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Subspecialty Abstracts (by category):

Scholars' Abstracts (by category):

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Subspecialty Abstracts

Airway Management

S-1.

COMPARISON OF AIRWAY INDICES, BODYMASS INDEX AND CORMACK LEHANE GRADING IN SNORERS AND NON SNORERS

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AFFILIATION: Department of Anesthesiology and Intensive care, Nizam's Institute of Medical Sciences, Hyderabad, India

INTRODUCTION: Difficulties with tracheal intubation significantly contribute to morbidity and mortality associated with anesthesia.1 Airway management is one of the greatest concerns of anesthesiologists and difficult intubation, is an event not easy to predict before induction of anesthesia. Snoring is increasingly prevalent and patients who snore pose a potential problem for securing an airway because of a narrow space between the base of the tongue and the posterior pharyngeal wall, and hence more prone to collapse under anesthesia2. The relationship between night time snoring and increase in Coramack Lehane grading is established3. We focussed on the utility of individual upper airway evaluation by physical examination and their usefulness in predicting a difficult airway among people who snore. We hypothesized that simple history of snoring in preanaesthetic evaluation along with airway morphology may predict difficult airway.

METHODS: After institutional ethics committee approval and informed consent 140 patients were recruited and were assigned to two groups; snorers group S and non snorers group NS based on the history given by them, their spouse or close relatives. During the pre-anaesthtic check-up (PAC), history of snoring, along with various parameters such as age, weight (kg), height, mouth opening, thyromental distance, sternomental distance, neck circumference, modified mallampatti grade, neck extension were noted. A single investigator performed laryngoscopy in all the cases and the investigator was blinded to the history of snoring. Glottic visualization was assessed based on Cormack Lehane classification and difficulty in intubation assessed based on the intubation difficulty score (IDS).

RESULTS: We found that snorers had higher neck circumference, BMI, modified mallampatti score (table I)Cormack Lehane grade (table II) and Intubation difficulty score which was statistically significant. Males outnumbered females. Bag and mask ventilation was also difficult in snorers. (Tables 1,2) Conclusions: A simple history of snoring can alert us to a probable difficulty with bag and mask ventilation and intubation. References: 1. Benumof JL. Airway management : Principles and practice. St Louis Mosby 1996: 121-1252. Friedman M. Sleep Apnea and Snoring: Surgical and Non-Surgical Therapy Saunders Elsevier publications 2008 3. The relationship between night time snoring and Cormack and Lehane grading, Acta Anesthsiologica Taiwanica . 2010

Table 1: Modified mallapati grade in Snorers and Non snorers

Modified mallampati classification	Non Snorers	Snorers	p value
Class I	29 (43.3%)	07 (10.4%)	<0.001
Class II	22 (32.8%)	25 (37.3%)	
Class III	16 (23.9%)	29 (43.3%)	
Class IV	00 (0.0%)	06 (9.0%)	

Table II: Cormack Lehane grading

Cormack Lehane grading	Non Snorers	Snorers	p value
Class 1	23 (34.3%)	01 (1.5%)	<0.001
Class 2a	26 (38.8%)	21 (31.3%)	
Class 2b	14 (20.9%)	12 (17.9%)	
Class 3	04 (6.0%)	30 (44.8%)	
Class 4	00 (0.0%)	03 (4.5%)	

S-2.

WITHDRAWN.

S-3.

FINESSE NOT FORCE: DIFFICULTIES DURING AIRWAY MANAGEMENT IN OCTOGENARIANS REGARDING INTUBATION, VENTILATION, AND OXYGENATION

AUTHORS: K. N. Johnson, L. Groban, Y. F. Bryan

AUTHORS: K. N. JOHNSON, L. GROBAN, Y. F. BRYAN;

AFFILIATION: Anesthesiology, Wake Forest Baptist Health, Winston-Salem, NC

INTRODUCTION: Octogenarians undergo anatomic and physiopathologic degradation, including an edentulous mouth, arthritic neck, and cognitive dysfunction[1-4]. Aging may also be associated with OSA, asthma, and COPD[5]. These changes may make airway management challenging due to difficulty visualizing the vocal cords or placing the endotracheal tube during intubation, difficult bag mask ventilation (BMV), and/or increasing the chance for oxygen desaturation. Current airway studies include elderly patients but do not focus specifically on techniques for the elderly. The aim of our study was to examine which component of airway management regarding intubation (I), ventilation (V), and oxygenation (O) was problematic in octogenarians.

METHODS: With waiver of consent, an IRB approved difficult airway prospective observational study in adults at Wake Forest School of Medicine from 2010-2015 was conducted. Inclusion criteria included airway features indicative of difficult airway, history of failed intubation, the planned use of specialized airway devices, and/or airway complications. Patients 80 years and older were analyzed. Demographic data collected were age, weight, BMI, gender, ASA class, airway indices, diagnosis, and procedures. Complications occurring during I (≥3 intubation attempts), V (CPAP > 20 cm H_2O or 2-person BMV), and O (SpO_2 < 95%) were analyzed. Results: See table 1 for demographics and figure 1 for diagnosis and procedures. 3 patients (7.3%) had complications with all three IVO. See figure 2 for the combination of outcomes (IV, IO, VO). 19.5% of patients experienced complications with I, 48.8% of patients experienced complications with V, and 34.1% of patients experienced complications with O. 17.1% of patients had a tachycardic response while 19.5% had a hypertensive response during airway management.

CONCLUSIONS: In octogenarians, we found a low incidence of problems when combining all three airway outcomes of IVO; however, a high frequency of problems were found individually with V and O. There were less complications with I, however patients had tachycardia and hypertension during I. The reason for greater problems with V and O may have been due to our patients being edentulous, creating a difficult seal during BMV, and/or due to OSA and COPD. In conclusion, our results suggest that alternative devices and airway techniques should be developed specifically for the elderly.

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Table 1. Demographics

	Mean ± SD (Range)
Age (years)	83.6 ± 5.5 (80-113)
Weight (kg)	73.7 ± 16.4 (42.8-113.4)
BMI (kg/m^2)	26.3 ± 5.0 (18.2-35.1)
	n / %
Female	22 / 53.7
Male	19 / 46.3
ASA	n / %
2	5 / 12.2
3	31 / 75.6
4	5 / 12.2
Mallampati Class*	n / %
I/II	20 / 51.3
III/IV	19 / 48.7
Thyromental Distance**	
< 3 FB	5 / 12.5
≥ 3 FB	35 / 87.5
Neck Range of Motion**	
Limited	26 / 65.0
All	14 / 35.0

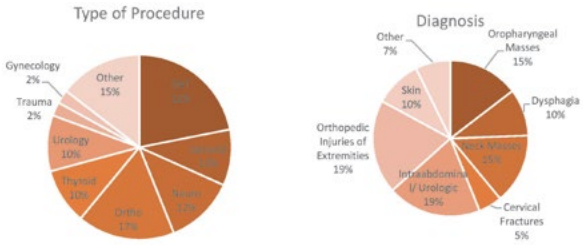

Figure 1.

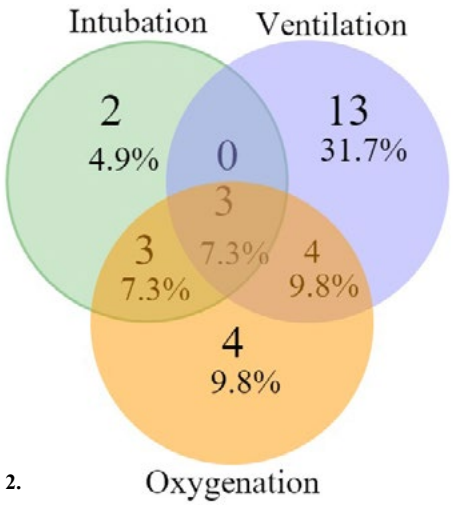

Figure 2.

S-4.

SUBGLOTTIC PERIOPERATIVE AIRWAY − TUBE INFLATION VIA RANDOMIZED EVALUATION WITH VARIABLE SYRINGE SIZE (SPAIR−TIRE) STUDY

AUTHORS: G. Williams[1], C. A. Artime[2], J. Tam[2], T. Burnett[2], O. L. Mancillas[2], T. A. Syed[2], C. A. Hagberg[2]

AFFILIATION: [1]Anesthesiology and Neurosurgery, The University of Texas Health Science Center at Houston (UTHealth) McGovern Medical School, Houston, TX, [2]Anesthesiology, The University of Texas Health Science Center at Houston (UTHealth) McGovern Medical School, Houston, TX

INTRODUCTION: An important component of endotracheal tube (ET tube) management is inflation of the endotracheal tube cuff (ETTC), which should ideally be inflated to a pressure of 22-32 cmH2O.[1,2,3] Decreased mucosal blood flow to the trachea begins when the cuff pressure exceeds 34 cmH_2O, with total obstruction of blood flow occurring at approximately 50 cmH_2O. We hypothesized that anesthesia providers will be able to more frequently achieve an endotracheal cuff pressure (ETCP) in the recommended range of 22-32 cmH_2O when a 5mL syringe is used to inflate the ETTC, as compared to a 10mL syringe.

METHODS: 200 patients were randomized to the use of a 5mL syringe (study group) or a 10mL syringe (control group) during ETTC inflation. For each patient, the determined syringe size was given to the anesthesia provider in the preoperative holding area. All other elements of the anesthetic preoperative evaluation and care were conducted as determined by the anesthesiologist. Following insertion of the ET tube, inflation of the ETTC was performed using a 5mL or 10mL syringe, with the final inflation volume being determined by the attending anesthesiologist. Afterwards, a member of the study team measured and recorded the ETCP using a standard hospital-provided manometer.

RESULTS: Our study demonstrated that neither a 5mL nor 10mL syringe was predictive at achieving an ETCP within the desired range of 22-32 cmH_20. The percentage of in-range cuff pressures for the study group was 10.53% and for the control group was 6.78%. The average cuff pressure for the study group was 55.8 cmH_20 versus 68.8 cmH_20 for the control group, a difference of 13 cmH_20 (p=.005). Overall, 84.21% (n=64) of the study group and 91.53% (n=54) of the control group had cuff pressures exceeding 30 cmH_20 (Figure 1). In addition, our data demonstrated that cuff pressure was not associated with height, weight, BMI, BSA, or the ET tube size. However, multivariate analysis showed that there was an association of higher cuff pressures with the use of a 10 mL syringe (p=.002), female gender (p=.011), and in non-smokers (p=.049).

CONCLUSION: Although our study did not show that syringe size was predictive of ideal cuff ranges, the data did demonstrate that using a 5mL syringe resulted in a lower degree of elevated pressure as compared to a 10mL syringe. Therefore, the use of a 5mL syringe should be considered during inflation of the ETTC, as this could potentially reduce risk of patient harm associated with elevated endotracheal cuff pressures.

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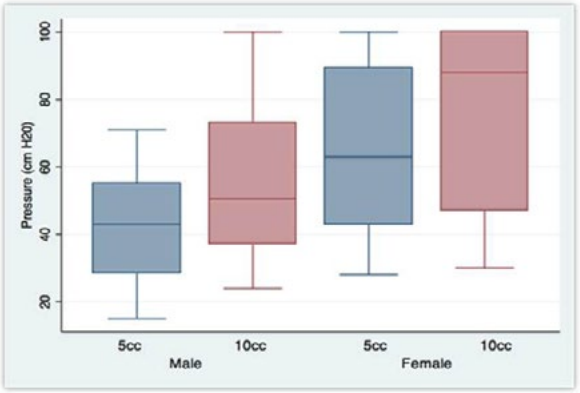
Figure 1: Boxplot of pressure distribution, organized by gender



S-5.

A COMPARISON OF THE KING VISION CHANNELED, KING VISION NONCHANNELED, AND COBALT GLIDESCOPE VIDEO INTUBATION SYSTEMS IN PATIENTS AT RISK FOR DIFFICULT INTUBATION

AUTHORS: S. Guzman-Reyes, G. Medina-Rivera, O. O. Nwokolo, T. H. Markham, S. D. Gumbert, T. Burnett, C. A. Hagberg

AFFILIATION: Anesthesiology, The University of Texas Health Science Center at Houston (UTHealth) McGovern Medical School, Houston, TX

INTRODUCTION: There are several advantages of video laryngoscopy; especially their ability to provide superior glottis visualization, as compared to traditional laryngoscopy.1-3 The purpose of this three arm study was to compare the efficiency and efficacy of the King Vision® Video Intubation Systems to the Cobalt GlideScope® in patients with anticipated difficult airways. We hypothesized that the King Vision™ Video Channeled Laryngoscope is more efficacious in terms of successful endotracheal intubation in comparison to the Cobalt GlideScope® Video Laryngoscope. It is further hypothesized that the King Vision™ Video Laryngoscope with Standard Blade (Non-Channeled) is equivalent to the Cobalt GlideScope®.

METHODS: 225 adult >18yo patients were randomized into 3 groups: Group A (n=75) Cobalt GlideScope®, Group B (n=75) King Vision® Channeled Video Laryngoscope and Group C (n=75) King Vision® Standard Video Laryngoscope. Patients who met two or more of the following inclusion criteria: MP III-IV, MO <4cm, neck circumference >43cm, and/or TMD <6cm were enrolled in the study. Laryngoscopy and intubation was performed by resident anesthesiologists under the direct supervision of an attending anesthesiologist. Intubation time, number of intubation attempts, and optimal Cormack-Lehane (C-L) view were recorded and analyzed.

RESULTS: Patient demographics and difficult airway predictors were similar in all 3 groups. The median intubation time was slightly longer in both Group B (42.0s) and Group C (43.1s), when compared to Group A (39.0s) (Table 1), but not statistically significant (p=0.92 and 0.64 for B vs A and C vs A, respectively); with first attempt intubating success advantaging Group C. The final intubating C-L grade view was similar between Group A and Group C (Table 1). Protocol deviations and incomplete cases were excluded from the following analysis.

CONCLUSION: Both King Vision® Channeled and Non-Channeled Video Laryngoscopes have unique features which help facilitate successful endotracheal intubation. Nonetheless, the King Vision® Non-Channeled Video Laryngoscope has more success facilitating endotracheal intubation on the first attempt by resident anesthesiologists. Furthermore, the data demonstrates that both King Vision® Video Laryngoscope Systems can be a viable alternative to the Cobalt GlideScope® Video Laryngoscope.

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Table 1: Comparison of Final intubation time, Number of attempts, and Final Cormack-Lehane (C-L) glottic view among three groups.

Variables	Device			P-value	P-value
	Group A GS (N=67)	**Group B** KVCh (N=54)	**Group C** KVNCh (N=72)	GS vs KVCh	GS vs KVNCh
Final intubation time (sec), **median** (Q1, Q3)	N=66 **39.0** (28.7, 58.9)	N=53 **42.0** (28.5, 60.1)	N=72 **43.1** (30.5, 57.3)	0.92#	0.64#
# of Attempts, n (%)					
1	**57** (85.1)	**46** (85.2)	**68** (94.4)	0.88*	0.13*
2	6 (9.0)	6 (11.1)	4 (5.6)		
3	3 (4.5)	1 (1.9)	0 (0)		
4 (all failed)	1 (1.5)	1 (1.9)	0(0)		
Final C-L view, n (%)	N=66	N=53	N=71	0.85*	0.93*
1	**57** (86.4)	**44** (83.0)	**59** (83.1)		
2a	7 (10.6)	6 (11.3)	9 (12.7)		
2b	2 (3.0)	3 (5.7)	3 (4.2)		

# denotes p-values obtained by Wilcoxon rank sum test; * denotes p-values obtained by Fisher's exact test.
Abbreviations: Q1, 1st quartile; Q3, 3rd quartile.

S-6.

PERIOPERATIVE AIRWAY CHANGES AND THEIR RETURN TO BASELINE IN PATIENTS UNDERGOING ELECTIVE SURGERY IN THE PRONE AND TRENDELENBURG POSITIONS: EARLY DATA

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AFFILIATION: [1]School of Medicine, Tufts University, Boston, MA, [2]Department of Anesthesiology, Tufts Medical Center, Boston, MA

INTRODUCTION: Both prone and Trendelenburg (T-burg) positioning intraoperatively may cause soft tissue edema and swelling affecting the head, neck and airway. Airway changes following prone spine procedures have been reported,[1] but no studies have investigated the postoperative time required for the airway to return to baseline. In this study we tracked airway changes in elective surgical patients from immediately prior to surgery through the first postoperative day (POD) to assess the effects of positioning and additional factors on postoperative airway changes and the time course of their resolution.

METHODS: Following written informed consent we enrolled patients requiring prone or T-burg positioning for spine, laparoscopic or robotic procedures. The Modified Mallampati Score (MMS; standard 4 classes plus an additional class, 4+) was used for airway evaluation at 6 time points (or until discharge): preoperatively; emergence (within 30 min of PACU arrival); 2, 3, and 4 hours after surgery; and POD 1. Data collection included patient characteristics, PMH, procedure duration, and intraoperative fluid and steroid administration. We analyzed the differences between preoperative and postoperative MMS scores with the paired t-test. The effects of prone versus T-burg positioning, procedure type (spine, laparoscopic, robotic), procedure duration, and intraoperative fluids on MMS changes were examined using mixed model and time-to-event analyses. Data are reported in means ± SD.

RESULTS: Seventy-seven patients aged 55 ± 14 years with a BMI of 29.78 ± 7.81 kg/m2 of whom 37, 22 and 17 underwent spine, laparoscopic and robotic procedures respectively were enrolled. For the entire cohort, a mean increase of 1.43 MMS classes, from 2.45 preoperatively to 3.88 at emergence, was observed (Fig. 1, 95% CI = 1.23, 1.63, p<0.0001). Position, procedure type, duration, and intraoperative fluid balance did not significantly influence these initial MMS changes. However, position, procedure type, and intraoperative fluid balance all significantly affected the duration for MMS return to baseline, with prone requiring longer than T-burg (Fig. 2, p=0.0021), spine and robotic both requiring longer than laparoscopic (Fig.3, p=0.0001), and fluid balances >1500mL requiring longer than those <1500mL (Fig. 4, p=0.0005). Procedure duration of >120 min compared to <120 min showed a trend for longer resolution of airway changes (p=0.052).

CONCLUSIONS: Our study demonstrates the development of clinically significant changes in MMS airway presentation immediately following procedures in the prone and T-burg positions. The procedure type, position and intraoperative fluid balance significantly affected the airway presentation's return to baseline, with longer procedure duration showing a trend for longer resolution time. These early data should be confirmed in a larger cohort to determine potentially modifiable risk factors. Anesthesia providers should be aware of these data and potential consequences for early postoperative airway management needs.

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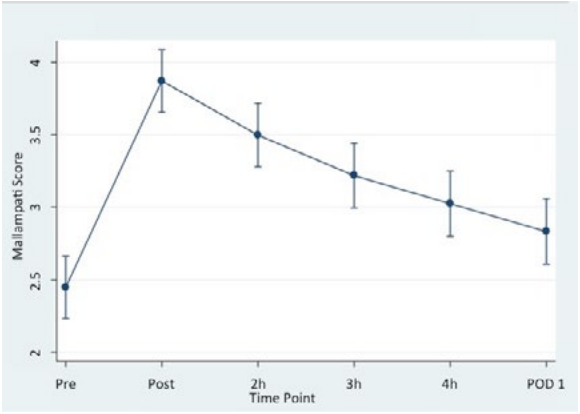

Figure 1. Mallampati score at six time points for the entire cohort.

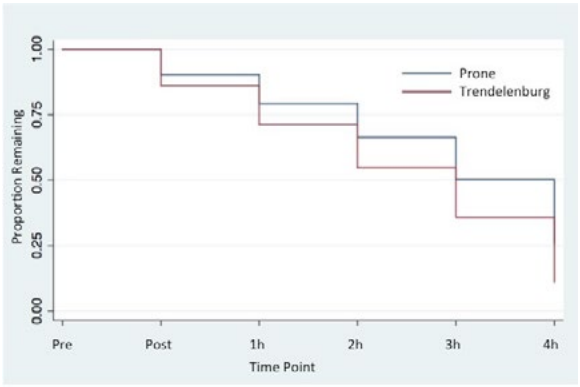

Figure 2. Intraoperative position and time to resolution of MMS changes.
Kaplan-Meyer time-to-event curves ($p = 0.002$)

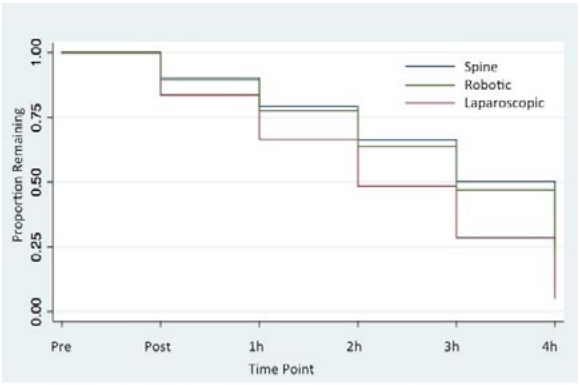

Figure 3. Type of procedure and time to resolution of MMS changes.
Kaplan-Meyer time-to-event curves ($p < 0.001$)

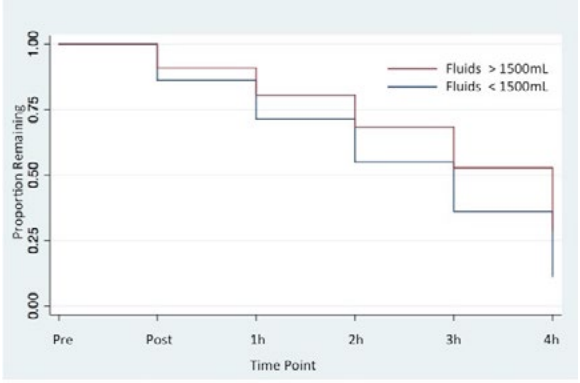

Figure 4. Fluid balance (intraoperative fluid administered – EBL and urine output) and time to resolution of MMS changes.
Kaplan-Meyer time-to-event curves ($p < 0.001$)

S-7.

COMPUTATIONAL MODELING OF DIRECT LARYNGOSCOPY AND THE EFFECT OF CERVICAL SPINE INJURY ON INTERVERTEBRAL KINETICS

AUTHORS: B. Gadomski[1], S. Shetye[2], B. Hindman[3], B. Santoni[4], M. M. Todd[3], R. Fontes[5], C. Puttlitz[1]

AFFILIATION: [1]Mechanical Engineering, Colorado State University, Fort Collins, CO, [2]McKay Orthopaedic Research Laboratory, University of Pennsylvania, Philadelpha, PA, [3]Anesthesia, University of Iowa, Iowa City, IA, [4]Research, Foundation for Orthopaedic Research and Education, Tampa, FL, [5]Neurosurgery, Rush University Medical Center, Chicago, IL

INTRODUCTION: Laryngoscopy and intubation in the presence of cervical spine injury can produce deleterious stress on the cervical spinal cord, leading to neurological injury (paralysis). Currently, it is not known which forms of cervical spine injury present a "high risk" to the cord during intubation. Further, experimental examination of cervical spine motion during intubation for all possible forms of cervical spine instability is practically impossible. Thus, our aim was to develop and validate a computational model of the cervical spine that is capable of simulating all types of cervical spinal injuries, predicting both cervical spine motion and cord stress during intubation.

METHODS: A high-fidelity finite element (FE) model of the cervical spine (C0-C7) using computed tomography data was created[3,4] using previously published material data [Fig 1]. The spinal cord was created using published human geometry data,[3] modeled with a hyperelastic material definition[4]. The FE model was loaded with experimental (patient and cadaver) intubation force distributions measured with two laryngoscopes (Macintosh and Airtraq) and validated against fluoroscopic intervertebral rotation (IVR) data from previous studies[5,6]. Differences between FE model predictions and experimental data were determined with a one-way analysis of variance and a Tukey post-hoc test (α=0.05). Additionally, a C3-C4 disc disruption injury (FE modeled by reducing the properties of the annulus fibrosis and nucleus pulposus by 90%) and a C2 odontoid fracture (Type II) injury (FE modeled via complete disassociation of the odontoid from the C2 vertebral body) were tested. The mean experimental Macintosh intubation force was applied to the FE model and model predictions were compared to experimental (cadaver) IVR data. For all simulations, the inferior surface of the C7 vertebral body was constrained to prevent movement while the C0 vertebral body (occiput) was allowed to rotate in place and translate inferiorly and superiorly.

RESULTS: No statistically significant differences in IVR between FE model predictions and clinical and cadaver data were observed with stable spines with Airtraq intubation forces [Fig 2]. With a stable spine, there was one significant deviation between the FE model prediction and clinical data at C3C4 with the application of the Macintosh loading profiles (p=0.012). In the presence of the Type II odontoid and C3C4 injuries, FE model predictions fell within one standard deviation of experimental measurements [Fig 3].

DISCUSSION: The data demonstrate a high degree of agreement between FE model predictions and experimental measurements when intubation forces are applied in scenarios involving both intact and injured cervical spines. This validated model will now be used to identify which cervical spine injuries present the greatest risk of deleterious spinal cord stress (stretch or compression) during intubation.

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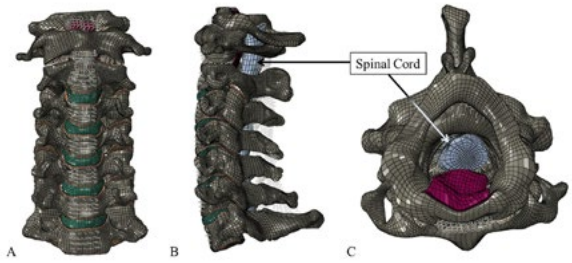

Figure 1. (A) Coronal, (B) sagittal, and (C) axial views of the C0-C7 cervical spine finite element model. The spinal cord and tectorial membrane can be visualized in the axial view.

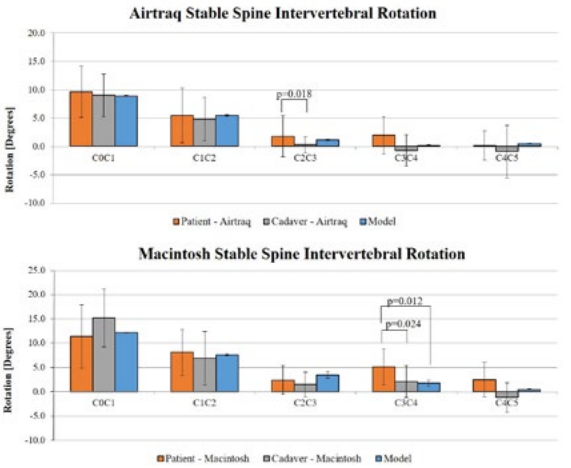

Figure 2. (Top) The finite element model predictions with the Airtraq laryngoscope fell within one standard deviation of both the patient cohort data as well as the cadaver data for the C1 through C5 levels [5]. (Bottom) The finite element model predictions with the Macintosh laryngoscope fell within one standard deviation of both the patient and cadaver data for the C1 through C5 levels. The finite element model kinetic predictions demonstrated a statistically significant difference at C3C4 as compared to the patient data [5].

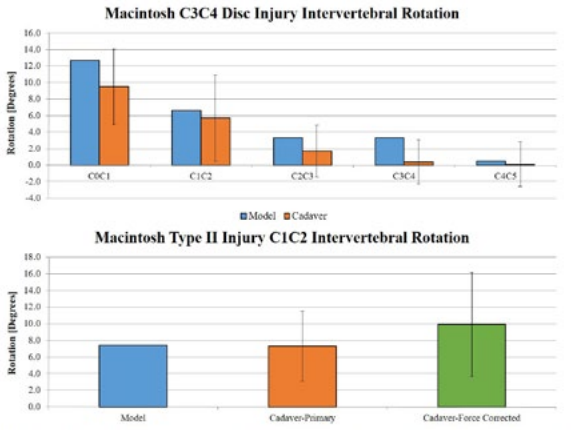

Figure 3. (Top) Model IVR predictions from C0C1 to C4C5 fell within one standard deviation of experimental measurements. (Bottom) Model IVR predictions at C1C2 fell within one standard deviation of primary cadaver measurements as well as force-corrected cadaver measurements [6].

S-9.

WITHDRAWN.

S-10.

A COMPARATIVE STUDY OF THE I-GEL VS AIR-Q SUPRAGLOTTIC AIRWAY DEVICES AS A CONDUIT FOR TRACHEAL INTUBATION WITHOUT THE AID OF FLEXIBLE FIBRESCOPE I ANAESTETHIZED PATIENTS

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INTRODUCTION: I-gel and Air-Q have been used to aid tracheal intubation in patients and manikins while using the standard more rigid poly vinyl chlorideendotracheal tube (ETT)[1-6]. However, fiberscopic guidance is recommended to perform tracheal intubation when using I-gel[2].Success rate of blind tracheal intubation via these two devices have not been compared and reported in literature. The objective of this prospective randomized controlled trial was to first note the percentage of glottic opening (POGO) via I-gel and Air-Q using fiberscope and then evaluate the success rate of tracheal intubation using armored ETT (which is longer and softer than the standard PVC ETT) through I-gel vs. Air-Q without the assistance of flexible fiberscope.

METHODS: After approval by the hospital Ethical Issues Committee, 60 ASA I-II adult patients without predictors of difficult tracheal intubation between 18-60 yr, weighing 30-70 kg of either sex and giving informed verbal consent were included in this study. All patients were to undergo elective surgical procedure needing endotracheal intubation. Patients were randomized into Group G (n=31) - tracheal intubation via I-Gel or Group Q (n=29) – tracheal intubation via Air-Q.A senior anesthetist well versed with the use of these devices performed tracheal intubation. Initial assessment of POGO scores via the device and subsequent success or failure to place the ETT without using fiberscope were recorded. Use of backward pressure over the thyroid cartilage was permitted in either group. Man Whitney U and X2 tests were used to analyze the data.

Group	Age (yr)	Weight (kg)	Gender (M/F)	Fiberscopic POGO Score (%)	Applying thyroid pressure No Yes	Intubation No Yes
Q	29 (19-60)	65 (42-70)	20/9	90 (0-90)	7 22	9 20
G	32 (16-60)	65 (35-70)	22/9	80 (0-90)	10 21	12 19
P value	0.68	0.78		0.52	0.54	0.94

Age, weight, and POGO score have been expressed as median (range) while the last two columns in the table gives patient numbers.

RESULT & CONCLUSIONS: Age, weight and gender of the patients were comparable in the two groups. We noteda slightly better POGO view with Air-Q. This suggests its better alignment to glottic aperture than I-gel resulting in more successful tracheal intubationswith this device. However, neither of theses two findings reached the level of statistical significance in comparison to I-gel. Both theses devices favor over 60% correct tracheal intubations.

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S-11.

THE EFFECT OF CRICOID PRESSURE ON APNEIC OXYGEN RESERVE IN ADULT PATIENTS UNDERGOING ENDOTRACHEAL INTUBATION FOR SCHEDULED SURGERY

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INTRODUCTION: Cricoid pressure is commonly used during anesthesia induction with planned endotracheal intubation. It is believed that applying cricoid pressure decreases a patient's risk to aspirate gastric contents between the time of anesthesia induction and endotracheal intubation. However, there is evidence that application of cricoid pressure increases heart rate and blood pressure, which may result in faster oxygen consumption[1]. This pilot study was designed to investigate the effect size such an increase in oxygen consumption could have on the time to desaturation.

METHODS: Adult patients 18-65 years scheduled for surgery including anesthesia with planned endotracheal intubation gave written consent to participate in this LLU IRB approved study. Exclusion criteria were suspected or known difficult mask ventilation/intubation; elevated ICP; ASA PS 4; ASA PS 3 with cardiopulmonary disease; planned cardiothoracic surgery; or risk for aspiration of gastric contents. Patients were randomly assigned to cricoid pressure or sham, with concealment until after consent. The surgical and anesthetic team and research staff collecting data were blinded to group allocation. Standard monitors were applied with processed EEG monitoring (PSI). Vital signs were continuously collected to computer, and noted every 60 seconds from anesthesia induction after intubation. Patients were preoxygenated to FeO_2/FiO2 > 0.9 prior to induction; or withdrawn for failure to attain this ratio. After administration of anesthetic and relaxant drugs and before endotracheal intubation, research staff placed their hands on the patients neck, concealed by a drape. The staff that applied cricoid pressure were trained and demonstrated ability to reliably reproduce 30N of force[2,3] prior to study participation. Timing started at the onset of apnea (lack of respiratory effort; no $EtCO_2$; time 0). No mask ventilation or supplemental oxygen was applied after time zero. Cricoid pressure patients had 30N of cricoid pressure applied at time 0; held until SpO_2 < 95% or 6 minutes had elapsed. Cricoid presssure was released prior to endotracheal intubation. Time to lowest SpO_2 and intubation were calculated. The primary outcome measure was the difference in time to lowest SpO_2. Secondary measures included difference in the lowest SpO_2 and the number of patients with SpO_2<95%.

RESULTS: 40 patients consented, with 2 from each group withdrawn for preoxygenation failure. There were no significant differences in patient characteristics (Fig 1). We did not find a significant difference in time to reach lowest SpO_2 or lowest SpO_2 (Fig 2, 3).

CONCLUSIONS: Application of 30N cricoid pressure was not associated with a difference in time to lowest SpO_2 or lowest SpO_2 in preoxygenated patients. Prior reports showing cardiovascular activation used 40N cricoid pressure. It is possible that excess pressure may cause more sympathetic response than the recommended 30N cricoid pressure.

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	Sham N = 18	Cricoid N = 18	Difference	p-value
Sex # (%) Female	11 (61.1%)	13 (72.2%)	11.1% -19.4 to 39.4%	0.480
ASA Physical Status # 1; 2; 3	2; 8; 8	3; 8; 7		0.875
Age years median 95% CI	39.5 30.5 to 48.5	45.4 38.7 to 52.1	-5.9 -16.8 to 5.0	0.278
Body mass index kg/m² mean; 95% CI	28.2 26.0 to 30.3	26.4 24.0 to 28.8	1.5 -1.3 to 4.9	0.243
Time to reach lowest SpO2 minutes median; 95% CI	6.4 5.5 to 7.6	6.3 3.8 to 7.8	0 -2.0 t 3.0	0.702
Lowest SpO2 median; 95% CI	93.8% 92.0 to 95.1%	94.8% 93.5 to 96.9%	-1.0% -3.0 to 1.0%	0.454
Lowest SpO2 <95% # (%)	14 (82.4%)	11 (64.7%)	-17.6% -44.2 to 12.6%	0.244

Figure 1: There were no significant differences in patient characteristics. We did not find a difference in time to lowest SpO2, lowest SpO2 or the number of patients with SpO2 <95% in those who had 30 N cricoid pressure held compared to sham treatment patients.

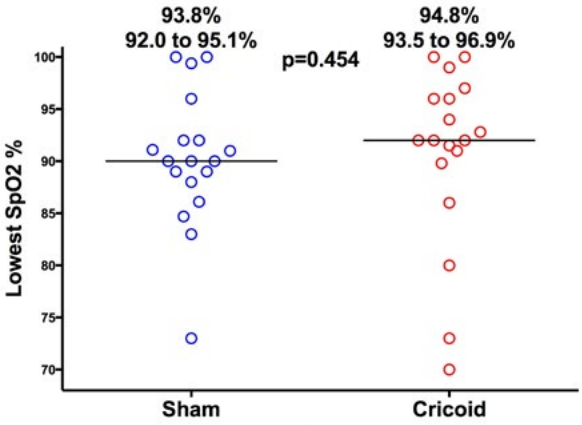

Figure 3: lowest recorded SpO2 (%, median; 95% CI) was not significantly different in patients who had 30 N cricoid pressure held compared to sham treatment patients.

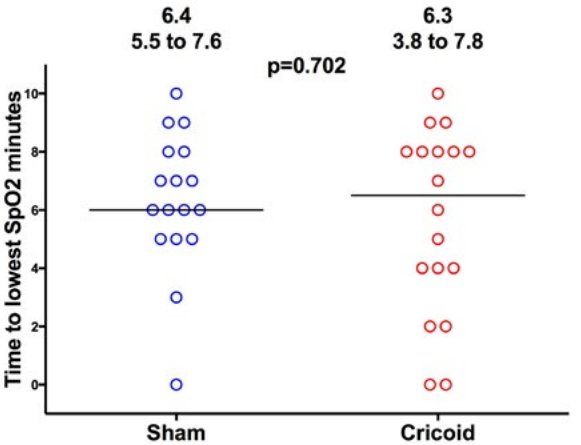

Figure 2: time (minutes, median; 95% CI) of apnea to reach lowest recorded SpO2 was not significantly different in patients who had 30 N cricoid pressure held compared to sham treatment patients.

S-12.

OPTOACOUSTIC ASSESSMENT OF ENDOTRACHEAL TUBE (ET) POSITION WITHIN THE TRACHEA

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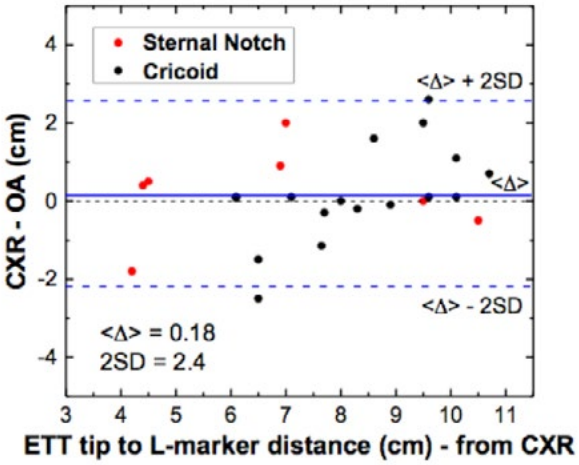
INTRODUCTION: Endotracheal tube (ET) malposition can be catastrophic. Currently available methods for determining the position of ETs within the trachea have substantial practical limitations. In particular, chest radiography represents a time-consuming snapshot that, because of the need for lifting and positioning the patient, actually represents a risk for accidental removal of ETs or other devices. The hypothesis of this clinical study was that a novel optoacoustic (OA) prototype device would determine as accurately as chest radiography whether an ET was properly positioned (not too far cephalad or caudad).

METHODS: The prototype consisted of: 1) low energy pulsed laser diode, 2) one mm pulse-transmitting optical fiber, 3) acoustic detector for OA signals generated in pre-tracheal tissues, and 4) a PC to display in real-time OA signal amplitude (maximum signal when the laser pulse is directly beneath the acoustic detector). We predicted that the peak OA signal from a properly positioned ET would occur when the optical fiber had been withdrawn from the ET tip to the top of the ET cuff. IRB informed consent was obtained from cardiac surgical patients (n=24). OA measurements were obtained immediately before the postoperative CXR. In the first group of patients (n=17), a radio-opaque marker placed at the level of the cricoid cartilage was the target for the top of the ET cuff; in the second group of patients (n=7), the radio-opaque marker was placed at the level of the sternal notch. We compared the distance that the optical fiber was withdrawn from the tip of the ET until a peak OA signal was obtained to the distance (by CXR) from the tip of the ET to the radio-opaque marker. Data were analyzed using regression analysis and Bland-Altman difference plots.

RESULTS: In 95% of patients, the external landmark, which represented the length of the ET from the tip to the estimated position determined by OA, was within 2.4 cm (2 SDs) of the CXR measurement (r2=0.81). Assessment of the data demonstrated unexpected difficulty correctly positioning the radio-opaque marker, especially in identifying the cricoid cartilage.

