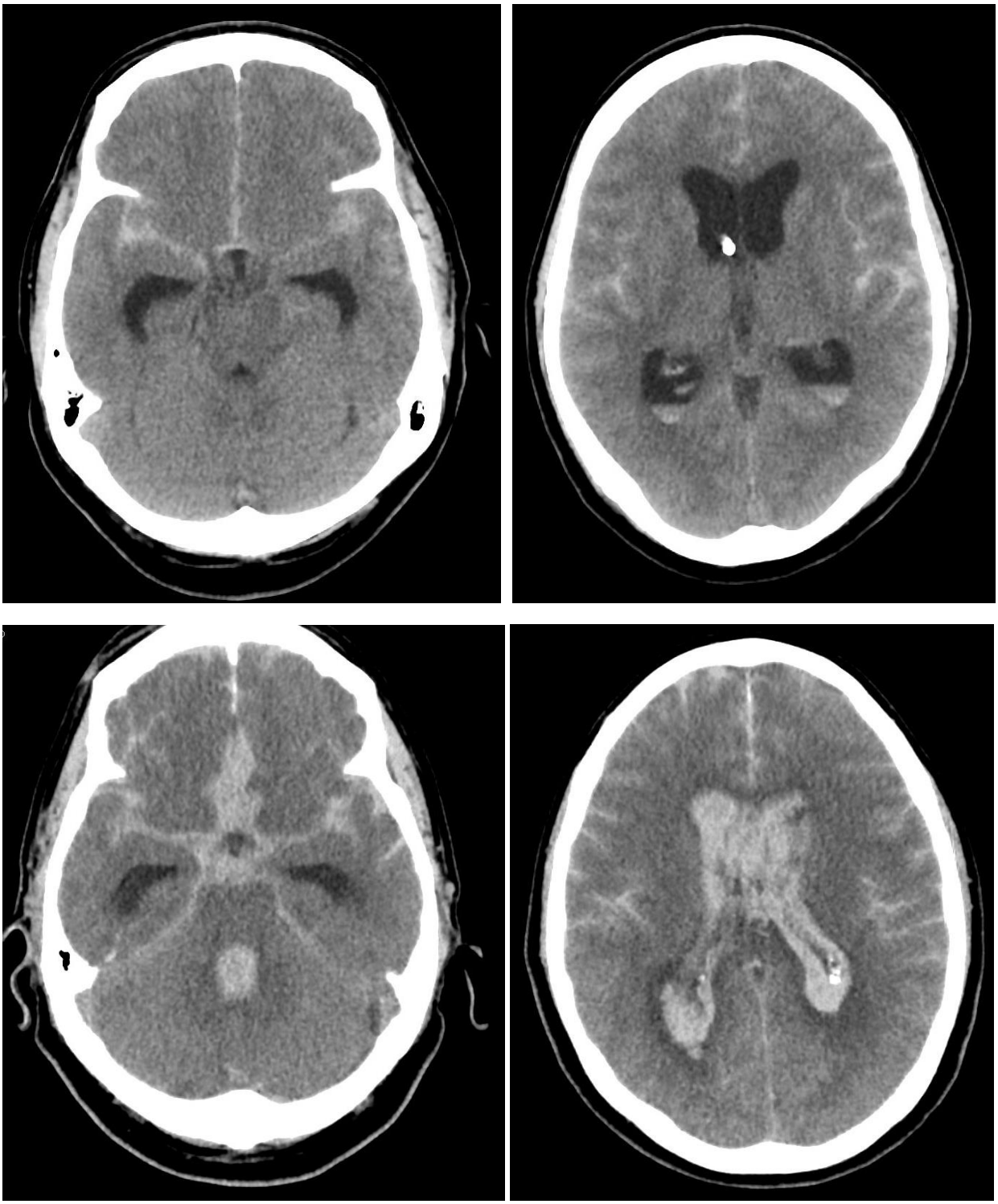


Figure 1. Computer tomography imaging of patient 1 (above) and 2 (below) showing diffuse thick subarachnoid hemorrhage with intraventricular blood.

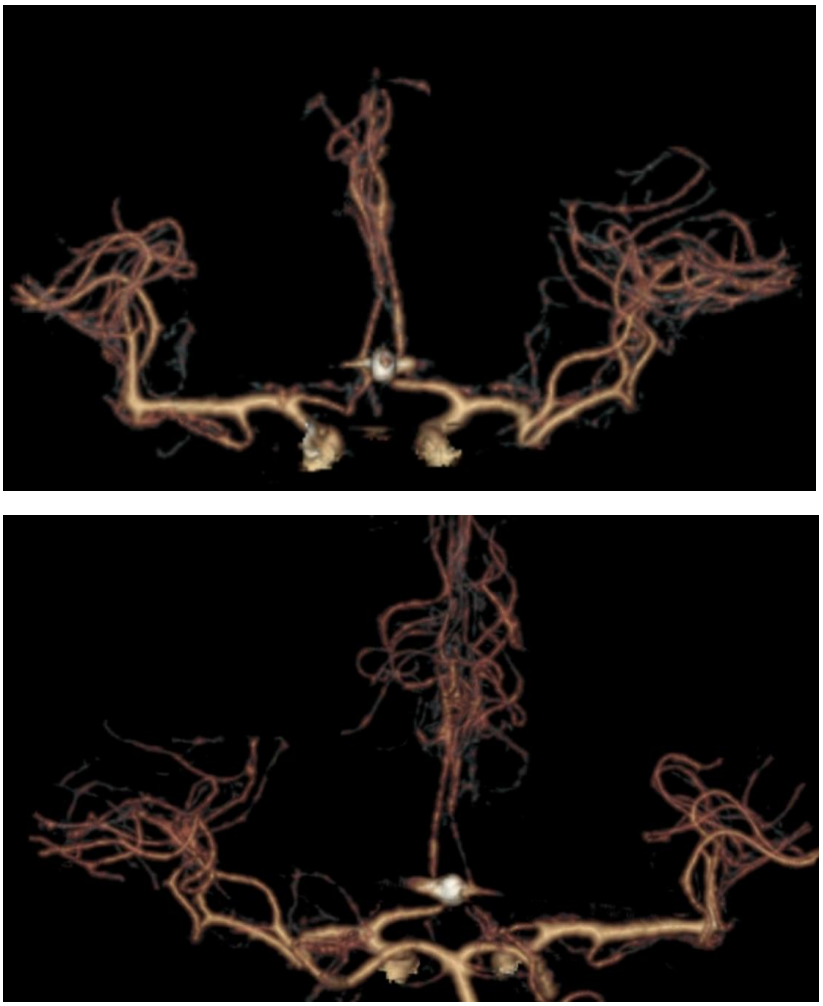
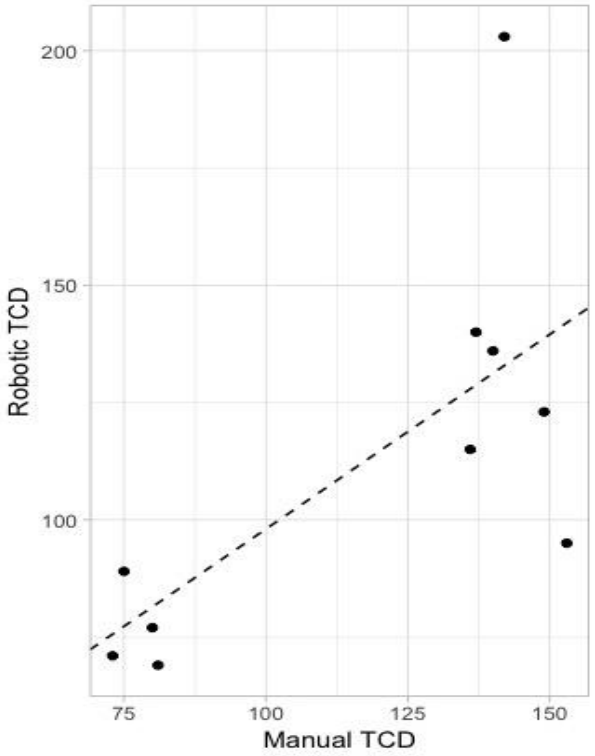


Figure 2. Angiographic findings in patient 2, initially demonstrating normal calibers in alll cerebral vessels but significant vasospasm in bilateral ACAs 6 days after ictus.

A



B

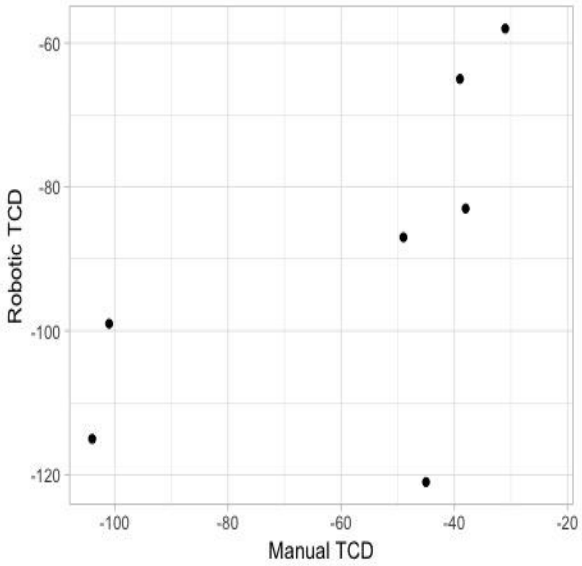
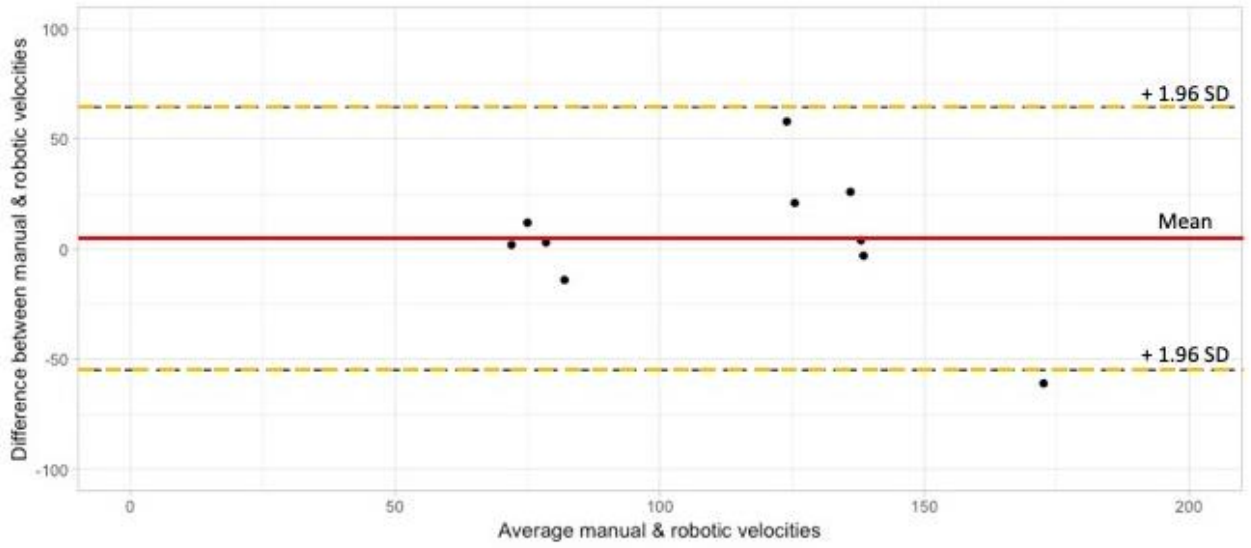


Figure 3. A) Moderate agreement between Trans cranial doppler (TCD) findings using robotic technique and TCD findings using manual technique for the middle cerebral artery (concordance correlation coefficient = 0.83 (95% COI = 0.52 - 0.95)) B) Poor agreement between Trans cranial doppler (TCD) findings using robotic technique and TCD findings using manual technique for the anterior cerebral artery (concordance correlation coefficient = 0.32 (95% COI = -0.15 - 0.68)

A



B

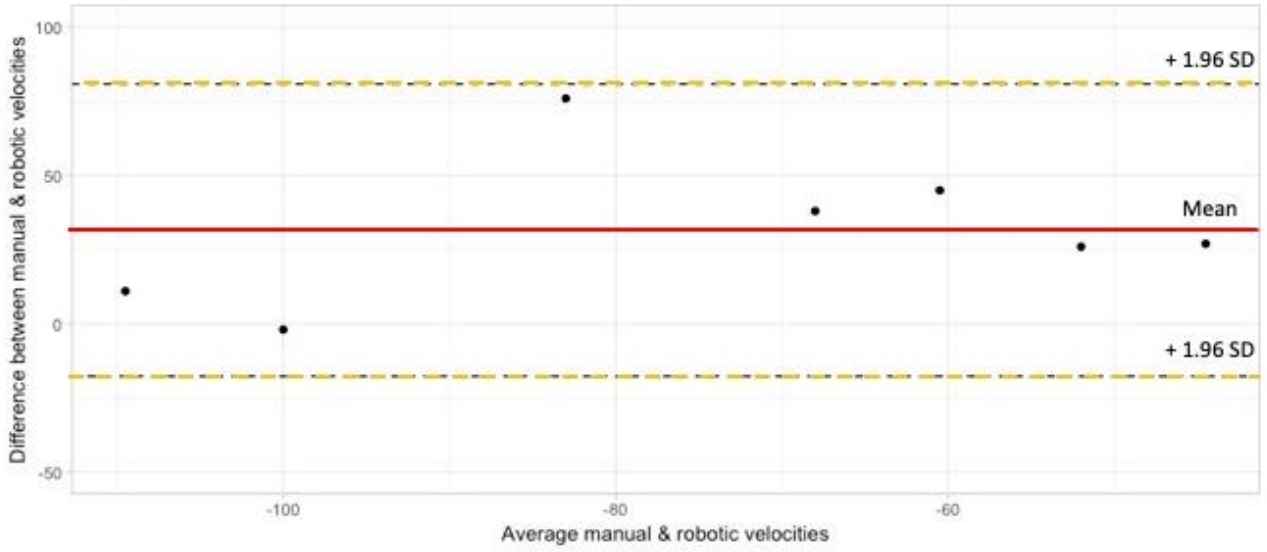


Figure 4. Bland-Altman plot shows no proportional bias, indicating agreement between the two methods for the middle cerebral artery (A) and anterior cerebral artry (B).