CONCLUSIONS: The OA prototype determined positioning of the ET within the trachea with acceptable accuracy and precision. The sternal notch group provided a clearer landmark and improved correlation in the last seven patients. These data suggest that 1) the OA can provide accuracy comparable to CXR, 2) that the OA technique could continuously monitor ET position, and 3) OA potentially could be used to guide repositioning of excessively cephalad ETs.



S-13.

EFFECT OF HEAD ROTATION ON EFFICIENCY OF FACE MASK VENTILATION IN APNEIC ADULT PATIENTS UNDER GENERAL ANESTHESIA: A PROSPECTIVE RANDOMIZED CROSSOVER STUDY

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INTRODUCTION: Upper airway obstruction (UAO) is a common problem after induction of general anesthesia (GA). It has been described that axial head rotation[1] or lateral recumbent position[2] can improve UAO. However, there have been no well controlled studies to assess the effectiveness of head rotation on efficiency of mask ventilation. The aim of this study was to determine if head rotation improves the efficiency of mask ventilation of adults under general anesthesia.

METHODS: Forty patients, ages 18-75, BMIs 18.5 to 35.0 kg/m^2, meeting ASA physical status classification I-III requiring GA and tracheal intubation for elective surgery were recruited. Study patients were randomized into two groups (A and B). When the patients were apneic after induction, face mask ventilation was started in a neutral head position (NP) or in a head position axially rotated 45° to the right (45RP). The mask was held with two hands and the jaw was positioned to optimize the airway. Mask ventilation was carried out for three minutes with pressure control ventilation at 10 breaths per minute, I:E ratio 1:2, peak inspiratory pressure 15 cmH_2O, and no PEEP. Head position was changed at one minute intervals (every 10 breaths) in the following sequences: group A; NP→45RP→NP, group B; 45RP→NP→45RP. The primary outcome was expiratory tidal volume (VTe) measured by using respiratory inductive plethysmograph. Each patient had own calibration curve which was obtained retrospectively after intubation. The last three breaths obtained from each head position were averaged and the mean value was used as a single data point for final analysis. Data are expressed as mean values or medians with interquartile ranges (IQRs) depending on the data distribution. Differences (ΔVTe %) between groups are expressed as medians with 95% confidence intervals (95% CIs). $P < 0.05$ was considered statistically significant.

RESULTS: Five patients were excluded due to severe airway obstruction or protocol violation and 35 patients were analyzed. The mean age was 62 yr and the mean BMI was 28 kg/m^2. The VTe was significantly larger in 45RP (7.8 [IQR, 4.5-10.4] mL/kg) than that in NP (7.4 [3.5-9.8] mL/kg, $p < 0.005$, Figure 1). The ΔVTe % for the 35 patients was 8.4 [95%CI, 1.5-21.8] %. In subgroup analysis, the ΔVTe % was significantly higher in patients with airway obstruction (n=20, VTe in NP/VTe after intubation at 15 cmH2O < 1.0) (23.9 [8.4-48.4] %) than those without airway obstruction (1.0 [-3.1-6.7] %; $p < 0.005$, Figure 2A), and higher in patients with low VTe (n=12, VTe in NP < 6 mL/kg) (39.4 [9.3-102.3] %) than those without low VTe (2.7 [-2.1-10.3] %; $p < 0.005$, Figure 2B).

CONCLUSION: In anesthetized, apneic adult patients, 45RP significantly increased the efficiency of mask ventilation comparing with NP especially in patients who presented airway obstruction and/or low VTe in NP.

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Figure 1. Effects of 45° head rotation on expiratory tidal volume

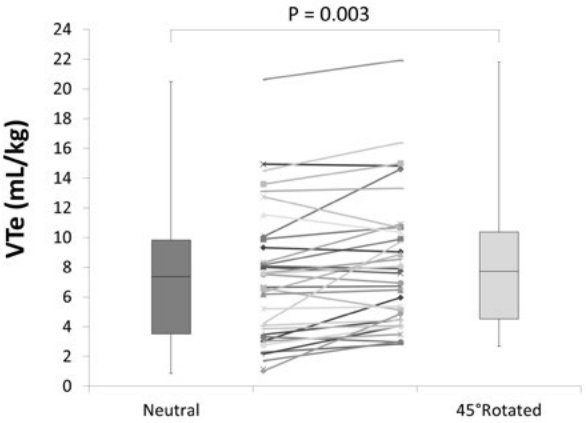
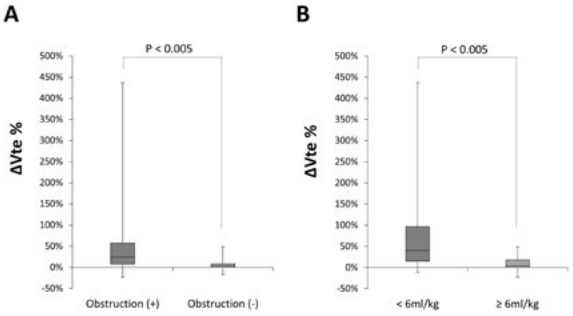


Figure 2. Differences in VTe (%) from NP to 45RP for patients with and without airway obstruction (A) and low tidal volume in NP (B)



S-14.

NON-DEPOLARIZING NEUROMUSCULAR BLOCKING AGENTS, REVERSAL, AND RISK OF POSTOPERATIVE PNEUMONIA

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BACKGROUND: Residual postoperative paralysis from non-depolarizing neuromuscular blocking agents is a known problem. This paralysis has been associated with impaired respiratory function, but the clinical significance remains unclear. The aims of this analysis were twofold: 1.) to investigate if receiving an intermediate-acting non-depolarizing neuromuscular blocking agent during surgery is associated with postoperative pneumonia, and 2.) to investigate if non-reversal of these agents is associated with postoperative pneumonia.

METHODS: Surgical cases (n=13,100) from the Vanderbilt University Medical Center National Surgical Quality Improvement Program database that received general anesthesia were included. We compared 1,455 surgical cases that received an intermediate-acting non-depolarizing neuromuscular blocking agent to 1,455 propensity score matched cases that did not, and 1,320 surgical cases that received an intermediate-acting non-depolarizing neuromuscular blocking agent and reversal with neostigmine to 1,320 propensity score matched cases that did not receive reversal. Postoperative pneumonia incidence rate ratios and bootstrapped 95% confidence intervals were calculated.

RESULTS: Patients receiving an intermediate non-depolarizing neuromuscular blocking agent had a higher absolute incidence rate of postoperative pneumonia (9.00 vs 5.22 per 10,000 person-days at risk) and the incidence rate ratio (IRR) was statistically significant (1.79, 95% bootstrapped CI: 1.08-3.07). Among surgical cases that received an intermediate non-depolarizing neuromuscular blocking agent, cases that were not reversed were 2.26 times as likely to develop pneumonia after surgery compared to cases that received reversal with neostigmine (IRR: 2.26, 95% bootstrapped CI: 1.65-3.03). Figure 1 shows the standardized differences between surgical cases that received an NMBA and those that did not. Figure 2 shows the standardized differences between surgical cases that NMBA reversal and those that did not.

CONCLUSIONS: Intraoperative use of intermediate non-depolarizing neuromuscular blocking agents is associated with developing pneumonia after surgery. Amongst patients that receive these agents, non-reversal is associated with an increased risk of postoperative pneumonia.

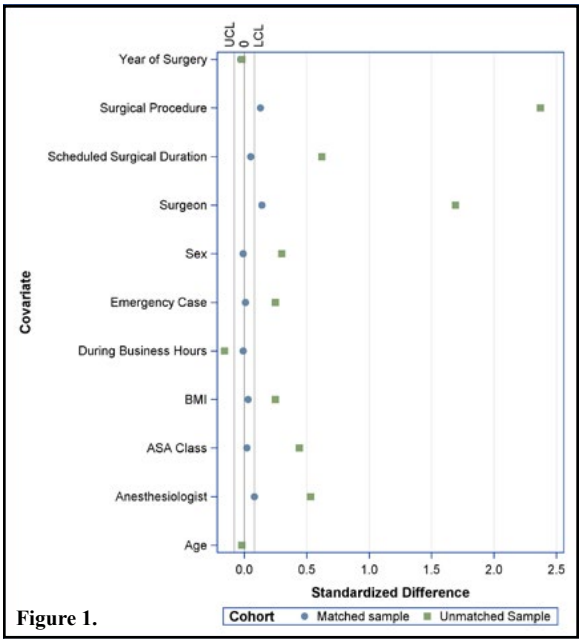

Figure 1.

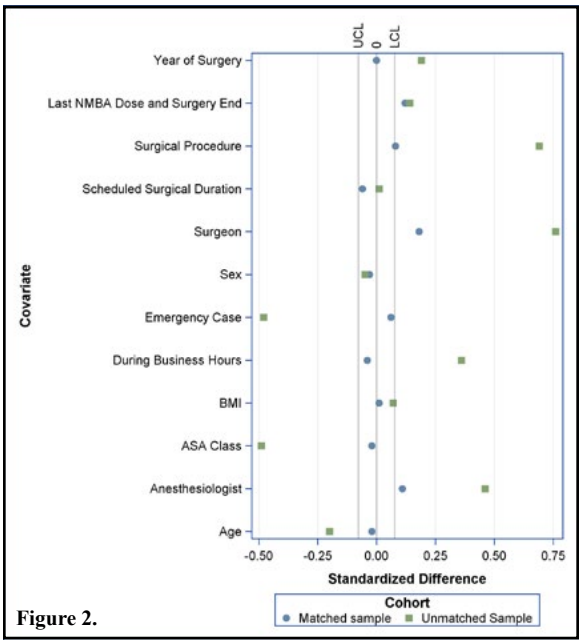

Figure 2.

S-15.

THE COMPARISON OF MCGRATH MAC, C-MAC, AND MACINTOSH LARYNGOSCOPE IN NOVICE USERS IN A MANIKIN

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INTRODUCTION: We hypothesized that McGrath MAC[1] (Aircraft Medical Lt., Edinburgh, UK) would decrease the time of intubation compared to the C-MAC[2] (C-MAC PM, Karl Storz, Tuttlingen, Germany) because of the closer position of the camera with the blade, narrower blade and the lesser weight of the equipment. In this study, we compared the time of intubation among the macintosh blade, McGrath MAC, and C-MAC in novice users using a manikin.

METHODS: Thirty-nine medical students who had experience of intubation less than 3 using the macintosh blade in the manikin were recruited (30 males and 9 females). SimMan manikin (Laerdal Medical Canada Ltd., Toronto, Ontario, Canada) was used. For intubation, we used three devices including the C-MAC, the McGrath MAC, and the Macintosh laryngoscope. The participants performed the intubations on the manikin in two different simulated settings including the normal airway and difficult airway (tongue edema) sequentially. Each participant was allowed to perform up to three intubation attempts with each device in each simulated airway setting. Intubation time, the success rate of intubation, Cormack-Lehane grade at laryngoscopy, and difficulty of using the device were recorded. The participant was also asked to answer which device was the most useful among the three devices.

RESULTS: In normal airway, one participant failed the intubation using the macintosh while all the intubations succeeded after the three attempts with the McGrath MAC and C-MAC. The intubation time of the first attempt was not significantly different among the three devices. However, the intubation times of the second attempt, third attempt, and overall attempts were significantly decreased in McGrath MAC and C-MAC compared to the macintosh. The success rate of intubation in each attempt increased significantly and Cormack-Lehane grade improved significantly in McGrath MAC and C-MAC compared to the macintosh. In simulated difficult airway (tongue edema), 12 participants failed intubation with the macintosh while one and two participants failed intubation with the McGrath MAC and C-MAC, respectively. The intubation times were similar among the three devices. The success rate of intubation increased significantly and the Cormack-Lehane grade improved significantly with the McGrath MAC and C-MAC compared to the macintosh. In both airway scenarios, the subjective difficulty of using the device was higher significantly with the macintosh compared to the McGrath MAC and C-MAC. The majority of participants selected the McGrath MAC as the most useful device in both airway scenarios, although there were no significant differences in all measured parameters between McGrath MAC and C-MAC.

CONCLUSIONS: In manikin with simulated normal and difficult airways, the intubation time, success rate of intubation, laryngeal view, and subjective difficulty were similar between the McGrath MAC and C-MAC although the majority of participants chose the McGrath MAC as the most useful device.

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S-16.

THE INFLUENCE OF HEAD AND NECK POSITION ON THE OROPHARYNGEAL LEAK PRESSURE USING AIR-Q® SP AIRWAY

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AFFILIATION: Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of.

INTRODUCTION: The ventilation through the laryngeal mask airway is influenced differently by the various head and neck positions according to the type of laryngeal mask airway.1-4 The Air-Q® self-pressurizing airway (Air-Q® sp airway, Mercury Medical, FL, USA) has an opening between the cuff and the airway tube making the cuff pressure self-regulated by the ventilation and the adjacent structures.5 We evaluated the influence of the various head and neck positions on the oropharyngeal leak pressure during ventilation with the Air-Q® sp airway.

METHODS: In this prospective randomized cross-over study, we enrolled 51 patients who were scheduled for the elective surgery under general anesthesia. Air-Q® sp airway of size 2.5 or 3.5 was placed in all patients and the mechanical ventilation was performed using volume-controlled mode with tidal volume of 10 ml/kg and respiratory rate of 12 per minute. Under the neutral head position, expiratory tidal volume and peak inspiratory pressure were recorded three times and the mean values were obtained. Oropharyngeal leak pressure and the fiberoptic view at the end of the Air-Q® sp airway were also assessed. The measurements were repeated under the extended, flexed, and rotated head positions in random order.

RESULTS: The oropharyngeal leak pressure and peak inspiratory pressure decreased significantly in extended position, compared to the neutral position, but increased significantly in flexed position ($P < 0.001$). The expiratory tidal volume decreased significantly in flexed and extended positions compared to the neutral position ($P = 0.027$ and $P < 0.001$, respectively). The ventilation score decreased significantly in extended position compared to the neutral position ($P < 0.001$) although there was no significant difference between flexed and neutral positions. The rotated position did not alter the oropharyngeal leak pressure and the ventilatory parameters significantly compared to the neutral position.

CONCLUSIONS: The flexed and extended positions affected significantly the oropharyngeal leak pressure, peak inspiratory pressure, and expiratory tidal volume compared to the neutral position during ventilation through the Air-Q® sp airway, although the ventilation score reduced significantly only in extended position. The rotated position did not affect significantly all parameters compared to the neutral position.

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Table 1. Characteristics of patients

	N = 51
Age (years)	43 ± 10 (22-64)
Gender (M/F)	0/51
Height (cm)	160 ± 5
Weight (kg)	56 ± 9
Size of the Air-Q® sp airway, 2.5/3.5	16 (31)/35 (69)

Values are expressed as the number of patients (percentage) or mean ± SD (range).

Table 2. Oropharyngeal leak pressure and Fibreoptic view.

	Neutral	Extended	Flexed	Rotated
Oropharyngeal leak pressure (cmH_2O)	22 ± 3	14 ± 6*	26 ± 4*	22 ± 3
Fiberoptic view, 1/2/3/4	0/0/46/5	0/0/46/5	0/14/33/4	0/0/46/5

Values are expressed as the number of patients or mean ± SD. *P < 0.05 compared to the neutral position. 1 = vocal cords not visualized; 2 = vocal cords plus anterior epiglottis visible; 3 = vocal cords plus posterior epiglottis visible; 4 = only vocal cords visible.

Table 3. Ventilatory parameters

	Neutral	Extended	Flexed	Rotated
Expiratory tidal volume (ml)	579 ± 82	491 ± 165*	538 ± 120*	570 ± 87
Peak inspiratory pressure (cmH_2O)	13 ± 2	11 ± 3*	16 ± 4*	13 ± 2
Ventilation score	3.0 ± 0.0 (3)	2.5 ± 0.4 (2-3)*	2.9 ± 0.4 (1-3)	3.0 ± 0.2 (2-3)

Values are expressed as mean ± SD (range). *P < 0.05 compared to the neutral position.

S-17.

WITHDRAWN.

S-18.

DIGITAL IMAGING SOFTWARE TO ASSESS THE ANATOMIC STRUCTURES OF THE ORAL CAVITY IN PATIENTS WITH THYROID MASSES; PILOT STUDY EVALUATING INTUBATION AND OXYGENATION DIFFICULTIES WHEN USING VIDEOLARYNGOSCOPY

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INTRODUCTION: Problems associated with airway and anesthetic management in patients undergoing thyroid/parathyroid surgery range from the size/type of thyroid mass to the number of poor airway indices which may lead to a potential difficult intubation and desaturation[1,2]. Patients with small mouth openings and high Mallampati scores may be difficult to intubate. Airway indices are subjective measurements due to inter-observer variability, therefore limiting assessment reliability[3]. Digital imaging (DI) technology using a software program has been used for airway evaluation to determine the area of unoccupied space in the mouth and to analyze the oral cavity[4]. Our aim was to use DI as an objective measurement of oral aperture to better predict the occurrence of airway and non-airway related complications during intubation, ventilation, and oxygenation in patients undergoing thyroid/parathyroid surgery.

METHODS: Patients undergoing thyroid/parathyroid surgery were consented for an IRB approved prospective observational study. Written consent was obtained from 11 patients. Mallampati score (I-IV), oral aperture (OA), thyromental (TM) distance, and neck range of motion (ROM) were evaluated and a photograph of the oral cavity was analyzed using ImageJ software. A mouse was used to outline the total area of the mouth, the area of the mouth occupied by the tongue and teeth, and the unoccupied space and the areas were calculated. Demographic data included age, weight, height, BMI, gender, ASA status. The anesthetic medications, agents, and techniques were at the discretion of the anesthesiologist. Additional data included the manual maneuvers and aids used during bag mask ventilation and videolaryngoscopy for intubation. Times for intubation and airway and non-airway related complications were also recorded.

RESULTS: Eleven patients were photographed and observed. Three were excluded. Two patients desaturated during intubation, and 5 patients required multiple intubation attempts with one desaturating. Age (yr) = 62±19.0, weight (kg) = 72.2±11.8, and height (m) = 1.64±0.06. The mean ± SD of total mouth area was 27.6 ±11.6 cm^2, occupied mouth area was 10.4±11.8 cm^2, unoccupied mouth area was 6.6 ± 4.7 cm^2.

CONCLUSIONS: We found DI to be easy to use to obtain an objective measurement of the space occupied by the teeth and tongue and unoccupied space in the oral cavity. Our measurements of the oral cavity may facilitate in deciding the size and shape of the airway devices used for intubation. These measurements may further help prevent airway complications by predicting which device best fits in the oral cavity.

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S-19.

BOUGIE ASSISTED ENDOTRACHEAL INTUBATION USING THE AIR-Q INTUBATING LARYNGEAL AIRWAY

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INTRODUCTION: Air-Q/Intubating Laryngeal Airway is an extraglottic airway (EGA) used as a primary airway device or as an adjunct to tracheal intubation (Fig. 1)[1].

Bougie assisted intubation (BAI) is known to improve success of intubation as compared to more expensive devices like the fiberoptic stylet and the Airway Scope[2,3].

We hypothesized that blindly introducing a bougie through the air-Q might improve the success rate of endotracheal intubation.

METHODS: After ethical committee approval and written informed consent, 140 patients of either sex,older than 18 years, ASA physical status I-II scheduled for elective surgical procedures under general anesthesia requiring tracheal intubation were randomly allocated to one of two groups of 70 patients each. Blind tracheal intubation was performed through the air-Q with either Bougie assistance (Group B) or without (Group Q).

After induction and muscle relaxation, an air-Q was inserted in the upper airway. An endotracheal tube was then blindly advanced to a depth of 12-15 cm in group Q. Tracheal intubation was deemed successful if ventilation through the ETT produced an adequate chest expansion & a normal capnographic curve.

In group B, the operator gently inserts a bougie through the air-Q. As it enters the trachea, a characteristic click is felt. The air-Q is then removed & ETT is railroaded over it.

In both groups, 3 attempts at device insertion and intubation were allowed. Intubation was only attempted when appropriate ventilation was obtained . If tracheal intubation through the device failed, it was performed by direct laryngoscopy.

RESULTS: Both groups were comparable regarding demographic data (table 1) and airway characteristics (table 2).

Table 3 shows comparable air-Q insertion characteristics between both groups while bougie insertion variables in Group B are shown in table 4.

The overall success rate for intubation was similar in both groups (64.3%) with significant longer total time of intubation in group-B (table 5).

There was statistical significant difference between both groups regarding ventilatory adjusting maneuvers required to apply ETT (table 6).

Group-B showed significantly higher rate of complications (trauma, sore throat, dysphonia & dysphagia). (Table 7)

Hemodynamically, there was significant elevated heart rate and mean arterial pressure in group-B compared to group-Q after endotracheal intubation (figure 1 &2).

CONCLUSION: Bougie guided tracheal intubation through air-Q didn't improve the overall success rate and required significant longer time with hemodynamic derangement & traumatic sequelae.

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Table 1: Demographic features of the two study groups.

	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
Age (yrs.)	35.07 ± 10.50	33.86 ± 8.77	0.459
Gender Female (♀) Male (♂)	50 (71.4%) 20 (28.6%)	45 (64.3%) 25 (35.7%)	0.366
Weight (kg)	80.07 ± 11.20	78.43 ± 5.87	0.279
Height (cm)	165.50 ± 7.24	164.64 ± 6.45	0.461
ASA-physical status **I** **II**	 60 (85.7%) 10 (14.3%)	 60 (85.7%) 10 (14.3%)	 1.000

Data were expressed as mean ± SD or number (%).

Table 2: Comparison of the airway characteristics between the two study groups

	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
Mallampati Score 1 2	 25 (35.7%) 45 (64.3%)	 20 (28.6%) 50 (71.4%)	 0.366
Mouth opening (cm)	4.79 ± 1.15	4.64 ± 0.92	0. 420
Thyromental distance (cm)	7.00 ± 1.14	7.21 ± 0.95	0.229
Neck circumference (cm)	37.79 ± 3.53	38.79 ± 2.41	0.053

Data were expressed as mean ± SD or number (%).

Table 3: Comparison of the Air-Q variables between the two study groups

Air-Q	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
Insertion time (sec)	21.21 ± 2.72	20.43 ± 2.94	0.103
Ease of insertion Easy Difficult	 65 (92.9%) 5 (7.1%)	 65 (92.9%) 5 (7.1%)	 1.000
Number of attempts **One** **Two**	 65 (92.9%) 5 (7.1%)	 65 (92.9%) 5 (7.1%)	 1.000
Grade of ventilation Adequate Possible	 65 (92.9%) 5 (7.1%)	 65 (92.9%) 5 (7.1%)	 1.000

Data were expressed as mean ± SD or number (%).

Table 4: Bougie variables in Group-B

Bougie	Group-B *(n= 70)*
Insertion time (sec)	20.11 ± 10.17
Ease of insertion Easy Difficult Failed	 30 (42.9%) 15 (21.4%) 25 (35.7%)
Number of attempts One Two Three	 30 (42.9%) 15 (21.4%) 25 (35.7%)

Data were expressed as mean ± SD or number (%).

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S-19 • continued

Table 5: Tracheal intubation variables & overall success rate in the study groups

	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
ETT number of insertion attempts			
One	30 (42.9%)	30 (42.9%)	0.483
Two	10 (14.2%)	15 (21.4%)	
Three	30 (42.9%)	25 (35.7%)	
ETT insertion time (sec)	26.67 ± 10.09	25.78 ± 7.97	0.644
Number of accidental esophageal intubation			
No	30 (42.9%)	30 (42.9%)	0.877
One	10 (14.3%)	12 (17.1%)	
Two	5 (7.1%)	3 (4.3%)	
Three	25 (35.7%)	25 (35.7%)	
Total time to insert ETT (sec)	48.11 ± 9.96	65.89 ± 14.50	0.001**
Overall success rate	45 (64.3%)	45 (64.3%)	1.000

Data were expressed as mean ± SD or number (%).
p> 0.05= not significant, **p< 0.01= highly significant
ETT= endotracheal tube

Table 6: Comparison of the needed adjusting maneuvers between the two study groups

Adjusting maneuvers	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
Nil	25 (35.7%)	25 (35.7%)	.0.001**
Pillow	5 (7.1%)	0 (0.0%)	
Cricoid pressure	5 (7.1%)	0 (0.0%)	
Neck extension	5 (7.1%)	0 (0.0%)	
Jaw thrust	25 (35.7%)	45 (64.3%)	
Jaw thrust + Neck extension	5 (7.1%)	0 (0.0%)	

Data were expressed as number (%).
p> 0.05= not significant; **p< 0.01= highly significant

Table 7: Comparison of the complications between the two study groups

Adjusting maneuvers	Group-Q *(n= 70)*	Group-B *(n= 70)*	*p*-value
Hypoxia	0 (0.0%)	0 (0.0%)	---
Mouth trauma	0 (0.0%)	5 (7.1%)	0.023*
Tongue trauma	0 (0.0%)	0 (0.0%)	---
Lips trauma	0 (0.0%)	0 (0.0%)	---
Blood on device	30 (42.9%)	40 (57.1%)	0.091
Sore throat			
Mild	5 (7.1%)	30 (42.9%)	0.001**
Moderate	5 (7.1%)	5 (7.1%)	
Dysphonia *(mild)*	0 (0.0%)	5 (7.1%)	0.023*
Dysphagia *(mild)*	5 (7.1%)	40 (57.1%)	0.001**

Data were expressed as number (%).
p> 0.05= not significant; *p< 0.05= significant , **p< 0.01= highly significant

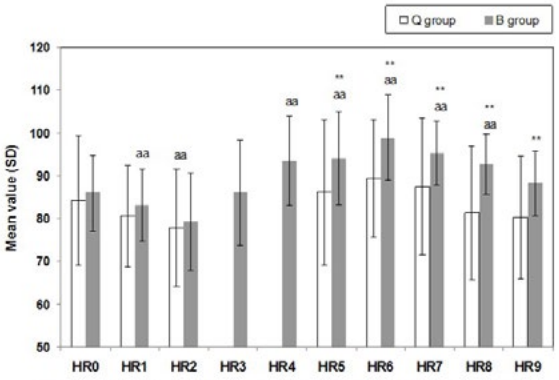

Figure-1: Heart rate changes throughout the study in the two study groups
***p< 0.01 relative to group Q. aap< 0.01 relative baseline (HR0) within the same group.*

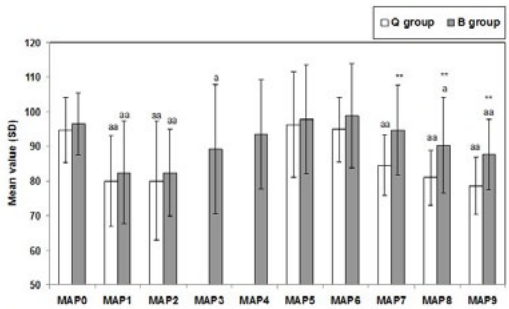

Figure-2: Mean arterial pressure changes throughout the study in the two study groups
***p< 0.01 relative to group Q, *p< 0.05 & **p< 0.01 relative baseline (MAP0) within the same group.*

S-20.

REDUCTION OF THE RESPIRATORY RATE BY HIGH-FLOW NASAL CANNULA OXYGEN THERAPY : A STUDY IN PATIENTS WITH ACUTE RESPIRATORY FAILURE IN THE INTENSIVE CARE UNIT

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Nowadays, high-flow nasal cannula (HFNC) therapy is increasingly used in the intensive care unit (ICU) and emergency care unit[1]. Data of a prolonged evaluation of the effects of the HFNC therapy on respiratory rates (RRs) of patients in the ICU are lacking. Therefore, this study aimed to elucidate the effects of the HFNC therapy on the RRs of patients with acute respiratory failure (ARF).

METHODS: This study identified 128 patients with hypoxemic respiratory failure who received HFNC therapy in the ICU and high care unit (HCU) between January 2013 and May 2015. Their medical records were retrospectively reviewed. The primary outcomes were alterations in the RRs after HFNC. Statistical analysis was performed using one-way repeated ANOVA followed by the Bonferroni post-hoc test.

RESULTS: Finally, 110 patients were included. The chief causes of ARF were pneumonia (26%), pulmonary fibrosis (17%), and post-extubation respiratory failure (17%). The mean RRs were 27.3 ± 8.9 (before HFNC), 23.3 ± 9.8 (15 min after HFNC), 22.0 ± 6.0 (30 min after HFNC), 22.1 ± 6.0 (45 min after HFNC), 24.8 ± 7.9 (1 h after HFNC), 24.4 ± 8.2 (2 h after HFNC), 23.7 ± 7.6 (3 h after HFNC), 24.1 ± 8.1 (4 h after HFNC), 23.8 ± 7.6 (5 h after HFNC), and 24.4 ± 8.0 (6 h after HFNC). The use of HFNC significantly reduced the RRs (before HFNC vs. 30 min, 45 min, 1 h, 2 h, 3 h, 4 h, 5 h, and 6 h after HFNC; $p < 0.05$).

CONCLUSIONS: The use of HFNC in patients with ARF significantly reduced the RRs. HFNC therapy might reduce respiratory distress.

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S-21.

AIRWAYS IN THE MORBIDLY OBESE: CAN DIFFICULT LARYNGOSCOPY BE PREDICTED BY BODY SHAPE?

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INTRODUCTION: Within the obese population there are two classical patterns of fat distribution; centripetal fat 'Apples' and peripheral fat 'Pears'. The impact of these body shapes on difficulty of laryngoscopy is not well understood. Body shape, as measured by 'A Body Shape Index' (ABSI), can be used to quantify the type of fat distribution and is suggested to represent a significant risk factor for mortality[1]. We analysed our bariatric airway database to determine to what extent ABSI was associated with an increased incidence of difficult laryngoscopy and to ascertain if any association was gender-specific.

METHODS: We analysed patient data collected prospectively from a single bariatric surgical centre over the last 7 years. Patients were included in the analysis if they had primary bariatric surgery and had complete data required to calculate ABSI and Cormack and Lehane (C&L) laryngoscopy grade. ABSI was calculated using the formula1: Waist Circumference / Body Mass Index$^{2/3}$ x Height$^{1/2}$. Patients were grouped into quartiles based on their ABSI and then C&L laryngoscopy grade was compared in each group. The incidences of difficult laryngoscopy (either C&L grade 3 or 4) were investigated. P values were calculated using the Fisher Exact test.

RESULTS: A total of 792 patients undergoing primary bariatric surgery had complete data (fig. 1). Of these, 79% were female, the median age was 45 years (range 17-71 years), the median weight 137kg (70-353kg) and the median body mass index 48kg.m-2 (27-98kg.m-2). Median ABSI was 7.88 (5.66-9.37, fig. 2). Fifty-two percent of males had an ABSI in the highest quartile vs 17% of females ("true Apples"); whereas 30% of females had an ABSI in the lowest quartile vs 5% of males ("true Pears"). The overall incidence of difficult laryngoscopy was 6.6% with no failed intubations.

Difficult laryngoscopy occurred more frequently in males if the ABSI was greater than the median value for the entire cohort of 792 patients (14.5% vs 5.9%, p=0.25). Difficult laryngoscopy occurred more frequently in males when divided above and below the male median ABSI (14.5% vs 10.8%, p=0.49). However this was not statistically significant due to the low total numbers of males analysed. In females there was a non-significant inverse correlation between increasing ABSI and difficulty of laryngoscopy (6.4% vs 3.5%, p=0.14).

CONCLUSIONS: Male bariatric patients have a greater than two-fold incidence of difficult laryngoscopy compared to females (12.7% vs 5%, p<0.01). Male patients with an apple shape, as defined by an ABSI above the gender-specific median, appear to have a somewhat higher rate of difficult laryngoscopy (14.5% vs 10.8%) but this trend is non-significant. This analysis is underpowered to demonstrate a significant difference and perhaps surprisingly does not really support the consensus opinion that male, 'Apple' shaped bariatric patients are more prone to difficult intubation. Further analysis of ABSI and laryngoscopy grade in a larger cohort would be welcomed.

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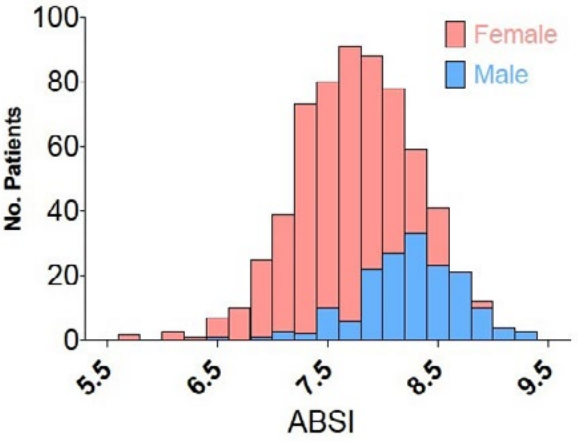
	Female	Male	Total	(Range)
Patients (n)	626 (79%)	166 (21%)	**792**	
Age (yrs)	44	47	**45**	(17-71)
Weight (kg)	131	161	**137**	(70-353)
Height (m)	1.65	1.79	**1.66**	(1.43-2.03)
BMI (kg.m^2)	49	50	**49**	(27-98)
Waist (cm)	133	152	**137**	(85-213)
ABSI	7.76	8.28	**7.88**	(5.66-9.37)
Difficult Laryngoscopy	5%	12.7%	**6.6%**	

Figure 1. Patient demographics. All values are median values unless stated.

Figure 2. Distribution of A Body Shape Index by gender



S-22.

IS THE VIDEO LARYNGOSCOPE REALLY TAKING OVER? INTUBATION TRENDS IN BARIATRIC SURGERY

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INTRODUCTION: Bariatric surgery has become more common in the United States due to the increasing prevalence of morbid obesity. Bariatric surgery patients may carry a higher incidence of difficult tracheal intubation due to obesity, neck circumference, and history of obstructive sleep apnea[1,2]. Over the past several years, the video laryngoscope (VL) has become more available, leading one to believe its use is more common, especially in obese patients. Studies have shown that VLs provided better airway exposure and displayed a more favorable learning curve[3,4]. Because of the lack of evidence for evaluating the trends in the use of VL, we evaluated the choice of laryngoscopy in bariatric surgery patients by anesthesia providers at an academic institution.

METHODS: We reviewed anesthesia records for the past three years (October 1, 2012 to September 30, 2015) of bariatric surgery patients to identify laryngoscope preference (i.e. video or direct laryngoscope) of resident physicians for obtaining an airway during general anesthesia. Bariatric surgery patients in this study were identified as patients who received one of the following surgical procedures: laparoscopic sleeve gastrectomy, robotic assisted laparoscopic gastric bypass, laparoscopic gastric band placement, gastric band port revision, and laparoscopic gastric band revision.

RESULTS: Preliminary results show no clear increase in the use of VL for intubation of bariatric patients at an academic institution. The percentages of VL intubations in bariatric patients are 28%, 9%, and 33% for Fall 2012, 2013, and 2014 respectively. When looking specifically at resident training level, the percent of VL intubations by intern, CA1, CA2, and CA3 were 29%, 22%, 29%, and 40% respectively.

CONCLUSIONS: Our preliminary results suggest that over the last three years, the use of VL has not increased in the bariatric surgery population. It would seem that the use of VL would have increased over the years since its availability has become widespread. There also does not seem to be an increase in or preference for the VL by resident physician training level. One may argue that the attending physicians who had originally been trained to use the DL may be hesitant to teach or support the use of VL in their residents. A future study may want to look to identify reasons that training physicians are not gravitating toward the use of VL.

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Subspecialty Abstracts

Ambulatory Anesthesia

S-23.

USE OF NON-INVASIVE MINUTE VENTILATION (EXSPIRON) REDUCES HYPOVENTILATION AND APNEA DURING TOTAL INTRAVENOUS ANESTHESIA (TIVA)

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INTRODUCTION: Death or serious brain injury are catastrophic events that can occur during general anesthesia. According to ASA closed claims database, 45% of these events are due to respiratory arrests. Despite advances in monitoring e.g., pulse oximetry and capnography, hypoventilation secondarily to anesthesia continues to be a significant cause of respiratory arrests. This problem is likely amplified in remote anesthesia locations due to limited personnel and available monitoring. We tested a novel non-invasive device that determines minute ventilation [MV} (ExSpiron 1XI monitor, Respiratory Motion Inc) in an effort to attenuate hypoventilation during GI endoscopies under anesthesia.

METHODS: This study was performed as a randomized clinical evaluation in our endoscopy suite in patients undergoing upper and lower GI endoscopies using total intravenous anesthetic (TIVA) with propofol +/- remifentanil. We evaluated a total of 65 patients that were ASA I-III, male and female, ages 30-84 and body weight 55-130 kg. For all patients, baseline minute ventilation was obtained prior to TIVA and then monitored and recorded (every 5 seconds or 0.2 Hz) throughout the duration of the case. Although the sensor and device were placed in the control group (n=38), the screen monitor was covered and data was collected but remained blinded to the anesthesia provider throughout the case.In the ExSpiron group (n=27), the anesthesia provider titrated TIVA to achieve MV between 40-80% of baseline value. All data (low MV, defined % time patients < 40% MV baseline, %MV per quartile, defined as total case time/4 X mean MV and # of apnea episodes, defined as zero MV > 15 seconds) was collected retrospectively from July to December 2015. A Student t-test was used for statistical comparisons.

RESULTS: Data shows that low MV = MV 40% baseline occurred in control group 32± 4% time. On the other hand, the use of ExSpiron to guide TIVA resulted in a significant 2 - 3 fold reduction in episodic low MV, or 12 ± 3 %of the time (p value = 0.0003). ExSpiron also resulted in a significantly higher MV over time compared to control group at quartile 3 & 4 ($p<0.05$). Additionally, there was a 25-30% reduction in apnea episodes with ExSpiron vs. control.

CONCLUSION: The use of bio-impedance respiratory monitoring (ExSpiron 1XI) for adjusting TIVA to minute ventilation can prevent episodes of inadequate ventilation. Our results show that patients spent significantly less time with a minute ventilation below 40% of their baseline. This monitoring does not replace pulse oximetry or capnography, but is an adjuvant that can provide valuable information and allow titration of anesthetics to maximize a patient's ventilation.

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S-24.

USE OF CPAP DEVICES IN AMBULATORY SURGERY CENTERS

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INTRODUCTION: Obstructive sleep apnea (OSA) is a relatively common sleep-related breathing disorder that is associated with significant perioperative complications[1]. Recently, the Society For Ambulatory Anesthesia (SAMBA) published a consensus statement on preoperative selection of adult patients with OSA scheduled for ambulatory surgery. In this statement, it is recommended that "Patients receiving preoperative continuous positive airway pressure (CPAP) should be instructed to bring their CPAP device to the ambulatory care facility, unless one is available at the facility"[1]. Because the compliance with this recommendation and the need for CPAP in the immediate postoperative period remains unknown, we decided to conduct a survey of medical directors of busy ambulatory surgery centers (ASC) located throughout the United States (US).

METHODS: We created a survey to investigate if the ASCs that accept OSA patients require the patients to bring their CPAP devices to the facility. In addition, we inquired if those ASCs used CPAP devices in the immediate postoperative period within the past two years. The survey was validated by five practitioners of busy ASCs to confirm whether or not any of the questions were difficult to understand or were ambiguous. The surveys were distributed via email and a reminder email was sent if no response was received within a month. The results of the survey were analyzed using spreadsheets and presented as percentages.

RESULTS: We had a response rate of 60.9% (67 of 110 ASC medical directors submitted the survey). The survey results encompass 408,147 cases among 1,946 providers. 59.7% (40/67) facilities require patients to bring their CPAP devices on the day of surgery. Only 17/67 (25.37%) of the facilities reported using a CPAP machine postoperatively in the past 2 years. Furthermore, the highest CPAP use was reported at 20 times over the past 2 years.

CONCLUSIONS: Our survey results reveal that 60% of the facilities followed the SAMBA recommendations. It is possible that the facilities that did not require their patients to bring the CPAP device had a CPAP device within the facility. Of note, 75% of the facilities never needed to use CPAP over the past two years. Further larger prospective studies are necessary to assess postoperative respiratory complications requiring the need for CPAP use.

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S-25.

COMPARISON OF NON-INVASIVE MONITORING TECHNIQUES DURING INTRAVENOUS PROPOFOL-BASED ANESTHESIA: RESPIRATORY VOLUME MONITORING VS. CAPNOGRAPHY

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INTRODUCTION: Capnography ($EtCO_2$) is the standard of care for monitoring ventilation in patients undergoing procedures under monitored anesthesia care (MAC) & general anesthesia. However, in non-intubated patients, $EtCO_2$ monitoring is challenging (eg, patient non-compliance/oral vs nasal breathers) or impossible (eg, upper endoscopy). Thus, clinicians often rely on pulse oximetry, a late indicator of respiratory depression, or on subjective assessment. A recently developed noninvasive respiratory volume monitor (RVM) provides accurate & continual monitoring of minute ventilation (MV), tidal volume (TV) & respiratory rate (RR) (errors <10% for MV/TV & <3% for RR)[1,2]. Here we compared RVM & EtCO2 monitoring in patients receiving propofol-based sedation.

METHODS: Simultaneous data were recorded by RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA) and capnography (Capnostream 20, SmartCapnoLine, Covidien, Mansfield, MA) from 11 colonoscopy patients (age: 51.9 ± 15.4 yrs; BMI: 27.4 ± 4.2 kg/m^2). RVM data was collected via a thoracic electrode PadSet. MAC was provided using propofol with midazolam and fentanyl. Clinical staff were blinded to RVM data. This study was IRB approved with written, informed consent. MV & TV were estimated as percent of baseline MV established during normal breathing prior to sedation. MV, TV, RR & $EtCO_2$ measurements were compared before & after a cumulative dose of 100 mg of propofol using paired t-tests. RR measurements from RVM & capnograph were also compared.

RESULTS: Following propofol, MV & TV decreased significantly (fig 1 a&b, $p<0.05$) while $EtCO_2$ remained unchanged (fig 1c, $p>0.5$). Measured RR by RVM & $EtCO_2$ was remarkably similar & unaffected by propofol (fig 1d). $EtCO_2$ stayed within a narrow range throughout the procedure despite decreasing TV & MV. In 9 patients, $EtCO_2$ did not exceed 10 mmHg of the mean & was 5 mmHg above the mean only 12.3 ± 4.9% of the time. Fig 2 shows a typical course where MV decreases after propofol, while $EtCO_2$ remains unchanged. During airway obstruction (fig 3), while the patient is apneic, both MV & $EtCO_2$ decrease & then recover after chin lift. There was good agreement in RR measurements across both devices. While the RVM's RR remained stable, the capnograph's RR became erratic at times, likely due to supplemental O_2 impeding the capnograph's ability to detect individual breaths (fig 4).

CONCLUSIONS: In non-intubated patients, the RVM reflects expected changes in ventilation with propofol and demonstrates reduction in TV & MV during obstruction and hypoventilation. The RVM provides reliable measurements when capnography data is unavailable and is not subject to the $EtCO_2$ limitations of nasal cannula placement, dilution with O_2, mouth breathing, & obstruction of the sensor during upper endoscopies. The RVM shows greater measurement fidelity in response to anesthetics & can identify decreases in ventilation sooner than $EtCO_2$. The RVM provides useful data that is similar to that provided by capnography and may provide a useful alternative to capnography.

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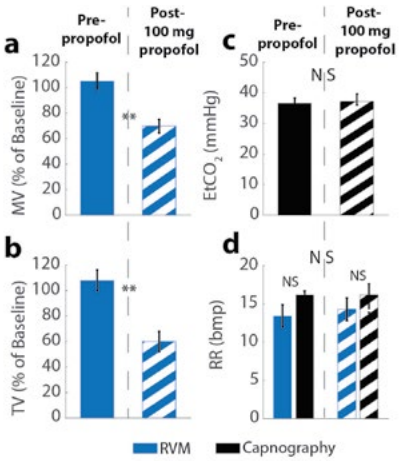

Figure 1: Effects of propofol on Minute Ventilation (MV) (a), Tidal Volume (TV) (b), $EtCO_2$ (c) and Respiratory Rate (RR) (d). Left side (solid): Averages ± SEM before sedation, Right side (hashed): Averages ± SEM after 100 mg cumulative dose of propofol. Results showed a significant decrease in MV and TV while $EtCO_2$ and RR remained essentially unchanged.
** $p < 0.05$
NS: Not significant ($p > 0.15$)

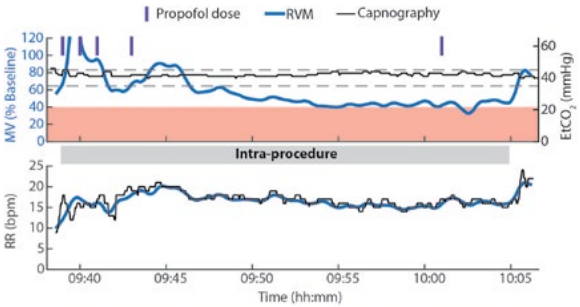

Figure 2: Representative example showing MV (blue) steadily decreased following propofol (purple) while $EtCO_2$ (black) stays nearly constant. RR measured by RVM and capnography are consistent.

S-25 • CONTINUED ON NEXT PAGE

S-25 • continued

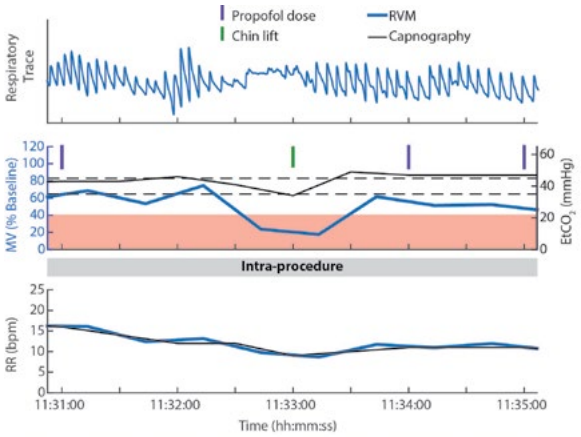

Figure 3: Example recording showing a patient with obstructed breathing which triggered a chin lift (green). Obstruction is clearly visible in the respiratory trace (top). MV decreases quickly from 75% to 18% and $EtCO_2$ decreases from 46 to 34 mmHg while the patient is apneic. Both MV and $EtCO_2$ recover following the chin lift.

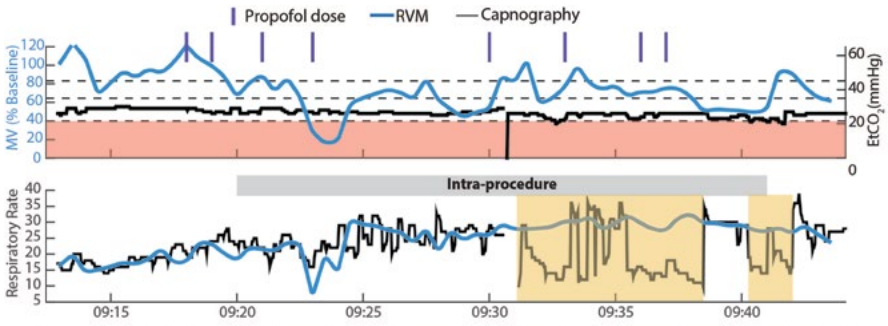

Figure 4: Example MV (top) and RR (bottom) trends of a patient with periods of poor agreement between RR readings highlighted in yellow. During these periods, the RR measurements from the capnograph are highly variable and lower than the RR measurement from the RVM.

S-26.

ANESTHESIOLOGIST-ADMINISTERED PROPOFOL SEDATION RESULTS IN LESS VENTILALTORY DEPRESSION THAN GASTROENTEROLOGIST-ADMINISTERED SEDATION FOR GI PROCEDURES

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INTRODUCTION: Monitoring respiratory function during sedation for gastrointestinal (GI) procedures can be challenging, and delayed detection of respiratory compromise may lead to an increase in patient morbidity and mortality. Hospitals often utilize dedicated anesthesiology personnel for higher-risk cases, while lower-risk cases are managed by GI staff. Choice of sedatives can also differ: propofol is commonly used by anesthesiology personnel, but not by GI staff. In this study we used a non-invasive respiratory volume monitor (RVM) to compare the degree of respiratory depression between upper endoscopy and colonoscopy procedures.

METHODS: An impedance-based RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA) was used to monitor patients undergoing GI procedural sedation. Endoscopy patients were sedated with propofol with or without other agents (fentanyl, ketamine, midazolam) and were managed by anesthesia personnel. Colonoscopy patients were sedated with a combination of meperidine and midazolam and were managed by GI staff. All patients received routine monitoring including capnography. All caregivers were blinded to the RVM measurements. Baseline MV (MVBASELINE) for each patient was acquired prior to sedation. Mirroring the ARDSnet criteria for extubation, we classified MV<40 %MVBASELINE as potentially un-safe.1 MV, TV & RR values were calculated. Values are reported as mean ± standard error of the mean (SEM), unless otherwise noted.

RESULTS: We enrolled 22 patients (13 females, age: 54±15 yrs, BMI: 27.3±6.6 kg/m2, mean±std) undergoing upper endoscopy procedures, and 25 patients (14 females, age: 60±8 yrs, BMI: 28.9±4.3 kg/m2, mean±std) undergoing colonoscopy. Upper endoscopy procedure times ranged from 14 to 64 min, with an average of 31.2±2.7 min. Endoscopy patients spent an average of 13.2%±3.0% of the procedure with un-safe MV (<40%MVBASELINE). Colonoscopy procedure times ranged from 7 to 39 min, with an average of 17.3±1.6 min. Colonoscopy patients spent an average of 21.7%±5.2% of the procedure below 40%MVBASELINE. While endoscopy procedures were on average 80% longer than colonoscopies, the fraction of time patients had potentially un-safe MV was 60% less (13.2%±3.0% vs. 21.7%±5.2%, Fig. 1). Notably, in the upper endoscopy group only 9.1% of the patients had un-safe MV for >1/3 of the procedure time, whereas in the colonoscopy group 20.0% of patients did so (Fig. 2). While no patients in the endoscopy group spent >1/2 of the procedure with unsafe MV, 16% of the colonoscopy patients did so.

DISCUSSION: Overall we observed a noticeably higher incidence and degree of respiratory depression in patients undergoing colonoscopy compared to those undergoing upper endoscopy despite the longer procedure times of the endoscopies and the close proximity of the airway to the proceduralist. This finding could be due to differences in sedating agent, procedure type, or sedation caregiver. Monitoring TV and MV during endoscopic and colonoscopic procedures may augment patient safety and improve outcome.

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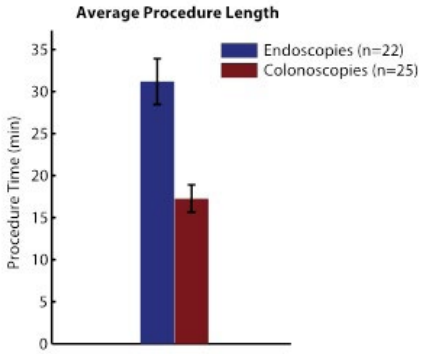

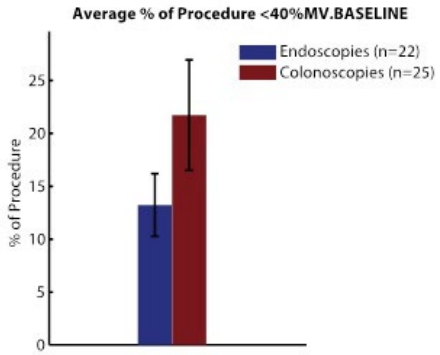

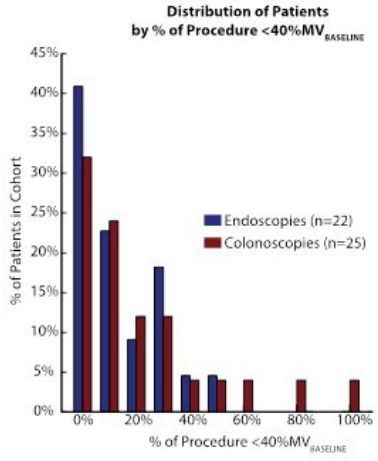

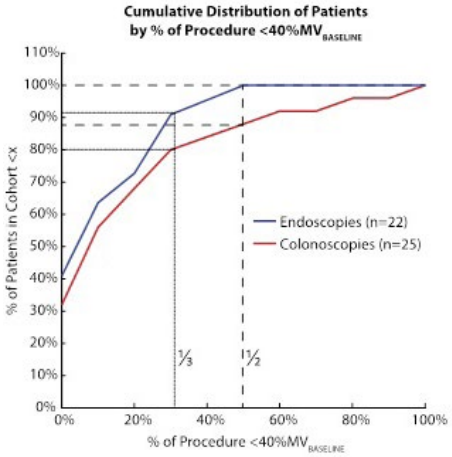

S-27.

THE EFFECT OF ZINC LOZENGES ON POSTOPERATIVE SORE THROAT SYNDROME: A PROSPECTIVE RANDOMIZED, DOUBLE BLINDED, PLACEBO-CONTROLLED STUDY

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INTRODUCTION: Postoperative sore throat (POST) is a common complication seen after endotracheal intubation. Zinc is a Group IIb metal, which is involved in diverse physiologic processes, such as growth, immune system as well as tissue repair[1], and has been demonstrated to be an effective antioxidant via protection of sulfhydryl groups against oxidation and inhibition of the production of reactive oxygen species by transition metals[2]. The aim of this study is to evaluate the effects of administration of zinc lozenges prior to endotracheal intubation on POST.

METHODS: Seventy nine patients undergoing low or moderate risk surgery were randomly assigned into two groups, to either receive placebo lozenges (control) or zinc lozenges (zinc) orally to be dissolved by sucking 30 min preoperatively. Patients were assessed for incidence and severity (four-point scale, 0-3) of POST at 0, 2, 4, and 24 h postoperatively. The primary outcome was sore throat at 4 h after surgery. The secondary outcome was the severity of POST at four evaluation time intervals postoperatively.

RESULTS: The incidence of POST at 4 h was 29% in control group and 7% in zinc group (P-0.025). The incidence of POST at 0 h was 0% in zinc group and 24% in control group (P-0.001); the highest incidence of POST occurred at the second hour after surgery, with the rate of 10% in the zinc group and 34% in the control group (P-0.017). The incidence of POST at 24 h was 13% in zinc group and 24% in control group which did not reach statistical significance (P-0.183). Additionally, the incidence of mild and mild to moderate POST was significantly reduced with zinc compared to placebo (P-0.016 and P-0.027). Additional factors found to be associated with increased incidence of POST were patient's weight, duration of surgery and Cormack-Lehane view during intubation; factors associated with increased severity of POST were initial cuff pressure of the endotracheal tube, and use of succinyl choline for intubation.

CONCLUSIONS: The administration of zinc lozenge 30 min preoperatively is effective to reduce both incidence and severity of POST in the immediate postoperative period.

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S-28.

RAPID ONSET OF PAIN RELIEF WITH OLICERIDINE (TRV130), A NOVEL μ RECEPTOR G PROTEIN PATHWAY SELECTIVE (μ-GPS) MODULATOR, VS. MORPHINE: A PHASE 2A/B STUDY ANALYSIS

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INTRODUCTION: Conventional opioids are widely employed for the management of moderate to severe acute pain. These opioid ligands bind to μ receptors and non-selectively activate two intracellular signaling pathways: the G protein pathway, associated with analgesia, and the β-arrestin pathway, associated with opioid-related adverse events (ORAEs) and inhibition of G protein-mediated analgesia. Opioids such as morphine may take up to 30 minutes to produce meaningful analgesia. The slow onset of action of morphine reduces its predictability and makes it difficult to titrate. Potential consequences include excessive dosing and increased risk of delayed ORAEs. These may be avoided by an analgesic with a rapid, predictable onset of pain relief with decreased ORAEs. Oliceridine (TRV130) is a novel μ receptor G protein Pathway Selective (μ-GPS) modulator that activates G protein with low β-arrestin recruitment to the μ receptor. In two randomized phase 2 studies, oliceridine demonstrated the potential to produce rapid and predictable analgesia, with a differentiated safety and tolerability profile compared to morphine. Here we present an analysis of the time to onset of pain relief from a randomized, double-blind, adaptive phase 2a/b study in patients experiencing postoperative pain following bunionectomy.

METHODS: Patients in the second phase of this adaptive study (N=195) were randomized to receive double-dummy oliceridine 0.5mg, 1mg, 2mg or 3mg every 3 hours (q3h); placebo; or morphine 4mg every 4 hours (q4h) intravenously in an 8:8:4:5 ratio. Categorical pain relief was assessed at baseline, 5, 10, 15, 30, and 45 minutes, and at various other time points between 1 and 48 hours using a 5-point scale ("none," "a little," "some," "a lot" and "complete"). Rescue analgesics were available as necessary.

RESULTS: At 5 minutes post the initial dose, the proportions of patients with "a lot" or "complete" pain relief were 0% and 13% with placebo and morphine, respectively, versus 20%, 29%, 58%, and 94% with oliceridine 0.5mg, 1mg, 2mg or 3mg, respectively (Figure 1). At 15 minutes, the proportions of patients with "a lot" or "complete" pain relief were 0% and 26% with placebo and morphine, respectively, versus 20%, 45%, 78%, and 90% with oliceridine 0.5mg, 1mg, 2mg or 3mg, respectively (Figure 2). Adverse events (AEs) associated with oliceridine were similar in nature to those observed with conventional opioids. There were no serious AEs reported.

CONCLUSIONS: In this analysis of a phase 2a/b study of patients with postoperative pain following bunionectomy, a significantly greater proportion of patients receiving oliceridine reported "a lot" to "complete" pain relief at 5 and 15 minutes following administration versus patients on morphine. When delivered as-needed, oliceridine's rapid onset of pain relief may allow for convenient and predictable titration and thereby may address the unmet need for an analgesic that can rapidly and effectively manage moderate to severe acute pain while possibly reducing ORAEs.

Figure 1: Proportion of Patients with "A Lot" of or "Complete" Pain Relief: 5 Minutes

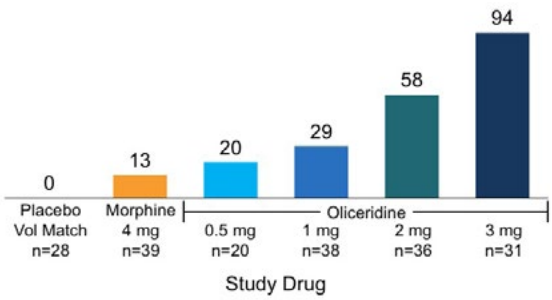
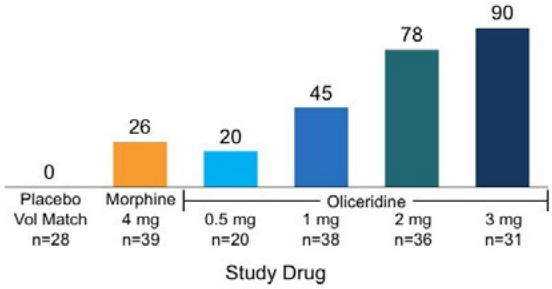


Figure 2: Proportion of Patients with "A Lot" of or "Complete" Pain Relief: 15 Minutes



S-29.

AN IN-VIVO PORCINE MODEL FOR VENOUS AIR EMBOLISM DURING VITRECTOMY SURGERY

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AFFILIATION: [1]Anesthesiology, University of Miami, Miami, FL, [2]Ophthalmology, University of Miami, Miami, FL, 3Surgery, University of Miami, Miami, FL

INTRODUCTION: Death is not an outcome associated with eye surgery. Yet, in the past decade intermittent case reports have documented acute and profound circulatory collapse, and even death, during the fluid-air exchange (FAX) phase of pars plana vitrectomy (PPV) surgery[1,2,3]. Although all clinical descriptions were suggestive of venous air embolism (VAE), the underlying pathogenesis remained unclear. A subsequent in-vitro experiment hypothesized that air infused through a misplaced scleral trocar could distend the suprachoroidal space; resulting in dilation of the emissary veins and propagation to the central venous circulation 4. This porcine model is the first in-vivo study that aims to corroborate that air egresses from the supra-choroidal space through the vortex veins into the central circulation; ultimately resulting in symptomatic or fatal VAE.

METHODS: This study received approval from the Institutional Animal Care and Use Committee. General anesthesia with spontaneous ventilation was administered to two pigs. Ophthalmic surgeons performed lensectomy and PPV (with FAX) in all eyes using a 25-gauge three-port technique. Monitoring included EKG, non-invasive BP, $ETCO_2$, intra-arterial catheter, trans-mucosal SpO_2 and trans-esophageal echocardiography (TEE).

RESULTS: In two eyes, attempted infusion into the suprachoroidal space via a misguided scleral trocar was unsuccessful. However, in the third eye the suprachoroidal space was identified. Air was infused at a pressure of 30 mm Hg and resulted in the development of a large choroidal detachment. The infusion pressure was then increased to 60 mm Hg. After 30 seconds intra-cardiac air was detected on TEE, and within one minute $EtCO_2$ declined precipitously. Hypotension and ischemic ECG changes were noted at three minutes. Notably, SpO_2 levels only plummeted at four minutes. The interval from detection of intra-cardiac air until death was six minutes. After death, the heart was opened under water. Profuse amounts of air bubbled out of the right ventricle.

CONCLUSIONS: This in-vivo porcine model confirms that pressurized air infused via a misplaced scleral trocar can enter the suprachoroidal space, exit the eye through the vortex veins, enter the central venous circulation and produce VAE. Vigilance and repeated assessments of trocar position during FAX, as well as rapid cessation of the infusion of air with flooding of the surgical field with saline should contain morbidity from this catastrophic complication of eye surgery. The anesthesiologist has a key role to raise OR awareness of the potential for VAE during FAX.

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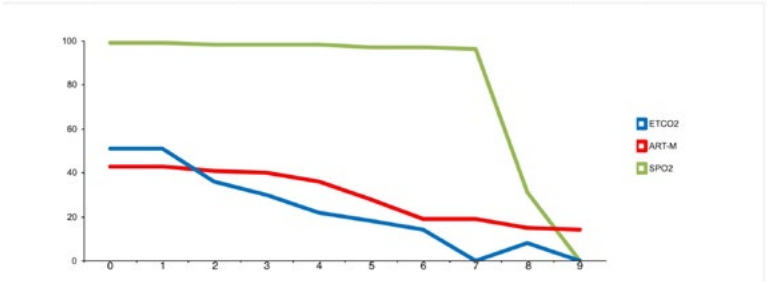
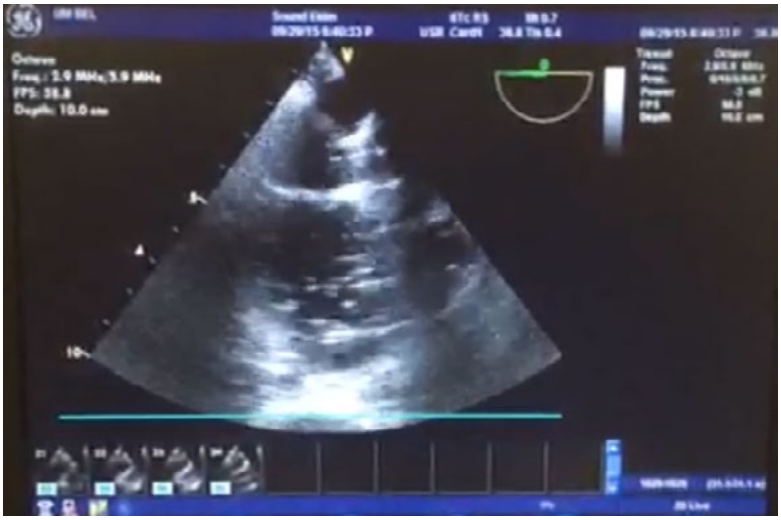
	Time (Min.) 0	Time (Min.) 1	Time (Min.) 2	Time (Min.) 3	Time (Min.) 4	Time (Min.) 5	Time (Min.) 6	Time (Min.) 7	Time (Min.) 8	Time (Min.) 9
Heart Rate	85	85	85	85	86	214	90	92	96	102
ART-S	67	68	64	64	60	48	39	105	63	25
ART-D	28	29	27	26	23	17	1	-50	9	11
ART-M	43	43	41	40	36	28	19	19	15	14
ETCO2	51	51	36	30	22	18	14	0	8	0
SPO2	99	99	98	98	98	97	97	96	31	0
Temp.	97.7	97.7	97.7	97.7	97.7	97.3	97.2	97.2	97	97





S-30.

A RANDOMIZED, PLACEBO- AND ACTIVE-CONTROLLED PHASE 2B STUDY INVESTIGATING OLICERIDINE (TRV130), A NOVEL μ RECEPTOR G PROTEIN PATHWAY SELECTIVE (μ-GPS) MODULATOR

AUTHORS: H. Minkowitz[1], D. Soergel[2], D. Burt[3], F. Skobieranda[2], T. J. Gan[4]

AFFILIATION: [1]Anesthesiology, Memorial Hermann Memorial City Medical Center, Houston, TX, [2]Clinical Development, Trevena, Inc., King of Prussia, PA, [3]Biostatistics, Trevena, Inc., King of Prussia, PA, [4]Anesthesiology, Stony Brook University, Stony Brook, NY

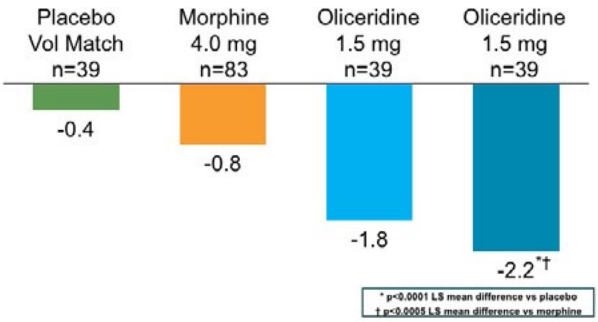
INTRODUCTION: Opioids are widely employed for management of moderate to severe acute pain; however, opioid-related adverse events (ORAEs), including respiratory depression and gastrointestinal dysfunction, can increase risk and may limit dosing required for analgesic efficacy. Conventional opioids bind to μ receptors and non-selectively activate two intracellular signaling pathways: the G protein pathway, associated with analgesia, and the β-arrestin pathway, associated with ORAEs and inhibition of G protein-mediated analgesia. Oliceridine (TRV130) is a novel μ receptor G protein Pathway Selective (μ-GPS) modulator that activates G protein while causing low β-arrestin recruitment to the μ receptor. This could result in opioid-like efficacy while mitigating ORAEs. The objective of this randomized, double-blind, adaptive patient-controlled analgesia (PCA) phase 2b study was to investigate the efficacy, safety, and tolerability of oliceridine compared to placebo (PBO) and morphine in patients (pts) with moderate to severe pain following abdominoplasty.

METHODS: Pts (N=200) experiencing postoperative pain following abdominoplasty were randomized to regimens of intravenous oliceridine (two 0.75mg loading doses followed by either 0.1mg or 0.35mg self-administered demand PCA doses), PBO, or morphine (4mg loading dose followed by 1mg demand PCA doses), in a 1:1:1:2 ratio. All treatment arms included a 6-minute PCA lockout period. The primary endpoint was time-weighted average change in numeric pain rating scale over 24 hours (NPRS TWA 0-24). Rescue analgesics were available as necessary.

RESULTS: Oliceridine 0.1mg and 0.35mg regimens reduced model based NPRS TWA 0-24 change vs PBO by 2.3 and 2.1 points, respectively ($p=0.001$ and $p=0.0005$ vs. PBO); similar to morphine (2.1 points; $p<0.0001$ vs. PBO). Pain intensity differences at 5 minutes after the 1.5mg oliceridine loading dose were -1.8 and -2.2 for the 0.1mg and 0.35mg groups, respectively, compared to -0.9 after the 4mg morphine loading dose (Figure 1). Median time to meaningful pain relief was 1.1 hours and 0.3 hours with oliceridine 0.1mg and oliceridine 0.35mg, respectively, compared with 1.1 hours with morphine. Adverse events (AEs) associated with oliceridine were similar in nature to ORAEs; however, both oliceridine dose groups had a significantly lower prevalence of hypoventilation, nausea, and vomiting than the morphine group (post hoc $p<0.05$ for both oliceridine regimens vs. morphine). There were no serious AEs reported in the study.

CONCLUSION: In pts with postoperative pain following abdominoplasty surgery, oliceridine achieved a magnitude of pain relief comparable to morphine over 24 hours. Pts receiving oliceridine 0.35mg also tended to experience a more rapid onset of meaningful pain relief compared to pts receiving morphine. Both dose groups of oliceridine had a lower prevalence of ORAEs than the morphine group including a lower prevalence of hypoventilation, nausea and vomiting. These results suggest that oliceridine, a novel μ-GPS, may widen the therapeutic window between effective, rapid analgesia and typical ORAEs.

Figure 1: LS Mean Pain Intensity Difference Change from Baseline: 0-15 Minutes



S-31.

PREDICTORS OF EARLY POSTSURGICAL PAIN IN CHILDREN UNDERGOING OUTPATIENT OPERATIONS

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INTRODUCTION: About 20-60% of children experience significant postoperative pain after ambulatory surgery. Several factors contribute to this. First, many procedures are of relatively short duration and less invasive compared to in-patient operations, which creates a tendency to assume that severe postoperative pain may not be a frequent accompaniment of these procedures. Second, because of a desire to improve and expedite patient throughput, practitioners are often reluctant to use powerful long-acting opioid analgesics for concerns about delayed emergence from anesthesia[1]. Given the growing number and complexity of pediatric outpatient procedures, identifying factors associated with early postoperative pain requiring treatment (PPRT) in the PACU is an important clinical goal. To date these factors are largely unknown. To this end, this prospective, observational study determined the incidence and risk factors for PPRT among children who underwent elective ambulatory surgery. PPRT indicates PACU administration of analgesic medication (overall, opioid, and non-opioid).

METHODS: Following IRB approval, clinical, demographic and anthropometric data were prospectively collected on 558 children aged 4-17yr who underwent ambulatory surgery. Primary outcome measure was PPRT while secondary measure was numeric pain scores. Univariate factors associated with PPRT were assessed with Chi-squared or t-test as necessary. Probability of PPRT was modeled using multivariable stepwise logistic regression analysis with age, gender, race, habitual snoring, surgical specialty, intraoperative morphine dose, intraoperative use of multi-modal analgesia and duration of surgery included as predictors.

RESULTS: Of 558 children, 54.3% were boys. The mean age of the subjects was 9.7 (4.0) yr. Overall, 37.1% of patients received some form of analgesia in the PACU, while 27.8% received at least one intravenous opioid analgesic. In bi-variable analysis, increasing arousal pain score ($p<0.001$), ENT or orthopedic surgery ($p<0.001$), longer surgical duration ($p<0.001$), higher intraoperative dose of morphine ($p=0.005$), and intraoperative use of multimodal analgesia ($p=0.035$) were significantly associated with PACU administration of any analgesia. Considering PACU IV opioid use, habitual snoring ($p=0.008$), OSA history ($p=0.002$), ENT or orthopedic surgery ($p<0.001$) and longer duration of surgery ($p<0.001$) were significantly associated with this outcome variable. On multivariable analysis, the factors depicted in Fig. 1 achieved statistical significance as predictors of PACU opioid requirement. Conclusion: In this prospective study, over one third of children undergoing outpatient surgery required one form of analgesic in the PACU. It is concerning that OSA history is a strong predictor of PACU opioid requirement given the potential for delayed respiratory depression after these children are discharged home. Efforts to personalize perioperative analgesia for children with OSA history are warranted.

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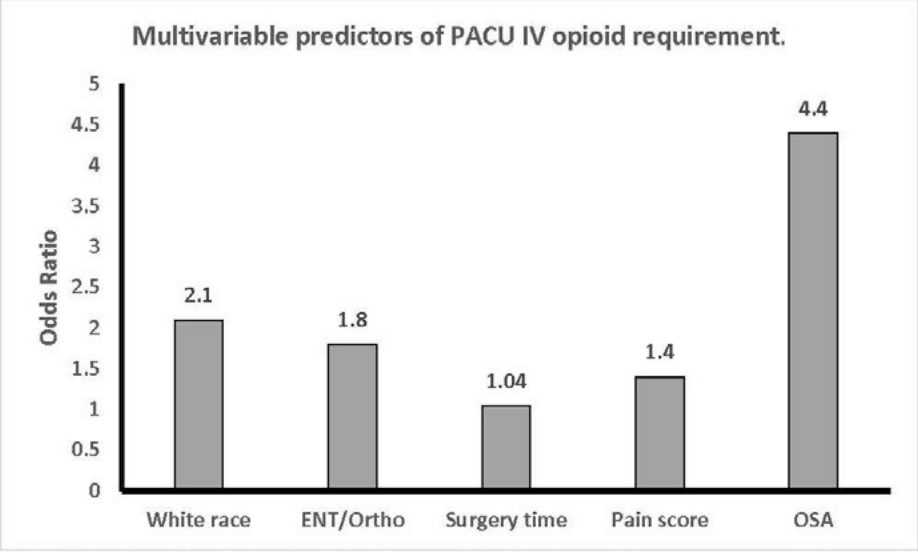

Fig.1. Showing adjusted odds ratios from multivariable logistic regression model Model adjusted for age, gender, race and the significant predictors.

Subspecialty Abstracts

Anesthetic Pharmacology

S-32.

PROLIFERATION OF C6 GLIOMA CELLS IS REGULATED BY TRANSIENT RECEPTOR POTENTIAL MELASTATIN 7 CHANNELS

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Calcium is essential for cancer cell proliferation. Receptor Potential Melastatin 7 (TRPM7) channels are implicated in mediating calcium homeostasis in cancer cells. Interaction with TRPM7 thus represents a potential target for anti-cancer therapy[1]. It has been shown that TRPM 7 channels present in head and neck cancer cells and play an important role in mediating cell proliferation[2]. Brain glioma is the most common malignant tumor with poor outcome. The presence of TRPM7 channels would provide a target for potential intervention. Here, we tested the presence of TRPM7 like currents by patch clamp whole cell recording in C6 glioma cells, and explored its role in cell proliferation measured by LDH assays with two TRPM7 blockers 2-APB and Gadolinium. We also tested the effects of knocking down TRPM7 expression with siRNA on TRPM7 currents and proliferation of C6 glioma cells.

METHODS: Electrophysiology TRPM7 currents were recorded with Axopatch-200B amplifier and pClampex 8.2 software by whole-cell patch clamp recordings. Rapid changes of extracellular solutions was achieved by a multibarrel perfusion system (SF-77, Warner Instruments, Hamden, CT). RT-PCR Isolation of total RNAs was performed using RNeasy Mini kit (Qiagen). An oligonucleotide primer pair was synthesized over regions specific for human TRPM7 cDNA (GenBank accession number NM017672). A primer pair for the detection of human glyceraldehyde-3-phosphate dehydrogenase (GAPDH; GenBank accession number M33197) was used as the internal control. RNA interference Briefly, dsRNAs 406-426 (TRPM7-siRNA) of human TRPM7 (NM_017672.4) were synthesized from Invitrogen. Cells were transfected with 30 nM siRNA using transfection reagent lipofectamineTM RNAiMAX (Invitrogen) according to the manufacturer's instructions. Non-targeting siRNA (Invitrogen) was used as a negative control. LDH assay Cytotoxicity Detection Kit (Roche Applied Science) was used to measure supernatant and maximal releasable LDH induced by 0.5% Triton X-100.

RESULTS: The application of calcium-free extracellular fluid results in an inward current in C6 cells, which is inhibited by TRPM7 channel nonspecific blocker Gadolinium and 2-APB (Figure 1 and 2). Proliferation of C6 glioma cells was inhibited by Gadolinium and 2-APB as indicated by microscopic observation and LDH release assays. The expression level of TRPM7 was measured by RT-PCR or real time PCR. Knockdown TRPM7 expression with TRPM7-siRNA inhibited TRPM7 currents and proliferation of C6 glioma cells (Figure 3).

CONCLUSION: TRPM7 is expressed in C6 glioma cells and mediates the proliferation of cell proliferation.

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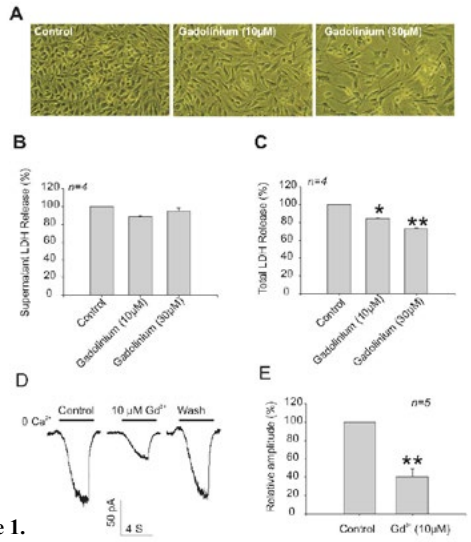

Figure 1.

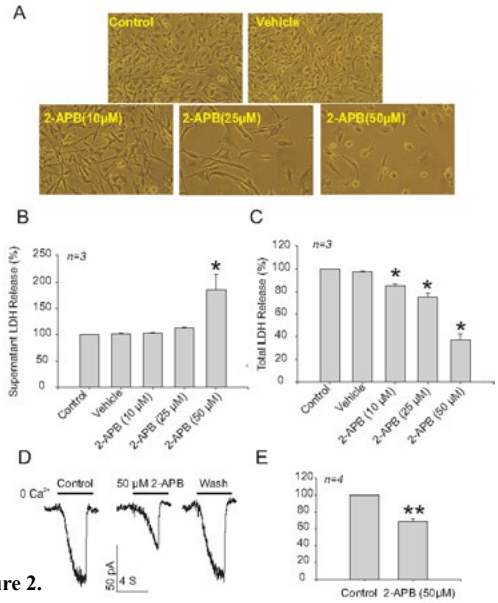

Figure 2.

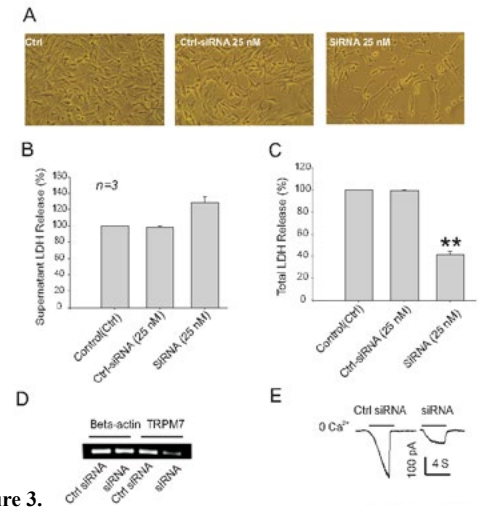

Figure 3.