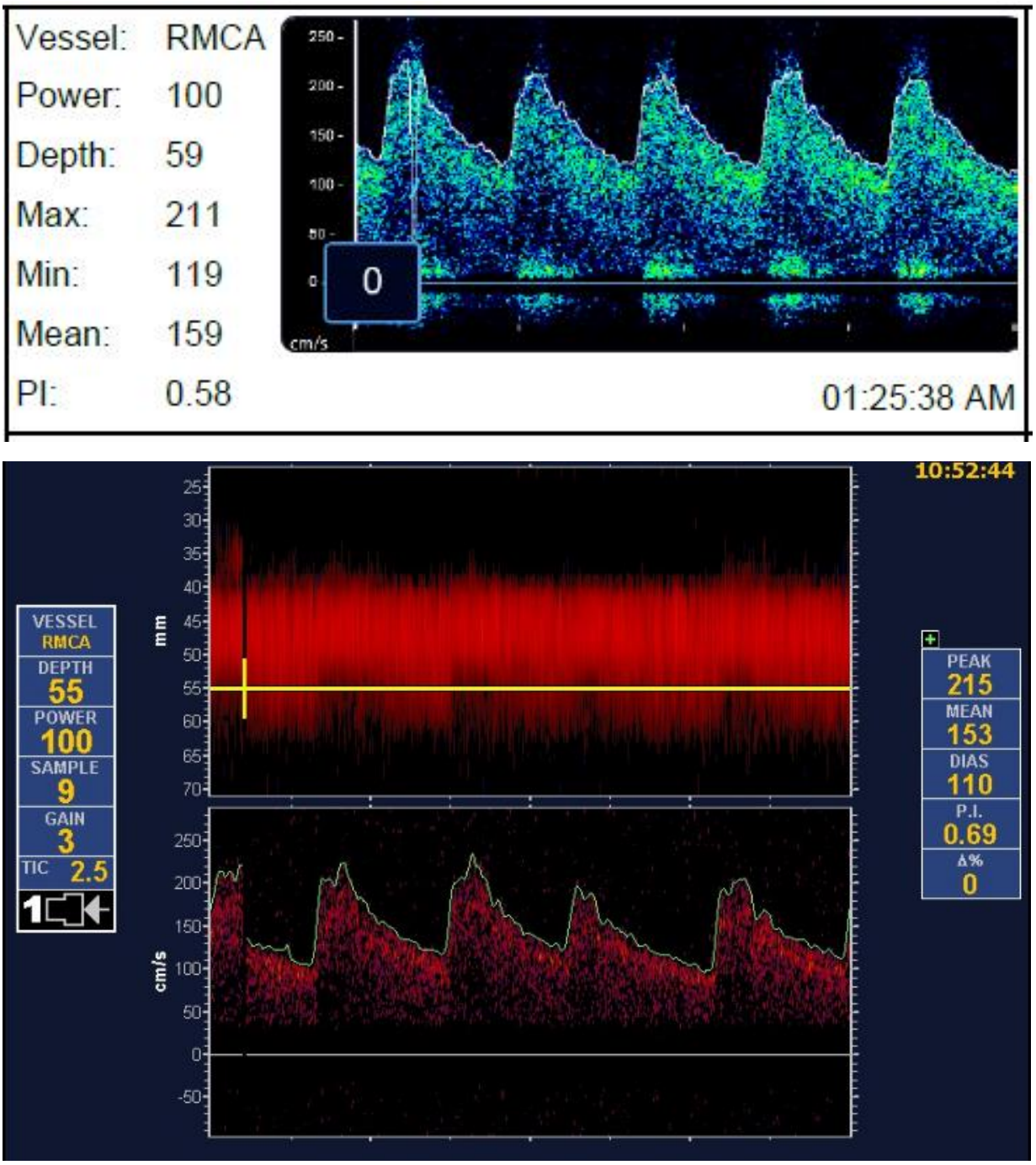


Figure 5. Robotic (above) and Manual (below) TCD waveform of the right MCA of Patient 1 on post-ictus day 10 demonstrating elevated right MCA mean flow velocity, consistent with vasospasm in both techniques.

Geriatric Anesthesia

Geriatric Anesthesia-1 Myiasis: Friend or Foe to a Comatose Patient?

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Introduction: Myiasis derived from the Greek word fly or 'myia' is a rare parasitic infection characterized by the infestation of living tissue by fly larvae (maggots). Severe myiasis is rare in developed countries (1). Risk factors include old age, low socioeconomic class, chronic wounds and poor hygiene. Maggots in most cases are parasitic causing harm to the host, however in some cases can be mutualistic. Facultative myiasis described as maggots decomposing wound tissue while sparing adjacent living tissue may prevent or treat an infection by cleaning the necrotic tissue, producing substances with bactericidal properties, and stimulating granulation (2, 3). Maggots may be beneficial initially, however as the infestation worsens the relationship becomes detrimental to the host. Possible complications of myiasis include local tissue destruction, invasion into deep tissues and secondary infection (4). We discuss a case of severe myiasis in a comatose patient.

Case Report: A 79-year-old male was found comatose in his backyard by neighbors who last reported seeing him three days prior. He was brought to the emergency department with multiple pressure wounds, hypothermic, hypotensive, and covered in maggots. He was intubated, resuscitated, imaged and was taken emergently to the operating room after imaging revealed large pneumomediastinum and pneumoperitoneum (Figure 1-3). After a negative exploratory laparotomy, bronchoscopy and endoscopy were performed revealing an ulcerated, necrotic lesion in his proximal left mainstem bronchus and a large maggot burden in the esophagus and bronchial tree (Figure 4). The airway was irrigated copiously and suctioned to reduce the maggot burden. His left proximal bronchial defect was later stented. On further investigation, the patient was found to have influenza A, necrotic pneumonia, and bacteremia. He eventually suffered fulminant sepsis with multi-system organ failure and expired a week after presentation despite aggressive medical therapy.

Discussion: Maggots can be parasitic or mutualistic. In this case, the patient had multiple necrotic wounds and pneumonia due to influenza and possible superimposed bacterial infection. He was lying outdoors unconscious for approximately three days presumably leading to myiasis. Initially the maggots may have been mutualistic enabling the patient to survive, however became parasitic causing an airway defect. Well known complications of myiasis include necrotic tissue ulceration, abscess formation, osteomyelitis, and amputation (5). It is up to the treating team to determine whether the maggots are therapeutic or malignant. In this case, the patient underwent multiple washouts and mechanical debridement. Despite aggressive treatment, the patient progressed to multisystem organ failure. It is unclear the exact role the maggots played in the disease course, however given the severity of his disease the significant maggot burden may have contributed to his death.

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Figure 1: Chest computed tomographic scan showing pneumomediastinum

Figure 2: Chest computed tomographic scan showing pneumomediastinum

Figure 3: Abdominal computed tomographic scan showing pneumoperitoneum

Figure 4: Bronchoscopy image at carina demonstrating maggot infestation

Liver

Liver-1 Dabigatran Reversal with Idarucizumab in a Patient Undergoing Orthotopic Liver Transplantation : A Case Report

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[1]University of Colorado, Denver, CO, [2]University of Colorado, Aurora, CO

Introduction: End stage liver disease (ESLD) is a challenging disease accompanied by many comorbid conditions. Protein synthetic disruption drives hemostatic instability such that patients are hypercoagulable and prone to significant bleeding.1 Portal vein thrombosis (PVT) is a particularly morbid complication affecting the portal vein trunk and intrahepatic portal branches.2 Prevalence of PVT is 8-25% of patients with ESLD awaiting liver transplantation (LT).3 Treatment of PVT with anticoagulation has been shown to increase the rate of recanalization 4 and prevent recurrence of thrombosis. Low-molecular weight heparins had been accepted as the standard in this patient population, however their efficacy can be impaired up to 40% due to lower levels of circulating antithrombin III 5 and their use limited by concomitant renal impairment.4 Direct acting oral anticoagulants (DOACs) have become a popular choice in this population due to pharmacokinetic stability and convenience.

Case Report: Our case is of a 42 year old male with chronic liver disease secondary to primary sclerosing cholangitis complicated by ascites necessitating TIPS placement and portal vein thrombus. Model for End Stage Liver Disease Score (MELD) was 18. His portal vein thrombus was initially treated with rivaroxaban (Xarelto) however in anticipation for a liver transplant he was changed to dabigatran for anticoagulation due to the availability of a reversal agent, idarucizumab. When an organ became available he discontinued any further dabigatran doses and proceeded to the operating room. His preoperative INR was 1.6, PT 21.9 (ref range 11.8-13.8), and aPTT 66.6 (ref range 23.8-34.4). Dilute thrombin and Ecarin times 5,6 were not measured. Total bilirubin was 4.8 mg/dL and serum creatinine was 0.51 mg/dL. General anesthesia was induced in the normal fashion. Prior to incision a single 5 gram dose of idarucizumab was administered intravenously. Intra-operatively the patient was transfused with 8 units of packed red blood cells, 13 units of fresh frozen plasma, 2.5 liters of crystalloid and 2.3 liters of Cell Saver blood collection was returned. Based on thromboelastography assessment, no units of cryoprecipitate or platelets were deemed necessary. Blood loss was estimated to be eight liters. The patient was extubated at the conclusion of the procedure and observed in the ICU for 24 hours due to concern for rebound bleeding, however he met no other ICU admission criteria. He was transferred to the floor on postoperative day (POD) #1 and discharged home on POD #9 having experienced no significant bleeding events postoperatively. Written consent was obtained to publish this case.

Discussion: Dabigatran was the first DOAC to be approved by the US Food and Drug Administration (FDA) for non-valvular AF and DVT/PE8 and works through direct inhibition of thrombin. Historically, reversal of dabigatran has been unreliable as the thrombin contained in prothrombin complex concentrate continues to be inhibited by circulating drug.9 Idarucizumab was approved in 2015 and is a monoclonal antibody reversal agent directed at dabigatran. It binds both free and thrombin bound dabigatran with 350x the affinity of dabigatran to thrombin in a 1:1 stoichiometric ratio and the complex is renally excreted.8,10 Trials have not shown hypercoagulability following reversal with idarucizumab in healthy subjects.10 To our knowledge, this is the second reported case of successful dabigatran reversal with idarucizumab prior to liver transplantation. Similar to our case, dabigatran was chosen for anticoagulation prior to transplant specifically because of the availability of a direct reversal agent.11 More recently, andexanet alfa has been approved for the reversal of rivaroxaban and apixaban, however due to its short half life must be administered as a bolus followed by an infusion to avoid rebound bleeding.8 We anticipate that as more patients with ESLD receive DOACs to treat venous thrombosis we will see these novel reversal agents utilized more frequently prior to LT. Much is still unknown about the efficacy of idarucizumab and other novel anticoagulant reversal agents in patients with ESLD and comorbid conditions and clinical trials are necessary to further investigate this question. Additionally, it is unknown if re-dosing reversal agents is required following significant blood loss as is often encountered during LT.

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11) Liver Transplantation. 2017;23:396-397

Liver-2 The Intraoperative Finding of a large Atrial Septum Defect Pre-Liver Transplantation: Proceed or Not-to-Proceed?

Lauren Hampton[1], Annette Rebel[1], Zaki-Udin Hassan[1], Malay B Shah[1]

[1]University of Kentucky, Lexington, KY

Introduction: Although liver transplantation remains a high-risk procedure, the presence of an atrial septal defect (ASD) or a patent foramen ovale (PFO) in a patient who is to undergo this procedure is often seen as a trivial finding and one without relevance in perioperative mortality 1,2. However, not every ASD is as insignificant as a PFO, and preoperative transthoracic echocardiography (TTE) may lead one to underestimate the size and shunt fraction of one such defect 3,4. The following presented case involves a postinduction transesophageal echocardiogram (TEE) finding with significant impact on the related surgical plan.