S-33.

MIDAZOLAM INDUCED PROLIFERATION LOSS IN HUMAN GLIOBLASTOMA BY SUPPRESSING TRPM7 CHANNELS

AUTHORS: J. Chen[1], C. Xiao[2], Y. Dou[3], W. Zhu[4], J. Lin[2]

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BACKGROUND: It has been shown that the melastatin-like transient receptor potential 7 (TRPM7) channel is overexpressed in a number of cancer cell lines including head and neck, breast, pancreatic and prostate cancer, compared with cells in normal tissues or pericarcinous tissues. In these cancer cells, TRPM7 has been implicated in proliferation or apoptosis, indicating TRPM7 an anti-anaplastic target[1]. However, the existence and role of TRPM7 in human glioma is largely unknown. Recurrence of malignant glioma following surgery is very high and accounts for the dismal outcome. Our previous study showed that benzodiazepine inhibited proliferation of human glioblastoma cells[2]. Here we further tested the hypothesis that midazolam suppress the growth of human glioblastoma cells by inhibiting TRPM7 currents and expression.

METHODS: Whole cell patch clamp recording was employed to measure the TRPM7 currents in human glioblastoma cells. Calcium imaging was used for intracellular calcium signals. Cell proliferation was determined by 5-bromo-2'-deoxyuridine (BrdU) incorporation assay. Cell viability was measured by MTT assay. Cell cycle distribution was examined by flow cytometry. rtPCR was used to quantitate the mRNA levels. Western blot was applied to detect cell cycle regulatory proteins.

RESULTS: TRPM7 channels were identified by immunostaining and characteristic TRPM7 channel currents in human glioblastoma MGR2 cells. TRPM7 current was blocked by a pharmacologic inhibitor Gd3+ (Figure 1). Midazolam inhibited the TRPM7 currents in a dose dependent and reversible fashion and also inhibited the TRPM7 expression (Figure 2). Its inhibition of TRPM7 currents correlates its inhibition of calcium influx, which was abolished by TRPM7 agonist bradykinin (Figure 3). Midozolam induced proliferation loss in MGR2 cells and G0/G1 phase cell cycle arrest (Figure 4). The effects of midazolam were independent on benzodiazepine receptors but TRPM7 mediated (Figure 5).

CONCLUSION: Midazolam suppress TRPM7 channels leading to proliferation loss and G0/G1 phase cell cycle arrest in human glioblastoma.

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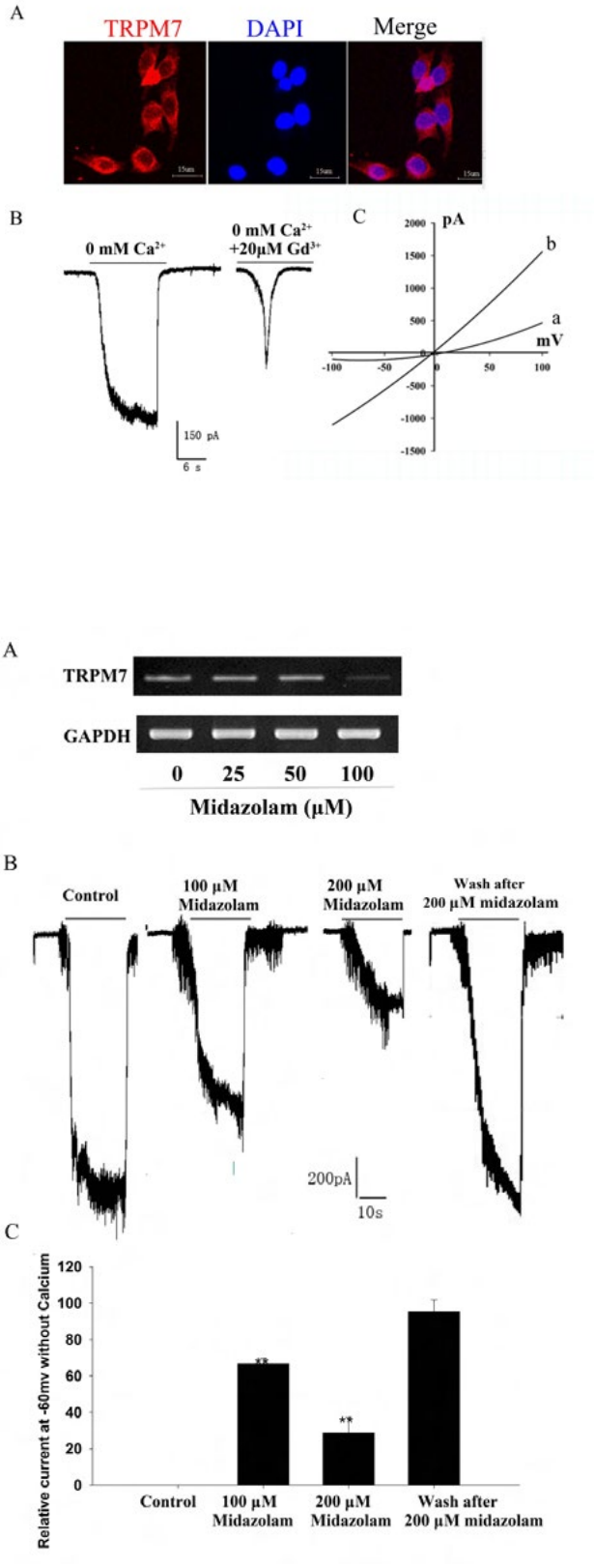

Figure 2.

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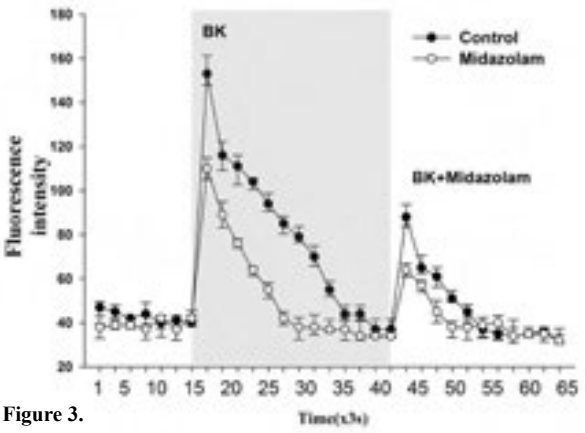

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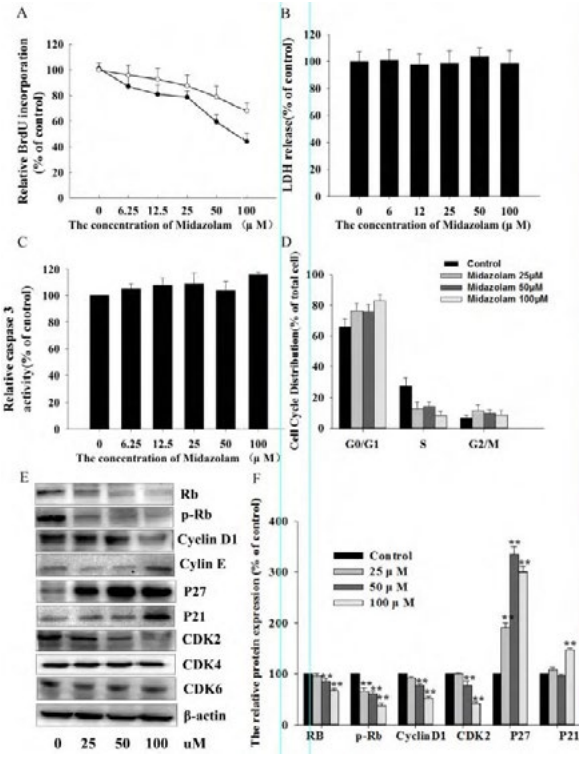

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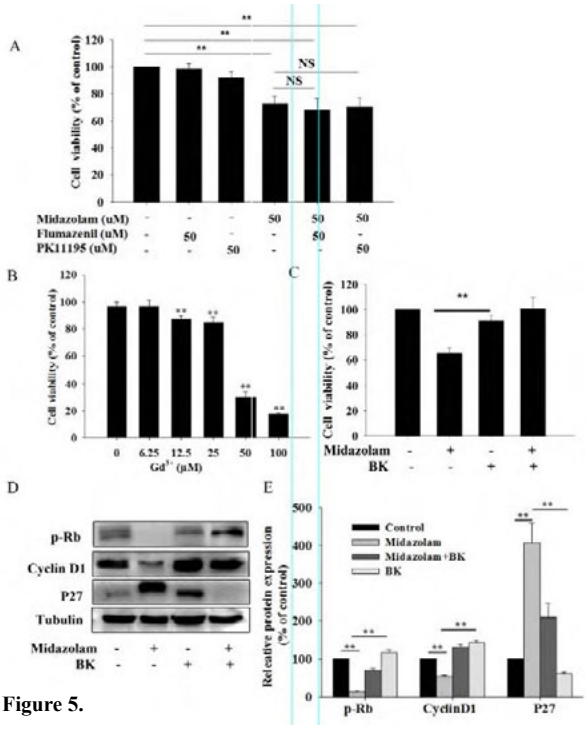

Figure 5.

S-34.

ANTIMICROBIAL SENSITIVITIES AND RESISTANCE OF METHICILLIN-SENSITIVE S. AUREUS (MSSA) IN A TERTIARY CARE HOSPITAL IN JAPAN; A VALIDITY OF THE USE OF US (UNITED STATES) GUIDELINES IN JAPAN

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INTRODUCTION: According to the guideline for antimicrobial prophylaxis of surgical site infection (SSI) published in 2013 in US, cefazolin (CEZ) is the drug of choice in most of the surgical procedures because it is the most studied antimicrobial agent with a proven efficacy. The predominant microbial organism that causes SSI after clean procedures is S. aureus, accounting for approximately 22.5% of SSI. In order to assess whether the guideline in US is also validated in Japan, we have evaluated antimicrobilal susceptibility profile of MSSA isolated in a tertiary care hospital in Japan.

METHODS: The study was conducted in a retrospective fashion after an IRB approval was obtained. The samples consisted of 695 MSSA isolates from 533 individuals during the 4-year period from 2012 to 2015. MICs(minimal inhibitory concentrations) for cefazolin, sulbactam/ampicillin, clindamycin, fluoroquinolones, aminoglycosides, minocycline, trimethoprim-sulfamethoxazole, rifampicin, and vancomycin were determined by a broth microdilution method according to the Clinical and Laboratory Standards Institute guidelines.

RESULTS: Of 695 MSSA isolates, no single resistance to CEZ was observed (resistance rate 0%). Seven out of 695 isolates showed resistance to sulbactam/ampicillin (resistance rate 1%). By contrast, clindamycin showed high resistance rate (129 out of 695 isolates were resistant; 18.5%) to MSSA. Although sensitivity to vancomycin was well preserved, 2 out of 695 isolates have been identified as vancomycin insensitive (MIC above 4-8 mg/L), supporting the prevuous notion that vancomycin is less effective than cefazolin for MSSA. Resistance rates to fluoroquinolones and aminoglycosides (except for arbekacin) are also high (135 out of 695 isolates and 214 out of 695 isolates, resistance rates 19.4% and 30.7%, respectively). For patients with a known history of β-lactam allergy, the potential alternatives to clindamycin might be minocycline (15 out of 695, resistance rate 2.1%), trimethoprim-sulfamethoxazole (resistance rate 0%), and rifampicin (9 out of 695, resistance rate 1.2%).

CONCLUSION: Ideally, microbial agent for SSI should prevent SSI and relating perioperative morbidity and mortality. To achieve these objectives, antimicrobial agents must be active against pathogens most likely to contaminate surgical site. Since local resistance patterns of microbial organisms may vary depending on several factors such as differences of institutions, nations, and the difference of availability of antimicrobial agents, resistance patterns of microbial organisms should take precedence before applying the guidelines. Here we show that the use of CEZ is apparently validated. However, the use of clindamycin for the patients with a known history of β-lactam allergy is not validated. To draw a definite conclusion, a nation-wide surveillance is required.

S-35.

PHARMACOKINETICS OF INTRAVENOUS ACETAMINOPHEN AND PHARMACODYNAMICS OF CONCOMITANTLY USED ACETAMINOPHEN AND FENTANYL IN PERIOPERATIVE PATIENTS

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INTRODUCTION: Intravenous (i.v.) acetaminophen (ACET) is administered during surgery for postoperative analgesia. However, little information is available on the pharmacokinetics of i.v. ACET and on the pharmacodynamics of concomitantly used i.v. ACET and fentanyl in Japanese patients.

METHODS: After approval by the Institutional Review Board and registration at the UMIN-CTR (UMIN000013418), patients, who were scheduled to undergo elective surgery under general anesthesia, were enrolled in the study with written informed consent. The recommended dose of ACET according to manufacturer guidelines was administered for either 15, 60 or 120 min during surgery. Prior to emergence from anesthesia, 100–200 mcg of fentanyl was administered intravenously. In selected patients, ACET concentrations were measured at time points from 0 to 480 min (15 or 16 samples per case) after starting ACET administration (Liquid Chromatography-Mass Spectrometry/Tandem Mass Spectrometry, limit of quantitation; 0.1 mcg/mL). Population pharmacokinetic analysis was performed using a nonlinear mixed-effect model based on the NONMEM program version 7.2 with PLTtools (http://www.pltsoft.com/). Plasma ACET concentrations and fentanyl effect-site concentrations at the time points of when patients first experienced postoperative pain (i.e., when the bolus button on the i.v. patient-controlled analgesia system was pressed) after discharge from the operation room, were simulated using pharmacokinetic models built in the present study and the Shafer model[1], respectively. PK/PD tools (http://www.pkpdtools.com/; under maintenance as of January 1st, 2016) were used for simulations.

RESULTS: Data from 40 patients who underwent body surface, oral, neck or endoscopic surgeries were analyzed (male/female = 17/23, 51.2 ± 15.3 years, 60.2 ± 10.4 kg). Using 185 data points (Figure 1) from 12 patients (Table 1), ACET pharmacokinetics were described by a two-compartment model with weight as a covariate. Final pharmacokinetic parameter values were as follows: V1 = 10.5 L, V2 = 29.9 × (weight/70 kg) L, CL1 = 0.22 × (weight/70 kg)0.75 L/min, and CL2 = 1.14 L/min. Median prediction error and median absolute prediction error were -1% and 13%, respectively (Figure 2). Age and sex were not included as covariates. Simulated plasma ACET concentrations and fentanyl effect-site concentrations when patients experienced postoperative pain were 10.1 ± 5.7 mcg/mL and 0.42 ± 0.28 ng/mL, respectively. Pharmacokinetic simulations of the recommended i.v. ACET dosage administered in 15 min with a range of body weight are shown in Figure 3.

CONCLUSION: We constructed a population pharmacokinetic model of i.v. ACET in Japanese patients and described the postoperative pharmacodynamics of iv ACET and fentanyl when used concomitantly.

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Patient backgrounds and clinical characteristics from the pharmacokinetic study

Male/Female(n)	7/5
Age(year)	54.5[38-74]
Height(cm)	163.2[153.4-171.0]
Weight(kg)	62.9[50.0-85.3]

Figure 1. Raw kinetic data

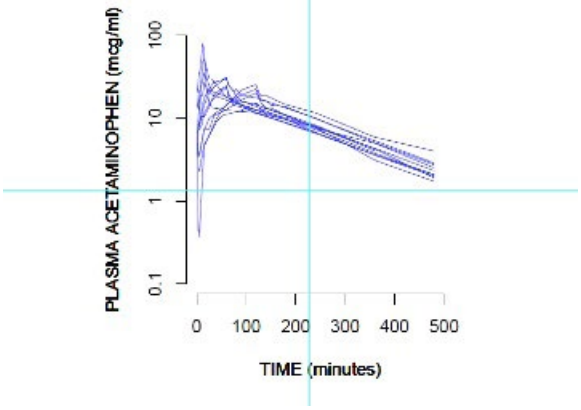


Figure 2. Observed/predicted vs. time for the final model

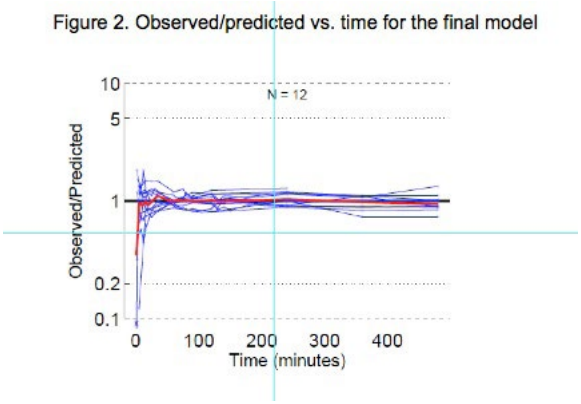
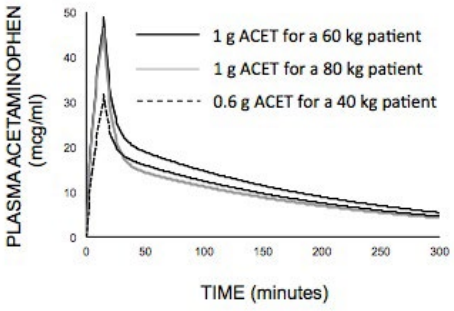


Figure 3. Pharmacokinetic simulations



S-36.

KETAMINE POTENTIATES GABA$_A$ RECEPTOR FUNCTION IN MICE

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AFFILIATION: [1]Physiology, University of Toronto, Toronto, ON, Canada, [2]Physiology and Anesthesia, University of Toronto; Aneshesia, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

INTRODUCTION: Ketamine is widely believed to depress brain function by inhibiting the NMDA receptor subtype of glutamate receptor[1]. However, high concentrations of ketamine have been shown to increase the activity of a subtype of GABAA receptors that contain α6 and δ subunits[2]. This subtype of GABAA receptor is expressed almost exclusively in the cerebellum. It is unknown whether clinically relevant concentrations of ketamine modulate other GABAA receptor subtypes that are expressed in other brain areas. The goal of this study is to determine whether ketamine modifies the activity of native GABAA receptors that are expressed in the hippocampus.

METHODS: The studies were approved by the local Ethics Committee. Whole-cell voltage clamp currents were recorded in cultured murine hippocampal neurons. Drugs were applied to the recorded neurons through a three-barrel fast perfusion system. All experiments were performed in the presence of the NMDA receptor blocker, DL-APV (20 μM). Data are reported as mean ± SEM.

RESULTS: Clinically relevant concentrations of ketamine (10-300 μM) increased GABA-evoked currents but only when neurons were perfused with low concentrations of GABA (0.3-0.5 μM, Figure 1). Ketamine (10-1000 μM) also potentiated tonic GABA current in a concentration-dependent and reversible manner (Figure 2). Higher concentrations of ketamine (0.3-50 mM) directly activated currents in the absence of GABA (EC50 = 6.4 ± 0.6 mM, Figure 3). Ketamine currents were blocked by the competitive antagonist, bicuculline (IC50 = 1.3 ± 0.1 μM) and the noncompetitive blocker, picrotoxin (IC50 = 15.2 ± 2.0 μM) confirming that the currents were generated by GABAA receptors. Interestingly, furosemide (300 μM), an antagonist of α6-containing GABAA receptors, failed to modify the potentiating and direct gating effects of ketamine on GABAA receptors. In addition, the effects of ketamine were similar between neurons from wild-type and δ subunit-deficient mice (Figure 4).

CONCLUSIONS: Clinically-relevant concentrations of ketamine potentiate GABAA receptors in hippocampal neurons, but only when receptors are activated by low concentrations of GABA. These results suggest that extrasynaptic GABAA receptors are preferentially sensitive to ketamine. The effects of ketamine are not unique to GABAA receptors containing α6 and ð subunits. These results are important because they implicate extrasynaptic GABAA receptors in mediating the anesthetic, analgesic and anti-depressant properties of ketamine.

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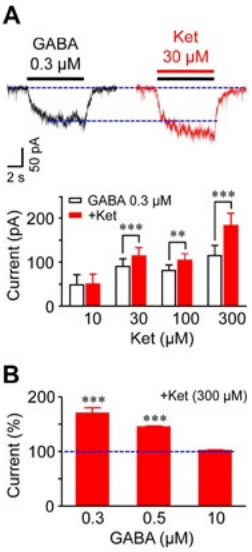

Figure 1. Clinically relevant concentrations of ketamine (10-300 μM) potentiate $GABA_A$ receptor function (**A**). The potentiating effects decrease with increasing concentrations of GABA (**B**). *n* = 6-8. ** *P* < 0.01, *** *P* < 0.001.

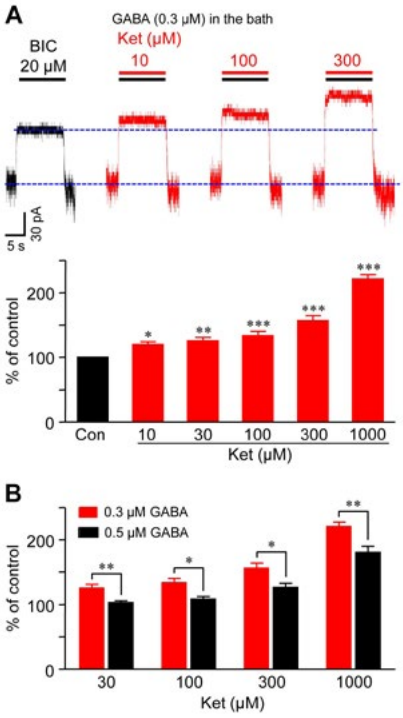

Figure 2. Clinically relevant concentrations of ketamine (10-300 μM) potentiate tonic GABA current mediated by extrasynaptic $GABA_A$ receptors (**A**). The potentiating effects decrease when the ambient concentration of GABA is increased from 0.3 μM to 0.5 μM (**B**). *n* = 8. * *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001.

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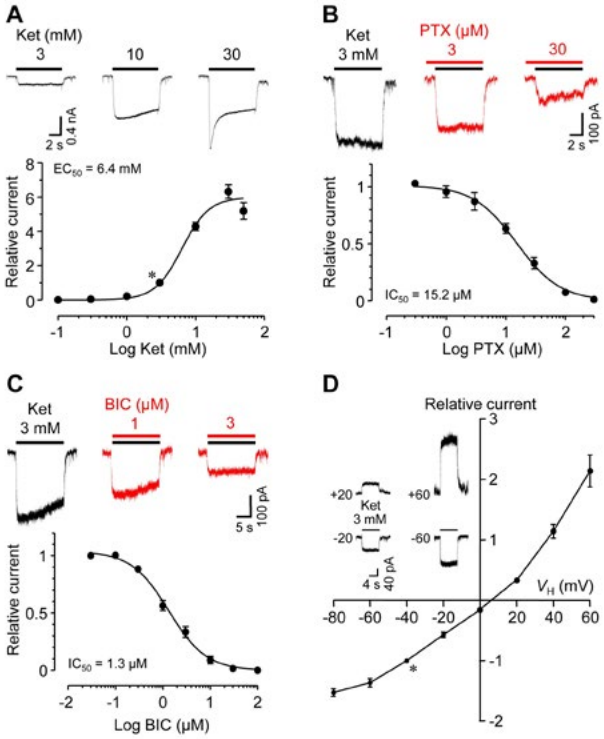

Figure 3. Higher concentrations of ketamine (0.3-50 mM) directly activate currents (**A**). The current is inhibited by a chloride channel blocker, picrotoxin (PTX, **B**) and by a competitive $GABA_A$ receptor antagonist, bicuculline (BIC, **C**) **D**. I-V curve shows that the reversal potential of the current is close to chloride equilibrium potential. *n* = 5-14.

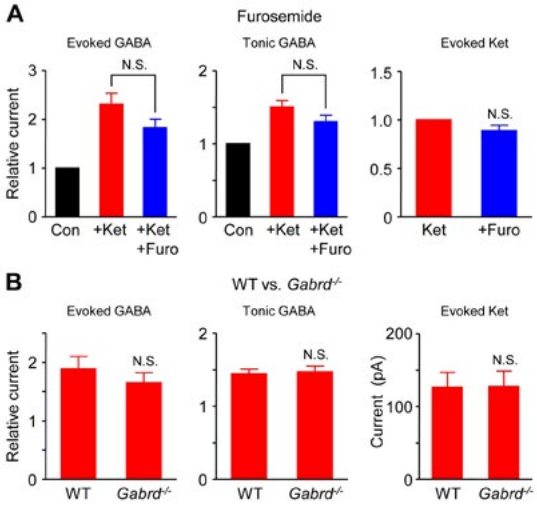

Figure 4. The effects of ketamine are not unique to $GABA_A$ receptors containing α6 and δ subunits. The up-regulating and direct gating effects of ketamine are not affected by the specific α6-containing $GABA_A$ receptor antagonist furosemide (300 μM, **A**) or genetic deletion of δ-containing $GABA_A$ receptors (**B**). *n* = 7-9. N.S.: no significance.

S-37.

INJECTABLE ULTRA-STABLE ISOFLURANE NANO-EMULSION: FORMULATION, STABILITY AND INDUCTION STUDIES IN RATS

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AFFILIATION: [1]Anesthesiology, University of Miami Miller School of Medicine, Miami, FL, [2]Surgery, University of Miami Miller School of Medicine, Miami, FL

INTRODUCTION: The discovery of the cytoprotective and immunomodulatory effects of volatile anesthetics (VA) has sparked interest in the reformulation of these compounds for safe intravenous delivery that will open up possibilities for its experimental use in a variety of novel applications[1]. However, recent researches to bioengineer safe emulsions have met with limited success due either to lack of long term stability or toxicity of the ingredients employed[2]. We have successfully bioengineered, preliminarily tested and patented an ultra-stable perfluorocarbon (PFC)-based isoflurane (Iso) nano-emulsion. In this paper we describe the characterization, efficacy and safety of this new formulation in small animal induction studies.

METHODS: Our Iso formulation consists of a mixture of PFC and Pluronic surfactant suspended in normal saline as the water phase. Iso/PFC nano-emulsions were manufactured by high-pressure microfluidization. Particle size stability and Iso content were assessed long term (>320 days) by dynamic light scattering (DLS) and attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR), respectively. The safety profile and efficacy of this emulsion were tested in Lewis rats with indwelling jugular vein catheters. Using a syringe pump, emulsions were delivered to the point of induction/anesthesia (loss of righting reflex, ciliary reflex and hind leg pain response) at a fixed infusion rate (2μL min-1 g-1). Propofol and carrier PFC emulsions were utilized as controls. Animals were monitored for liver enzymes and histopathology of multiple organs was assessed.

RESULTS: The manufactured emulsions displayed long-term particle size and Iso content stability when stored at room temperature. Over the 320 day measurement period, there was no significant change in mean particle size (125.17±8.64 vs 126.53±8.97nm, n = 3 emulsions). Initially, polydispersity was less than 15%, then increased to 20%, and was ~5% by the end of the study. Quantitative Iso content indicated little change over the 320 days (6.42±0.72 vs. 6.37±1.37 % v/v). The pre-emulsification content was 10% v/v, indicating that there was substantial loss during the emulsification but that these losses were reproducible maintaining comparable concentrations from batch to batch. The Iso/PFC emulsions achieved anesthetic effect significantly faster than Propofol (49±5 vs 110.28±19.43 sec, P =0.012 by Mann-Whitney test) and exhibited a significantly shorter duration of effect (87±38 vs 233.3±25.12 sec, P = 0.011) and time to recovery (137±37 vs 343.5±25.4 sec, P = 0.011). No significant changes in liver or pancreatic enzymes were observed compared to Propofol or when comparing baseline. No values were greater than 2-fold that of baseline levels. Histopathological analysis of major organs showed no overt pathological changes.

CONCLUSIONS: These preliminary studies demonstrate the stability, safety and efficacy of this new VA emulsion as induction agent, with potential novel applications.

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S-38.

SELECTIVE ALKYLPHENOL ANESTHETIC BINDING TO $GABA_A$ SUBUNITS IN NATIVE NEURONAL TISSUE

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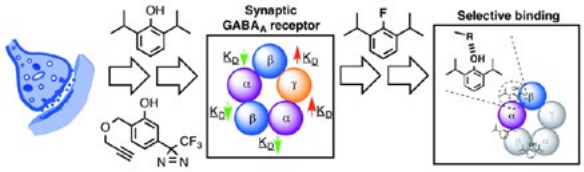
INTRODUCTION: Propofol is a positive modulator of the GABAA receptor, but the mechanistic details, including the relevant binding sites, remain disputed.

METHODS: Here, we designed and synthesized a photoaffinity tandem bioorthogonal propofol ligand, ortho-alkynyl-meta-azipropofol (AziPm-click), for the unbiased identification of propofol-binding proteins in their native milieu within mouse synaptosomes. After confirmation of retained GABAergic and in vivo anesthetic character by our probe, we developed our affinity-based protein profiling strategy combined with quantitative mass spectrometry for the identification of propofol synaptic protein targets. GABAA receptor subunit selectivity was further investigated with molecular dynamics simulations and potential molecular recognition elements were studied with a previous developed propofol analogue.

RESULTS: Our affinity-based protein profiling strategy identified ~4% of the synaptosomal proteome as potential propofol-specific protein targets, including five α or β GABAA receptor subunits. γ subunits were not identified, a finding that was not due to low abundance. Molecular dynamics simulations allowed the hypothesis that the higher affinity interactions for propofol at α/β relative to γ-containing interfaces were due to differential hydrogen-bonding. Application of a hydrogen-bond null propofol analogue supported this hypothesis.

CONCLUSIONS: This investigation provided the first experimental evidence for direct propofol interaction with specific GABAA receptor subunits within native tissue. Further, these results expand the list of potential alkylphenol molecular targets.



S-39.

PI3K/AKT MEDIATES LIDOCAINE PROTECTING RAT PC12 CELLS FROM AMYLOID-BETA TOXICITY

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INTRODUCTION: Amyloid-beta is neurotoxic and plays an important role in the etiology of Alzheimer's disease. Lidocaine is a common local anesthetic, which has been shown to be neuroproctective at antiarrhythmic dose against hypoxia in animal[1] and suggested to be beneficial for postoperative cognitive function in patients undergoing cardiopulmonary bypass[2]. We have observed the protective effects of lidocaine against beta-amyloid neurotoxicity on neuron cell line PC12 cells and mouse cultured neurons (IARS, 2014). Here we further explored the involvement of PI3K/Akt and the MAPK pathways, the two most important pathways in neuronal survival[3].

METHODS: The MTT assay was used to determine the viability of PC12. Western blot analysis was performed with antibodies against phospho -FoxO3a, phospho-IGF-1R, phospho-Akt (Ser473), phospho-ERK1/2 or anti-GAPDH antibodies.

RESULTS: *Lidocane protected PC12 cells* The protective effect of lidocaine was seen and significant at 0.1 nM and increased further when the concentration of lidocaine increased and maximal at 3-10 nM. The protection was decreased when concentration was higher such as 30 nM. *Lidocaine time-dependently stimulated the phosphorylation of p-FoxO3a, Akt and Erk in PC12 cells* The effect of lidocaine on the PI3K/Akt and the MAPK pathways, the two pathways most important in neuronal survival, were tested[4]. Our results showed that lidocaine time-dependently stimulated the phosphorylation of Akt in PC12 cells (Figure 2). Lidocaine also induced the phosphorylation of FoxO3a, a main downstream target of Akt. Lidocaine has a minimal effect on the activation of MAPK, which was only observed at about twenty min. These results suggested that PI3/Akt/FoxO3a is the main pathway of lidocaine. *PI3K inhibitor LY294002 and Akt inhibitor Akt inhibitor IIIV abolished the effect of lidocaine* To see if above pathway are involved in the protective effect of lidocaine, we pretreated PC12 cells with LY29400 or Akt inhibitor IIIV to inhibit the activation of PI3K or its downstream kinase Akt respectively. Our results showed that the blockage of either PI3K by LY294002 or Akt by Akt inhibitor IIIV abolished the protective effect of lidocaine on the survival of PC12 cells from Aβ25-35. PD98059 and U0126, two specific inhibitors of MAPK pathway have no effect (Figure 3). Conclusion Our results suggest that lidocaine protected neuronal cells from beta amyloid toxicity via the PI3K/Akt pathway.

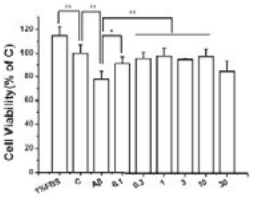

Figure 1. Lidocane promoted survival of PC12 cells from toxicity of beta amyloid Aβ25-35. PC12 cells treated with various concentration of lidocane (0.1-30 nM) were treated with 10 um AB25-35 for 24 hours and the viability of cells was determined by MTT assay. Data are shown as the mean ± SEM. and represent assays from at least three independent experiments. *p<0.05,** p<0.01 (n = 4).

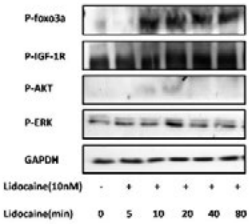

Figure 2. Lidocaine time-dependently stimulated the phosphorylation of p-FoxO3a, Akt and Erk in PC12 cells.

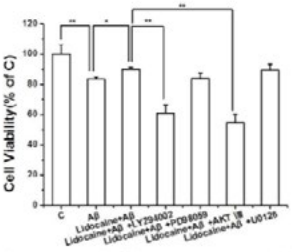

Figure 3. PI3K inhibitor LY294002 and Akt inhibitor Akt inhibitor IIIV abolished the effect of lidocaine.

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S-40.

LIDOCAINE ALTERS MIGRATION AND TRPM7 CHANNEL EXPRESSION OF Human A549 LUNG CANCER CELLS

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INTRODUCTION: Surgery is a crucial step in the treatment of lung cancer. Patients often die from recurrence or metastasis after surgery[1]. Retrospective studies indicated that addition of regional anesthesia is associated with a longer recurrence-free period in breast, colon and prostate cancer patients[2-4]. Thus the anesthetic technique and/or choice of anesthetic may be an important consideration. To uncover any beneficial effects of regional anesthesia, it is necessary to determine the effects of local anesthetics on cancer cell behavior. TRPM7, a calcium-permeable ion channel highly expressed in cancer cells, has been implicated in mediating the proliferation and migration in a number of cancer cells. Here, we seek to determine the effects of a common local anesthetic lidocaine on lung cancer cell A549, and to explore the potential role of TRPM7 in mediating the effects of lidocaine.

METHODS: Human lung adenocarcinoma cells (A549) were exposed to 0.3-10 mM lidocaine for 48 hours in an incubator. The cells were studied with the following assays:- MTT Trans-well migration Immunohistochemistry and Western blot analysis. All data are expressed as mean ± SE. P values less than 0.05 were considered significant.

RESULTS: A549 cell viability judged by the MTT assay was normal at 0.3 - 1 mM lidocaine. However, at 3 and 10 mM lidocaine, viability decreased significantly after 48 hour incubation (Fig 1). The trans-well cell migration assay revealed that 3 and 10 mM lidocaine suppressed cell migration and invasion (Fig 2). Both immunohistochemistry (3A, 3B) and western blot data (3C, 3D) indicate that 1 and 3 mM lidocaine decreased expression of TRPM7 in A549 cells after 48 hours treatment.

CONCLUSION: Lidocaine suppresses the growth and migration of human lung A549 cancer cells. Reduced expression of TRPM7 channels following lidocaine treatment was observed and could be the cause for the decrease of A549 cell proliferation and migration seen in direct microscopic observation and MTT assays. It is possible that lidocaine directly blocks the TRPM7 channel in A549 cells and contributes to the results. Further study is warranted for elucidating the underlying mechanisms.

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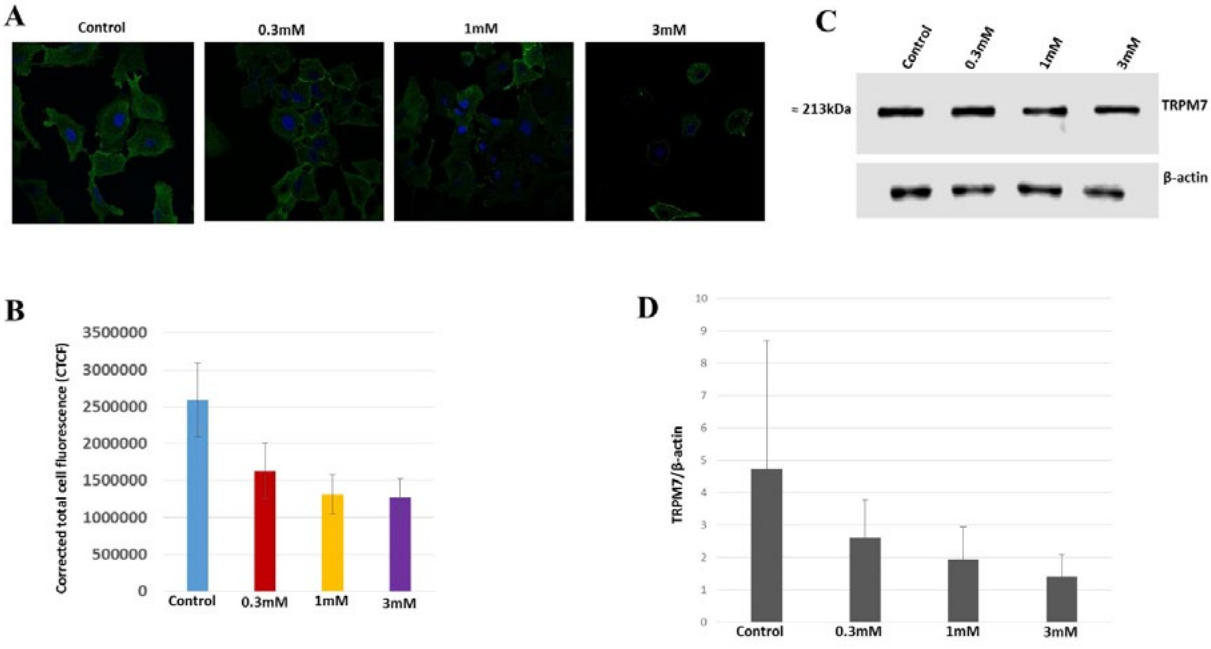

S-41.

CONCORDANCE OF SUBSTITUTED TRYPTOPHAN SENSITIVITY VS. SUBSTITUTED CYSTEINE MODIFICATION-PROTECTION WITH ANESTHETIC PHOTOLABELING IN GABAA RECEPTORS

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BACKGROUND: Photolabel analogs of potent intravenous anesthetics have identified residues located in transmembrane inter-subunit pockets of GABAA receptor structural models. In α1β3γ2 and α1β3 receptors, both azi-etomidate and *m*-azi-propofol (azi-Pm) photolabel α1M236[1,2]. A barbiturate photolabel, mTFD-MPAB, and azi-Pm both photolabel β3M227[2,3]. Alphaxalone does not block these photolabeling reactions. Mutation-based strategies, including substituted tryptophan drug sensitivity and substituted cysteine modification-protection have also been used to probe for anesthetic contact residues[4-8]. We examined concordance among these approaches.

METHODS: We mutated α1M236 and β3M227 to both Cys (C) and Trp (W). Mutant or wild-type α1β3γ2 receptors were expressed in *Xenopus* oocytes and studied with two-microelectrode voltage-clamp electrophysiology. In wild-type and Trp mutant receptors, enhancement of EC5 GABA responses by etomidate, mTFD-MPAB, propofol, and alphaxalone, each at 2 x ED50 for loss-of-righting-reflexes, was compared using two-way ANOVA. In Cys mutants, apparent rates of covalent modification by p-chloromercuribenzene sulfonate (pCMBS) were tracked electrophysiologically and compared in the absence vs. presence of anesthetics[8]. To analyze concordance between photolabeling and other methods for probing drug-residue interactions, we calculated the percentage agreement of both positive and negative findings as well as Cohen's kappa, a measure to index agreement between pairs of methods. Frogs were used with IACUC approval.

RESULTS: The α1M236W mutation reduced modulation by etomidate, propofol, and alphaxalone. β3M227W reduced sensitivity to only mTFD-MPAB. Receptors with α1M236C or β3M227C mutations were modulated by all four anesthetics. Etomidate and propofol, but not mTFD-MPAB or alphaxalone, significantly slowed pCMBS modification of α1M236C. β3M227C was protected from pCMBS by mTFD-MPAB and propofol, not etomidate or alphaxalone. The agreement between photolabeling and substituted cysteine modification-protection was perfect, with 100% concordance (kappa = 1.0). However, the concordance with tryptophan mutant sensitivity was only 75% (kappa = 0.50).

DISCUSSION: Substituted cysteine modification-protection correctly identifies, among four drugs, those with photolabel analogs that modify the two amino acids we examined, without false positives or negatives. While Trp substitutions at azi-etomidate and mTFD-MPAB photolabeled residues reduce sensitivity to the corresponding site-selective drugs, both false positive and false negative results were obtained with this method. Substituted cysteine modification-protection is thus the better strategy for probing other putative anesthetic contact residues in $GABA_A$ receptors and other targets.

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S-42.

OPTIMAL DOSE OF DEXMEDETOMIDINE FOR SEDATION DURING EPIDURAL ANESTHESIA

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INTRODUCTION: Sedation in epidural anesthesia can reduce patient's anxiety and discomfort. Dexmedetomidine has a sedative, hypnotic, analgesic, and minimal respiratory depression effect. However, use of the dexmedetomidine is associated with prolonged recovery. This study was designed to investigate the optimal dose of intravenous dexmedetomidine for proper sedation with minimal recovery time in epidural anesthesia.

METHODS: Sixty three patients, ASA physical status I - II were recruited. After performing the epidural anesthesia, a loading dose of dexmedetomidine (1 μg/kg) was administered for 10 min, followed by the maintenance infusion of the following: Group A (n = 32; dexmedetomidine 0.6 μg/kg/hr) and Group B (n = 31; dexmedetomidine 1.0 μg/kg/hr). Heart rate, blood pressure, and the bispectral index score (BIS) were recorded during the operation. In the recovery room, modified aldrete score (MAS) was measured. Results: BIS was not significantly different between two groups from baseline to 150 min after the infusion of dexmedetomidine. BIS were significantly increased in Group A at 160min ($P < 0.05$) (Fig. 1). Mean blood pressure of Group B was significantly higher in PACU (Fig. 2). MAS was higher in Group A at 30 min of PACU ($P < 0.05$) (Fig. 3).

CONCLUSIONS: The loading dose (1 μg/kg/10 min) followed by maintenance dose (0.6 μg/kg/hr) of dexmedetomidine was sufficient for surgery of less than 160 min.

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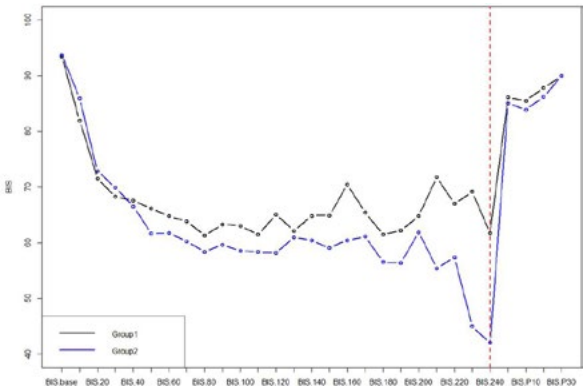

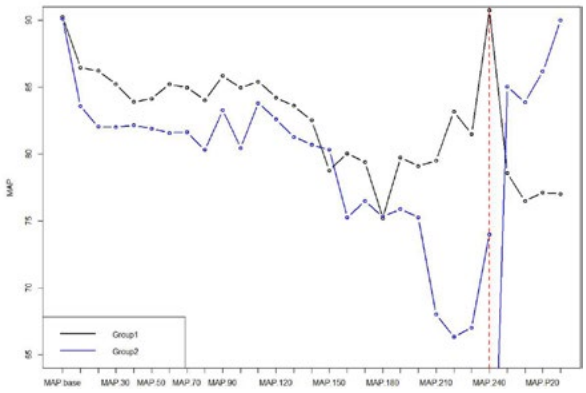

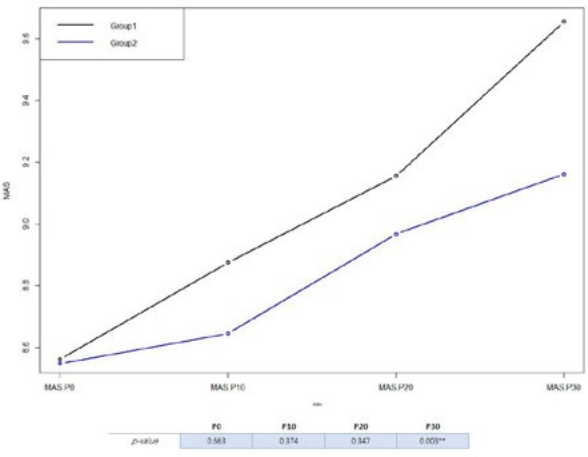

S-43.

HEMODYNAMIC CHANGES DURING CLOSED-LOOP INDUCTION OF ANESTHESIA

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INTRODUCTION: Closed-loop controlled anesthesia continually adjusts drug infusion rates using depth of hypnosis feedback. This method has been shown to effectively control anesthetic drug administration during induction and maintenance of anesthesia[1]. It has been previously reported that the effect of propofol on depth of hypnosis occurs more rapidly than its effect on systolic blood pressure[2]. The purpose of this study is to evaluate the effects of closed-loop induction of anesthesia on hemodynamic vital signs and depth of hypnosis.

METHODS: As part of a larger clinical trial (NCT01771263), with local research ethics board approval and written informed consent, vital signs data were obtained during closed-loop controlled induction of total intravenous anesthesia (TIVA) with propofol and remifentanil. Invasive mean arterial blood pressure (MAP) and heart rate (HR) were acquired using the Carescape B850 multi-parameter monitor (GE Healthcare, Buckinghamshire, UK), which was slaved to a LiDCO Rapid (LiDCO Limited, London, UK) to obtain a cardiac output (CO) measure. Depth of hypnosis was measured using the WAVCNS index obtained by the NeuroSENSE NS-701 monitor (NeuroWave Systems, Cleveland Heights, OH). Vital signs data, covering the interval from the start of propofol infusion until intubation, were plotted and analyzed using MATLAB (The Mathworks Inc, Natick, MA).

RESULTS: Data, in which arterial line placement preceded the start of anesthesia induction, were available for 11 participants (all males) with median (range) age of 64 (54-76) years and BMI of 28.7 (22.6-32.4) kg/m^2. At the time of intubation, the median (range) propofol effect site concentration (Ce, calculated using the Schnider model[3]), was 4.6 (2.7-8.2) mcg/ml. Induction of anesthesia was associated with a median (range) decrease in HR of 6 (-7-16) bpm, a decrease in MAP of 37 (8-50) mmHg, a decrease in CO of 2.16 (-0.77-3.54) L/min, and a decrease in WAVCNS of 38.9 (27.6-73.7) units (see Figure 1 for curve fitted plots). There was no clear age-dependent effect for the magnitude of hemodynamic change in any of the reported vital signs; while they were all negatively correlated with age, the correlation coefficient was small (R2 of 0.01, 0.26, 0.04, and 0.13 respectively). The change in MAP preceded the change in WAVCNS in 8/11 (73%) participants; in these cases 6/8 participants (75%) experienced burst suppression after intubation (see Figure 2 for example cases).

DISCUSSION: A clinically significant reduction of MAP and CO was observed during closed-loop induction with TIVA. The temporal relationship of TIVA-induced hypotension and reduction in WAVCNS contradicts the findings in the literature for the Bispectral Index (BIS)[2]. Future work includes incorporating hemodynamic changes into the design of the closed-loop controller, which will be particularly beneficial in older and sicker patients.

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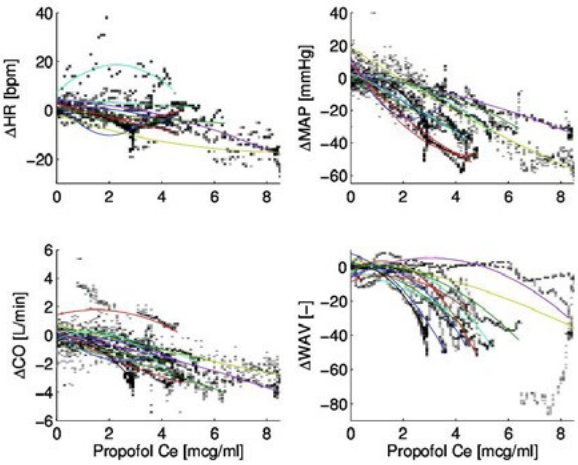

Figure 1: Vitals sign changes during induction of total intravenous anesthesia.
Data were normalized to the sample at the time the first non-zero value obtained for propofol effect site concentration (Ce), and are plotted as heat maps with log-transformed intensities. Quadratic regression lines, identifying each participant's data, are overlaid. The subplots in clockwise order from left to right are: change in heart rate (HR), mean arterial blood pressure (MAP), cardiac output (CO), and depth of hypnosis (WAV).

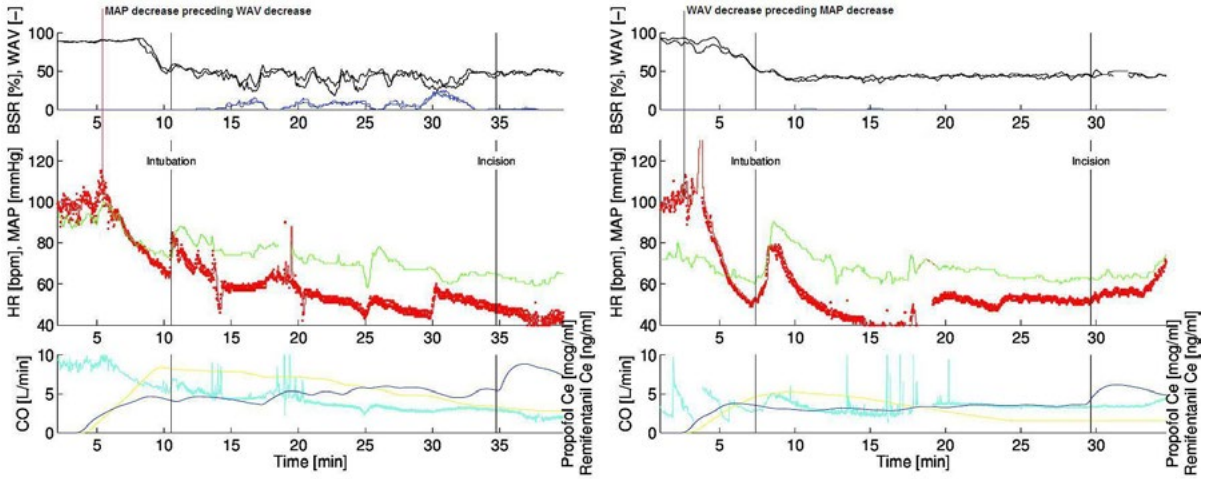

Figure 2: Examples of two cases with different temporal relationships with respect to depth of hypnosis (WAV) decrease and mean arterial pressure (MAP) decrease. The top subplot shows WAV in black, as well as burst suppression ratio (BSR) in blue. The middle subplot shows MAP in red and heart rate (HR) in green. The bottom subplot shows cardiac output (CO) in aqua, as well as propofol effect site concentration (Ce, in yellow) and remifentanil effect site concentration (Ce, in blue).

S-44.

ISOFLURANE IMPACTS MELANOMA GROWTH IN MICE IN AN IMMUNE DEPENDENT AND SEX SPECIFIC MANNER

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INTRODUCTION: Emerging clinical data heighten the importance of choice of anesthetic on cancer survival during tumor surgery in general and in melanoma surgery in particular. Immune system activation plays an important role in cancer development and progression and is characterized as one "hallmark of cancer". Immune cells can comprise up to 50% of the tumor mass and thus can critically influence both positively and negatively tumor progression. The impact of anesthetics on various aspects of the immune system has been observed for decades but remains poorly understood. In addition, sex differences have not been described though male and female immune systems vary drastically.

METHODS: Male and female B6 mice were injected with the melanoma cell line B16 and subsequently exposed to isoflurane for 2hrs (single exposure). Tumor growth was measured in a blinded fashion on predetermined days. This was repeated in RAG (Recombination Activating Gene) -/- mice lacking adaptive immunity and in RAG-/- x gamma chain (γc) -/- mice lacking adaptive immunity and natural killer cells of the innate immune system. Tumor infiltrating leukocytes were characterized on day 10 of tumor growth by flow cytometry.

RESULTS: Isoflurane exposure in male mice showed an increase in tumor size compared to control animals not exposed to isoflurane ($p=0.007$). This difference was not seen in female mice ($p=0.95$). Immune deficient male mice with the same genetic background did not show a difference in tumor size ($p= 0.79$ for RAG-/- and $p= 0.27$ for RAG-/- x γc -/-) indicating an immune modulatory effect of isoflurane in male mice only. In 2 preliminary experiments tumors of isoflurane exposed mice displayed less lymphocytes ($p=0.04$), but a higher proportion of neutrophils ($p=0.007$). In summary, our results demonstrate that isoflurane hastens melanoma growth in male mice only in an immune dependent fashion. Tumor infiltrating leukocytes (TIL) differ significantly between anesthetized and non anesthetized mice.

CONCLUSION: Isoflurane alters the immune system to allow faster tumor growth in males. Choosing a less immune modulating anesthetic may therefore be of crucial importance especially for male individuals undergoing surgery related to melanoma removal.

S-45.

OLICERIDINE (TRV130), A NOVEL μ RECEPTOR G PROTEIN PATHWAY SELECTIVE (μ-GPS) MODULATOR, HAS A DIFFERENTIATED PROFILE OF G PROTEIN AND β-ARRESTIN SIGNALING VERSUS OPIOIDS

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INTRODUCTION: Opioids are widely employed for management of moderate to severe acute pain; however, opioid-related adverse events (ORAEs), including respiratory depression and gastrointestinal dysfunction, may limit dosing required for analgesic efficacy. Conventional opioids (morphine, oxycodone, hydromorphone, oxymorphone, fentanyl, and sufentanil) bind to μ receptors and non-selectively activate two intracellular signaling pathways: the G protein pathway, associated with analgesia, and the β-arrestin pathway, associated with ORAEs and inhibition of G protein-mediated analgesia. Oliceridine (TRV130) is a novel μ receptor G protein Pathway Selective (μ-GPS) modulator that activates G protein with low β-arrestin recruitment to the μ receptor. This could result in opioid-like efficacy while mitigating ORAEs. The objective of this study was to assess G protein activation and β-arrestin recruitment with oliceridine versus conventional opioids.

MATERIALS AND METHODS: Both G protein and β-arrestin responses were measured across a broad concentration range for oliceridine, morphine, oxycodone, hydromorphone, oxymorphone, fentanyl, and sufentanil using the same human embryonic kidney (HEK)-293 cell line expressing the human μ receptor. G protein-mediated responses were quantified by measuring reduction in forskolin-stimulated cAMP (HTRF, CisBio). β-arrestin recruitment was measured using enzyme fragment complementation per manufacturer's instruction (DiscoveRx). cAMP accumulation assays were run in parallel with β-arrestin recruitment, using the same cells, drug dilutions, and assay buffers. Data were normalized as a percentage of maximal assay responses to morphine.

RESULTS: Oliceridine displays strong G protein pathway activation similar to that seen with other opioids including morphine, oxycodone, hydromorphone, oxymorphone, fentanyl, and sufentanil, in the cAMP assay. Oliceridine was more potent (EC50 = 8 nM) than morphine (50 nM) and similar to fentanyl (6 nM) in the cAMP assay. In the β-arrestin assay oliceridine produces little to no response as compared to morphine, fentanyl, and sufentanil.

DISCUSSION: Oliceridine had similar G protein signaling, which is associated with analgesia, compared to morphine, oxycodone, hydromorphone, oxymorphone, fentanyl, and sufentanil. In contrast, oliceridine elicited almost no β-arrestin recruitment to the μ receptor, which is associated with ORAEs and inhibition of G protein-mediated analgesia, as compared to morphine, oxycodone, hydromorphone, oxymorphone, fentanyl, and sufentanil. In fact, both fentanyl and sufentanil recruited higher levels of β-arrestin than morphine. These results provide strong mechanistic support that oliceridine can activate G protein mediated-analgesia while mitigating β-arrestin-mediated ORAEs compared to conventional opioids. This novel mechanism of μ receptor activation may be responsible for the wider therapeutic window of oliceridine between analgesia and ORAEs in the management of moderate to severe pain.

S-46.

AGE AND RESIDUAL NEUROMUSCULAR BLOCKADE

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INTRODUCTION: Murphy et al. recently reported an association between age and the incidence of residual neuromuscular blockade (NMB) in the PACU.[1] These data were collected in a qualitative intraoperative NMB monitoring environment, with an overall incidence of residual paralysis [defined as a Train-of-Four (TOF) ratio less than 0.9] of 44%. In 2011, we instituted quantitative electromyographic intraoperative NMB monitoring, with a resultant decrease in the incidence of residual paralysis.[2,3] In the course of the project (thru July 2015), quantitative TOF ratio's were determined in 851 extubated PACU patients who had received a nondepolaring agent. These data were reexamined to determine whether age was associated with residual paralysis. This retrospective analysis was approved by the IRB.

METHODS: Residual paralysis was found in 161 (18.9%) patients. Patients with residual paralysis were older (57.0 ± 12.8 years, mean ± SD) than those without (51.6 ± 17.2 years, P = 0.0002). However, because of potentially confounding variables, this comparison may be misleading. We hence developed a logistic model to determine if age remained associated with residual paralysis in the presence of other potentially relevant variables (including the use of quantitative monitoring, which changed over time). First, the differences in all variables gathered during our project were univariately compared between patients with and without residual paralysis. Significant differences were found for age, body mass index (BMI), ASA physical status class, surgical service (e.g., neurosurgery, orthopaedics), total intraoperative rocuronium dose (mg/kg), the use and dose of neostigmine, the use of quantitative neuromuscular monitoring to assess reversal (yes/no), and, if yes, the last recorded intraoperative TOF ratio. These variables were tested for their significance in a multivariate logistic regression model using a stepwise model selection technique. Quantitative monitoring was forced to remain in the model. Results: Age remained significantly and independently associated with residual paralysis (Odds Ratio= 1.022, 95% CI =1.010-1.036, P=0.0006), even when adjusted for other variables. The observed odds ratio corresponding to a 37 year age difference - the difference between the two groups in Murphy et al (i.e. 38 vs 75 years) - was 2.27 (95% CI: 1.42 to 3.64). This is indistinquishable from the 1.92 fold increase in the risk of residual paralysis with age observed by Murphy et al.[1]

CONCLUSION: Even though the overall incidence of residual paralysis reported by Murphy et al is over twice that seen in in our institution, the relative impact of age was not different, suggesting that age remains an independent risk factor for residual paralysis even when quantitative monitoring is widely used.

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S-47.

INTRAOPERATIVE ANTIBIOTIC PROPHYLAXIS BY CONTINUOUS INFUSION VS INTERMITTENT BOLUSES FOR PANCREATIC SURGERIES

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INTRODUCTION: Prophylactic antibiotics (Abx) are given preoperatively to prevent surgical site infections (SSIs). They can be given as intermittent bolus or bolus followed by a continuous infusion. Re-dosing during surgery can be as often as every 2 hrs depending on the antibiotic half-life.[1] For the time-dependent Abx bactericidal action only occurs when the plasma concentration of the drug is above the effective minimum inhibitory concentration. (MIC). Using intermittent bolus dosing there are times when the plasma Abx concentration is below the MIC (especially right before next scheduled re-dosing), which may predispose to an increased risk of SSI (fig. 1).[2] To prevent sub MIC between intervals some use a bolus dose followed by a continuous infusion. We retrospectively studied if either method is better for preventing SSI in high SSI risk pancreatic surgery. An intentionally exaggerated schematic displays a plot of Abx concentration versus time using intermittent bolus dosing (solid black line) versus bolus followed by continuous infusion (teal line) in relation to a target minimal inhibitory concentration (MIC) (dashed line). The "decisive period" is from I to shortly after end surgery. The time below MIC during the decisive period is represented by the crosshatched. BI = bolus ± infusion; I = incision; ES = end surgery; EI = end infusion.

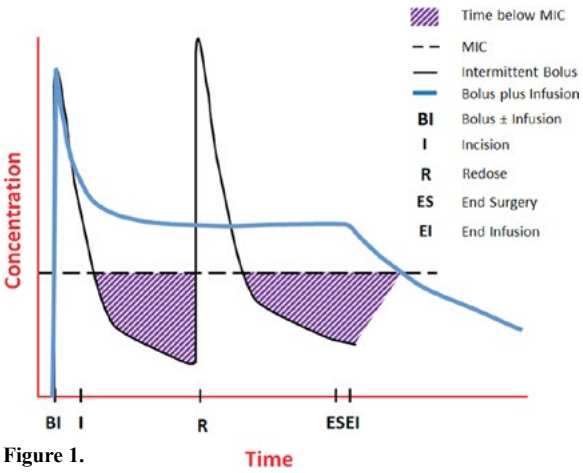

Figure 1.

METHODS: After IRB approval we performed a retrospective chart review. Inclusion criteria: Surgeries with these three ICD-9 codes: 52.5 (Partial pancreatectomy), 52.6 (Total pancreatectomy), 52.7 (Radical pancreaticoduodenectomy) The sub-groups were: 1) bolus Group: received prophylactic Abx with intermittent bolus re-dosing, 2) infusion group: received prophylactic Abx bolus followed by continuous infusion Exclusion Criteria: received Abx within 72 hours prior to surgery, documented infection within 72 hours prior to surgery, death within 30 postoperative days. Official CDC definition criteria and exclusion parameters for SSI up to 30 days postoperatively. Data were analyzed with using a Fisher's exact test to assess frequency differences. .P < .05 was considered statistically significant. An odd ratio OR, with 95% confidence intervals, was also calculated to assess the odds of SSI in the bolus group as compared to the infusion group; if the 95% confidence interval does not include 1.0, the OR is considered statistically significant. Results: 124 cases July 1,2014- August 15, 2015 • Cases with Bolus intraop Abx: 85 cases; • Cases with Continuous intraop Abx infusion (after bolus): 33

Table # 1, Summary

	No SSI	SSI	Total	Rate of SSI
Bolus group	75	10	85	11.76%
Infusion group	29	4	33	12.12%
Differences between groups (Fisher's exact test)				p = 0.99
Odds ratio (95% CI)				0.87 (0.25-3.05)
Exclusion			6	
Total			124	

CONCLUSIONS: Based on our preliminary data the rates of SSI in both bolus and infusion group are similar. The data are however very underpowered (assuming a baseline SSI rate 10% over 3000 cases will be needed to see a 2% deviation from the baseline). In the meantime prophylactic antibiotic administration approach can remain per individual preference.

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S-48.

EFFECT OF ABCB1 RS12720464 AND RS1055302 POLYMORPHISMS IN CHINESE PATIENTS ON THE TIME-COURSE OF ACTION OF ROCURONIUM ADMINISTERED AS A SINGLE DOSE

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OBJECTIVE: To determine whether ABCB1 gene polymorphisms affect the time-course of action of rocuronium in Chinese patients.

METHODS: This study included 105 unrelated Chinese patients undergoing general anesthesia with propofol, fentanyl and rocuronium. Neuromuscular monitoring was performed with calibrated acceleromyography. Patients were allowed to recover spontaneously from the neuromuscular block. The time interval between the first maximum depression of the train of four (TOF) and spontaneous recovery TOF ratio of 0.25/0.7/0.8/0.9 was recorded. The Sequenom MassArray® SNP detection technology was used to detect the genotypes of the *ABCB1* rs12720464, rs1055302. Demographic and non-genetic clinical data were also collected.

RESULTS: In the present study, the mean time to spontaneous recovery of TOF ratio 0.8/0.9 in *ABCB1* rs12720464 GG genotype was longer compared to that observed in ABCB1 rs12720464 AG genotype (56.77 ±14.23 min vs. 49.50 ±10.49 min, and 62.58 ±18.16 min vs. 53.20 ±12.56 min, respectively, $p<0.05$). Further, the time to spontaneous recovery of TOF 0.7/0.8/0.9 in ABCB1 rs1055302 GG genotype was longer than that in *ABCB1* rs1055302 AG genotype (52.00 ±12.10 min vs. 44.83 ±7.38 min, 55.96 ±13.92 min vs. 46.83 ±7.67 min, 61.66 ±17.70 min vs. 49.50 ±8.44 min, respectively, $p<0.05$).

CONCLUSION: In Chinese patients administered a single-dose rocuronium, the genetic variants *ABCB1* rs12720464, and rs1055302 contribute to the individual variability of time-course of action. Clinical trial registration number: ChoCTR-PRP-15007205.

S-49.

SIMULATION-BASED ASSESSMENT OF AWARENESS TO RACE DIFFERENCES IN PROPOFOL PHARMACODYNAMICS

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INTRODUCTION: Ethnic variability to propofol anesthesia has been described[1,2]. As part of the transition from formulaic to personalized medicine, we hypothesized that patient ethnicity should be taken into account, especially when administering potent drugs such as propofol for sedation and analgesia, and we performed a simulator-based study to evaluate that hypothesis.

METHODS: We adapted data on ethnicity and propofol[1,2] to scale the loss and recovery of consciousness (LOC, ROC) thresholds in the Fechner propofol model[3] for different ethnic groups, based on personal communication from Dr. Fechner that the data was from a Caucasian population. Thus, using Caucasians as the norm (1.0), the mean propofol consumption to achieve similar bispectral index value was set for African Americans at 0.82 and for South Asians (from the Indian subcontinent) at 0.78, and the mean time to eye opening from propofol anesthesia was set for African Americans at 1.6 and for South Asians at 1.9. We did not simulate inter-patient variability within an ethnic group because it would have been a confounding factor. With IRB approval and informed consent, a convenience sample of 22 2nd-, 3rd- and 4th-year medical students administered propofol sedation and analgesia to a mixed reality simulator (male, 32 years old, 66-68 kg) for an upper GI endoscopy. The virtual physical appearance and the programmed pharmacokinetics and pharmacodynamics (PK/PD) can be readily altered to represent 3 different ethnicities (African American, South Asian, Caucasian).

RESULTS:

Race	Time Duration of Loss of Consciousness (s); Mean ± SD
Caucasian	81.72 ± 130.12
African American	289.54 ± 188.0
Asian	313.81 ± 166.49

LOC duration, used as a measure of over-sedation, was significantly higher for the African-American ($P=0.003$) and South Asian ($P<0.05$) patient compared to the Caucasian patient. Patients from ethnicities with known sensitivity to propofol were over-sedated.

CONCLUSIONS: Our data indicate that our study participants possess a lack of awareness of the ethnic variability the response to propofol and the possible need for education and training in ethnic variability to drugs at medical schools and PK/PD models for model-driven training simulators that vary based on the ethnicity of the simulated patient. As globalization shrinks our world and makes patients more diverse, and as personalized medicine gains momentum, we expect these two trends to emphasize the need to address these potential learning gaps. We are in the process of repeating this study with anesthesiology residents and faculty.

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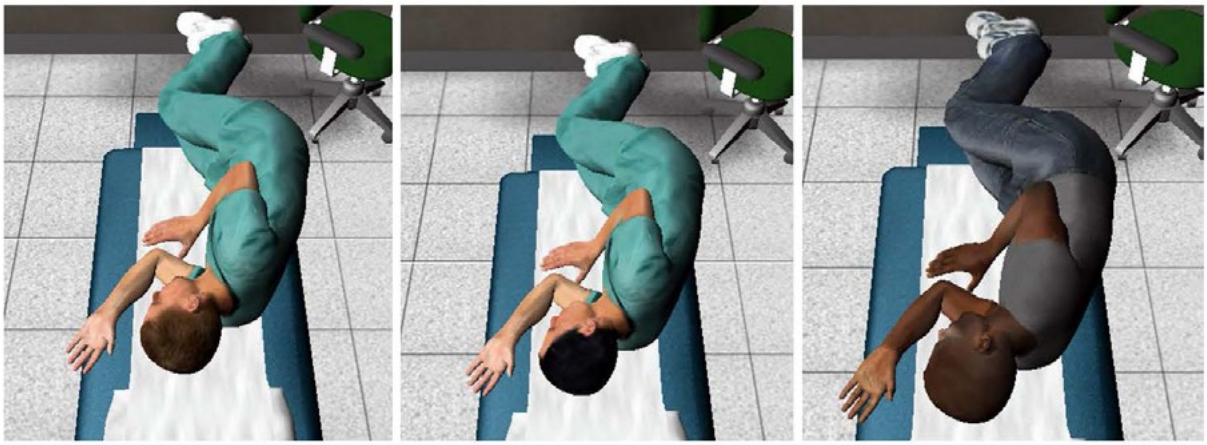
Figure.



S-50.

EVALUATION AND CONTROL OF WASTE ANESTHETIC GAS (WAG) IN THE POST-ANESTHESIA CARE UNIT (PACU) WITHIN PATIENT AND CAREGIVER BREATHING ZONE

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INTRODUCTION: The objective of this clinical study was to evaluate waste anesthetic gas (WAG) in the PACU, as well as the potential safety and scavenging utility of the ISO-Gard® Mask. NIOSH recommends maximal occupational exposure to volatile inhaled anesthetics to 2 ppm and 1 hour to prevent potential health hazard. We hypothesized that WAG in the recovery unit exceeds the recommended levels in the PACU and that the ISO-Gard® Mask minimizes WAG.

METHODS: 125 post-operative patients were randomized to receive either the standard oxygen delivery mask or the ISO-Gard mask. Inclusion criteria included: non-terminal status, adult outpatient surgical procedures scheduled for at least 2 hours, and use of inhaled anesthetic gas. Each group was divided into two sub-groups receiving either sevoflurane or desflurane. Continuous particulate concentrations were measured using infrared spectrophotometers placed within 6-inches of virtual breathing zones for both patients and PACU nurses.

RESULTS: Data was collected on 56 patients in the traditional mask (Group 0), 52 patients in the ISO-Gard mask (Group 1), and their respective nurse counterparts (Table 1). The mean data collection times for both patients (Table 2) and PACU nurses (Table 3) were comparable. The median duration of MAX-WAG values >2ppm for patients in Group 0 and in Group 1 are 19.5 and 13.5 minutes while the values for nurses in Group 0 and Group 1 are 3.0 and 1.0 minutes, respectively. Due to the variability of data collection duration from patient to patient, we calculated the proportion of the duration with MAX-WAG values >2ppm relative to the collection period of each individual. The median proportion of MAX-WAG values >2ppm for patients in Group 0 and Group 1 are 32.2% and 22.4%, while the values for nurses in Group 0 and in Group 1 are 14.7% and 2.0%, respectively. We conducted a similar analysis for the sevoflurane and desflurane subgroups.

CONCLUSIONS: Our data suggests a statistically significant difference in the distribution of the duration of MAX-WAG values >2ppm between the study and control groups for both the patient (p-value=0.02) and the PACU nurse (p-value<0.01). The median proportion of MAX-WAG values >2ppm in both patient's and nurse's breathing zones were also significantly different between the two groups (p-value=0.03) and (p-value<0.01). We observed a statistically significant difference in the duration and the proportion of MAX-WAG values >2ppm between the two groups using desflurane, but no difference with sevoflurane, which may be due to limited sample size. Patients and PACU nurses were exposed to WAG levels greater than 2 ppm during the 1 hour post-operative period. The ISO-Gard mask effectively reduced the amount of WAG detected in the immediate 1 hour post-operative recovery phase.

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Table 1: The use of gas by groups

Variable	*Randomization Group*		P-value
	Traditional Mask (control)	ISO-Gard Mask	
GAS, n (%)			
desflurane	32 (57.1)	31 (59.6)	0.79
sevoflurane	24 (42.9)	21 (40.4)	

p-value was obtained by Chi-square test..

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S-50 • continued

Table 2: MAX-WAG values within Patient breathing zone

Variable	Randomization Group		P-value
All patients			
	Traditional Mask (control) (N=56)	ISO-Gard Mask (N=52)	
Collection duration (minutes), mean±SD	58.7±8.1	56.7±10.2	0.26*
Duration of MAX-WAG >2ppm (minutes) , median (Q1, Q3)	19.5 (12.0, 37.6)	13.5 (3.2, 24.0)	0.02
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	32.2 (20.4, 61.1)	22.4 (6.4, 40.4)	0.03
Patients with Desflurane used			
	Traditional Mask (N=32)	ISO-Gard Mask (N=31)	
Collection duration (minutes), mean±SD	59.6±7.6	58.4±9.0	0.57*
Duration of MAX-WAG >2ppm (minutes) , median (Q1, Q3)	21.0 (13.5, 43.2)	14.7 (2.5, 26.3)	0.03
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	33.7 (22.8, 75.6)	23.6 (4.2, 41.0)	0.04
Patients with Sevoflurane used			
	Traditional Mask (N=24)	ISO-Gard Mask (N=21)	
Collection duration (minutes), mean±SD	57.4±8.7	54.1±11.6	0.28*
Duration of MAX-WAG >2ppm (minutes) , median (Q1, Q3)	19.0 (11.0, 23.1)	13.5 (3.5, 21.0)	0.27
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	29.7 (19.8, 47.2)	21.2 (6.5, 39.8)	0.33

Abbreviations: SD, standard deviation; Q1, 1st quartile; Q3, 3rd quartile;
* denotes p-values obtained by t-test; other p-values were obtained by Wilcoxon rank sum test.

Table 3: MAX-WAG values within PACU nurse breathing zone

Variable	Randomization Group		P-value
All patients			
	Traditional Mask (N=56)	ISO-Gard Mask (N=52)	
Collection duration (minutes), mean±SD	60.6±20.6	56.9±9.7	0.24*
Duration of MAX-WAG >2ppm (minutes) , median (Q1, Q3)	3.0 (1.5, 6.5)	1.0 (0, 3.0)	<0.01
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	4.7 (2.4, 9.8)	2.0 (0, 5.7)	<0.01
Patients with Desflurane used			
	Traditional Mask (N=32)	ISO-Gard Mask (N=31)	
Collection duration (minutes), mean±SD	64.0±25.9	58.1±9.1	0.24*
Duration of MAX WAG >2ppm (minutes) , median (Q1, Q3)	3.8 (1.5, 9.5)	1.0 (0, 3.0)	<0.01
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	5.9 (2.6, 15.0)	1.5 (0, 5.7)	<0.01
Patients with Sevoflurane used			
	Traditional Mask (N=24)	ISO-Gard Mask (N=21)	
Collection duration (minutes), mean±SD	56.0±8.7	55.1±10.6	0.76*
Duration of MAX-WAG >2ppm (minutes) , median (Q1, Q3)	2.0 (1.0, 5.4)	1.5 (0.5, 3.0)	0.21
Proportion of MAX-WAG >2ppm during collection (%), median (Q1, Q3)	4.0 (1.7, 8.0)	2.6 (1.0, 5.8)	0.24

Abbreviations: SD, standard deviation; Q1, 1st quartile; Q3, 3rd quartile;
* denotes p-values obtained by t-test; other p-values were obtained by Wilcoxon rank sum test.

S-51.

INHIBITION OF TRPM7 CHANNELS IN HEK-293 CELLS BY LOCAL ANESTHETICS

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INTRODUCTION: Transient Receptor Potential M7 (TRPM7) is a non-selective, outwardly rectifying, cation channel. It is a major pathway for calcium and magnesium entry into non-excitable cells, which is essential for cancer cell proliferation. TRPM7 is highly expressed in lung cancer cells and mediates their motility . We have shown that benzodiazepines suppress the growth and proliferation of glioma cells by targeting TRPM7[4]. Moreover, we have found that local anesthetics suppress the proliferation of lung cancer cell line A549 (companion abstract at this meeting). Here we test whether lidocaine (Lido) or bupivacaine (Bup) blocks currents through TRPM7 channels expressed in HEK293 cells.

METHODS: HEK TRPM7 cells (gift of L. Runnells, Rutgers Univ), plated in 30 mm dishes, were prepared for whole-cell recording. Expression of TRPM7 was induced with tetracycline 48 hrs before recording. Bath and perfusion solutions contained (in mM) 140 NaCl, 5 KOH, 2 $CaCl_2$, 20 HEPES, 10 glucose. Patch electrodes were filled with 145 Cs-methane sulfonate, 8 NaCl, 10 HEPES, 4 MgATP. Cells were perfused with ±anesthetic-containing solutions during whole-cell recording. Voltage ramps from -80 to +80 mV were applied. Voltage-dependent currents increased after the whole-cell mode was attained and usually stabilized in 5-10 min. Current-voltage curves were fit to a V-dependent block after subtraction of a linear leak. The current at +80 mV was used to assess current inhibition. Data was included only if the current after removal of anesthetic was ±20% of control. Results are presented as mean ± SD.

RESULTS: The potent TRPM7 channel blocker 2-aminoethyl diphenylborinate (100 µM) reversibly blocked >90% of the V-dependent current in the cells, suggesting that this current was due to TRPM7 channels. Application of Bup at 3 or 5 mM concentrations decreased the current at +80 mV to 70±11% (n=6) and 78±2% (n=3) of control respectively. Inhibition and recovery occurred within 2 min of applying and removing Bup. A t-test indicated that there was no significant difference between the effects of the two concentrations of Bup. Application of 3, 5 or 10 mM Lido decreased currents to 80±5% (n=3), 79±9% (n=3) and 77±6% (n=3) of control respectively. There was no significant Lido concentration dependence of the inhibition.

CONCLUSION: Local anesthetics reversibly block currents through TRPM7 channels, but are neither potent nor efficacious inhibitors of the channel at +80 mV. One caveat is that this voltage is not physiological. At normal cell potentials, however, the current through TRPM7 is considerably reduced because extracellular Ca++ permeates the channel slowly and suppresses the overall current carried by monovalent cations. Measurements of Ca++ flux through the channel must be performed to better assess the effects of local and other anesthetics on this channel.

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S-52.