Case Report: Case Report The 59 yr old male patient with end-stage liver disease (MELD 17) secondary to polycystic liver disease and nonalcoholic steatohepatitis (NASH) underwent the pre-liver transplantation assessment including TTE which revealed an intracardiac shunt (positive bubble study) with minor shunt volume. Intraoperatively, the post-induction TEE led to the discovery of a large ASD with a significant left-to-right shunt (Figure 1). Interventional cardiology was consulted to discuss the option of ASD closure with a transcatheter closure device before proceeding with the liver transplant. Two hours post anesthesia induction, the patient was transported to the interventional cardiology suite. Using intracardiac echocardiography for guidance, the ASD was measured to be approximately 32 mm in diameter, and it was noted that this defect extended inferiorly and posteriorly into a region that was poorly visualized by TTE and TEE. Due to the lack of posterior margins, the intracardiac closure device could not be placed 5,6. The perioperative care team decided not to proceed with the liver transplantation, since the significance of the ASD and its possible implications on postoperative outcome could not be discussed with the patient after anesthesia induction. The available donor organ was offered to the backup recipient (approx. 5hrs post donor cross-clamp placement). To assess the full extend of the intracardiac defect and to discuss surgical repair options, the patient underwent a cardiac MRI several weeks after the planned procedure (Figure 2)

Discussion: Conclusion This case report documented the failure to identify a large ASD/inferior venosus defect in the preoperative screening process for liver transplantation. The intraoperative finding of a large ASD altered the perioperative risks involved in a scheduled orthotopic liver transplantation and lead to the cancellation of the procedure with possible wasting of the donor organ. This case raises several questions: 1) Could the liver transplantation could have been performed with acceptable perioperative risk? 2) Why did the pre-transplantation screening procedures not identify the severity of the intracardiac abnormality? 3) What systemic modifications should be considered to optimize the transplantation screening process, preventing similar situations? The finding of a positive bubble study during a transthoracic echocardiogram should not be trivialized and may require further diagnostic examination of the patient.

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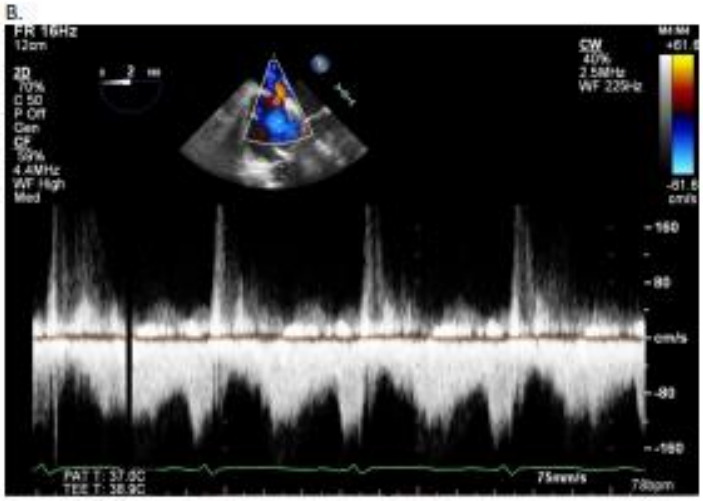
Figure 1: Transesophageal Echocardiography Images Obtained After Anesthesia Induction

A.

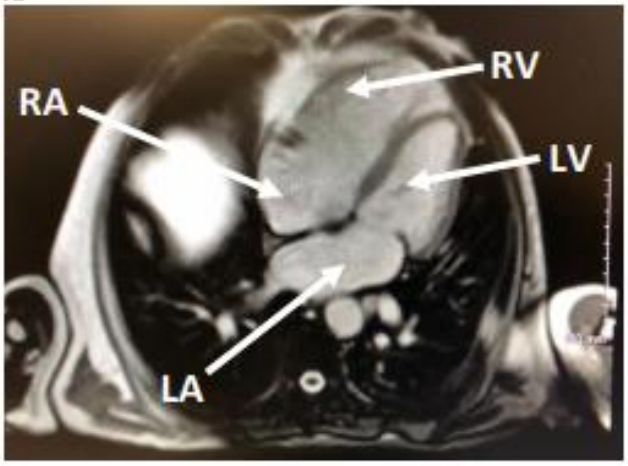
B.



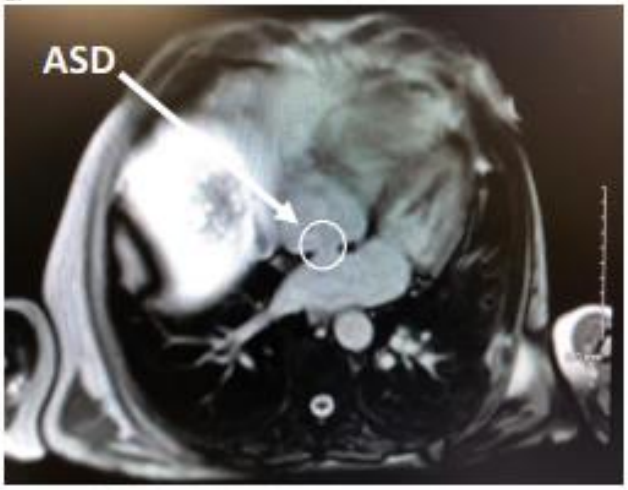
A. This image is a midesophageal four-chamber view that is focused on the right atrium and ventricle. The arrow labeled "RA" the right atrium, the arrow labeled "PAC" points to the artifact created by the pulmonary artery catheter, the arrow labeled "LA" points to the left atrium, and the yellow arrow points to an atrial septal defect (with its size in systole).
B. This image is of continuous wave Doppler that indicates almost constant left-to-right flow across an atrial septal defect. The image involves a similar probe position as that which is involved in A., and it provides a view that is similar to that which is in A.

Figure 3: Images from Cardiac Magnetic Resonance Imaging

A.



B.



A. This CINE_4CH image depicts the four chambers as marked with arrows (an arrow labeled "RA" points to the right atrium, an arrow labeled "LA" points to the left atrium, an arrow labeled "RV" points to the right ventricle, and an arrow labeled "LV" points to the left ventricle), showing a dilated right atrium and ventricle.
B. This image is a modified CINE_3CH view, showing an atrial septal defect.

Obstetric Anesthesiology

Obstetric Anesthesiology-1 Catheter-directed thrombolysis as a successful treatment for submassive pulmonary embolism in a pregnant patient at 33-weeks gestation

Danielle Laufer[1], Jennifer Lucero[2], Nasim Sobhani[1], Lee-lynn Chen[3]

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Introduction: Pulmonary embolism (PE) is responsible for 9% of maternal deaths during pregnancy in the United States (1). In 2011, the American Heart Association published updated guidelines classifying pulmonary embolisms into three types: massive, submassive, and low risk. They define massive PE as an acute PE with sustained hypotension or requiring inotropic support. Submassive PE is defined as an acute PE without systemic hypotension, but with either right ventricular (RV) dysfunction or myocardial necrosis. Lastly, low risk is a PE that does not fit into the two prior categories (2). Hemodynamically stable patients with normal RV function have an excellent short-term prognosis, while patients with massive PE physiology have mortality rates as high as 65%, for which aggressive treatment with IV thrombolytics is the standard of care (3). What is less clear, is the treatment of patients in the submassive group, especially those with an above average risk of bleeding. Catheter directed thrombolysis (CDT) is an alternative method to systemic thrombolysis. Catheters are placed percutaneously under fluoroscopic guidance into the pulmonary arteries and infuse a thrombolytic agent for 12-24 hours. Given that the total thrombolytic dose is lower with CDT compared to IV thrombolysis, CDT may be an attractive alternative in patients with a high risk of hemorrhage, such as a pregnant patient.

Case Report: We present a case of a 37-year-old G3P0 female at 33 weeks gestation who presented with acute onset tachycardia and shortness of breath. Her past medical history includes being a heterozygous carrier for prothrombin G20210A gene mutation and a recent knee injury that left her immobile for the past two weeks. She was admitted to the ICU on a heparin infusion. She was tachycardic with a stable blood pressure, dyspneic, saturating 92% on 4L nasal cannula. Her troponin I was elevated and a CT PE demonstrated saddle PE. Transthoracic echo (TTE) revealed severe RV dilation and dysfunction, positive McConnell's sign and PASP of 46 mm Hg. Thrombus was visualized in the proximal pulmonary arteries. Given the degree of RV strain, concern for further decompensation, and her heart's likely inability to tolerate the stress of labor in this state, decision was made to proceed with CDT via bilateral pulmonary artery EKOS catheters. Upon arrival to the IR suite, sedation was accomplished with small divided doses of midazolam and fentanyl. The pulmonary arteries were accessed through the right internal jugular vein and tPA was infused into the pulmonary arteries for a 24-hour period. At this time, the patient's tachycardia had resolved, and she was saturating well on 2L nasal cannula. Repeat TTE showed improvement in RV size and function. PASP decreased to 34 mm Hg and thrombus was no longer visualized in the pulmonary arteries. She did not have any bleeding complications as a result of the CDT. The patient was transferred from the ICU to the obstetric unit two days after catheter removal. She was discharged four days later and returned for a planned readmission at 39-weeks gestation for induction of labor where she delivered a healthy baby girl via spontaneous vaginal delivery without complications.

Discussion: Labor is associated with catecholamine-induced increase in heart rate and stroke volume which we did not think our patient would tolerate in the setting of a submassive PE. Given her increased risk of pre-term labor, our concern was that on a heparin infusion alone, the PE would not resolve before the start of labor and associated hemodynamic changes. Alternatively, systemic thrombolysis was also not without significant risk. A systematic review of 124 cases of severe PE in pregnant patients treated with IV thrombolysis resulted in major bleeding in 17.5% of cases during pregnancy and 58.3% of cases in the post-partum period (4). CDT appeared to be the best treatment option for our patient given the ability to rapidly decrease the clot burden and reduce the risk of significant bleeding compared to IV thrombolysis. Improvement in RV function on TTE was seen immediately following tPA infusion demonstrating that CDT was successful in reducing the clot burden within 24 hours of treatment. Additionally, our patient's heart was able to tolerate the hemodynamic changes associated with labor six weeks later. Although our case is an example of successful use of CDT in a pregnant patient, we still need more data of its efficacy and safety profile in pregnancy.

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33 WKS PREGNANT
SADDLE PE
122 bpm

33 WKS PREGNANT
SADDLE PE
119 bpm

Pain Medicine

Pain Medicine-1 Sickle Cell Pain Crisis: Clinical Guidelines for the Use of Oxygen: Oxygen therapy may prevent the vaso-occlusion and disruption of tissue oxygenation that lead to painful sickle cell disease crisis

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Introduction: Sickle cell disease (SCD) was first described by Herrick in 1910 regarding a dental student who presented with pulmonary symptoms. He further described the 'peculiar sickle-cell shape' of the red blood cells of the patient.1 In 1927, Hahn and Gillespie suggested that hypoxia caused the sickling of red blood cells by saturating a cell suspension with carbon dioxide to induce shape changes.2. Eaton, et al, stated: 'The rates of oxygen binding and dissociation are so fast (milliseconds) that the fractional saturation of normal Hb during the ˆ¼1-second duration of blood flow through the microcirculation is determined only by the oxygen pressure.'Gelation may be induced by deoxygenation of hemoglobin S molecules.and consists of polymerization of hemoglobin S molecules into fibers and the alignment of these fibers to form a crystalline phase. The aligned fibers rigidify the red cell and produce the shape distortion referred to as sickling. HbS polymerization in SCD results in a very complex cascade of processes that include erythrocyte sickling, intravascular hemolysis with release of cell-free hemoglobin, increased adhesion of red cells to the endothelium of blood vessels, activation of platelets, production of inflammatory cytokines, and ultimately vascular occlusion. Pathophysiological triggers that may contribute to vaso-occlusive crisis (VOC) include: hypoxia, daytime exertion, waking up earlier with a shortened duration of sleep, daytime exertion, stress, fatigue, exercise, exposure to cold, ingestion of alcohol, airline travel, altitude that exceeds 2,000 ft, infection, malaria, or pregnancy. In patients with SCD, VOC tends to occur most often at night, due to the relative hypoxia as a result of varying degrees of sleep apnea, or due to a trigger the patient may have been exposed to during the day. During sleep, minimum oxygen saturation is significantly lower. Castele, et al,27 performed 5 full-night and 7 daytime studies to examine this further. According to the findings: 'For all patients the mean (+/- SEM) of the median oxygenation values was 93.3% +/- 0.4% during wakefulness and 91.4% +/- 0.8% during sleep. During wakefulness the lowest saturation was 90% +/- 0.5%; during sleep there was a fall in the lowest oxygen saturation to 86.5% +/- 0.9%. In all patients a fall in oxygen saturation was associated with a decrease in respiratory depth without a change in respiratory frequency.' This nocturnal hypoxemia is a prelude to VOC.8

Case Report: In the past decade, the advent of battery-powered portable oxygen concentrators, which generate oxygen from ambient air, has freed people from a need to have sources to supply and refill oxygen cylinders. Oxygen by nasal canula, prior to sleep or at bedtime, was prescribed to 20 patients with SCD. Oxygen was administered by nasal canula at a rate of 1.5-2 liters/minute, continuous flow, delivered by a home or portable oxygen concentrator, to maintain an oxygen saturation of > 95%.Portable oxygen concentrators include the SeQual Eclipse, Inogen, Respironics, AirSep, and others, that extract oxygen from ambient air.