LOCAL ANESTHETICS INHIBITED BREAST CANCER CELL GROWTH

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INTRODUCTION: Addition of regional anesthesia to general anesthesia has been shown to be associated with a longer recurrence-free period for breast cancer patients following surgery[1]. There may be multiple reasons for this. One possibility is that there are direct effects of local anesthetics on cancer cells. It has been suggested that a better understanding of how anesthetics effect cancer cell biology may lead to cancer-specific anesthesia regimens for cancer patients undergoing surgery[2]. Here, we evaluate the effect of three common local anesthetics lidocaine, mepivacaine, and ropivacaine on proliferation and motility of two breast cancer cell lines MDA-MB-231 and MCF-7. MDA-MB-231 was derived from a patient with recurrence of breast carcinoma[3]. MCF-7 has characteristic for its extreme long longevity (over 90 weekly passages)[4] and was the first found hormone-responsive breast cancer cell line[5]. Methods: The cell lines were obtained from American Type Culture Collection. Seventy-two hours after plating, the stated concentration of local anesthetic was added to the culture medium. Cell viability was assessed after 48 h of exposure to anesthetic. Cell viability was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT; Sigma) assay. Absorbance at 571nm was measured and the "% Cell Viability" was calculated from the ratio of absorbance in the drug-treated cells to the drug-free control. The data are presented as the mean ± SD (n=5). All values were compared among groups using one way ANOVA test. In the graphs, * signifies $p<0.05$, ** signifies $p<0.01$. Results: All three local anesthetics suppressed the growth of both breast cancer cell lines in a dose dependent manner. Figures 1 and 2 show the effects of 48h exposure to lidocaine, mepivacaine, and ropivacaine at 0.3, 1, 3, 10 mM on MCF-7 and MDA-MB-231 respectively. No data is shown for MDA-MB-231 cells with 10 mM ropivacaine because it formed a precipitate when added to the media (DMEM) which impeded absorbance measurements. MCF-7 cells were more sensitive than MDA-MB-231 cells to the anesthetics. A significant decrease in viability was observed with 0.3 mM local anesthetics compared to the control in the MCF-7 cells. The difference between the cell lines is most pronounced with ropivacaine. 3 mM ropivacaine killed fewer MDA-MB0-231 cells than 0.3 mM ropivacaine applied to MCF-7 cells. The high toxicity of 10 mM lidocaine or mepivacaine resulted in very few cells being visible under direct microscopic observation.

CONCLUSION: Our results indicates that local anesthetics exert significant direct effects on the growth of breast cancer cells.

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Figure 1. The effect of lidocaine, mepivacaine, and ropivacaine on MCF-7 cell viability

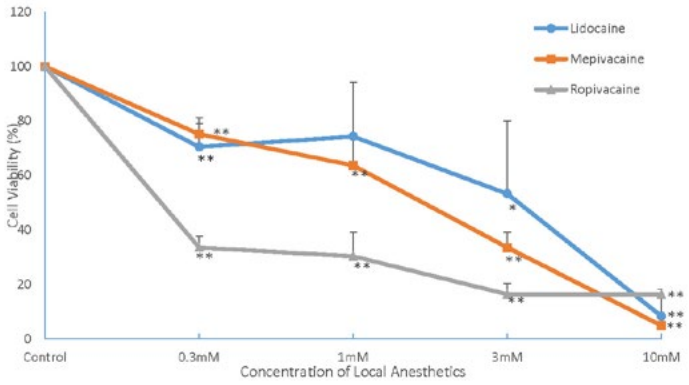
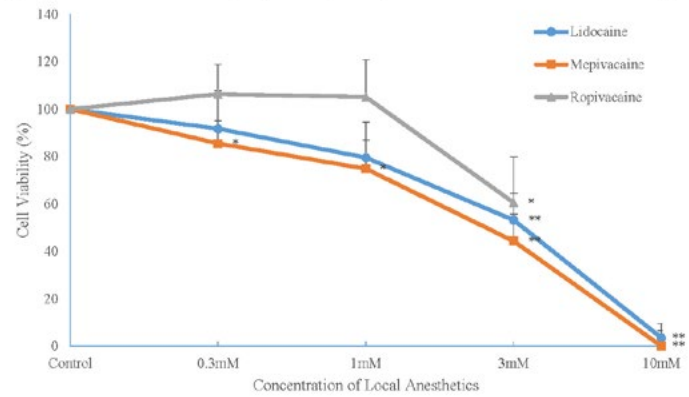


Figure 2. The effect of lidocaine, mepivacaine, and ropivacaine on MDA-MB-231cell viability



S-53.

A PHASE 1 DOSE OPTIMIZATION STUDY OF ABP-700 WITH OPIATES AND/OR MIDAZOLAM PRE-MEDICATION IN HEALTHY ADULT VOLUNTEERS TARGETING INDUCTION OF GENERAL ANESTHESIA

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INTRODUCTION: ABP-700 is a novel, second-generation metabolically labile etomidate analogue in development for procedural sedation and general anesthesia. Pre-clinical and Phase I studies show minimal hemodynamic and respiratory depression, no adrenocortical suppression, and rapid emergence from sedation and anesthesia[1,2]. Like etomidate, ABP-700 is associated with involuntary muscle movement (IMM) that is attenuated with opiate pre-medication[2]. This study aimed to determine a safety, pharmacokinetic, and pharmacodynamic profile of IV bolus and a bolus as infusion dose of ABP-700 when administered after pre-medication (PM) with commonly used opiates, midazolam or their combination.

METHODS: An open label, Phase I study was performed with ethics approval in accordance with the Declaration of Helsinki. Doses of ABP-700 were selected based on prior Phase I results showing a safety, efficacy and tolerability profile consistent with clinical utility for induction of general anesthesia. All PM was given as IV bolus 5 min prior to ABP-700. Eighty-Four subjects (50% male), ages 18 to 53, were studied in 10 cohorts: 5 cohorts (n=40) received fentanyl (2 mcg/kg), sufentanil (0.2 mcg/kg), midazolam (15 or 30 mcg/kg), or midazolam-fentanyl (15 mcg/kg-0.5 mcg/kg) followed by 0.25 mg/kg ABP-700; 3 cohorts (n=24) received midazolam (15 or 30 mcg/kg) or midazolam-fentanyl combination followed by 0.35 mg/kg ABP-700. One cohort (n=4) received remifentanil infusion (0.5 mcg/kg/min) for 5 min prior to 0.25 mg/kg ABP-700 and continued for 5 min thereafter at 0.25 mcg/kg/min. One cohort (n=16) received fentanyl followed by 0.7 mg/kg ABP-700 given as a 4 min infusion.

Safety assessments included clinical labs, hemodynamic, respiratory and adverse event (AE) monitoring. Hypnotic effect was determined with MOAA/S scoring and BIS monitoring.

RESULTS: All doses of ABP-700 were well tolerated with good hemodynamic stability. ABP-700 given as bolus effected a mean time to unconsciousness (MOAA/S < 3) of 37-44 sec, which did not differ by PM. The 0.7 mg/kg infusion dose evoked 433 sec mean duration of sedation. Duration of sedation ranged from 144-398 sec for 0.25 mg/kg to 218-248 sec for 0.35 mg/kg boluses. Full recovery occurred 30-60 seconds after the first MOAA/S > 0. Most AE's were reported as mild; one subject experienced moderate IMM. Apnea requiring intervention occurred in 3 subjects given high dose remifentanil; 2 additional subjects had 15 seconds of apnea without need for intervention.

CONCLUSIONS: ABP-700 is safe and generally well-tolerated when given with commonly used PM regimens. With the exception of remifentanil, the duration of sedation and safety profile of ABP-700 did not appreciably differ among PM regimens. IMM among all PM combinations was generally mild. Only high dose remifentanil was associated with clinically significant respiratory depression. ABP-700 used in combination with commonly used PMs warrants further investigation of possible clinical utility for deep sedation and induction of general anesthesia.

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Subspecialty Abstracts

Cardiovascular Anesthesiology

S-54.

WITHDRAWN.

S-55.

COLLOIDS IN CARDIAC SURGERY-FRIEND OR FOE

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BACKGROUND: The ideal fluid for keeping optimal balances in clinical settings is controversial. Due to large fluid shifts and a relatively high risk of bleeding and acute kidney injury (AKI), cardiac surgery seems to be an optimal setting to test efficacy and safety of colloids. Due to reported increase in AKI[1], use of hydroxyethyl starch solutions (HES) is presently not recommended in critically ill patients[2]. Human albumin (HA) was suggested as a more safe option compared with HES[3], but may carry a dose-dependent risk of AKI. Following, most departments have experienced a dramatic shift from the use of starches towards crystalloids when treating perioperative hemodynamic disturbances. However, during the last years we have seen a rapidly increasing use of HA. The purpose of this investigation is to address whether the use of colloids has adverse effects on postoperative outcomes compared to each other and against crystalloids in a large cohort of cardiac surgery patients.

METHODS: From the mandatory regional heart registry were included 7,496 consecutive cardiac surgery patients (2012-2014) from 3 university hospitals. Patients were grouped according to use of colloids/crystalloid (figure 1). Analysis was made on HES/crystalloids, HA/crystalloids and HES/HA all with the help of propensity score matching (figure 2). Primary outcome parameters were 30-days mortality, in hospital stroke, myocardial infarction and new dialysis. Secondary outcomes were mortality and new ischaemic event defined as a CAG and/or PCI within 6-month. In further analyses the propensity matched data was adjusted for perioperative treatment variables.

RESULTS: The groups were fully comparable in each individual analysis (table 1). In analysis of HES versus crystalloids the only independent impact was found on stroke, both crude and adjusted analysis. HA versus crystalloid demonstrated that in crude analysis negative impact of HA was found on all outcomes while after adjustment analysis impact remained on mortality and new postoperative dialysis (table 2). When evaluating HES versus HA negative impact of HA was seen on mortality and new postoperative dialysis in crude analysis, while only negative impact on dialysis remained after adjustment.

CONCLUSION: In this large cohort analysis made in a transition process from colloids to crystalloids and back, we could only demonstrate a negative impact of HES on the frequency of postoperative stroke. Human albumin had negative impact on mortality and dialysis after adjustments compared to crystalloids while a comparison between HES and HA demonstrated an independent negative impact of HA on postoperative dialysis.

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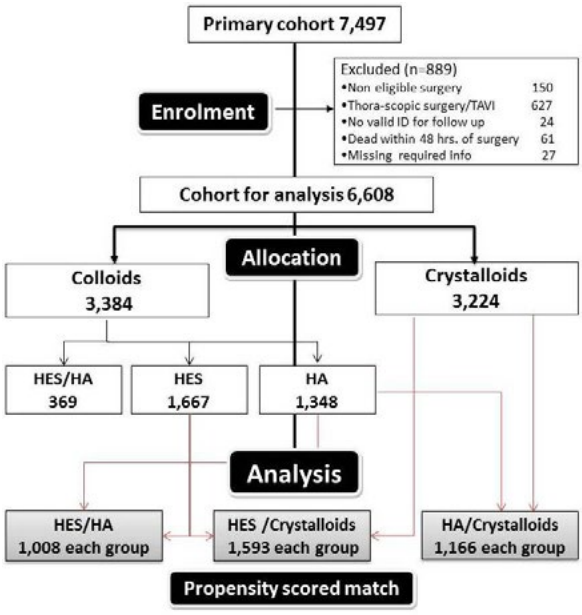

Figure 1. Cohort for analysis. Non-eligible surgery was heart transplant, thymectomy and pericardiectomy. HES=hydroxyl-ethyl starch; HA=human albumin; TAVI=transcutaneous aortic valve insertion.

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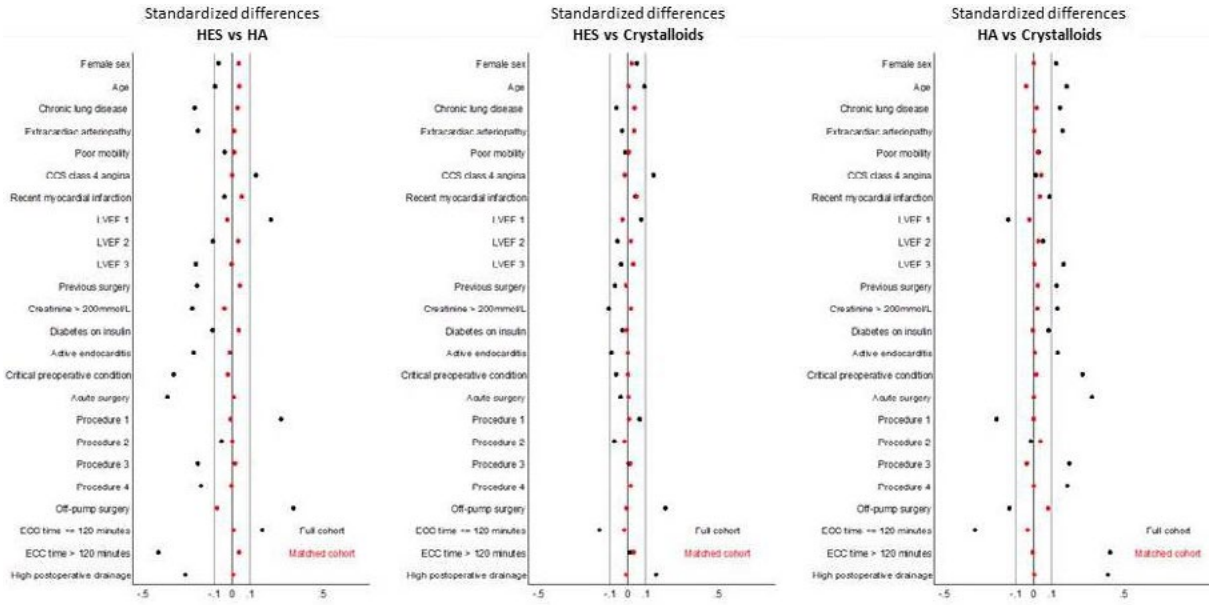

Figure 2. Standardized differences before and after propensity score of the three cohorts.

Factor	HA	Crys	*P-value*	HES	Crys	*P-value*	HA	HES	*P-value*
Number of patients	1,166	1,166		1,593	1,593		1,008	1,008	
Age (Yrs)*)	67.82	68.30	*0.283*	66.60	66.55	*0.901*	68.31	67.88	*0.377*
EuroSCORE I and II parameter									
Female	0.28	0.28	*1.000*	0.24	0.23	*0.534*	0.30	0.28	*0.434*
COLD	0.13	0.13	*0.710*	0.08	0.07	*0.294*	0.12	0.11	*0.534*
Peripheral artery disease	0.12	0.12	*0.950*	0.08	0.07	*0.334*	0.11	0.10	*0.828*
Previous CNS disease	0.05	0.04	*0.611*	0.04	0.04	*0.856*	0.04	0.04	*0.828*
Unstable angina	0.02	0.01	*0.327*	0.03	0.04	*0.626*	0.02	0.02	*1.000*
Myocardial infarction < 90 days	0.18	0.17	*0.412*	0.17	0.15	*0.188*	0.19	0.17	*0.250*
Previous cardiac surgery	0.07	0.06	*0.610*	0.04	0.04	*0.781*	0.05	0.04	*0.349*
s-Creatinine > 200 µmol/L	0.03	0.03	*0.632*	0.01	0.01	*0.636*	0.01	0.01	*0.314*
Insulin dependent DM	0.07	0.08	*0.875*	0.05	0.06	*0.816*	0.07	0.06	*0.416*
Endocarditis	0.03	0.03	*0.908*	0.01	0.01	*1.000*	0.02	0.02	*0.730*
Critical preoperative state	0.05	0.05	*0.772*	0.02	0.02	*1.000*	0.02	0.03	*0.581*
Acute surgery	0.08	0.08	*1.000*	0.03	0.03	*0.916*	0.05	0.05	*0.833*
Post OP. bleeding > 1200 ml	0.13	0.13	*0.950*	0.09	0.09	*0.802*	0.14	0.14	*0.898*
Left ventricular function									
Normal	0.66	0.67		0.73	74.6		0.67	0.68	
Moderately reduced	0.26	0.25	*0.813*	0.22	21.3	*0.629*	0.26	0.25	*0.775*
Severely reduced	0.08	0.08		0.05	4.1		0.07	0.07	
Type of surgery									
CABG only	0.42	0.42		0.52	0.52		0.43	0.44	
Single procedure	0.33	0.31	*0.752*	0.30	0.31	*0.917*	0.31	0.31	*0.988*
Double procedure	0.23	0.24		0.16	0.16		0.23	0.22	
Triple procedure	0.03	0.03		0.02	0.01		0.03	0.03	
Extra corporal circulation time									
Off pump	0.08	0.06		0.16	0.17		0.06	0.08	
< 120 minutes	0.52	0.54	*0.151*	0.58	0.59	*0.670*	0.55	0.54	*0.152*
≥ 120 minutes	0.41	0.41		0.26	0.25		0.40	0.38	

Table 1. Demographic and treatment factors divided on propensity matched cohorts.
*)Mann-Whitney test. All other χ2-test. COLD=chronic obstructive lung disease; CNS=central nervous system.

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Outcome parameter	Crude OR (95 % CI)	Adjusted OR (95 % CI)
	HES versus Crystalloid	
30-day mortality	1,50 (0,72-3,11)	1,36 (0,56-3,31)
6^{mth} mortality	1,56 (0,96-2,52)	1,25 (0,68-2,30)
New postoperative dialysis	1,30 (0,57-2,96)	1,00 (0,06-16,0)
Postoperative stroke	2,53 (1,39-4,61)	2,46 (1,26-4,79)
Postoperative MI	1,36 (0,92-2,01)	1,46 (0,96-2,21)
6 mth ischaemic event	1,00 (0,74-1,35)	0,98 (0,72-1,33)
	HA versus Crystalloid	
30-day mortality	3,38 (1,82-6,28)	2,45 (1,21-4,96)
6^{mth} mortality	3,04 (1,93-4,78)	1,80 (1,03-3,16)
New postoperative dialysis	7,13 (3,40-14,9)	4,84 (1,91-12,2)
Postoperative stroke	2,27 (1,23-4,16)	1,47 (0,71-3,07)
Postoperative MI	1,65 (1,08-2,52)	1,36 (0,79-2,33)
6^{mth} ischaemic event	1,69 (1,19-2,41)	1,37 (0,91-2,05)
	HES versus HA	
30-day mortality	0,35 (0,19-0,66)	0,65 (0,30-1,39)
6^{mth} mortality	0,52 (0,35-0,79)	0,95 (0,57-1,59)
New postoperative dialysis	0,20 (0,10-0,41)	0,31 (0,13-0,76)
Postoperative stroke	0,90 (0,54-1,51)	1,76 (0,87-3,58)
Postoperative MI	0,98 (0,65-1,47)	1,34 (0,82-2,20)
6^{mth} ischaemic event	0,87 (0,60-1,26)	0,93 (0,60-1,43)

Table 2. Conditional regression analysis on cohorts. Adjusted parameters are perioperative inotropes and vasoconstrictors together with transfusions of blood, plasma and platelets. OR=odds ratio; CL=Confidence limits; MI=myocardial infarction

Outcome factor	Dead 30-days	Dead 6-month	New dialysis	Stroke	Myocardial infarction	6-month ischaemic event
Hydroxy-ethyl starch	0,65 (0,30-1,39)	0,95 (0,57-1,59)	0,31 (0,13-0,76)	1,76 (0,87-3,58)	1,34 (0,82-2,20)	0,93 (0,60-1,43)
Perioperative constrictors	0,36 (0,08-1,73)	0,82 (0,31-2,12)	1,30 (0,25-6,91)	1,41 (0,52-3,81)	1,14 (0,58-2,24)	0,81 (0,41-1,61)
Perioperative inotropes	2,60 (0,75-9,03)	1,76 (0,81-3,86)	1,78 (0,42-7,45)	1,12 (0,45-2,82)	2,16 (0,97-4,81)	1,96 (0,94-4,10)
Blood transfusion	1,51 (1,05-2,18)	1,38 (1,14-1,68)	1,23 (0,96-1,57)	1,58 (1,11-2,23)	1,04 (0,92-1,18)	1,02 (0,94-1,10)
Plasma transfusion	0,79 (0,53-1,17)	0,83 (0,65-1,06)	0,91 (0,64-1,29)	0,71 (0,51-1,01)	0,96 (0,80-1,15)	0,84 (0,72-0,99)
Platelet transfusion	1,02 (0,57-1,84)	1,00 (0,73-1,37)	0,92 (0,62-1,36)	0,90 (0,58-1,39)	1,08 (0,77-1,53)	1,24 (1,01-1,51)

Table 3. Impact of individual factors used in adjustment in conditional regression analysis in hydroxyl-ethyl starch versus human albumin. All expressions are Odds-ratio and (95% CL).

S-56.

EXPOSURE TO CARDIOPULMONARY BYPASS DURING CORONARY ARTERY BYPASS SURGERY AND POSTOPERATIVE DELIRIUM

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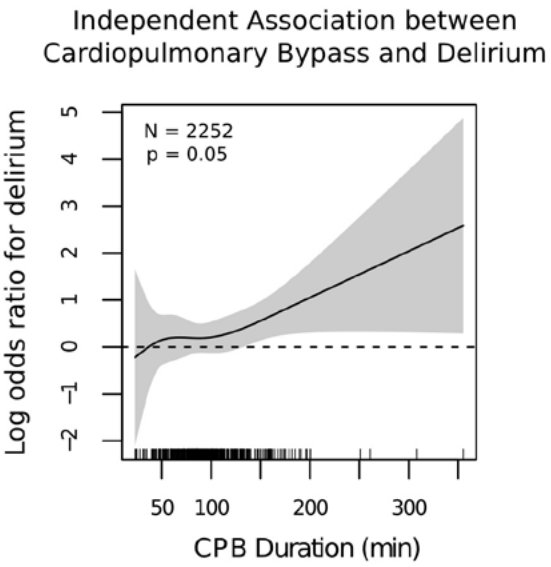
INTRODUCTION: Up to 50% of patients over 60 years of age develop delirium following cardiac surgery[1]. ICU delirium may lead to long-term cognitive impairment similar to Alzheimer's disease[2]. Cardiopulmonary bypass (CPB) alters perfusion, lyses erythrocytes, and induces a significant inflammatory response that may increase the risk for delirium, although to date, no studies have examined the association between CPB and postoperative delirium in patients receiving coronary artery bypass surgery. We hypothesized that CPB during coronary artery bypass surgery would correlate with an increased odds of delirium.

METHODS: We reviewed clinical data from two prospectively collected databases at our medical center, the Cardiac Surgery Perioperative Outcomes Database and the Society of Thoracic Surgeons (STS) Database, and included all patients who underwent elective on-pump coronary artery bypass grafting or elective off-pump coronary artery bypass grafting cardiac surgery from November 1, 2009 to June 30, 2015. Patient who also had valve surgery or other procedures were excluded. Delirium was defined as any positive confusion assessment method for the intensive care unit (CAM-ICU) exam following surgery during the ICU course. ICU standard practice directs bedside nurses to perform a CAM-ICU twice per 12 hour shift. We performed logistic regression to isolate the association between CPB exposure (use and duration) and the incidence of delirium from potential confounders and risk factors for delirium, including a history of cerebrovascular disease, history of cardiac surgery, and age.

RESULTS: Two thousand two hundred and fifty-two patients underwent elective coronary artery bypass surgery during the study period. Four hundred and twelve of these (18.3%) were exposed to CPB and 1840 (82.7%) were not. Delirium was diagnosed in 442 patients (19.6%). Median age in the cohort was 63 years, 23.3% were female, 79.0% had hypertension, 17.4% had cerebrovascular disease, and 3.2% had a history of cardiac surgery. CPB use and duration were associated with an increased odds of postoperative delirium (p=0.05). The association with CPB was strongest with longer CPB durations. For example, relative to off-pump procedures, the odds of delirium were greater by 58% (95% CI: [6%, 84%]) among patients who were exposed to CPB for 140 minutes (90th percentile of CPB duration), but only 18% (95% CI: [-29%, 100%]) greater among those on CPB for 54 minutes (10th percentile)

CONCLUSIONS: CPB was associated with increased odds of delirium in patients undergoing coronary artery bypass surgery. Future studies are needed to examine potential mechanisms of this association.



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S-57.

IMPACT OF PREOPERATIVE STATIN OR BETA BLOCKER USE AND DELIRIUM FOLLOWING CARDIAC SURGERY

AUTHORS: J. B. O'Neal[1], X. Liu[2], M. S. Shotwell[2], Y. Liang[1], A. Shaw[1], A. Shah[3], F. T. Billings[1]

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INTRODUCTION: Postoperative delirium occurs in up to 50% of patients over 60 years old after cardiac surgery and is associated with increased morbidity and mortality. The pathophysiology of delirium is poorly understood; however, a link between neuroinflammation and delirium has been proposed. Statins have anti-inflammatory properties in ex vivo, preclinical, and some clinical studies and might affect postoperative delirium. Beta blockers (BBs), on the other hand, may alter cerebral concentrations of serotonin and melatonin and could increase delirium in patients recovering from surgery, as has been observed in a study of patients recovering from vascular surgery[1]. The majority of cardiac surgery patients use statins and BBs daily. We hypothesized that preoperative statin use would decrease the odds of delirium but preoperative BB use would increase the odds of delirium.

METHODS: We reviewed clinical data from two prospectively collected datasets at our hospital, the Surgery Perioperative Outcomes Database and the Society of Thoracic Surgeons (STS) Database, and included all patients who underwent elective coronary artery bypass grafting (CABG), CABG + valve, or valve cardiac surgery from November 1, 2009 to June 30, 2015. Preoperative statin and BB use was defined by STS guidelines as patients receiving a statin or BB within 24 hours of surgery. Delirium was defined as any postoperative positive confusion assessment method for the intensive care unit (CAM-ICU) exam during the ICU course. ICU standard practice directs bedside nurses to perform a CAM-ICU twice per 12 hour shift. Logistic regression analyses were performed to investigate the associations between statin use and BB use and the incidence of postoperative delirium while adjusting for potential confounders and risk factors including exposure to cardiopulmonary bypass (CPB), CPB duration, age, dyslipidemia, hypertension, and cerebrovascular disease.

RESULTS: Four thousand and forty-three patients underwent elective CABG, CABG + valve, or valve surgery during the study period. Of these, 2,367 patients (58.5%) received a statin, and 2,738 patients (67.7%) a BB within 24 hours prior to surgery. Nine hundred and twenty-six patients (22.9%) were diagnosed with delirium during their ICU stay. Median age in the cohort was 65 years old, 32.1% were female, 39.0% had dyslipidemia, 73.2% had hypertension, and 17.8% had cerebrovascular disease. There was no evidence that either preoperative statin use or BB use had an independent association with postoperative delirium (statin odds ratio, 1.02 [95% CI, 0.86-1.20], P=0.83; BB odds ratio, 0.96 [95% CI, 0.81-1.15], P=0.67).

CONCLUSIONS: Neither preoperative statin use nor BB use was significantly associated with the incidence of delirium following cardiac surgery. Alternative pharmacologic interventions should be investigated.

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S-58.

DECREASING FORCE DEVELOPMENT IN HYPERCONTRACTILE CARDIAC RATS MUSCLES BY FROPOFOL: POTENTIAL IMPLICATIONS TO TREATMENT OF HEART DISEASES WITH HYPERCONTRACTILE STATES

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INTRODUCTION: A hypercontractile state has only recently been recognized as an important factor in the pathogenesis of certain types of heart failure. At present, efficacious agents to decrease contractility in the hypercontractile state have not been available[1]. Here, we hypothesize that the small molecule fropofol, a propofol derivative with no anesthetic activity[2],reduces force development in hypercontractile muscles. We also aim to demonstrate that the depression of force is a result of direct myofilament action.

METHODS: Hypercontractile trabecular muscles from hypertrophied right rat ventricles were superfused with Krebs-Henseleit solution[3]; force and intracellular Ca^{2+} ($[Ca^{2+}]_i$) were measured. Steady-state activations were obtained in the presence and absence of fropofol. Fresh working myofibrillar samples were isolated from rat heart and steady-state actomyosin ATPase-pCa relationships were determined.

RESULTS: Fropofol decreased force without significantly altering $[Ca^{2+}]_i$ in a dose-dependent manner in both normal and hypercontractile muscles. Similarly, fropofol also significantly decreased diastolic force in hypercontractile muscles. During steady-state activations, fropofol depressed maximal Ca^{2+}-activated force (F_{max}, control: from 84.5±2.5 to 49.6±4.4 mN/mm^2, p=0.000; hypercontractile, from 115.5±4.2 to 69.9±4.2 mN/mm^2, p=0.000) and the $[Ca^{2+}]$i required for 50% of activation (Ca_{50}, control: from 0.62±0.11 to 0.95±0.17 μM, P=0.001; hypercontractile, from 0.67±0.08 to 0.97±0.13 μM, P=0.046) in these muscles. The Hill coefficient was unaffected. After skinning, the same muscles showed significant decreases in Fmax (control: from 86.1±5.2 to 44.8±5.6 mN/mm2+, P=0.000; hypercontractile: 142.8±8.3 to 86.7±5.5 nM/mm2, P=0.000) and Ca_{50} (control: from 1.58±0.2 to 2.26±0.28 μM, P=0.002; hypercontractile: 1.7±0.22 to 2.39±0.27 μM, P=0.002) with no changes in Hill coefficient in the presence of fropofol. The myofibrillar ATPase-Ca^{2+} relationship was not affected by fropofol in normal and hypercontractile muscles.

CONCLUSIONS: Fropofol depressed cardiac force development by decreasing myofilament Ca^{2+} responsiveness in normal and hypercontractile states. The clinical implications of these findings are significant given that fropofol is a nonanesthetic myocardial contractility depressive small molecule targeting myofilament proteins and does not alter intracellular Ca^{2+} cycling thus not disturbing Ca^{2+}-dependent pathways. It decreases diastolic force thus improving diastolic function. These results pave the way to test fropofol in hypertrophic cardiomyopathy.

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S-59.

MITOCHONDRIAL TRPV1 REGULATES ENDOTHELIAL DYSFUNCTION IN DIABETIC RATS AND HUMAN ENDOTHELIAL CELLS

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INTRODUCTION: Patients with diabetes mellitus are at risk for perioperative adverse cardiovascular complications[1]. A biomarker estimating existing vascular pathology for pre-operative risk stratification is currently unavailable. High glucose levels induce increased lipid peroxidation in endothelial cells and can cause endothelial dysfunction[2]. The lipid peroxidation product, 12-hydroxyeicosatetraenoic acid (12-HETE), shares structural similarity with capsaicin (Fig. A). Further, 12-HETE is considered the endogenous activator of the transient receptor potential vanilloid 1 (TRPV1)[3]. Therefore, we hypothesize 12-HETE is increased in diabetes and induces endothelial dysfunction by activating mitochondrial TRPV1.

METHODS: Male Sprague-Dawley rats were given either streptozotosin (65mg/kg) to induce diabetes or vehicle. Rats were maintained without insulin for 2 weeks. Blood samples drawn via tail vein were used to measure 12-HETE plasma concentrations in diabetic and non-diabetic rats by mass spectrometry. Further, TRPV1 expression was investigated in human umbilical vein endothelial cells (HUVECs) employing immunohistochemistry. HUVECs were subjected to stimulation with the TRPV1 agonist capsaicin (30uM) or 12-HETE (100uM). Changes in mitochondrial calcium and transmembrane potential by flow cytometry of rhodamine-2 and JC-10 aggregate emission was performed. Mitochondrial function was also assessed using a Seahorse Extracellular Flux Analyzer, endothelial cell function by in vitro capillary tube formation, and cell viability via annexin V/propidium iodide binding. Statistical analysis was performed using ANOVA followed by Bonferroni correction.

RESULTS: In diabetic rats, a higher plasma concentration of 12-HETE was detected compared to non-diabetic rats (117±23 vs. 37±9 ng/mL, *P<0.05, n=5-7, Fig. B). TRPV1 was located primarily at endothelial cell mitochondria. Stimulation with capsaicin or 12-HETE induced mitochondrial calcium influx (*P<0.05 or **P<0.01 vs. DMSO or ethanol-vehicle control, respectively, n=4-6, Fig. C) and caused a decline in mitochondrial transmembrane potential (P<0.01 and P<0.05, n=4-5). Capsaicin also induced mitochondrial dysfunction (P<0.001; n=4) and reduced endothelial cell capillary formation, similar to 12-HETE (***P<0.001 and **P<0.01, n=3, Fig. D). These effects occurred independent of cell viability.

CONCLUSIONS: We identified a key endogenous lipid peroxidation product, 12-HETE, is elevated during diabetes and in human endothelial cells can induce changes in mitochondrial dynamics leading to endothelial cell dysfunction. Although further studies are needed, our results suggest 12-HETE plasma concentration mirrors in diabetics the severity of vascular dysfunction. 12-HETE could thus serve as a potent biomarker to assess perioperative risk in patients with known or previously undiagnosed diabetes mellitus.

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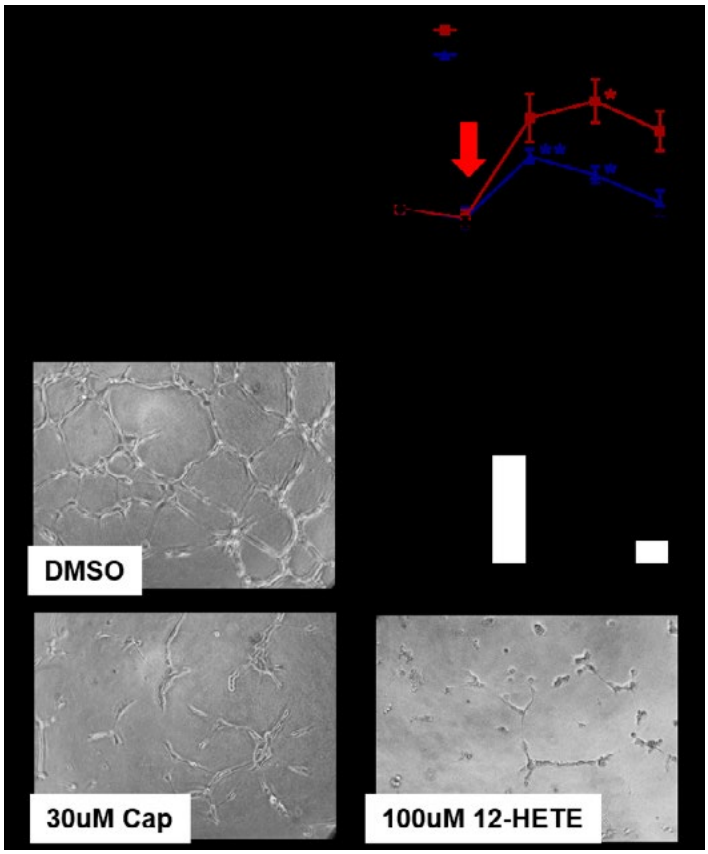

S-60.

IMPACT OF PACKED RED BLOOD CELL TRANSFUSIONS ON MORTALITY IN PATIENTS UNDERGOING CARDIAC SURGERY

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INTRODUCTION: In the last years a growing body of evidence emerged, showing that restrictive transfusion triggers might be beneficial to prevent transfusion-associated risks in various settings[1,2]. These risks are particularly transfusion-associated immunomodulatory effects (TRIM), lung injuries (TRALI), and a circulatory overload[3]. Ultimately, these conditions may outweigh the risks of anemia and thus lead to increasing mortality[1-3]. In this study, we investigated the effect on packed red blood cell (pRBC) transfusions on mortality in patients undergoing major cardiac surgery.

METHODS: In this retrospective analysis, all patients undergoing cardiac surgery at a European University hospital in seven consecutive years were screened for eligibility. Patients were included if the lowest hemoglobin level at any time during the post-operative ICU stay was 8.0 g/dl. Patients were grouped according to the number of postoperatively received packed red blood cell units (Group 0: none; group 1: 1 unit. group 2: 2 units). Patients that received more than 2 units of pRBC were excluded. Propensity-score matching (1:1:1) and non-parametric testing were applied to assess the impact of post-operative pRBC transfusion on outcome.

RESULTS: In total, 5.740 cases with complete electronically available records were identified. Of these, 3.411 patients fulfilled inclusion criteria and were included in analyses. In-hospital mortality (Group 0: 1.29%. Group 1: 2.71%. Group 2: 6.58%) as well as length of stay on the ICU and in the hospital differed significantly among groups (see Figure 1 for unmatched population). After adjusting for confounding factors, the observed findings in patient outcome remained consistent (see Figure 2 for propensity-matched population). Kaplan-Meier graphs for survival are presented in Figure 3.

CONCLUSION: The reported data suggest that pRBC transfusion may increase mortality even with a restrictive transfusion strategy. Trading off the risks of anemia and transfusions is challenging, especially in surgical patients. Further investigations are necessary to identify a transfusion threshold that balances risks and benefits based on patients' individual conditions.

	No units RBC N=2628	1 unit RBC N=479	2 units RBC N=304	p.overall
Patient characteristics:				
Age [y]	68.0 [60.0;74.0]	70.0 [63.0;75.0]	70.0 [63.0;75.0]	<0.001
Gender (Female)	706 (26.9%)	146 (30.5%)	88 (28.9%)	0.226
Type of surgery:				<0.001
CABG	1558 (59.3%)	278 (58.0%)	181 (59.5%)	
Valves	825 (31.4%)	121 (25.3%)	85 (28.0%)	
Both	245 (9.32%)	80 (16.7%)	38 (12.5%)	
APACHE II	17.0 [13.0;22.0]	18.0 [13.5;24.0]	19.0 [15.0;25.0]	<0.001
Arterial hypertension	1977 (75.2%)	351 (73.3%)	233 (76.6%)	0.532
Coronary heart disease	2002 (76.2%)	396 (82.7%)	244 (80.3%)	0.004
Left heart failure (>NYHA II)	562 (21.4%)	138 (28.8%)	94 (30.9%)	<0.001
COPD	394 (15.0%)	82 (17.1%)	54 (17.8%)	0.265
Diabetes mellitus	898 (34.2%)	204 (42.6%)	132 (43.4%)	<0.001
Peripheral vascular disease	391 (14.9%)	106 (22.1%)	57 (18.8%)	<0.001
Atrial fibrillation	590 (22.5%)	146 (30.5%)	105 (34.5%)	<0.001
Patient outcome:				
Mortality (In-hospital)	34 (1.29%)	13 (2.71%)	20 (6.58%)	<0.001
LOS (ICU) [d]	4.00 [3.00;6.00]	6.00 [4.00;9.00]	6.00 [4.00;10.0]	<0.001
LOS (In-hospital) [d]	11.0 [8.00;16.0]	12.0 [9.00;17.0]	14.0 [10.0;22.0]	<0.001

Figure 1.

	No units RBC N=304	1 unit RBC N=304	2 units RBC N=304	p.overall
Patient characteristics:				
Age [y]	70.0 [63.0;76.0]	70.0 [64.0;76.0]	70.0 [63.0;75.0]	0.960
Gender (Female)	91 (29.9%)	91 (29.9%)	88 (28.9%)	0.954
Type of surgery:				0.400
CABG	170 (55.9%)	180 (59.2%)	181 (59.5%)	
Valves	80 (26.3%)	84 (27.6%)	85 (28.0%)	
Both	54 (17.8%)	40 (13.2%)	38 (12.5%)	
APACHE II	18.0 [15.0;24.0]	18.5 [14.0;25.0]	19.0 [15.0;25.0]	0.696
Arterial hypertension	229 (75.3%)	230 (75.7%)	233 (76.6%)	0.925
Coronary heart disease	245 (80.6%)	243 (79.9%)	244 (80.3%)	0.979
Left heart failure (>NYHA II)	95 (31.2%)	91 (29.9%)	94 (30.9%)	0.935
COPD	60 (19.7%)	56 (18.4%)	54 (17.8%)	0.817
Diabetes mellitus	118 (38.8%)	122 (40.1%)	132 (43.4%)	0.493
Peripheral vascular disease	53 (17.4%)	53 (17.4%)	57 (18.8%)	0.887
Atrial fibrillation	106 (34.9%)	107 (35.2%)	105 (34.5%)	0.986
Patient outcome:				
Mortality (In-hospital)	4 (1.32%)	11 (3.62%)	20 (6.58%)	0.003
LOS (ICU) [d]	5.00 [3.00;6.00]	6.00 [4.00;9.00]	6.00 [4.00;10.0]	<0.001
LOS (In-hospital) [d]	12.0 [9.00;18.0]	13.0 [10.0;18.0]	14.0 [10.0;22.0]	0.001

Figure 2.