Discussion: The frequency of vaso-occlusive crises was decreased by 85% to 90%. This oxygen therapy has been simple but transformed their lives, according to patient reports. There has been not a single patient who applied oxygen at bedtime who woke up in a crisis. Patients who did experience a crisis were those who forgot to apply oxygen in the presence of another vaso-occlusive trigger (eg, daytime exertion) or patients with an underlying infection. Other patients had daytime crises as a result of exposure to triggers such as cold, dehydration, infection, etc. In the author's clinical experience, upon onset of a crisis, oxygen administration after the first few minutes is no longer preventive but may be part of an abortive protocol. Vascular occlusion and disruption of tissue oxygenation can result in severe pain, acute chest syndrome, avascular necrosis, and organ damage. The most frequent occurrence of painful crisis is during sleep when there is a decrease in oxygen saturation. Prevention of most episodes of sickle cell crisis, and thus organ damage, may be rapidly achieved by administration of oxygen at bedtime or prior to sleep. Oxygen should be administered prior to sleep when the individual is exposed to a VOC trigger.

Reference(s):

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Patient Safety

Patient Safety-1 REDUCED PREOPERATIVE LAB-ROUTINE MAY PUT PATIENT SAFETY AT RISK: A FATAL CASE REPORT

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Introduction: Cutting costs is a major issue in medicine. Some 20 years ago, otherwise healthy patients received an ECG, a chest X-ray and numerous laboratory tests prior to surgery. Nowadays, guidelines only recommend a minimal preoperative check-up, if at all (1,2). In the absolute majority of cases, this is cost-effective and safe. However, in rare cases this may have fatal consequences, as presented in the following:

Case Report: A 78 year old lady was admitted to our hospital due to lower back pain based upon a metastasizing tumor of the urinary bladder. She was scheduled for a ureterorenoscopy. Lab-test included a normal hemoglobin and hematocrit, normal white blood cell and platelet counts, and an INR und aCT within normal range. In terms of electrolytes, sodium, potassium and chloride were within normal range. On day 10, the patient developed a fever, and an antibiotic treatment was initiated. With a qSOFA of 1, the patient remained on the regular ward. Two days later, she presented a GCS of 3, and the medical emergency team was involved. The patient was intubated and transferred to the ICU. On admission there, a point-of-care lab-test was performed and revealed a total calcium of 6,00 mmol/l serum. This value was controlled in our central laboratory: 6,03 mmol/l. In the meanwhile, the patient required a high-dose vasopressor therapy (norepinephrine) due to septic vasoplegia. She underwent CPR, repetitively. A Shaldon catheter was placed and dialysis was initiated immediately. Finally, our patient developed a pulseless electric activity and died, consecutively. On autopsy, a parathyroid adenoma was diagnosed (diameter: 3,2 cm).

Discussion: A primary hyperparathyroidism remained undiagnosed during our patients 2-weeks hospital stay, because serum calcium as its key parameter is no longer part of our reduced lab-routine. Thus, the elevated calcium level remained undetected for 12 days. It was only diagnosed on autopsy with a parathyroid adenoma as its histomorphological correlate.

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Patient Safety-2 Management of an Inadvertent Cannulation of Subclavian Artery Complicated by Stroke

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Introduction: Inadvertent puncture of a non-compressible artery such as the subclavian artery, though rare, may be associated with life-threatening sequelae, including hemomediastinum, hemothorax, and pseudoaneurysm (1). They usually have a late clinical presentation with pain, swelling or other compressive symptoms. The optimal treatment in this situation is still a matter of debate. (2). Inadvertent placement in the subclavian artery is considered to be one of the most challenging complications to the vascular specialist, which is mainly due to its deep anatomical location(2) .Described herein is a successful endovascular management of inadvertent left subclavian artery cannulation during insertion of a triple lumen central line catheter.

Case Report: A 64-year-old- gentleman with a history of multiple sclerosis not on disease-modifying therapy with a baseline right sided weakness presented with urosepsis and bacteremia related to right obstructing uretropelvic junction (UPJ) stone underwent right percutaneous nephrostomy tube placement. Patient was admitted to SICU for broad spectrum IV course of antibiotic, resuscitation and hemodynamic monitoring. Left subclavian access was obtained using a surface landmark approach. After non-pulsatile backflow convinced to be venous blood, dilator over the guidewire was used, a 7.5 Fr CVC catheter was then placed. Imaging post CVC placement arose the suspicion of inadvertent subclavian artery cannulation. The catheter was left in place and vascular surgery and interventional cardiology teams were involved. The provisional treatment plan was to use arterial closure device. Since the patient was bacteremic, the procedure was postponed till next day. The elected overnight recommendation was to continuously transduce and to intermittently flush the line to maintain patency. Around two hours later, Patient was found to have tunnel vision and pressure-like headache behind his bilateral eyes in which CT head without contrast, at that time, excluded any acute pathology. Further examination revealed left homonymous hemianopsia. MRI confirmed Right acute PCA distribution area of infarct (image 1 & 2) extending from medial right occipital lobe (image 3) to right para-hippocampal gyrus (image 4).

Discussion: Discussion: CVC access appeared to be deployed frequently in critically ill patients, presenting with shock in particular. Although most reported CVC Cannulations are placed using external landmarks, a lot of literature supports the use of ultrasonography during CVC placement to avoid inadvertent injuries. In the present case, we reported a complication related to CVC placement using surface landmarks in form of right occipital lobe infarct and subsequent left superior quadrant field cut with mild left inferior quadrant acuity impairment. A risk that can be decreased by using ultrasound. Other preventive measure that might have been helped is introducing the angiocatheter into the cannulated vessel and subsequently transducing it before dilatation and actual catheter placement. However, absence of pulsatile flow may be misleading in hypotensive and volume depleted patient. A situation that is well descried and equally contributory to the development of the complication reported herein. The clinical picture that was noticed in our case is mainly related to artery-to-artery embolism from dislodged plague or air embolus secondary to mispositioned subclavian catheter extending to aortic arch. In our experience, septic embolism was less likely, based on the absence of valvular vegetations on TTE, negative bubble study and rapid clearance of blood culture.

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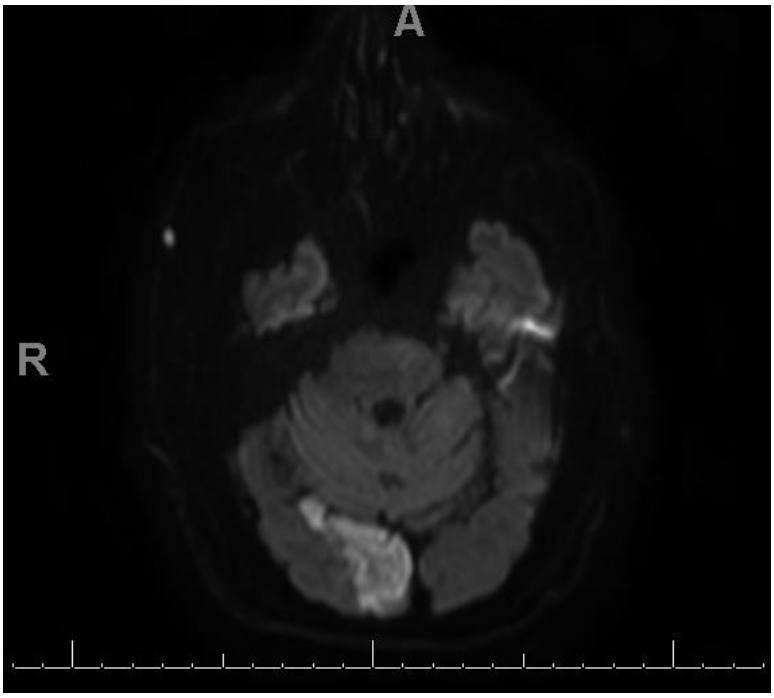
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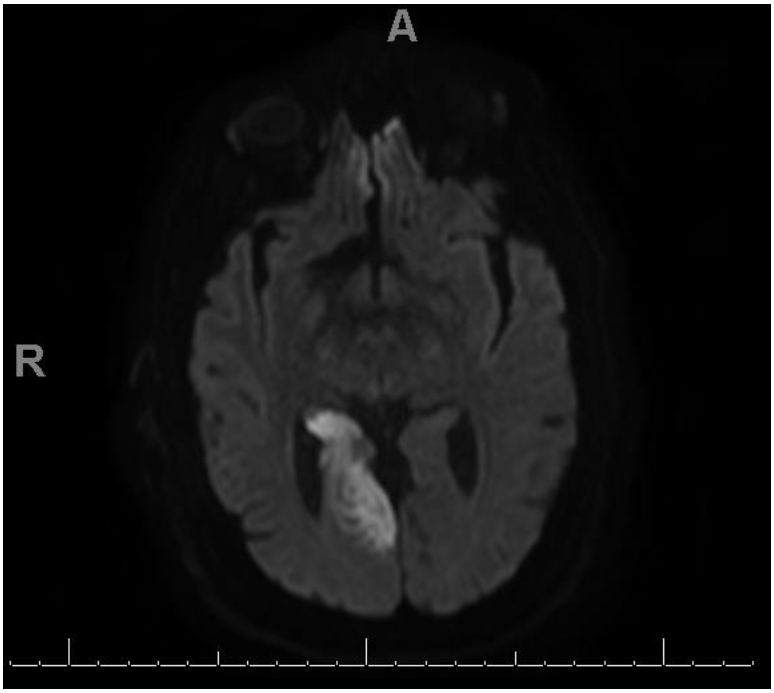
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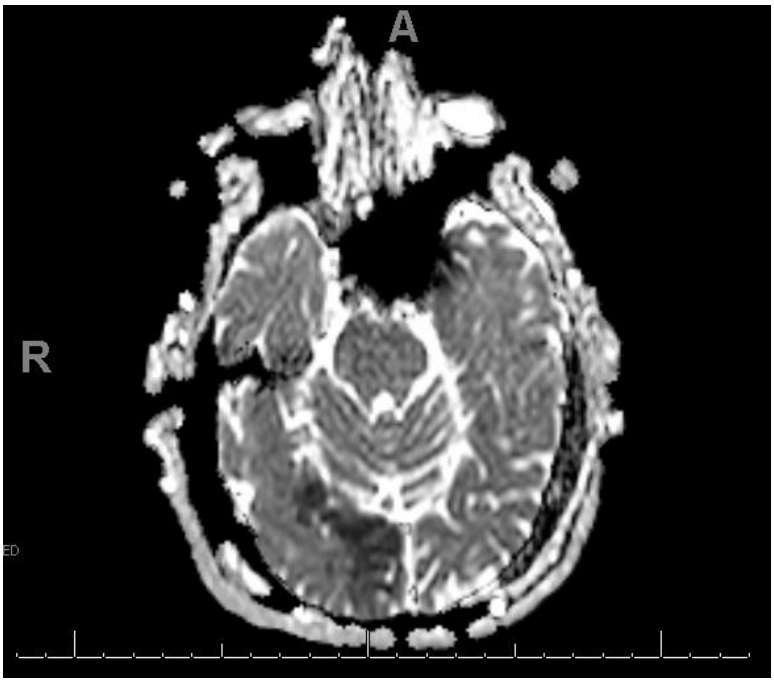
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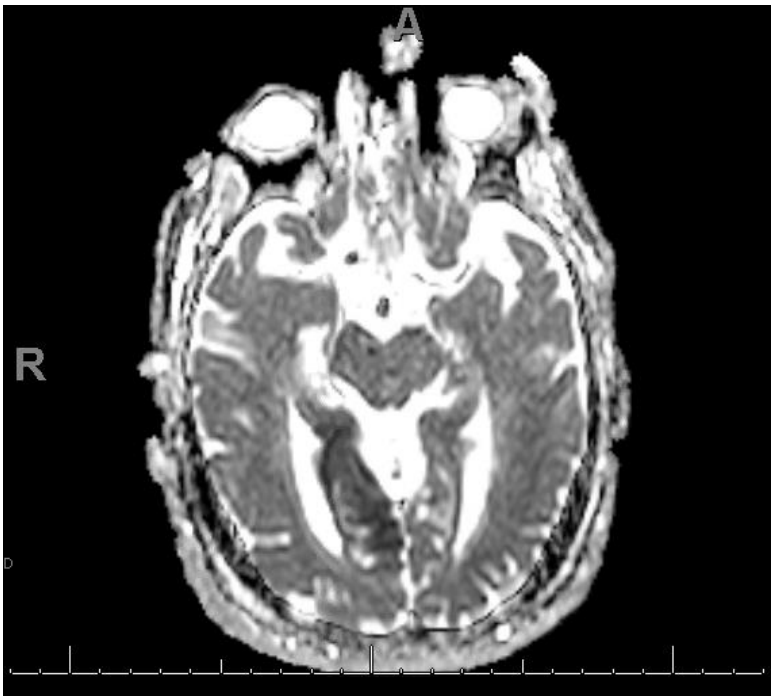
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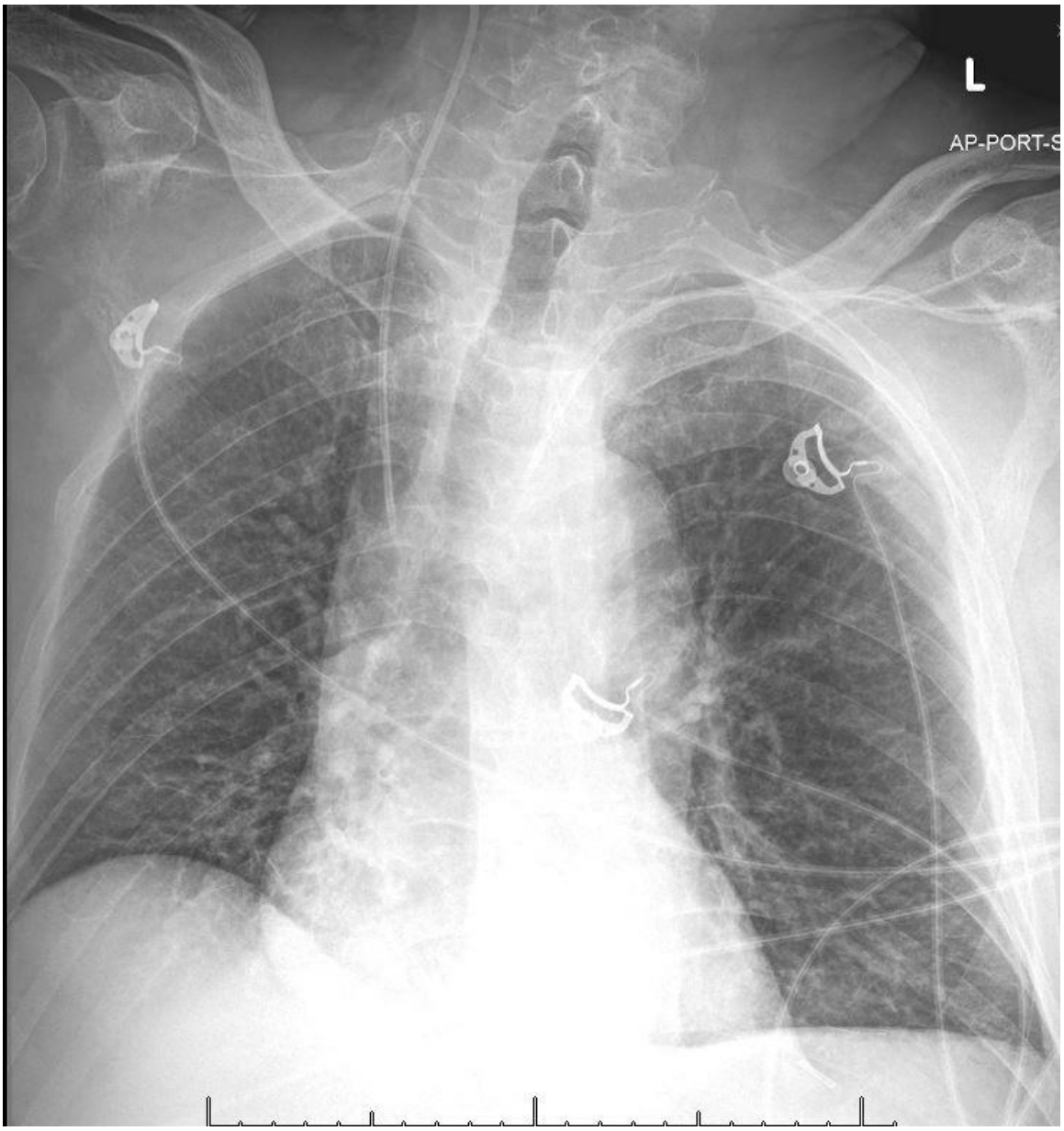
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AP-PORT-S

Perioperative Anesthesia

Perioperative Anesthesia-1 Intraoperative Fluoroscopic-Assisted Placement of Cerebrospinal Fluid Drains (CSFD) by Anesthesiologists for Patients Undergoing Endovascular Aortic Aneurysm Repair: Pearls and Pitfalls

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Introduction: Placement of CSFDs for endovascular aortic aneurysm repair surgery is a Class 1 recommendation for spinal cord protection in patients at high risk for spinal cord ischemic injury. Drains have traditionally been placed by anesthesiologists intraoperatively on the day of surgery or preoperatively in the non-OR setting, necessitating a pre-hospital admission to the intensive care unit (ICU). A systematic review of 4714 patients undergoing CSFD placement for open and endovascular repair of thoracic and thoracoabdominal aortic pathologies observed a rate of any reported complications at 9.9% and severe complications at 2.7%. Complications can be broadly categorized according to 1) technical or anatomic complications during the attempt to access and place the catheter itself and 2) later complications encountered in the OR during the intervention or subsequently in the ICU. Notable factors which make catheter placement more technically challenging include elevated BMI or anatomic abnormalities including scoliosis, severe osteoarthritis, prior lumbar spine instrumentation or hardware, and lumbar spinal stenosis. Prior studies have suggested an improvement in CSFD success rate with fluoroscopically-guided placement. These studies have not, however, provided any specific guidance with respect to the development of a fluoro-based approach. We describe our experience with the adoption of fluoro-based CSFD placement and focus on the technical challenges encountered.

Case Report: Case series of fluoroscopic-guided CSFD placement by anesthesiologists 34 patients undergoing endovascular aortic aneurysm repair with CSFD placement (September 2018 to January 2020) Outcome variables obtained by chart review and included demographics, anatomic level, approach (midline versus paramedian), technique (landmark or fluoroscopic), and CSFD-related early and late complications

Discussion: 25 unique patients with fluoroscopic-assisted CSFD placement 4 case cancellations 1 procedure aborted (bloody spinal fluid) 1 procedure aborted (inability to pass drain catheter) 2 procedures aborted (in same patient) (inability to access intrathecal space prone) No post-dural puncture headaches Illustrative example of failed procedure Access to intrathecal space with 14-gauge Tuohy with CSF return at multiple lumbar levels confirmed with radiopaque contrast injection. Physician unable to thread intrathecal catheter to any meaningful depth with sufficient return of CSF. MRI of lumbar spine reported moderate to severe canal stenosis (L1 to L5). Spinal cord injury (SCI) is one of the most devastating and dreaded complications of endovascular thoracic aortic repair with contemporary series suggesting incidences as high as 10%. Cerebrospinal fluid (CSF) drainage by means of an intrathecal drain inserted at the lumbar level has been shown to reduce the incidence of postoperative paraplegia and is a recommended adjunct for the care of patients undergoing both open and endovascular repair of the thoracic aorta. Unfortunately, the risk of major CSFD-related complications is not negligible and has the potential for severe morbidity. Intraoperative fluoroscopic-guided CSFD placement is a viable alternative technique with the potential to reduce the risk of CSFD-related complications, especially if difficult placement is anticipated. We present a case series of 25 fluoroscopic-guided CSFD placements and provide illustrative examples of successful and unsuccessful attempts. A formal training process including credentialing, lecture-based education, and practical training and oversight was developed at our institution to introduce the practice change of anesthesiologists performing CSFD placement under fluoroscopy. Some early challenges have included operator proficiency with the technique, anatomical considerations including degenerative joint disease, patient positioning and implications on CSF and epidural venous plexus pressure, and needle design. As the technique is refined for anesthesiologists, intraoperative fluoroscopic-guidance has the exciting potential to decrease placement failures, traumatic attempts, procedure cancellations, pre-operative ICU admissions, and resource utilization - particularly at lower volume centers. Further studies are needed to determine whether fluoroscopic-guidance minimizes the risk of CSFD-related complications and in which populations the technique may be most beneficial.

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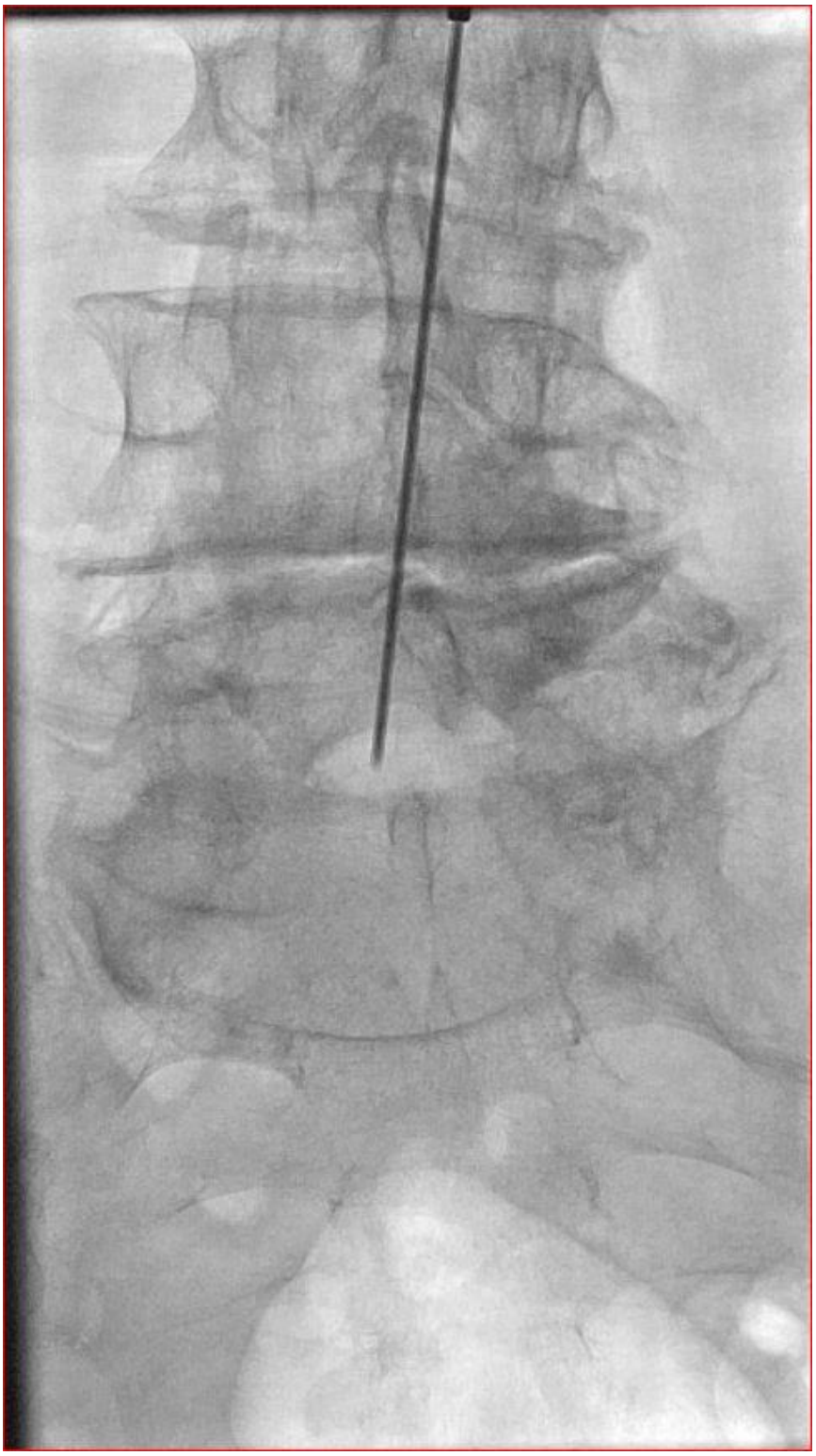