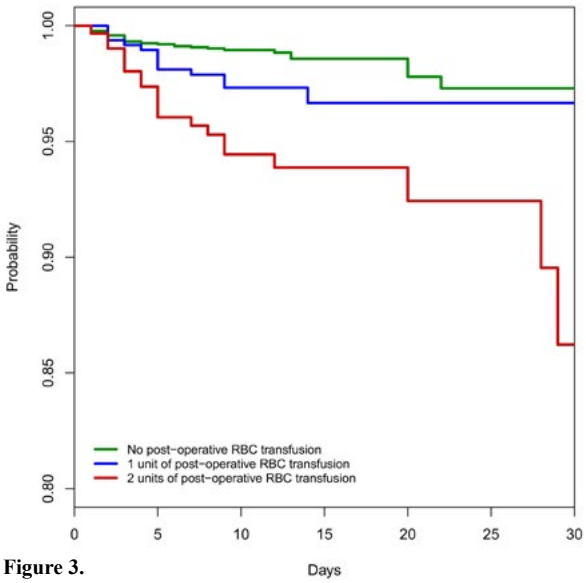

Figure 3.

S-61.

ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY AMONG PATIENTS WITH AND WITHOUT PRE-EXISTING CHRONIC KIDNEY DISEASE: EFFECTS OF PERIOPERATIVE CRYSTALLOID CHOICE

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INTRODUCTION: In observational studies, increased peri-operative AKI has been associated with the use of chloride-liberal (0.9% saline) rather than chloride-restrictive (Plasma-Lyte, PL, or Ringer's Lactate, LR) crystalloids,[1-4] but a recent randomized trial (SPLIT study) reported no such differences.[5] Studies also suggest that Cardiac Surgery associated-Acute Kidney Injury (CSA-AKI) increases with pre-existing Chronic Kidney Disease (CKD).[6] To explore possible reasons for discordance between observational studies and the SPLIT study, we examined whether the variation in CSA-AKI is influenced by perioperative crystalloid choice in relation to baseline CKD.

METHODS: After IRB approval, we used data contained in the Cerner Healthfacts repository of Electronic Health Records (Cerner Inc., Kansas City, MO) to identify all adults that had undergone cardiac surgery (CS) between January 2009 and June 2013 (Figure 1). We then categorized patients as with or without baseline CKD (based on ICD-9-CM codes). We compared rates of incident CSA-AKI, in-hospital mortality, and differences in peak versus baseline (delta) serum chloride values among patients receiving saline exclusively (chloride-liberal group) versus those also receiving PL or LR (chloride-restrictive group) using propensity score (PS) based matching and multivariate regression methods for risk-adjustment of baseline differences.

RESULTS: The odds of CSA-AKI (KDIGO Stage > 0) and in-hospital mortality were lower without (total n=4378 in the PS matched cohort) versus with baseline CKD (total n=702 in the PS matched cohort, Figure 2). Unlike the SPLIT study, we found that rates of incident CSA-AKI differed with exposure to chloride-liberal versus chloride-restrictive crystalloids in patients with baseline CKD (KDIGO>0 rate of 59% versus 46%, respectively) and without CKD (KDIGO>0 rate of 25% versus 19%, respectively). Delta chloride values were higher with CKD (mean increase in chloride 2.25 versus 1.35 mEq/L) despite similar volume-adjusted chloride-load (Table 1). The mean baseline creatinine among patients with CKD in our study (1.66-1.96) was significantly higher than in the SPLIT study (0.98-0.99, Table 1).

CONCLUSIONS: We found that rates of CSA-AKI were significantly higher when patients had CKD at baseline and, differences relative to crystalloid choice were greater with CKD than without (OR 0.57 vs. 0.72, respectively, when PL or LR was received versus saline only). Results of the SPLIT study may differ from observational studies for several reasons including potential unmeasured confounding or inadequate risk-adjustment in observational studies, use of PL as the default fluid in the SPLIT study, and better baseline renal function in the SPLIT study. Further study of the effects of crystalloid choice is warranted, especially among patients with CKD.

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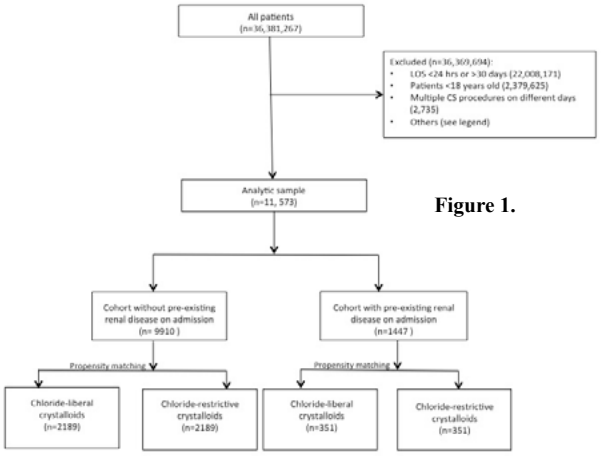

Figure 1.

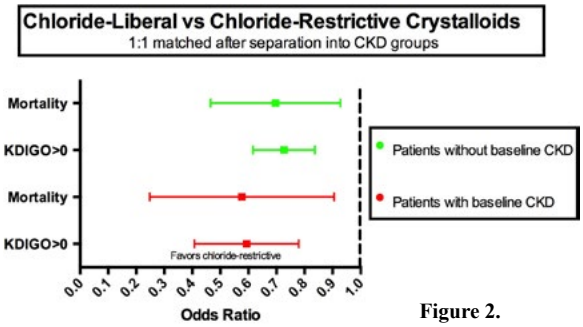

Figure 2.

S-61 • CONTINUED ON NEXT PAGE

S-61 • continued

Table 1.

	Cohort with normal baseline renal function			Cohort with abnormal baseline renal function		
EXPOSURE	**0.9% saline** **Mean (SD)** **n=2189**	**0.9% saline plus LR or PL** **Mean (SD)** **N=2189**	**p-value**	**0.9% saline** **Mean (SD)** **n=351**	**0.9% saline plus LR or PL** **Mean (SD)** **N=351**	**p-value**
Study Fluid Volume (mL)-total	1593	3402		1893	3741	
Saline	1593	1608		1893	1970	
LR	0	1263		0	1211	
PL	0	531		0	560	
Volume-adjusted Chloride Load mEq/L	154	124		154	131	
Baseline serum creatinine (mg/dL)	0.92 (0.33)	0.88 (0.25)	<0.0001	1.96 (1.6)	1.66 (1.3)	0.02
Max serum creatinine (day 1 to 7; mg/dL)	0.91 (0.38)	0.86 (0.32)	0.0002	1.99 (1.5)	1.64 (1.0)	0.002
Delta chloride 72 hours post surgery	1.6 (3.8)	1.1 (3.8)	0.0006	2.1 (4.3)	2.4 (4.0)	0.38
OUTCOMES	**0.9% saline** **% (n)** **n=2189**	**0.9% saline plus LR or PL** **%(n)** **N=2189**	**p-value**	**0.9% saline** **%(n)** **n=351**	**0.9% saline plus LR or PL** **%(n)** **N=351**	**p-value**
Rate of AKI (KDIGO >0)	24.5 (537)	19.2 (420)	<0.0001	59.0 (207)	45.9 (161)	0.0005
KDIGO stage			0.0003			0.002
0	75.5 (1652)	80.8 (1769)		41.0 (144)	54.1 (190)	
1	18.5 (404)	14.8 (323)		39.9 (140)	33.6 (118)	
2	4.5 (99)	3.2 (69)		11.4 (40)	6.0 (21)	
3	1.6 (34)	1.3 (28)		7.7 (27)	6.3 (22)	

S-62.

WITHDRAWN.

S-63.

PERIOPERATIVE GLUCOSE MANAGEMENT DURING CARDIAC SURGERY REDUCES INCIDENCE OF STERNAL WOUND INFECTIONS

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INTRODUCTION: Hyperglycemia during cardiac surgery with cardiopulmonary bypass (CPB) is common and reflects increased perioperative insulin resistance in both diabetics and non-diabetics. Hyperglycemia is thought to impair wound healing by inducing inflammatory cytokines[1]. A growing body of evidence shows perioperative hyperglycemia is an independent predictor of mortality in patients undergoing cardiac surgery and is associated with increased risk of sternal wound infections (SWIs)[2], but the ideal target range for glycemic control remains uncertain. In January 2014, we implemented a protocol for stringent glucose management during adult cardiac surgery. We sought to investigate whether patients managed under this protocol experienced fewer SWIs and other complications.

METHODS: We retrospectively reviewed hospital records of 164 adults undergoing cardiac surgery by a single surgeon. Patients were placed into pre-protocol and protocol groups. The protocol group was treated with insulin (IV bolus and continuous infusion) to maintain perioperative glucose in a target range of 120-150 mg/dL. In the pre-protocol group, hyperglycemia was treated at the anesthesiologist's discretion.

Demographic, surgical procedure, and 30-day complications data was collected. Glucose measurements were collected at the start of surgery, every 30 minutes during CPB, and at critical time points after CPB. Arterial K+ and base excess were collected at critical time points. Categorical variables were compared by chi-squared or Fisher's tests. Continuous variables were analyzed by Student's t-test or Wilcoxon rank-sum test.

RESULTS: Three patients who underwent emergency aortic dissection repair were excluded. 161 patients were included in the final analysis, with 81 in the pre-protocol group (date of surgery Jun-Dec 2012) and 80 in the protocol group (Jan-May 2015).

The protocol group experienced fewer SWIs by 30 days post-operatively (0% vs. 5.1%, p=0.050). Rates of other 30-day complications were similar in the two groups. No demographic differences were observed between the groups. Median cardiopulmonary bypass time was shorter (99 vs. 126 minutes; p=0.0005) in the protocol group, which also underwent more mitral repairs than the pre-protocol group. Serum glucose was similar at baseline and at start of surgery between both groups; patients in the protocol group had significantly lower glucose and similar K+ levels throughout CPB and at post-op time points (Fig 1 and Table 3).

CONCLUSIONS: Strict perioperative glucose control to target range of 120-150 mg/dL reduced incidence of SWIs following cardiac surgery at our institution, without increasing rates of other complications. While not statistically significant, there was a trend showing decreased acute kidney injury (AKI) in the protocol group. These results are encouraging as we continue to evaluate the safety and efficacy of this glucose management protocol. We plan to expand our study population to examine changes in composite outcomes under this protocol.

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Table 1- Baseline Data and Demographics

	Pre-protocol (n=81)	Protocol (n=80)	*p-value*
Age at surgery (years)	66.0 ± 12.4	65.0 ± 11.7	0.612
Female (%)	40.7 (n=33)	40.0 (n=32)	0.924
Race (%)			
White	39.5 (n=32)	42.5 (n=34)	0.699
Black	13.6 (n=11)	21.3 (n=17)	0.199
Asian	18.5 (n=15)	23.8 (n=19)	0.415
BMI (kg/m2)	27.6 ± 5.5	27.8 ± 4.9	0.879
Problem History (%)			
Diabetes mellitus	41.9 (n=34)	39.7 (n=31)	0.775
Atrial fibrillation	9.9 (n=8)	12.5 (10)	0.597
Chronic kidney disease	8.6 (n=7)	10 (n=8)	0.767
Hemoglobin A1c (%)	8.4 ± 14.0	6.4 ± 1.2	0.217

Table 2- Surgical Procedure Data

	Pre-protocol (n=81)	Protocol (n=80)	*p-value*
Off-pump technique (%)	1.3 (n=1)	5.1 (n=4)	0.21
Procedure (%)			
CABG	59.3 (n=48)	46.3 (n=37)	0.098
# of grafts (mean±SD)	3.7±1.3	2.8±1.2	0.058
Valve	54.3 (n=44)	66.3 (n=53)	0.122
Aortic valve replacement	32.5 (n=26)	32.5 (n=25)	0.997
Mitral valve replacement	12.5 (n=10)	14.3 (n=11)	0.742
Mitral valve repair/annuloplasty	**12.5 (n=10)**	**24.7 (n=19)**	**0.049**
Minimally invasive approach	6.2 (n=5)	12.8 (n=10)	0.152
Duration of cardiopulmonary bypass (minutes; median)*	**126**	**99**	**0.0005**

* Off-pump procedures excluded

Figure 1- Glucose Measurements

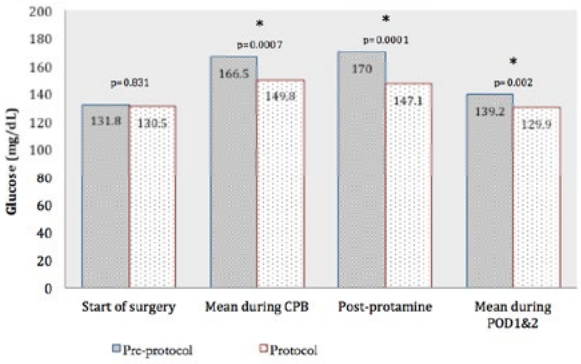

Table 3- Glucose Measurements

	Pre-protocol (n=81)	Protocol (n=80)	*p-value*
Day -1			
Serum [glucose]	122.6 ± 42.7	118.3 ± 43.8	0.54
Start of surgery	-	-	-
Arterial [glucose]	131.8 ± 38.9	130.5 ± 44.3	0.831
Arterial [K+]	4.0 ± 0.3	3.9 ± 0.3	0.119
Arterial base excess	0.6 ± 2.7	0.9 ± 2.9	0.482
During CPB*			
Peak arterial [glucose]	**199.9 ± 47.2**	**176.7 ± 31.4**	**0.0004**
Nadir arterial [glucose]	**135.7 ± 38.8**	**125.0 ± 29.7**	**0.053**
Mean arterial [glucose]	**166.5 ± 35.6**	**149.8 ± 24.7**	**0.0007**
Post-protamine			
Arterial [glucose]	**170.0 ± 40.4**	**147.1 ± 31.8**	**0.0001**
Arterial [K+]	4.1 ± 0.5	4.0 ± 0.6	0.533
Arterial base excess	**(2.5) ± 2.0**	**(1.8) ± 2.2**	**0.05**
During POD 1 & 2			
Peak serum [glucose]	185.1 ± 40.9	176.6 ± 42.9	0.205
Nadir serum [glucose]	**100.0 ± 15.2**	**94.8 ± 14.9**	**0.029**
Mean serum [glucose]	**139.2 ± 19.6**	**129.9 ± 16.8**	**0.002**

* During entire surgery for off-pump procedures

Table 4- Complications Within 30 Days

	Prior to protocol	Post protocol implementation	*p-value*
Death (%)	0	0	
Length of hospital stay after surgery (days; mean±SD)	6.95 ± 5.0	6.96 ± 4.3	0.987
Sternal Wound Infections (%)**	**5.1 (n=4)**	**0**	**0.05**
Return to operating room (%)**	6.3 (n=5)	3.75 (n=3)	0.719
Readmission (%)	13.8 (n=11)	13.8 (n=11)	1
Time to extubation (minutes; median)	420	416	0.939
Cerebrovascular accident or stroke (%)**	1.3 (n=1)	2.5 (n=2)	1
Acute kidney injury (%)**	6.3 (n=5)	1.3 (n=1)	0.117
New-onset atrial fibrillation (%)	20.9 (n=17)	30.0 (n=24)	0.207

S-64.

THE EFFECT OF REMOTE ISCHEMIC PRECONDITIONING ON DELIRIUM AFTER CARDIAC SURGERY

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INTRODUCTION: Delirium occurs is common after cardiac surgery and is associated with increased morbidity and mortality. A leading hypothesis for the etiology of delirium is unrecognized cerebral ischemia. Remote ischemic preconditioning (RIP) represents a novel strategy to potentially attenuate the effects of ischemia.[1] In piglets exposed to deep hypothermic circulatory arrest, RIP was shown to improve neurocognitive outcomes—including reduced brain lactate, faster recovery of EEG activity and decreased cerebral injury.[2] In human trials of RIP in cardiac surgery, results have been mixed, with several trials showing no benefit,[3,4] and other trials showing reduced mortality and troponin release[5] and reduction in acute kidney injury.[6] We conducted a pilot trial to examine whether RIP could reduce delirium or other complications after cardiac surgery.

METHODS: This was a pilot randomized (1:1 ratio) masked trial, with IRB approval and written informed consent. Significant inclusion criteria were age greater than 65 y/o undergoing coronary artery bypass graft (CABG) and/or valve surgery. Prior to bypass, patients in the intervention arm had 3 cycles of arm blood pressure cuff inflation to 200 mm Hg for 5 minutes followed by 5 minutes of deflation. Patients in the control arm had a cuff placed on their arm, but without inflation. The primary outcome was any episode of delirium, as assessed on 3 of the first 4 postoperative days using the Confusion Assessment Method (CAM) or CAM-ICU. Secondary outcomes were maximum rise in creatinine, acute kidney injury (AKIN criteria) length of stay (LOS), LOS-ICU, stroke, and inotropic drug greater than 24 hours. The primary analysis was by intention-to-treat using the chi-squared test.

RESULTS: Thirty-four out of a planned 50 patients have been enrolled in this pilot. Patient and surgical characteristics are shown in Table 1 and were similar. The incidence of delirium was identical between the control (42% [7/17]) and the intervention arms of the trial (42% [7/17]; p=1.0). The severity of delirium was also similar (median 4 [IQR 4-8] vs. median 4 [IQR 3.5-8.5] respectively; p=0.80). Finally, the number of delirium days was similar (median 1 [IQR 1-2] vs. median 1 [IQR 1-3] respectively, p=0.41). There was no difference in the control compared to intervention groups in the maximum increase in creatinine (0.23±0.46 mg/dL vs. 0.32±0.45 mg/dL; p=0.57) or the incidence of any acute kidney injury (41.2% vs. 43.8%; p=0.88). There were also no differences in other outcomes between the control and the intervention groups, including LOS-ICU (median 25h [IQR 22-46] vs. median 43h [IQR 23-95]; p=0.14), LOS (median 7d [IQR 6-7] vs. median 6d [IQR5-8]; p=0.85), stroke (0% vs. 5.9%; p=1.0), and inotropic drugs after 1 day (11.8% vs. 1.8%; p=1.0).

CONCLUSIONS: In a small sample, RIP prior to cardiopulmomary bypass did not prevent postoperative delirium or other complications after cardiac surgery.

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Table 1: Patient and Surgical Characteristics

	Control (n=17)	Intervention (n=17)	p-value
Age (years), mean ±SD	73.3 ±5.7	74.9 ±6.9	0.45 [a]
Male, n(%)	8 (47%)	12 (71%)	0.30 [b]
Caucasian, n(%)	13 (76%)	16 (94%)	0.16 [b]
Mini-mental state examination, med(IQR)	29 (28-30)	28 (26-29)	0.06 [c]
Prior stroke, n(%)	1 (5.9)	4 (23.5)	0.34 [b]
Obstructive sleep apnea, n(%)	4 (23.5)	2 (11.8)	0.66 [b]
Congestive heart failure, n(%)	0 (0)	4 (23.5)	0.10 [b]
Diabetes, n(%)	7 (41.2)	5 (29.4)	0.72 [b]
Chronic renal insufficiency, n(%)	1 (5.9)	0 (0)	1.0 [b]
Log EuroSCORE, med(IQR)	3.7 (3.1-6.4)	3.1 (2.5-9.3)	0.92 [b]
Prior cardiac surgery, n(%)	1 (5.9%)	2 (11.8%)	1.0 [b]
Coronary artery bypass surgery, n(%)	10 (58%)	10 (58%)	1.0 [b]
Midazolam (mg), mean±SD	4.7 ±2.3	4.9 ±1.7	0.8 [a]
Packed red blood cell transfusion intraoperatively, med (IQR)	0 (0-2)	0 (0-2)	0.79 [c]
Maximum epinephrine intraoperatively (mcg/kg/min), mean±SD	0.48 ±0.20	0.49 ±0.19	0.83 [a]

[a] Student's t-test; [b] Fisher's exact test; [c] Wilcoxon rank-sum test

S-65.

COMPARISON OF SEER SONORHEOMETRY WITH ROTATIONAL THROMBOELASTOMETRY AND LABORATORY PARAMETERS IN CARDIAC SURGERY

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INTRODUCTION: The Quantra™ Hemostasis Analyzer is a novel, ultrasound-based diagnostic device using Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry to characterize dynamic changes in viscoelastic properties of blood[1,2]. Cardiac surgery with cardiopulmonary bypass (CPB) is associated with significant impact on the coagulation system, often resulting in coagulopathy. In this study, we aimed to compare SEER Sonorheometry results from the QuantraTM with rotational thromboelastometry (ROTEM®) and conventional laboratory parameters in patients undergoing cardiac surgery with CPB at baseline, during and after CPB.

METHODS: The Research Use Only preliminary model QuantraTM uses a multi-well cartridge capable of performing 4 independent measurements with different reagents, including Clot Time, Clot Stiffness, Fibrinogen and Platelet Contribution (Figure 1). Clot Time was compared to ROTEM® INTEM clotting time and adjusted partial thromboplastin time. Clot Stiffness was compared to ROTEM® EXTEM. Fibrinogen Contribution was correlated to ROTEM® FIBTEM as well as fibrinogen level by Clauss method. Platelet Contribution was compared to absolute platelet count and ROTEM®-determined clot elasticity attributable to platelets. These comparisons were done at three different times: pre-CPB, while heparinized on CPB, and after protamine reversal of heparin following weaning from CPB.

RESULTS: Fifty-five adult patients undergoing elective cardiac surgery with CPB were enrolled in this prospective observational study. SEER Clot Time exhibited a strong correlation with ROTEM® INTEM CT (r = 0.84) and aPTT (r = 0.73) at baseline (Figures 1a, 1b). Figures 2a and 4b show the correlation of SEER Clot Time with ROTEM® INTEM CT (r = 0.66) and aPTT (r = 0.89) after CPB. Clot Stiffness exhibited a strong correlation with ROTEM® EXTEM A10 (r = 0.85) (Figures 3a, 3b). Fibrinogen Contribution correlated strongly with ROTEM® FIBTEM A10 (r = 0.85) (Figure 4a and 4b) as well as with the Clauss fibrinogen concentration (r = 0.73). We found poor correlation between numerical platelet count and the platelet contribution to clot stiffness (r = 0.48) (Figure 5a), underscoring the importance of platelet function as compared to numerical count in coagulation assessment. There was good correlation between Platelet Contribution and ROTEM®-determined clot elasticity attributable to platelets (r = 0.79) (Figure 5b).

CONCLUSIONS: SEER Sonorheometry demonstrates good level of correlation with ROTEM®-determined parameters for Clot Time, Clot Stiffness and Fibrinogen Contribution, but weaker correlation with numerical platelet count.

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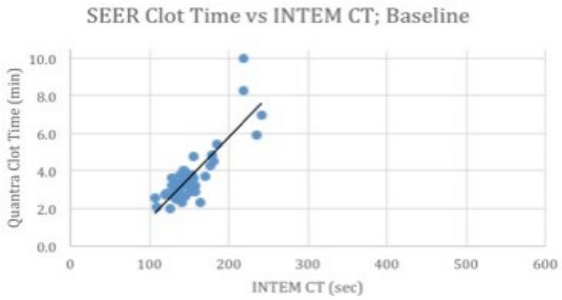
Figure 1a:



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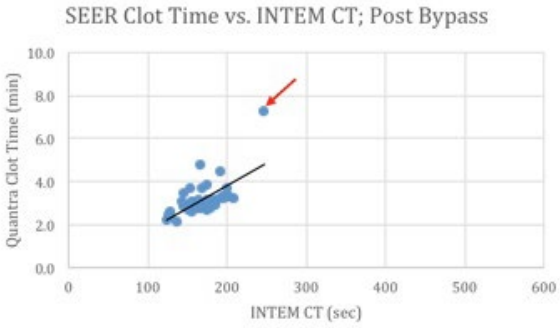

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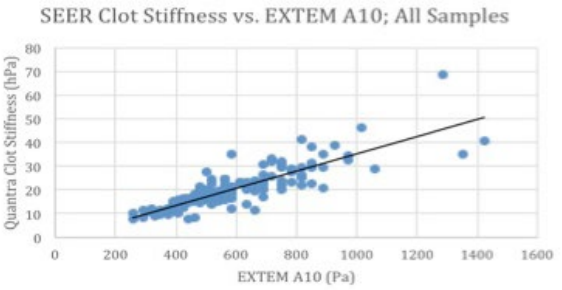

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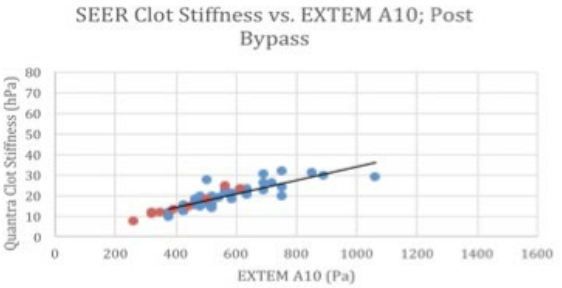

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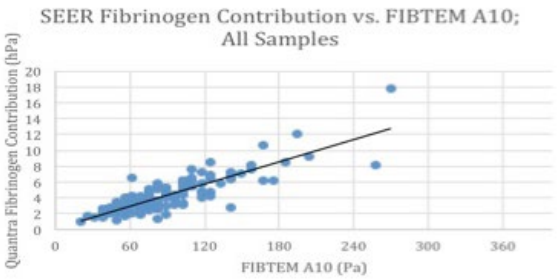
Figure 4a:



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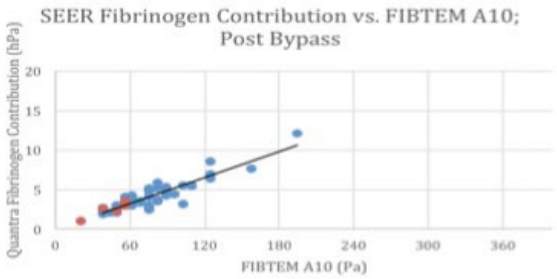

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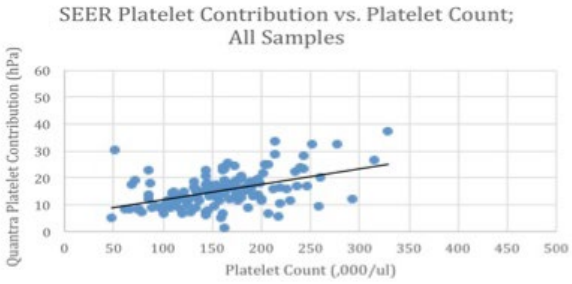
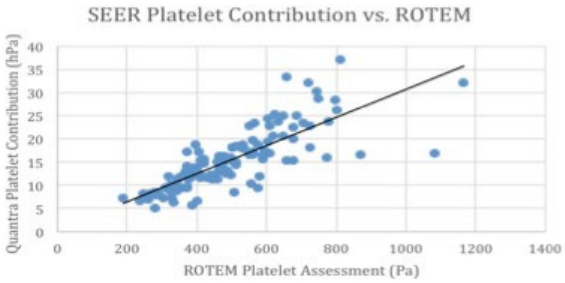


Figure 5b:



S-67.

PREOPERATIVE ASPIRIN AND MAJOR PERIOPERATIVE OUTCOMES IN PATIENTS WITH HYPERTENSION UNDERGOING CARDIAC SURGERY

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INTRODUCTION: Hypertension is prevalent in patients undergoing cardiac surgery and associated with higher incidence of cardiovascular complications. Aspirin has been shown to prevent cardiovascular events in patients with high-risk of cardiovascular disease. However, very few studies have been done on aspirin and hypertension. Its effects on patients undergoing cardiac surgery remain unknown[1,2].

METHODS: 6,514 consecutive patients receiving cardiac surgery (including coronary artery bypass graft [CABG], valve surgery, CABG plus valve surgery, or other cardiac surgery) in two tertiary hospitals from 2001 to 2014 were included in this retrospective cohort study. Of all the patients, 3,290 hypertension patients met inclusion criteria and were divided into two groups: with preoperative aspirin (aspirin) or without (control); they also were divided into three groups: hypertension plus heart failure (HHF), plus chronic kidney disease (CKD, defined as estimated glomerular filtration rate [eGFR] <60 ml/min/1.73m2 (HCKD), or without heart failure or CKD (HTN). Outcomes include major adverse cardiocerebral events (MACE), 30-day mortality, renal failure, intensive care unit (ICU) stay and readmission. MACE includes perioperative myocardial infarction (MI), heart block, cardiac arrest, permanent stroke, transient ischemic attack, coma, and renal failure.

RESULTS: Among 3,290 patients with HTN, 71.2% had preoperative aspirin, 28.8% not (control). Among hypertensive patients, 13.3% had heart failure and 14.7% CKD. Overall, there was a tendency toward unfavorable outcomes in patients with heart failure and CKD. 30-day mortality rates were 4.1%, 4.8%, 7.1% in the HTN, HCKD and HHF group respectively (Table 1). The patients with HTN taking aspirin presented significantly more with comorbidities including more diabetes, peripheral vascular disease and previous MI. With propensity scores adjusted and multivariate logistic regression, however, the results of this study (Table 2) showed that preoperative aspirin therapy (vs non-aspirin) significantly reduced the risk of 30-day mortality (3.7% vs 6.8%, OR: 0.593, 95% CI: 0.408-0.863, P = 0.006), postoperative renal failure (4.2% vs 8.0%, OR: 0.570, 95% CI: 0.404-0.805, P < 0.001), ICU stay (mean 109.1 vs 133.7 h, P < 0.001) and MACEs (9.1% vs 12.7%, OR: 0.765, 95% CI:0.589-0.995, P<0.05) in the patients with hypertension undergoing cardiac surgery. Readmissions did not show a significant difference between the two groups.

CONCLUSIONS: Preoperative aspirin therapy is associated with a significant decrease in the risk of MACEs, renal failure, ICU stay and 30-day mortality but does not increase the risk of readmissions in patients with hypertension undergoing cardiac surgery, indicating, for the first time, that preoperative aspirin is beneficial for patients with hypertension undergoing cardiac surgery. In addition, hypertensive patients with CKD or heart failure are more likely to experience higher risk of mortality following cardiac surgery.

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Table 1. Postoperative complications and mortality in hypertension patients undergoing cardiac surgery

No. of patients	No. 3290 (%)			P
	HTN 2419 (73.5)	HCKD 496 (15.1)	HHF449 (13.6)	
MACE	238 (9.8)	48 (9.7)	55 (12.2)	0.279
Total Hrs ICU (h)	106.32 ± 172.79	123.95 ± 192.28	166.78 ± 226.38	< 0.001
Readmission	330 (13.6)	72 (14.5)	78 (17.4)	0.114
30-day mortality	100 (4.1)	24 (4.8)	32 (7.1)	0.021

HTN, hypertension without heart failure or chronic kidney disease; HCKD, hypertension with chronic kidney disease; HHF, hypertension with heart failure. Among patients with HCKD and HHF, 74 had both heart failure and chronic kidney disease.

Table 2.Effects of aspirin on postoperative complications and mortality in hypertension patients undergoing cardiac surgery

No. of patients	Outcome No. (% of incidence) Preoperative aspirin 3290		Univariate OR (95% CI)	P	Adjusted OR(95% CI)	P
	Yes 2342 (71.2)	No948 (28.8)				
MACE	213 (9.1)	122 (12.7)	0.677 (0.535-0.858)	0.001	0.765 (0.589-0.995)	0.046
Renal failure	99 (4.2)	76 (8.0)	0.506 (0.372-0.690)	<0.001	0.570 (0.404-0.805)	0.001
Total Hrs ICU (h)	109.11±164.77	133.65±223.16		<0.001		
Readmission	343 (14.6)	128 (13.5)	1.099 (0.883-1.368)	0.396	1.126 (0.887-1.431)	0.329
30-day mortality	86 (3.7)	64 (6.8)	0.527 (0.377-0.734)	<0.001	0.593 (0.408-0.863)	0.006

S-68.

ROLE OF MACROPHAGE AUTOPHAGY IN THE PATHOPHYSIOLOGY OF AORTIC ANEURYSM IN MICE

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INTRODUCTION: Aortic aneurysms are common among the elderly population, and their rupture results in severe mortality and morbidity. Surgical intervention for unruptured aortic aneurysms still carries significant risks of mortality and morbidity. Therefore, pharmacological stabilization of aneurysms that prevents growth and rupture of aortic aneurysms has been vigorously sought. To develop such a strategy, underlying mechanisms of aortic aneurysm formation and growth need to be elucidated in an animal model that recapitulates key features of human aortic aneurysms. Autophagy regulates cellular homeostasis and integrates the cellular pro-survival machinery. It has been known that autophagy dysfunction can increase atherosclerotic lesion, and investigated that whether autophagy would modify aortic aneurysm growth or not by pharmacological approach. In this study, we investigated the role of autophagy in the mouse aortic aneurysm model by genetic approach.

METHODS: We used macrophage-specific ATG5-null mice, commonly used models of autophagy deficiency. To generate aortic aneurysms, angiotensin II and β-aminopropionitrile, a lysyl oxidase inhibitor were administrated subcutaneously through osmotic pump for 4 weeks in 8-week-old. Mice were euthanized and assessed at the end of the 4 weeks. Aneurysms were defined as a localized dilation of the aorta of >50% of its adjacent intact portion of aorta.

RESULT: The incidence of aortic aneurysm in autophagy-deficient group was significantly increased than control group (12/14; 86% vs 5/13; 38%, $p<0.05$, respectively). The majority of aneurysms were located in the ascending aorta and the aortic arch.

CONCLUSION: Lack of macrophage autophagy increased the incidence of aortic aneurysms. Macrophage autophagy may play a key role in the formation of aortic aneurysms.

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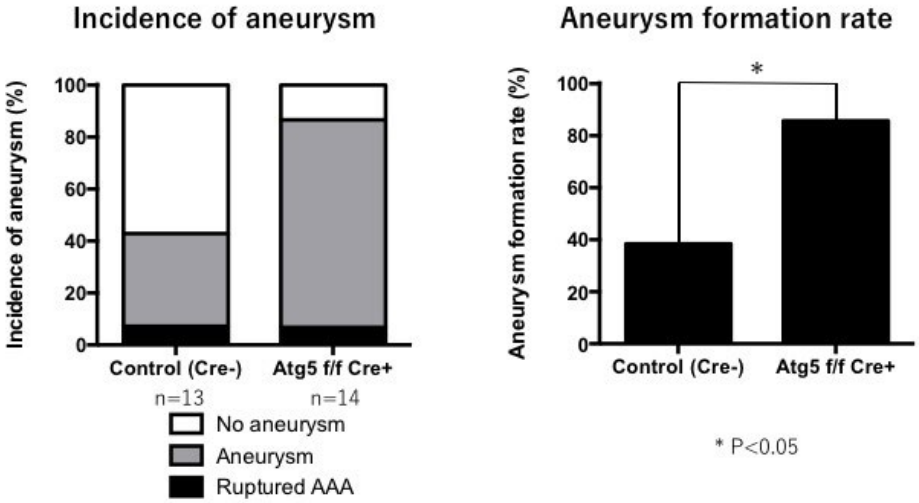

S-69.

IMPACT OF HEART RATE ON POST-INDUCTION PULSE PRESSURE VARIATION IN NON-LUNG INJURED PATIENTS

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INTRODUCTION: Pulse pressure variation (PPV) is a dynamic indicator of fluid responsiveness which can be used to guide fluid therapy but has several limitations. Elevated respiratory rates have been shown to lead to a reduction in measured PPV, likely secondary to a low heart rate to respiratory rate (HR/RR) ratio. Previous work has shown PPV to be inaccurate in predicting response to fluid bolus in lung-injured patients who require high RRs for lung protective ventilation.[1,2]

This study aims to determine if elective surgical patients who lack lung injury but have low resting HRs, such as those who are beta-blocked, have lower PPV values compared to their counterparts with normal HRs.

METHODS: Study protocol is shown in Figure 1. The primary endpoint is the difference in mean PPV between the group. Secondary outcomes include the difference in mean PPV between Beta-blocked and Non-beta-blocked groups, and the change in PPV after adjusting for patient position and fluid administration.

RESULTS: Tables 1 and 2 show results over the first 3.5 minutes of the study (when all patients were supine) and over the study duration (when some patients were in other positions), respectively. When all patients were supine, there were no significant differences between mean PPV between the Low versus Normal HR groups or between the Beta-blocked versus Non-beta-blocked groups, though there was a trend towards lower PPVs in the Low HR group. Over the study duration, patients in the Low HR group had significantly lower PPVs. There was no significant difference between PPVs in the Beta-blocked group versus the Non-beta-blocked group, though there was a trend towards higher PPVs in the Beta-blocked group. There were not enough patients in this preliminary analysis to permit comparison based on position, fluids, or vasoactive medications.

CONCLUSIONS: Preliminary results of this underpowered study show a trend toward lower PPV values in patients who have low resting HRs. Mean PPV was significantly lower in patients with low HR when not accounting for position. A major limitation is the assumption that all patients were equally fluid responsive due to fluid abstinence. Future results will analyze the impact of position and fluids on PPV values by subgroup.

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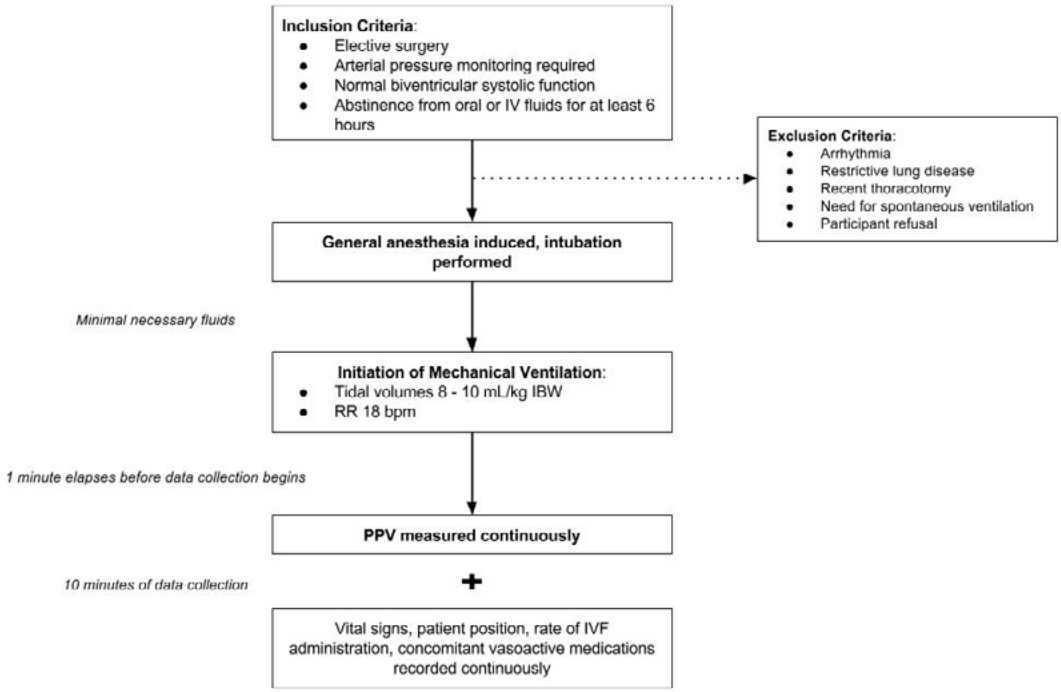

Figure 1: Study inclusion and exclusion criteria and overview of protocol.