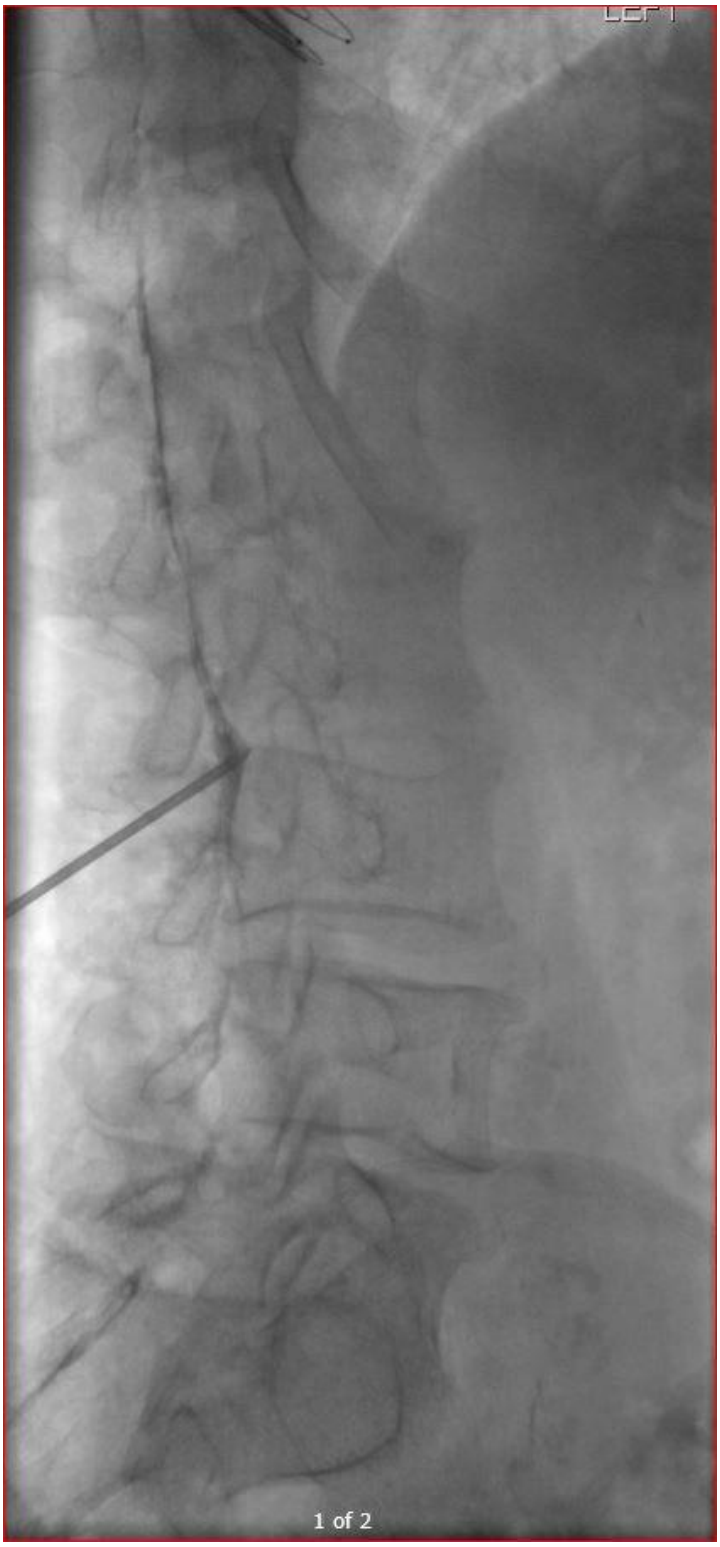
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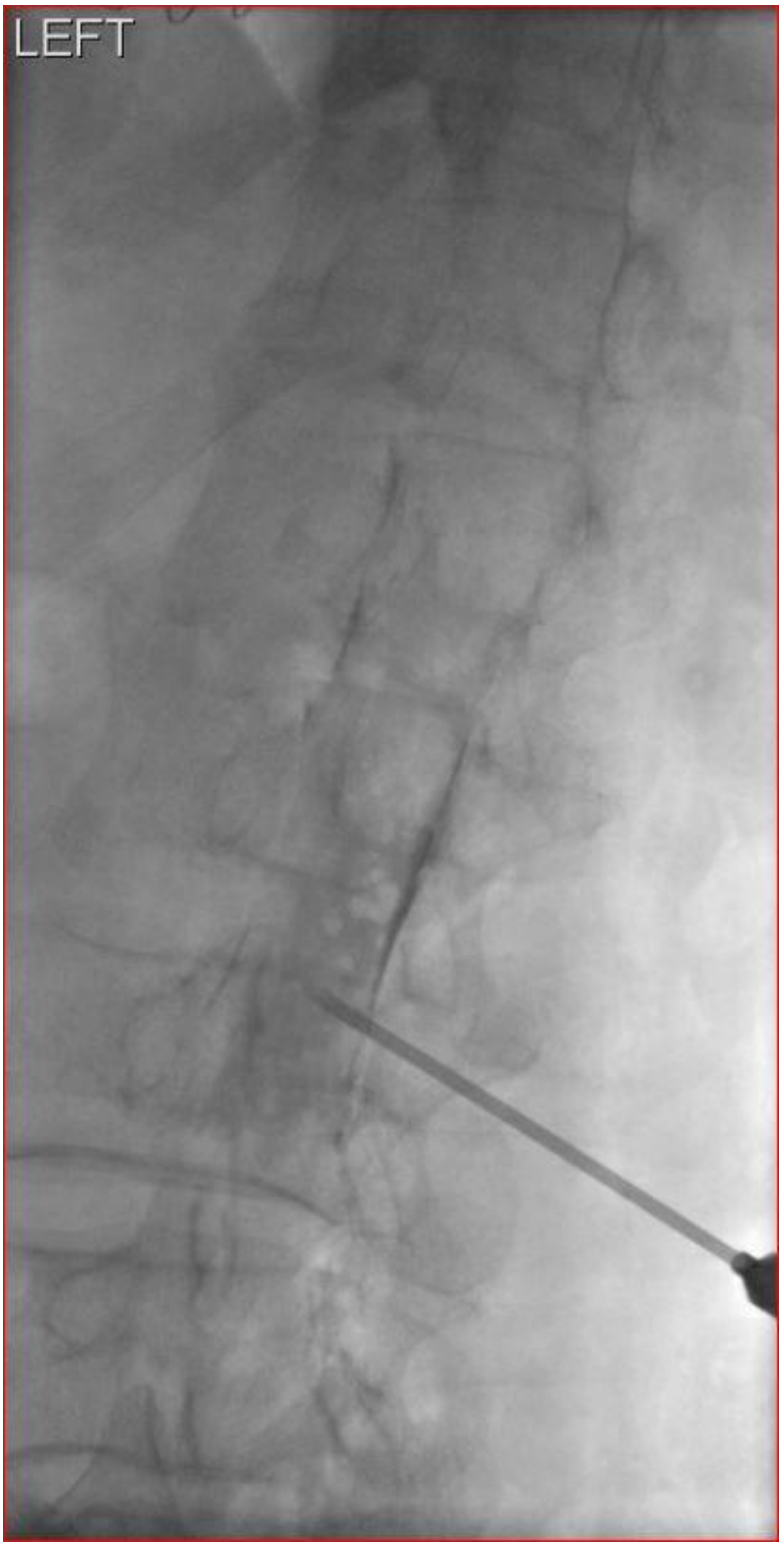
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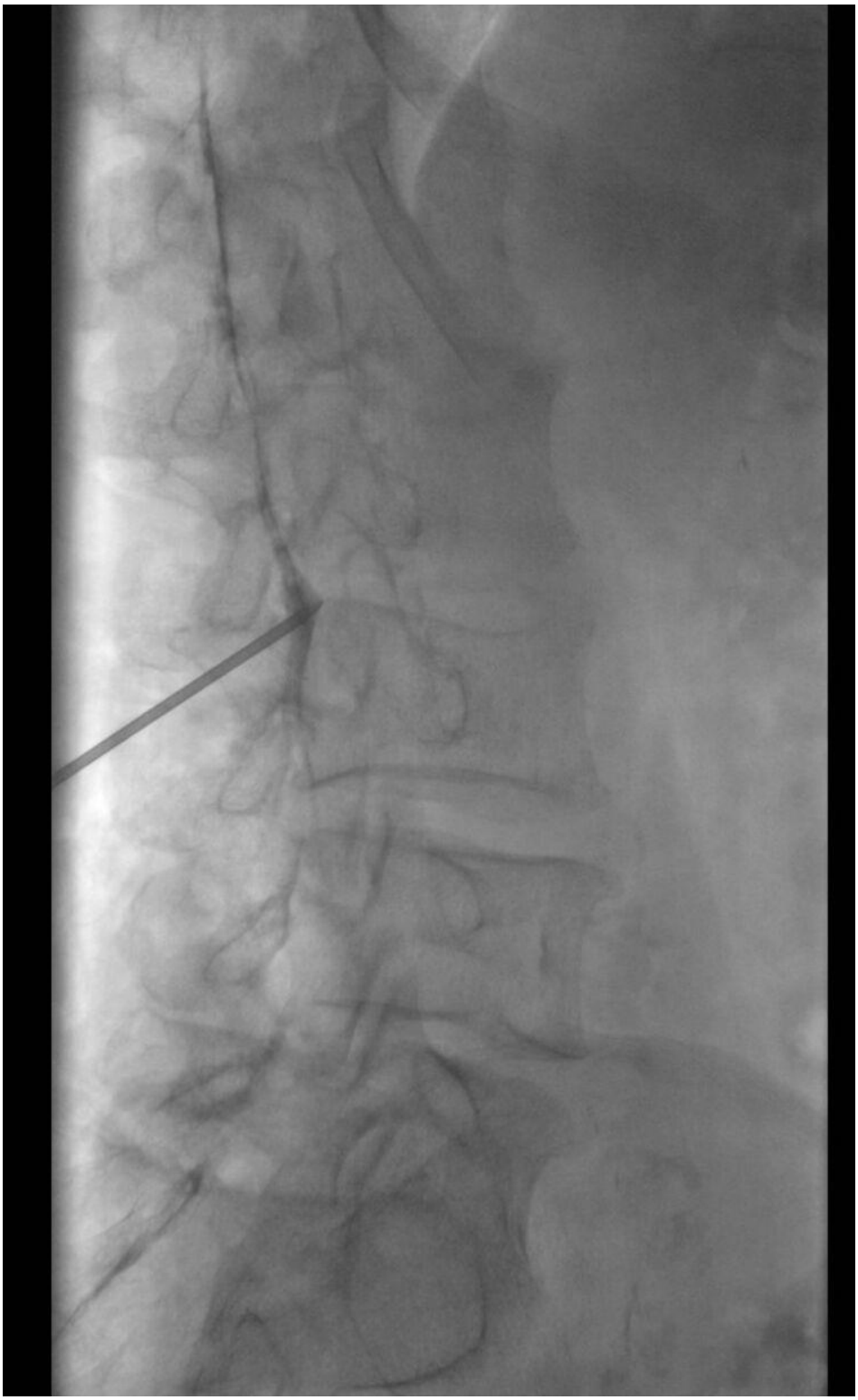

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Perioperative Anesthesia-2 Management of undiagnosed para-aortic mass in the intra-operative setting.

Kyle Kreft[1], Caleb Kennon[2], Chris Denny[1]

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Introduction: Paragangliomas (PGs) are rare tumors that derive from chromaffin tissue releasing catecholamines and, less commonly, serotonin[1]. Pre-operative optimization of known PG's includes an array of antihypertensives such as alpha-blockade, calcium channel antagonists, beta-blockade, and alpha methyl-para-tyrosine prior to surgical intervention[2]. Rarely, however, these tumors go undiagnosed and require immediate intraoperative management to avoid significant morbidity or mortality[3]. Currently, most of the research and recommendations surrounding PG's pertain to preoperative and intraoperative management when the diagnosis has already been made[2]. Several case reports exist of previously undiagnosed PG's that were discovered upon surgical manipulation. Our case report serves to add to this small cohort for future intraoperative management recommendations. In this case report, we discuss a 51 y/o female undergoing open resection of a retroperitoneal/para-aortic mass discovered to be an extra adrenal paraganglioma.

Case Report: The patient was a 51 y/o female undergoing scheduled open removal of a paraaortic mass. Pre-operative evaluation was significant for a vague history of migraine/headaches, paroxysmal tachycardia, and a cerebrovascular accident secondary to a ruptured aneurysm resulting in residual neurological deficits. Her presenting symptoms included dizziness and loss of consciousness. Previous EKG revealed sinus tachycardia and an unremarkable echocardiogram. The surgical team's working tumor diagnosis was that of a benign schwannoma or a mass associated with her history of surgeries for congenital gastroschisis. During surgical resection, manipulation of the mass elicited cardiovascular instability manifested as systolic blood pressures exceeding 300mmHg and tachycardia refractory to typical anesthetic management. The use of esmolol and nitroglycerin boluses and infusions, as well as a nicardipine infusion was required to regain cardiovascular stability. Upon pathologic sectioning of the tumor, it was determined to be an extra-adrenal paraganglioma. Post operatively the patient required norepinephrine for blood pressure support and was extubated without complication the following day.

Discussion: Historically, the morbidity and mortality during resection of a previously diagnosed PG's is high, with surgical mortality as much as 3.9%[1]. This number increases to as high as 80% when diagnosed intraoperatively[3]. Many factors go into successful management, including proper pre-operative documentation of symptoms and comorbid conditions, generous intravenous access, adequate blood pressure monitoring, communication with surgical team members, and immediate pharmacologic treatment not the least of which involves a vigilant anesthesiology clinician. Ultimately, early detection from high clinical suspicion in conjunction with swift pharmacologic treatment by the clinician(s) is imperative to minimize poor outcomes.

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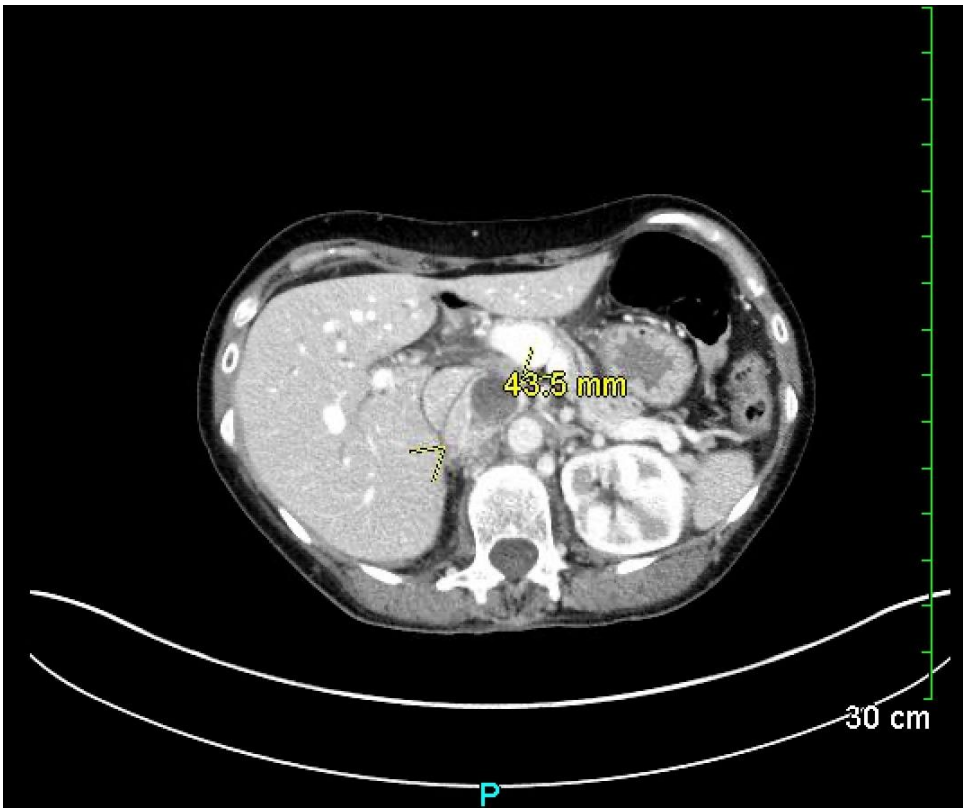
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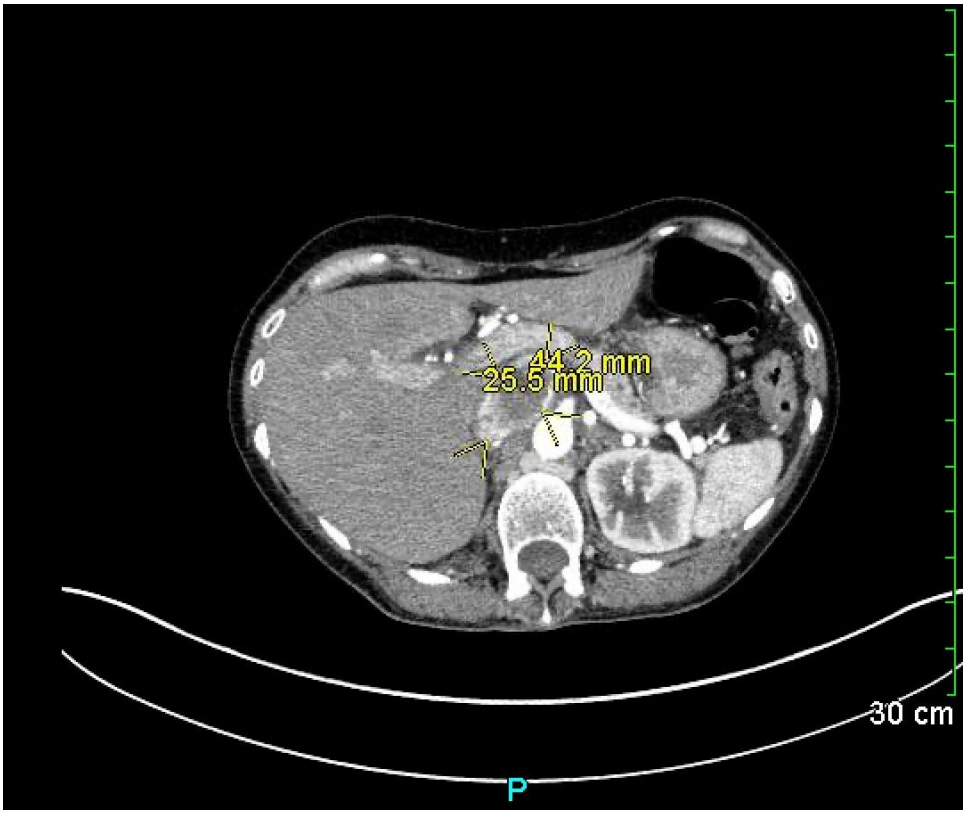
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Regional Anesthesia

Regional Anesthesia-1 Phrenic Nerve Block as a Bridge to Permanent Treatment for Intractable Hiccups after Coronary Artery Bypass Grafting

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Introduction: The patient is a 49 years old male suffering from constant, intractable hiccups after coronary artery bypass grafting surgery performed 14 months prior to this encounter. One month prior to this visit he underwent Nissen Fundoplication surgery for a paraoesophageal hernia, which was believed to be the cause for his intractable hiccups. The Nissen operation provided good relief of patient's gastrointestinal symptoms, but no relief of his hiccups. The patient had frequent hiccups (several per minute) despite multiple attempts to treatment with different classes of medications (including Thorazine, Neurontin, Baclofen).

Case Report: Upon obtaining informed consent, an ultrasound-guided diagnostic left sided phrenic nerve block was performed. The phrenic nerve was visualized as it branches from the upper trunk of the Brachial plexus with a 50/6 Hz high frequency linear probe of a Sonosite S2 ultrasound machine. Bupivacaine 0.5% in the amount of 2 ml, were injected via a Sonoplex Stim Pajunk 22G, 80 mm needle, with sudden relief of patient's hiccups. A total of 6 ml of Bupivacaine 0.5% was injected in divided doses, with complete resolution of patient's hiccups for approximately 8 hours. After the complete resolution of patient's hiccups, the left sided phrenic nerve block was deemed successful, and the patient was referred to a thoracic surgeon for clipping of his left phrenic nerve.

Discussion: Hiccupping is a characteristic noise caused by a sudden closure of the glottis after repeated, involuntary, spasmodic contraction of the respiratory muscles. Some hiccups are associated with certain diseases or occur postsurgical, and life-restricting intractable hiccups should be treated. The phrenic nerve injury can occur with whole body hypothermia, use of ice-slush around the heart and mammary artery harvesting. Most frequent cause of the hiccups after the CABG in injury or irritation of the left phrenic nerve due to the close anatomy to the heart. The conventional treatments for hiccups are either non-pharmacological, pharmacological or a nerve block treatment. It has been described in the literature, in the Korean Journal of Pain a case of ultrasound guided pulsed radiofrequency ablation of the phrenic nerve after a coronary bypass case in which the patient had intractable hiccups for seven years, which were complete stopped after pulsed radiofrequency ablation of the phrenic nerve, Kang et al. (4) During intraoperative continuous hiccups, ultrasound guided phrenic nerve block may be an alternative treatment option when physical methods and drug therapy are not effective noted Zhang et all in British Medical Journal of Anesthesiology. (2) It has been described a successful reversible phrenic nerve block for intractable hiccups accompanying pleural effusions, which consisted of thoracoscopic nerve clipping under general anesthesia and reversal under local anesthesia, Kim in surgical laparoscopic endoscopic percutaneous technique.(3) Given the benefit that he achieved with a temporary nerve block, and the disabling nature of the symptoms, we are describing here a case of blocking the phrenic nerve as a bridge to a more permanent way of stopping the hiccups. Patient was consented for a more permanent procedure, and he was explained the benefits and the risks including unilateral diaphragm paralysis which could lead to temporary or permanent shortness of breath. Pulmonary function tests were performed before the permanent procedure, which showed an FEV1 of 98% of normal. The DLCO could not be measured, due to his inability to hold breath because of his hiccups. Understanding the risks versus the benefits of the procedure the patient agreed to further proceed. The following procedure was done by an experienced thoracic surgeon, who via a thoracoscopic procedure, placed a permanent clip on the left phrenic nerve and the patient immediately after A phrenic nerve block may be a suitable treatment choice because it can quickly and effectively terminate hiccups when physical or medical treatments are not effective. An ultrasound-guided block can improve the success rate and reduce the potential for complications and can be a guideline for a more permanent solution.

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Trauma

Trauma-1 A modified pediatric facemask provided nasal CPAP pre-oxygenation and apneic nasal oxygenation in an obese trauma patient with hemothoraces and worsening respiratory distress during RSI/ETI

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Introduction: Trauma patients with pneumothorax or hemothorax have limited O2 reserve which may cause severe O2 desaturation during rapid sequence induction (RSI) of general anesthesia (GA) and endotracheal intubation (ETI), despite adequate pre-oxygenation with a facemask. A pediatric facemask has been used to maintain oxygenation by delivering nasal CPAP, pressure-support or pressure-control ventilation in adult patients with obstructive sleep apnea (OSA) during sedation, GA induction, and awake/asleep video-laryngoscopy (VL) assisted or oral fiberoptic ETI (Fig. 1).1-3 We used a modified pediatric facemask to provide nasal CPAP pre-oxygenation and apneic oxygenation in a trauma patient during RSI of GA.

Case Report: A 66-year-old obese male, 5'6', 239 lbs, BMI 38.6 kg/m2, s/p motor cycle accident, with multiple rib fractures, sternal fracture, bilateral hemothoraces and worsening respiratory distress for urgent thoracotomy, repair of fractured ribs and chest tube revision. The patient had a Mallampati Class II airway, mouth opening >3 cm and a thick neck. He had moderate bilateral rhonchi and was tachypneic with a facial CPAP mask. As soon as he was transported to OR with a non-rebreathing mask, a modified infant mask (size #2) was secured over his nose with elastic head-straps and connected to the anesthesia machine via a breathing circuit (Fig. 1). The APL valve was adjusted to deliver 6-8 cm H2O CPAP with 4 L O2/min. His tachypnea was immediately resolved and he breathed more comfortable than before. After he was pre-oxygenated for 10 min, his SpO2 maintained 100% and his ET/FI O2 reached 82-95% (Fig. 2-3). RSI of GA with cricoid pressure was then induced with fentanyl, lidocaine, propofol and succinylcholine. With the nasal mask delivering apneic oxygenation, ETI using a video-laryngoscopy was quickly accomplished (Fig. 4). He maintained 100% SpO2 and stable hemodynamics throughout RSI and ETI (Fig 3). He tolerated the 7-hour procedure well and was extubated on postoperative Day 2 without any complications.

Discussion: This simple modified infant mask assembly provided nasal CPAP pre-oxygenation and apneic oxygenation in an obese trauma patient with multiple fractured ribs, hemothoraces and worsening respiratory distress during RSI of GA and ETI. It takes less than 2 mins to modify a tear-drop shaped pediatric facemask to a triangular-shaped nasal mask to fit most adult noses (Fig. 5). It utilizes the existing anesthesia equipment and may improve patient safety at a low cost.

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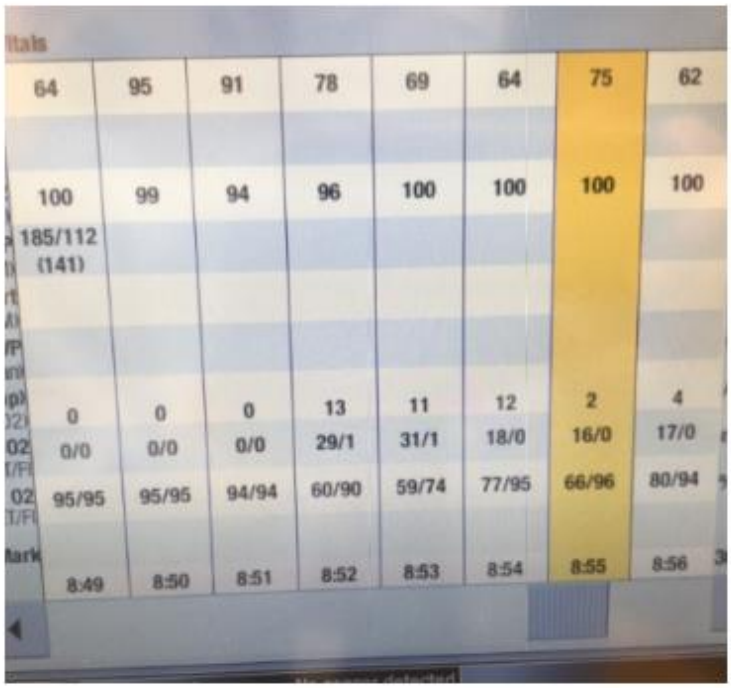

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100	99	94	96	100	100	100	100
185/112 (141)							
0	0	0	13	11	12	2	4
0/0	0/0	0/0	29/1	31/1	18/0	16/0	17/0
95/95	95/95	94/94	60/90	59/74	77/95	66/96	80/94
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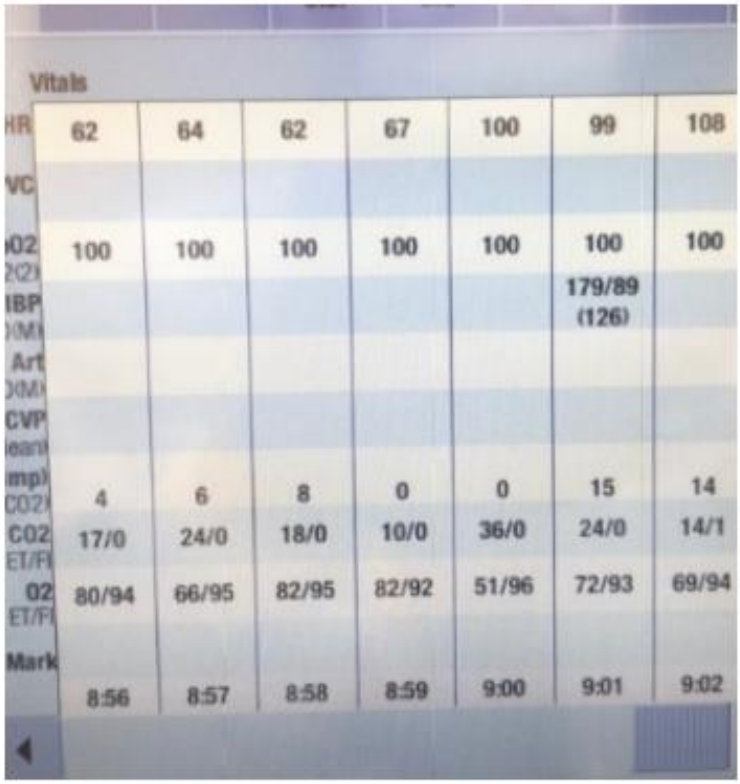

Vitals

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100	100	100	100	100	100	100
					179/89 (126)	
4	6	8	0	0	15	14
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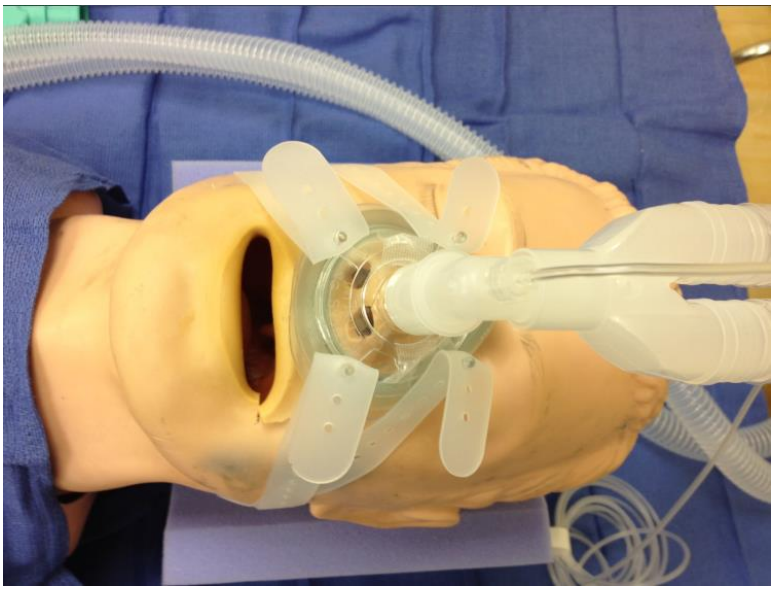

Trauma-2 Delayed Tracheoesophageal Fistula after Penetrating Chest Injury Requiring Extracorporeal Membrane Oxygenation Support

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Introduction: Penetrating thoracic injuries may lead to a constellation of injuries ranging from benign superficial wounds to aerodigestive injuries. Tracheoesophageal fistulae (TEF) may be attributed to iatrogenic, inflammatory, infectious and traumatic causes (either blunt or penetrating in nature). The presentation is commonly delayed secondary to subacute necrosis of the devitalized tissue. Operative mortality of TEF is roughly 15% and the procedure is significantly more challenging when hypoxemia is present prior surgery as selective lung ventilation become crucial to facilitate the surgical approach.1-4 We describe the case of a 29-year-old patient who developed a TEF following a gunshot wound to the chest and required veno-venous (VV) extracorporeal membrane oxygenation support (ECMO) due to severe acute respiratory distress syndrome (ARDS). Prompt diagnosis and multidisciplinary management becomes paramount to assure favorable clinical outcomes in these patients.

Case Report: A 29-year-old patient presented to our facility after sustaining several gunshot wounds to his left back and neck. Imaging revealed multiple bullet fragments along the left 1st and 2nd thoracic vertebrae. The patient was endotracheally intubated on arrival due to confusion and agitation. Since scant bloody secretions were noticed from the endotracheal tube, the patient was taken to the operating room (OR). Esophagoscopy revealed a superficial lesion, 25 centimeters from the incisors, and bronchoscopy revealed a submucosal tracheal hematoma 2 centimeters from the carina. Computerized tomography of the chest did not to demonstrate any signs of mediastinitis and the patient was hemodynamically stable. On hospital day (HD) #4 the patient met extubation criteria and the endotracheal tube was subsequently removed. He initially tolerated extubation however three hours later developed increasing respiratory distress, persistent cough and hypoxemia requiring re-intubation. Bronchoscopy revealed a distal carinal mucosa injury with protrusion into the airway with positive pressure. Mucosal ulceration was noted in the region with presumed gastric secretions entering the airway through a small orifice. Gastric secretions were noted in the left middle and lower lobes. The patient had persistent hypoxemia with saturations in the low 90's on 100% fraction of inspired oxygen. The decision was made to return to the OR for exploration of the neck and chest with possible thoracotomy. In the OR, a repeat esophagoscopy revealed a large lesion 25 centimeters from the incisors and bronchoscopy showed a moderate sized distal posterior tracheal defect. At this point, on anticipation of a right thoracotomy, both the trauma surgery and anesthesia teams decided that the patient would require right-sided lung isolation and given his level of hypoxemia would not likely tolerate selective lung ventilation; therefore, the decision was made to initiate bi-femoral VV-ECMO. Adequate flows were obtained and hypoxemia improved. A bronchial blocker was positioned for lung isolation and a right thoracotomy was performed. Both the tracheal and esophageal defects were primarily repaired and an intercostal flap was placed in between. The patient tolerated the procedure well and was admitted to the Intensive Care Unit. Daily bronchoscopy evaluations revealed an intact surgical repair. He was eventually decannulated from VV-ECMO on HD#13 and liberated from mechanical ventilation on HD#24. Follow up esophagograms were unremarkable and the patient was discharged home on HD#37.

Discussion: The body of literature citing ECMO support as an adjunct for the management of a TEF is scarce. Early recognition of a TEF is important as early treatment can prevent complications. This case presents the successful management of a TEF with VV-ECMO support due to severe ARDS and assist with intraoperative one-lung ventilation.

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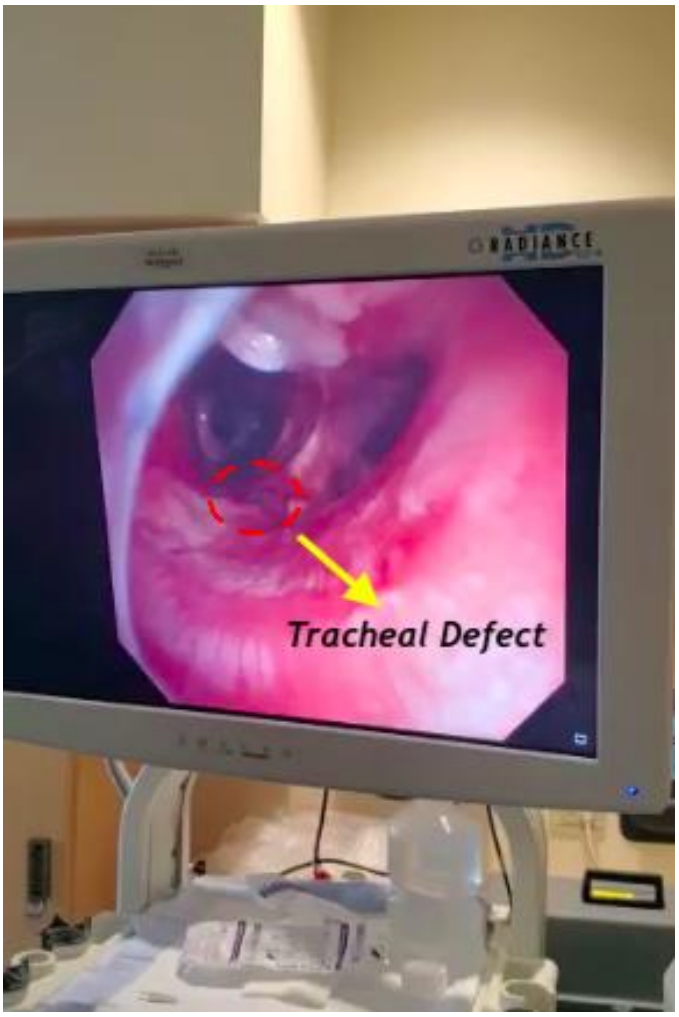
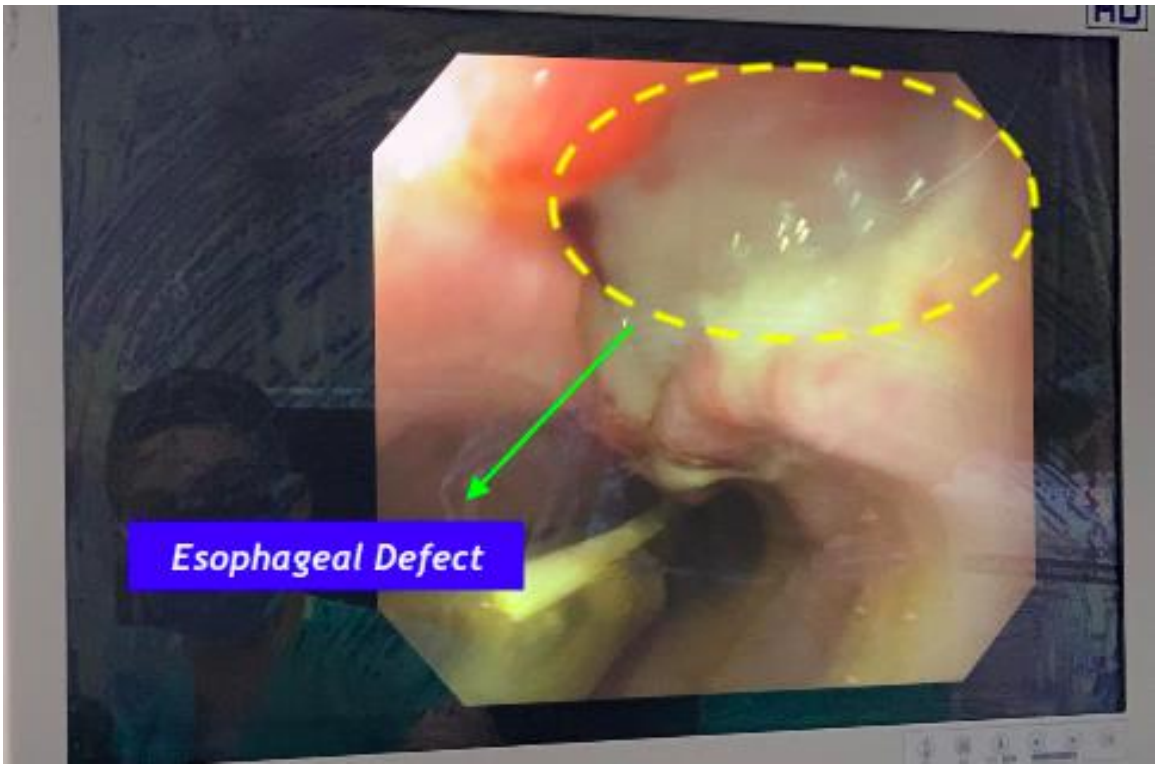

RADIANCE
Tracheal Defect


Esophageal Defect

Trauma-3 Development of a new tourniquet device which uses EHD phenomenon in emergency and surgery

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Introduction: After an emergency or disaster, subsequent trauma can cause severe bleeding and this can often prove fatal, so promptly stopping that bleeding is crucial to preventing avoidable trauma deaths. A tourniquet is often used to restrict blood flow to an extremity. In operation and hospital, the tourniquet systems currently in use are pneumatically actuated by an air compressor, so they must have a steady power supply. These devices have several drawbacks: they vibrate and are noisy since they are pneumatically actuated and they are far from portable since they are large and heavy .

Case Report: A tourniquet cuff (width 12 mm × length150 mm, material: polyolefin) was placed on the thigh of Wistar rats and pressure was applied for 2 hours by a device that uses EHD phenomena to generate pressure(an EHD pump)(figure1). Animals were divided into four groups based on how much compressive pressure was applied with a tourniquet: 40 kPa (300 mm Hg, n =13), 30 kPa (225 mm Hg, n = 12), 20 kPa (150 mm Hg, n = 15), or 0 kPa (controls, n = 25). Blood was sampled and biochemically assessed and creatine kinase (CK) levels were measured . We measured blood flow by Doppler.

Discussion: CK levels were 497 ± 173 IL/U in the control group, 662 ± 487 IL/U in animals to which a tourniquet was applied at a pressure of 20 kPa, 621 ± 314 IL/U in animals to which a tourniquet was applied at a pressure of 30 kPa, and 942 ± 649 IL/U in animals to which a tourniquet was applied at a pressure of 40 kPa. CK levels were significantly elevated in animals to which a tourniquet was applied at a pressure of 40 kPa which comparison to control group .(figure2) Blood flow by Doppler were 14±3.5ml/min/100g in the control group, 1.7±1.3ml/min/100g in animals to which a tourniquet was applied at a pressure of 20 kPa, 0.5±0.0ml/min/100g in animals to which a tourniquet was applied at a pressure of 30 kPa, and 0.3± 0.1 IL/U in animals to which a tourniquet was applied at a pressure of 40 kPa. A significant difference was noted in levels of CK between the 40-kPa and control groups. Blood flow by Doppler decreased at 20 kPa, and completely disappeared at 30 and 40 kPa. The optimum pressure to prevent musculoskeletal complications was around 30kPa.New tourniquet systems with an EHD pump will continue to be developed and improved for use as medical equipment and for future use in clinical settings.