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	Number of Subjects	Minimum PPV	Maximum PPV	Standard Deviation	Mean PPV	P Value
Low HR Group (<60 bpm)	10	5.0	16.7	3.5	10.0	0.10
Normal HR Group (≥ 60 bpm)	17	4.6	25.5	5.9	13.5	
Beta-blocked Group	22	4.6	25.5	5.6	12.6	0.49
Non-beta-blocked Group	5	5.1	15.5	4.1	10.7	

Table 1: Mean PPV results for first 3.5 minutes, by group. All patients were supine in the first 3.5 minutes of data collection. Some patients were in other positions (e.g. Trendelenburg) during the remainder of the study duration. P values are shown for comparison of mean PPV.

	Number of Subjects	Minimum PPV	Maximum PPV	Standard Deviation	Mean PPV	P Value
Low HR Group (<60 bpm)	10	5	14.6	2.7	9.2	0.049
Normal HR Group (≥ 60 bpm)	17	5.4	25.3	5.2	12.3	
Beta-blocked Group	22	5.0	25.3	4.7	11.8	0.13
Non-beta-blocked Group	5	5.5	12.9	3.2	8.3	

Table 2: Mean PPV results for entire study duration (10 minutes), by group. Some patients were in positions other than supine (e.g. Trendelenburg) after the first 3.5 minutes. P values are shown for comparison of mean PPV.

S-70.

PULSE OXIMETER USE BEYOND SATURATION DETERMINATION: PPG AUGMENTED INDEX & ARTERIAL COMPLIANCE

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INTRODUCTION: The pulse oximeter is one of the standard monitors used in the operating room. It is designed to monitor the patient's arterial oxygen saturation and heart rate. Study of the pulse oximeter waveform (PhotoPlethysmoGraph - PPG) provides valuable information regarding patient physiology. It has been reported that PPG waveforms can provide breath-to-breath changes in intravascular blood volume.[1] In addition, it has been suggested that the ratio of beat-to-beat volume change (provided by PPG amplitude) to pulse pressure (provided by arterial pressure waveform) reflects changes in vascular resistance, and compliance, in response to vasoconstrictors.[2] The diastolic reflected wave (as detected by the dicrotic notch position) has been shown to be influenced by arterial resistance and stiffness.[3] Vasodilators, as well as exercise, will dilate muscular arteries and thereby reduce the arterial augmented index and diastolic augmented index (figure 1), this effect will reduce left ventricular load.[4] The aim of this work was to study the relationship between PPG and arterial derived variables. The variables compared were the PPG augmented index and arterial compliance (PPG amplitude/arterial pulse pressure) to the blood pressure measured from radial artery during pheochromocytoma surgery. During the surgery multiple doses of vasodilators were used in an attempt to control blood pressure.

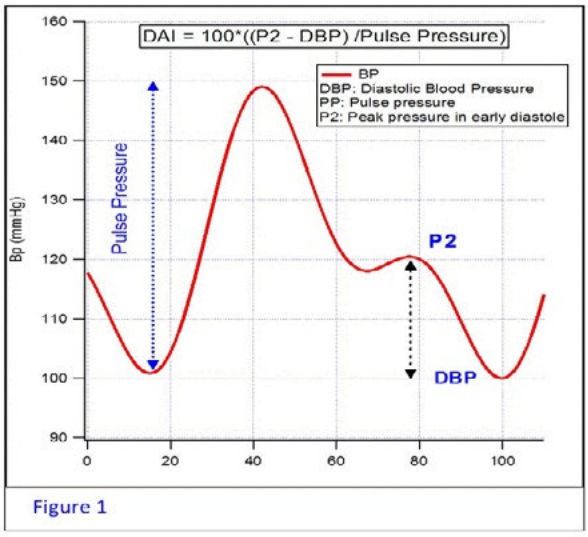

Figure 1

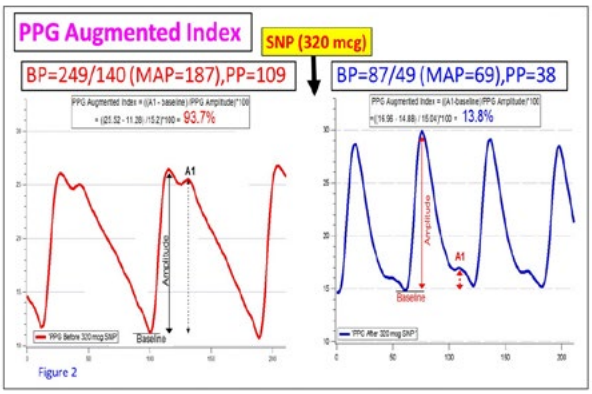

Figure 2

METHODS: This was an observational study performed with IRB approval. Arterial blood pressure (BP), finger PPG were recorded at 100 Hz from clinical monitors (GE; Fairfield, CT) with a data acquisition system (Collect 5/S - GE; Fairfield, CT). We used LabChart 7.37 (ADInstruments, Boulder CO) to analyze these waveforms. PPG augmented index is calculated as shown in (figure 2).

RESULTS: Over a wide range of blood pressures from 75 to 340 mmHg, the PPG augmented index tracked well the changes in the Systolic BP (SBP), Diastolic BP (DBP) and Mean BP (MAP), the correlation was 0.78, 0.85 and 0.82 respectively (figure 3-A). There was a very good negative correlation between the arterial compliance derived from PPG and SBP, DBP & MAP, the correlation was - 0.84, - 0.8 and - 0.82 respectively (figure 3-B). The effect of vasodilators on PPG augmented index is showed in (figure 4).

CONCLUSION: These PPG derived variables might be a useful tool in hemodynamic monitoring. It is hypothesized that the position of PPG dicrotic notch can provide valuable vascular tone information. We observed that during hypertension, the position of the dicrotic notch is close to the peak, thus indicating high vascular tone. With the use of vasodilators, the position of the PPG dicrotic notch moved downward towards the baseline. It is proposed that the position of PPG dicrotic notch might allow for tracking of the vascular tone and that it is a mirror image of arterial compliance. The sensitivity and specificity of this measurement remains to be determined.

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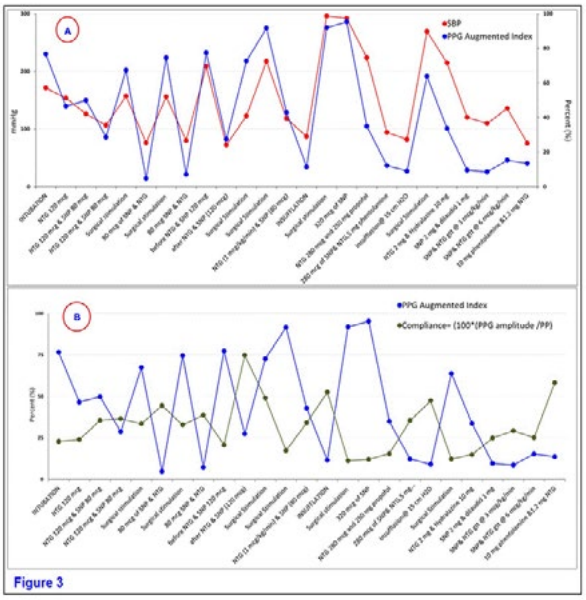

Figure 3

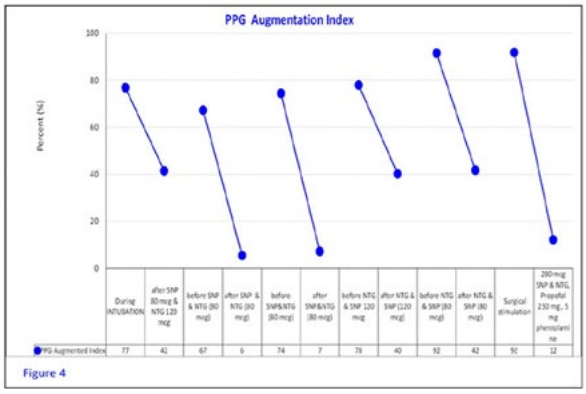

Figure 4

S-71.

STATIC AUTOREGULATION REMAINS INTACT DURING DEEP HYPOTHERMIA IN NEONATAL SWINE

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INTRODUCTION: Clinical studies measuring cerebral blood flow in infants during deep hypothermia have demonstrated diminished cerebrovascular pressure autoregulation.[1,2] The coexistence of hypotension in these cohorts confounds the most obvious conclusion that deep hypothermia impairs cerebrovascular pressure autoregulation. Our objective was to compare the lower limit of autoregulation (LLA) and the static rate of autoregulation (SRoR) between normothermic and hypothermic neonatal swine. We hypothesized that deep hypothermia impairs autoregulation in a non-bypass neonatal swine model controlled for arterial blood pressure.

METHODS: Twenty anesthetized neonatal piglets (5-7 days old; 10 normothermic and 10 hypothermic to 20°C) had continuous measurements of cortical red cell flux using laser-Doppler flowmetry while hemorrhagic hypotension was induced. LLA was determined for each subject using piecewise regression and SRoR was determined above and below each LLA as (%change cerebrovascular resistance/%change cerebral perfusion pressure). Study metrics were compared between the hypothermic and normothermic groups with Mann Whitney test to compare LLA, and Kruskall-Wallis test with Dunn's multiple post hoc comparisons (on SRoR data) for the two temperature groups above and below LLA. A difference in the SRoR > 0.5 (the difference between a perfect value of 1 to the upper limit of abnormal 0.5) would be detected with this sample size at a power of 0.94 given normal distribution, standard deviation of 0.3, and alpha 0.05.

RESULTS: There was no significant difference in LLA between the normothermic and hypothermic piglets (median LLA of 39 mmHg [IQR 38-51] versus 35 mmHg [31-50] respectively). Intact steady-state pressure autoregulation was defined as SRoR > 0.5 and was demonstrated in all normothermic subjects (SRoR =

0.72 [0.65-0.87]) and in 9/10 of the hypothermic subjects (SRoR = 0.65 [0.52-0.87]) with no significant difference.

CONCLUSIONS: Intact steady-state cerebrovascular pressure autoregulation is demonstrated in a swine model of profound hypothermia. LLA and SRoR were similar in hypothermic and normothermic subjects. Deep hypothermia alone may be inadequate to explain the loss of autoregulation observed during infant cardiopulmonary bypass.

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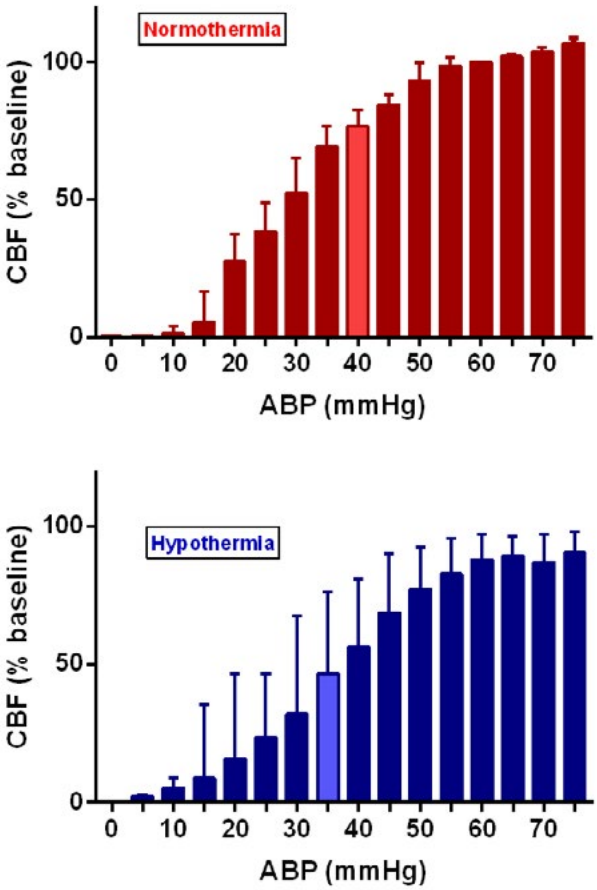

Figure 1. Autoregulation curves for normothermic and hypothermic cohorts. The highlighted bar shows the median lower limit of autoregulation (LLA) for the cohort. Figure 2: the static rate of autoregulation (SRoR) was measured above and below the lower limit of autoregulation (LLA) for each cohort. For both cohorts, SRoR was normal above LLA and abnormal below LLA.

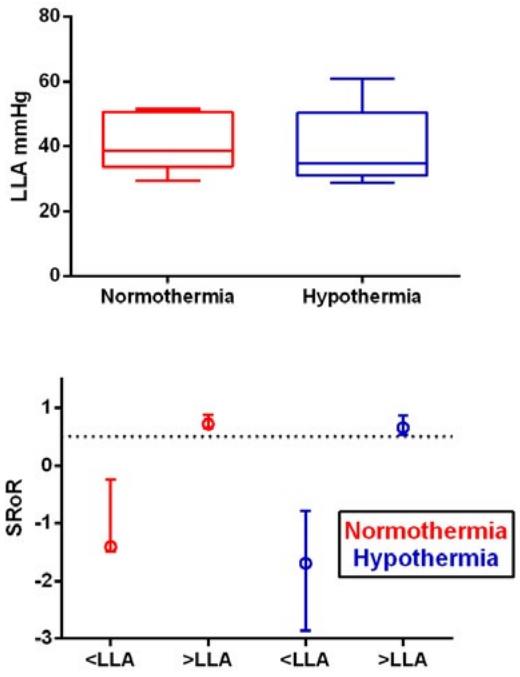

Figure 2.

S-72.

EXTRACORPOREAL CIRCULATION DURING LUNG TRANSPLANTATION PROCEDURES: A META-ANALYSIS

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BACKGROUND: Extracorporeal circulation is an inevitable tool in lung transplantation. Over the past years, an increasing number of centers changed their standard for intraoperative extracorporeal circulation from cardiopulmonary bypass (CPB) to extracorporeal membrane oxygenation (ECMO) – with differing result[1-6]. This meta-analysis reviews the existing evidence.

METHODS: An online literature research on Medline, Embase, and Pubmed has been performed. Two persons independently judged the papers found using the ACROBAT-NRSI tool of the Cochrane collaboration. Meta-analyses and meta-regressions were used to determine whether ECMO resulted in better outcomes versus CPB.

RESULTS: Six papers were included in the analysis. All were considered to have serious bias due to heparinization co-intervention. Forest plots showed the benefit of ECMO in blood transfusions (packed red blood cells with average mean difference of -0.46 units [95% CI=-3.72, 2.80], fresh-frozen plasma with average mean difference of -0.65 units [95% CI=-1.56, 0.25], platelets with average mean difference of -1.72 units [95% CI=-3.67, 0.23]). Duration of ventilator support with average mean difference of -2.86 days [95% CI=-11.43, 5.71] and ICU length of stay with average mean difference of -4.79 days [95% CI=-8.17, -1.41] were shorter in ECMO patients. ECMO treatment tended to be superior regarding 3 month mortality (odds ratio=0.46, 95% CI=0.21-1.02) and 1 year mortality (odds ratio=0.65, 95% CI=0.37-1.13). However, only ICU length of stay reached statistical significance. Meta-regression analyses showed that heterogeneity across studies (sex, the year that the ECMO was implemented and underlying pathology) influenced differences.

CONCLUSION: These data indicate a benefit of the intraoperative use of ECMO during lung transplant procedures regarding short-term outcome (ICU stay). The superiority of ECMO in lung transplantation patients remains to be determined in larger multi-center randomized trials.

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S-73.

ANESTHETIC MANAGEMENT OF CAROTID BODY TUMOR EXCISION: A CASE SERIES

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INTRODUCTION: Carotid body tumors (CBT) are rare neuroendocrine tumors. Due to a rich vascular supply, involvement of cranial nerves, possible secretory function, and potential for airway compromise, CBT excision demands a thoughtful approach to perioperative management. Because of the rarity of CBT excision, personal experience or anecdotal evidence may be insufficient for the clinician preparing for perioperative management of these patients. The purpose of this study was to use a multi-institutional case series to describe the contemporary anesthetic management of CBT resection. We further sought to identify patient and surgical factors that could be used to guide anesthetic planning.

METHODS: This retrospective case series reviewed 21 adult patients who presented for CBT resection at 2 tertiary institutions during 2003-2014. Perioperative data was extracted from medical records. The Mann-Whitney test was used to compare quantitative variables while Spearman's correlation coefficients were generated for quantitative and ordinal values. Nominal variables were compared using the chi-square or Fisher's Exact test. Significance was assessed at $p<0.05$.

RESULTS: Of 21 patients, average age was 49 years (range 24-80), 62% (n=13) were female, and ASA physical classification was I-III (n= 1-I, 14-II, 6-III). With respect to surgical factors, 90% (n=19) presented with sporadic disease (2 had familial CBT), 48% (n=10) had nerve involvement with the tumor, and 24% (n=5) sustained nerve injury during CBT. Anesthetic technique involved 100% general endotracheal anesthesia, no patients received supplemental nerve blockade, 86% (n=18) were orally intubated while 3 were nasally intubated, 86% (n=18) had an arterial catheter placed, and 10% (n=2) required mandibular subluxation. Mean estimated blood loss was 216 mL (range 10-1000mL) and no transfusions were administered. Tables 1-3 show additional perioperative data.

CONCLUSIONS: Our data suggest that many patients will require cardiovascular pharmacologic interventions during anesthesia, with a tendency toward negative chronotropes and vasodilators during emergence and post-operatively. Post-operative adverse events are common and typically involve airway, although none of the patients in our study required reintubation. Knowledge of tumor length and tumor volume can assist the anesthesiologist in anticipating blood loss and surgical duration. In summary, this analysis may aid clinicians in providing anesthetic care for CBT excisions.

Table 1. Pharmacologic Cardiovascular Interventions During Anesthetic Care. % of patients (n)

Anesthetic Phase	Positive inotrope/ chronotrope or vasoconstrictor	Negative inotrope/ chronotrope or vasodilator
Induction	33% (7)	0
Maintenance	76% (16)	29% (6)
Emergence	0	24% (5)
PACU	0	43% (9)

Table 2. Post-operative Adverse Events (after discharge from PACU)

Event	% (n)
Hypertension requiring therapy	29% (6)
Hoarseness	19% (4)
Difficulty swallowing	14% (3)
Vocal cord paralysis	5% (1)
Re-intubation	0

Table 3. Select Comparisons

Factors	P value	r_s
Estimated blood loss higher with:		
Nerve involvement	0.043	n/a
Greater tumor length	0.029	0.477
Greater tumor volume	0.009	0.571
Longer operative duration	0.001	0.684
Operative duration greater with:		
Greater tumor length	0.009	0.557
Greater tumor volume	0.001	0.695
Hospital length of stay longer with:		
Higher Shamblin class	0.001	0.691
Greater tumor length	<0.001	0.754
Greater tumor volume	0.003	0.631

r_s Spearman's rho. Shamblin classification is a grading system describing vasculature intimacy with CBT.

S-74.

SEPIAPTERIN ATTENUATES INCREASED MITOCHONDRIAL FISSION AND RESTORES ANESTHETIC CARDIOPROTECTION IN HUMAN CARDIOMYOCYTES EXPOSED TO HIGH GLUCOSE

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INTRODUCTION: Anesthetic preconditioning (APC) by volatile anesthetics has been shown to reduce infarct size after a myocardial ischemia/reperfusion (I/R) injury. This protective effect is abolished under diabetic conditions (e.g., high glucose) in both human and animal models, but the causal mechanisms have not been completely elucidated. Previous studies have indicated that reactive oxygen species (ROS) and increased mitochondrial fission may play a role in cardiomyocyte death during I/R injury. Sepiapterin, a BH4 analog, could decrease ROS by increasing nitric oxide synthase (NOS). In this study, we investigated the role of glucose-induced increase in ROS production and subsequent increase in mitochondrial fission on the attenuation of APC, and the effects of high glucose on the relationship between mitochondrial fission and nitric oxide (NO) signaling pathways. We hypothesized that high glucose-induced ROS production and mitochondrial fission contribute to the attenuation of APC, and that modulation of BH4/NO signaling with sepiapterin can restore APC under high glucose conditions via inhibition of mitochondrial fission.

METHODS: Human induced pluripotent stem cells (iPSC) were cultured to confluency and differentiated into cardiomyocytes (CMs). Contracting cells were immunostained for sarcomeric a-actinin and troponin T expression to confirm >90% purity of CMs. CMs were cultured in 5 mM glucose for 4 days, and then exposed to 5 or 25 mM glucose for 1 or 3 days with or without sepiapterin. CMs were exposed to 1 minimum alveolar concentration of isoflurane for 30 or 60 min followed by 6 h of H_2O_2 exposure. Cell viability (LDH release or propidium iodide staining) and ROS generation (ethidium fluorescence) end-points were used to assess the effects of various treatment conditions. Mitochondria were loaded with Mitotracker Green and imaged using confocal microscopy. The images were analyzed using the ImageJ software to assess the form factor (mitochondrial branching) and aspect ratio (mitochondrial length/width ratio). Expression of activated dynamin-related protein 1 (DRP1), a key protein responsible for mitochondrial fission, was assessed by Western blot.

RESULTS: CMs in 5 mM glucose were protected against oxidative stress by isoflurane exposure as demonstrated by increased cell viability, decreased ROS generation, decreased mitochondrial fission, and decreased expression of DRP1 in isoflurane-treated CMs. However, CMs exposed to 25 mM glucose had an attenuation of cardioprotection accompanied by increased ROS generation, increased mitochondrial fission, and increased expression of DRP1. Addition of sepiapterin reduced mitochondrial fission and increased cell viability in CMs cultured in 25 mM glucose conditions.

CONCLUSIONS: We have shown a novel interaction between NO signaling, ROS generation, and mitochondrial fission, through treatment with sepiapterin in attenuation of APC conferred by high glucose. Further experiments detailing the mechanism by which this occurs may reveal new therapeutic targets to reduce the detriment of perioperative cardiovascular events.

S-75.

GABA$_A$ RECEPTOR ACTIVATION DECREASES MYOGENIC TONE IN SMALL RESISTANCE ARTERIES IN MICE

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INTRODUCTION: Hypertension is a large national health problem effecting approximately 70 million people in the United States (29% of the adult population)[1]. It is a common clinical observation that patients with hypertension have dramatic reductions in blood pressure upon exposure to GABAergic anesthetics. Yet, despite this well recognized clinical effect, the potential role for direct anesthetic activation of GABAA receptors on vascular smooth muscle of small resistance arteries has not been investigated. Although there are many contributing factors that lead to hypertension, smooth muscle tone (more specifically myogenic tone) in small resistance arteries is a major determinant of vascular resistance. We hypothesized that direct anesthetic effects at peripheral GABAA receptors expressed on vascular smooth muscle (VSM) cells modulate myogenic vascular tone.

METHODS: Mouse tail small resistance arteries (95-110 µm diameter) were dissected in ice-cold Krebs-Ringer solution and transferred to a vessel chamber for pressure myography recordings. The proximal and distal end of the artery were cannulated with a tapered glass pipette and secured. The chamber was superfused with Krebs-Ringer solution at 37°C, pH 7.4 (gassed with 95% O_2-5% CO_2), and placed on the stage of an inverted microscope. The internal diameter of the vessel was measured continuously by a video dimension analyzer (Living Systems) and recorded using a BIOPAC (Santa Barbara, CA) data acquisition system. Intraluminal pressure was increased from 0 to 90 mm Hg in a single step before and after treatments of GABAergic agonists (propofol 100nM in 0.1%DMSO or muscimol 100uM). Statistical analysis was performed on the change in maximal diameter and plateau diameter in the absence and presence of treatment using a paired Students t-test.

RESULTS: A step increase in intraluminal pressure of mouse tail resistance arteries from 0 to 90mm Hg resulted in a change of intraluminal maximum diameter (29.7 +/- 6.0um) and plateau diameter (15.25 +/- 3.0um), (mean +/- SEM n=4) (Fig. 1). However after GABAA agonist pre-treatment, the vessel response to the increase in intraluminal pressure demonstrated a significant enhancement in the change of both intraluminal maximum diameter (37.0 +/- 7.1um) and plateau diameter (29.5 +/- 7.6um), (mean +/- SEM n=4) (Fig. 1) when compared to control ($p<0.05$ for both maximum and plateau).

CONCLUSION: The data suggests that modulation of myogenic tone can be achieved with pharmacologic activation of GABAA receptors expressed on resistance arteries.

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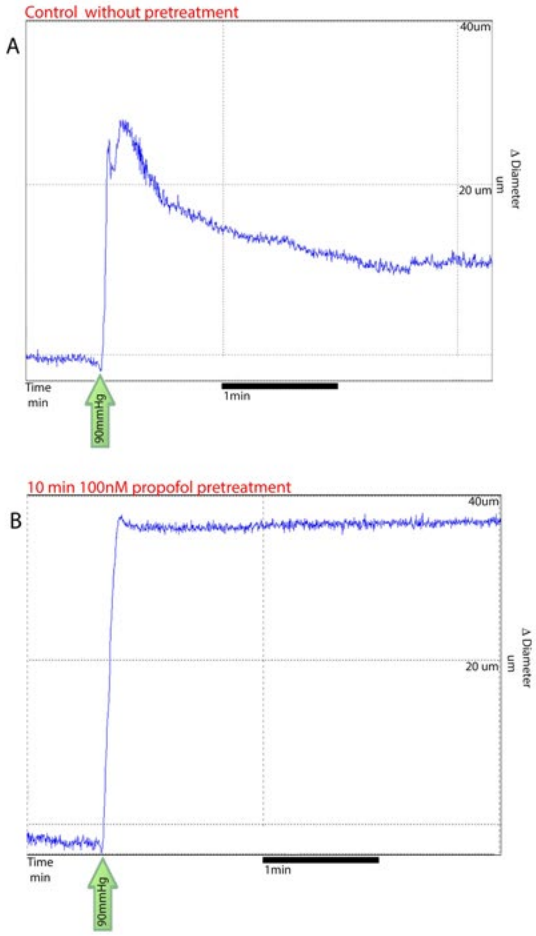

Figure 1. Representative tracings of myogenic tone in *ex vivo* mouse tail resistance artery. Using pressure myography, a cannulated mouse resistance artery was exposed to an increase in intraluminal pressure (0-90mm Hg) indicated by the green arrow. Tracing displays a change in luminal diameter in response to increased intraluminal pressure. **A control:** A max change in diameter of 27 um and a recontraction to a a plateau of 15 um was measured. **B GABA$_A$ agonist treated:** After a 2 min pretreatment of 100nM propofol a maximal change in diameter of 40 um and a recontraction to a plateau of 39 um was measured.

S-76.

COMPARISON OF FERUMOXYTOL (FERRAHEME) AND GADOLINIUM AS INTRAVENOUS CONTRAST AGENTS IN PEDIATRIC PATIENTS UNDERGOING CARDIAC MAGNETIC RESONANCE IMAGING (MRI) UNDER GENERAL ANESTHESIA

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BACKGROUND: Ferumoxytol is a contrast agent used for vascular MRI due to its improved safety profile in renal impairment and long intravascular half-life. Its strong signal enhancement enables faster and more reliable image data acquisition with less need for suspended respiration. However, its administration has been associated with hypotension in pediatric populations. This study was conducted to evaluate anesthetic outcomes and associations between contrast agent and incidence of hypotension in pediatric patients undergoing cardiac MRI.

METHODS: Following IRB approval, medical records of patients less than18 years of age who underwent cardiac MRI with general anesthesia between 5/1/2014 and 9/30/2015 were reviewed. Baseline demographic and medical characteristics, as well as imaging and anesthetic duration and technique, vital signs throughout the anesthetic, and need for vasoactive support were collected. Hypotension was defined as a sustained or frequent decrease (>/= 5 readings) in systolic or mean blood pressure by more than 20% from baseline and/or the use of intravenous vasopressors. Continuous data were compared using Wilcoxon rank sum test. Categorical data were compared using chi square test; $p < 0.05$ was defined as statistically significant.

RESULTS: Seventy-nine patients were identified, 51 in the ferumoxytol group and 28 in the gadolinium group (Table 1). There were no significant differences between groups with respect to age, weight, or baseline blood pressures. The incidence of low blood pressure was identical (65%) in both groups. There was no difference in sustained hypotension or use of vasopressors between groups. Baseline blood pressures between patients who did and those who did not receive vasoactive medications were similar. Patients who received vasoactive medications or had sustained hypotension had longer anesthetic times (140 vs 95 min, p=0.04) and time to PACU discharge (219 vs 161 min, p=0.05) as compared to patients without hypotension. The image acquisition time (45 vs 68 min, p=0.002) and anesthesia duration (102 vs 140 min, p=0.02) were shorter in the ferumoxytol group. None of the study patients required post-anesthesia vasoactive agents and there were no post-anesthesia complications. The time to discharge from the PACU did not differ between groups.

CONCLUSIONS: Although transient low blood pressure was common in children undergoing cardiac MRI with anesthesia, the incidence of hypotension did not differ between the contrast agents ferumoxytol and gadolinium groups. Use of ferumoxytol was associated with significantly shorter MRI scan time and anesthesia duration in this population as well as decreased need for neuromuscular blockade.

Table 1. Demographic, medical, and procedural characteristics

	Ferumoxytol N=51	Gadolinium N=28	p-value
Age (yrs)	4 (2-6.5)	4.5 (2-7)	0.53
Weight (kg)	17 (10.8-24.5)	18 (12.8-25.2)	0.74
Diagnosis			0.17
Congenital heart disease – single ventricle	8 (16%)	3 (11%)	
Congenital heart disease – biventricular	37 (73%)	17 (61%)	
Cardiomyopathy or other	6 (12%)	8 (29%)	
Image acquisition time (min)*	45 (35-57)	68 (51-81)	0.002*
Anesthesia duration (min)*	102 (86-135)	140 (102-199)	0.02*
Time to PACU discharge (min)	166 (139-208)	193 (164-233)	0.14
Baseline systolic blood pressure (mmHg)	100 (92-110)	101 (90-112)	0.60
Baseline mean blood pressure (mmHg)	73 (66-86)	73 (67-80)	0.66
Lowest systolic blood pressure (mmHg)	70 (70-78)	73 (65-79)	0.61
Lowest mean blood pressure (mmHg)	43 (40-48)	45 (42-49)	0.31
Any decrease in mean of systolic blood pressure by 20% or more during the study	30 (65%)	17 (65%)	0.99
Vasoactive medications administered	10 (20%)	2 (7%)	0.15
Hypotension	20 (43%)	11 (42%)	0.99
Neuromuscular blockade *	6 (12%)	11 (40%)	0.003*
Endotracheal intubation	9 (17%)	10 (37%)	0.052

Data are presented as median (quartile 1 – quartile 3) or frequency (% of total). Statistically significant values are indicated with an astresik (*). Hypotension was defined as a sustained decrease or frequent decreases (>/= 5 readings) in systolic or mean blood pressure by more than 20% from baseline and/or the use of intravenous vasopressors.

S-77.

ACUTE KIDNEY INJURY DEFINED BY AKIN CRITERIA IS NOT SENSITIVE AFTER CARDIAC SURGERY

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INTRODUCTION: Acute kidney injury (AKI) after cardiac surgery increases morbidity and mortality[1]. Stage I AKI is commonly defined by the AKIN criteria[2] as an increase in serum creatinine by more than 0.3 mg/dL within 48 hours of injury. Hemodilution after cardiac surgery caused by use of cardiopulmonary bypass may delay a substantial increase in creatinine. Furthermore, it is not known whether transient increases in serum creatinine may have less effect on outcome than a sustained increase.

METHODS: This is a retrospective study of all cardiac surgery patients at one institution in 2011. AKI was defined according to AKIN criteria as an increase in serum creatinine by more than 0.3 mg/dL within 48 hours of surgery. Transient AKI was defined as AKI that normalized by 72 hours. Sustained AKI was defined as a persistent increase in creatinine for 72 hours or longer. Late AKI was defined as an increase in creatinine by more than 0.3 mg/dL that occurred only after 48 or more hours following surgery. Short term (90-day) and 1-year mortality was determined using the US Social Security index.

RESULTS: This study included 1580 patients. 109 patients developed transient AKI (6.9%), 183 patients had sustained AKI (11.6%), and 106 patients had late AKI (6.7%). Serum creatinine during the first postoperative week is depicted in figure 1. Ninety-day and 1-year survival was significantly better for patients without AKI ($p<0.0001$), but there was no difference in survival between AKI groups (table 1 and figure 2). However, there was a significant difference in the length of stay (LOS) after surgery between the groups (ANOVA $p<0.0001$). Normal patients had shorter LOS than all other groups ($p<0.0001$), and patients with transient AKI had shorter LOS than patients with sustained and late AKI ($p<0.005$, Tukey's post hoc test). There was no difference in LOS between patients with sustained versus late AKI (figure 3).

DISCUSSION: Of all cardiac surgery patients who developed AKI in our cohort, 7% developed AKI after 48 hours and would not have fulfilled AKIN criteria. Therefore, AKIN criteria is not sensitive enough to capture all episodes of AKI in this population. The mortality was high for patients with AKI independent of whether it was transient, sustained, or late AKI. However, among patients with AKI, those with transient AKI had a shorter length of stay compared to the other groups. This may indicate that transient postoperative increases in serum creatinine are less detrimental than sustained or late AKI.

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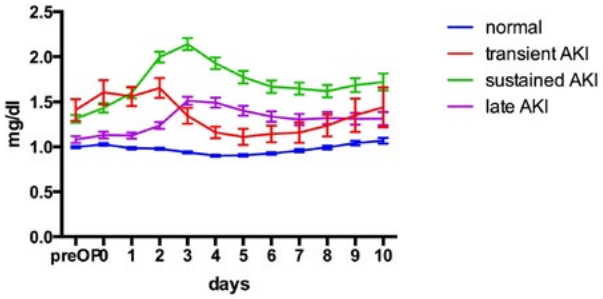

Figure 1. Serum creatinine after cardiac surgery

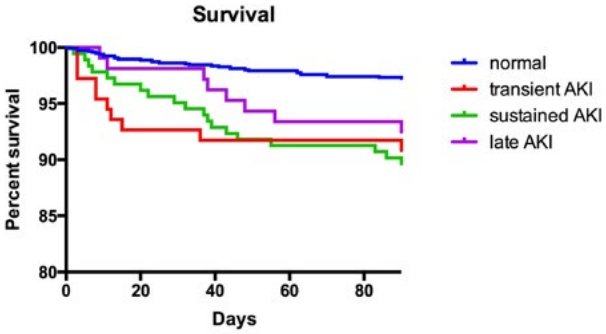

Figure 2. Kaplan-Meier Survival curves

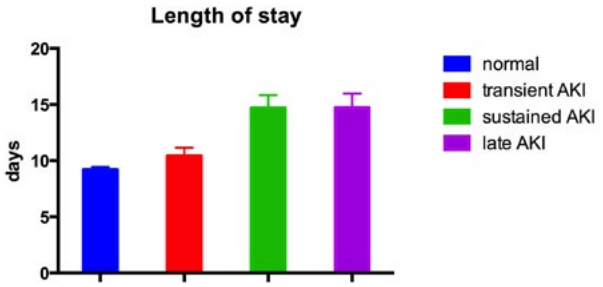

Figure 2. Length of stay after cardiac surgery

Table 1: Mortality after cardiac surgery in patients with or without AKI

	Normal	Transient AKI	Sustained AKI	Late AKI	Others
n	1159	109	183	106	23
90-day mortality	32 (2.8%)	9 (9.0%)	18 (10.9%)	7 (7.1%)	3 (15%)
1-year mortality	52 (4.7%)	14 (15.7%)	24 (15.1%)	12 (12.8%)	4 (21.1%)

S-78.

TYPE OF ANESTHESIA AND OUTCOMES AFTER TRANS-CATHETER AORTIC VALVE IMPLANTATION

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INTRODUCTION: The purpose of this study was to compare postoperative outcomes after general anesthesia (GA) with tracheal intubation and conscious sedation with dexmedetomidine in patients undergoing trans-femoral trans-catheter aortic valve implantation (TAVI) procedures[1,2]. We hypothesized that conscious sedation with dexmedetomidine would be a non-inferior anesthetic modality compared to historical controls with GA approach[3,4].

METHODS: After the Research Ethics Board approval, a prospective cohort of 50 consecutive patients undergoing trans-femoral TAVI under conscious sedation with dexmedetomidine (DEX group) were matched by age and sex on 1:1 basis with 50 historical controls receiving general anesthesia (GA group). In the GA group, anesthesia was induced with fentanyl 1-3g/kg, and propofol 0.5-2mg/kg. Tracheal intubation was facilitated with rocuronium 0.6mg/kg.5 Anesthesia was maintained with isoflurane 0.5-2.0%, or sevoflurane 1.5-2.5%. In DEX group, patients received dexmedetomidine bolus 0.4-1µg/kg over 10-20min followed by an infusion 0.5-1.4µg/kg/h until the end of procedure[5]. Transesophageal and transthoracic echocardiography were utilized in GA and DEX groups respectively. Both groups were compared with respect to demographic data, past medical history, medications, surgical characteristics, postoperative morbidity and mortality, and length of hospital stay. Statistical analysis was performed on the intent-to-treat basis. P &lt 0.05 was considered statistically significant.

RESULTS: Both groups were similar with respect to demographic data and surgical characteristics. Four patients in DEX group were converted to GA during the TAVI procedure. All patients in GA group were extubated in the operating room (OR). The OR times were 133 ± 42min in DEX group vs 158 ± 41min in GA group, p=0.0036. There was no difference with respect to postoperative morbidity and mortality between the two groups. (Table) The median difference in hospital length of stay was 2 days favoring DEX group, however, this difference did not reach statistical significance, p =0.07.

CONCLUSIONS: Conscious sedation with dexmedetomidine resulted in a non-inferior anesthetic modality compared to historical controls with general anesthesia approach 6. Potential benefits included shorter OR times and expedited hospital discharge.

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Postoperative Morbidity and Mortality

	DEX Group (n = 50)	GA Group (n = 50)
Myocardial Infarction	1 (2)	1 (2)
Stroke/Transient Ischemic Attack	1 (2)	1 (2)
Highest creatinine, mmol/L	104 [55, 311]	103.5 [65, 576]
Dialysis	1 (2)	2 (4)
Delirium	3 (6)	5 (10)
Hospital length of stay, days	5 [1, 64]	7 [2, 41]
Death	0 (0)	1 (2)

Data expressed as number of patients (%), and median [range].

S-79.

OPTIMIZING CEREBRAL SATURATION IN CARDIAC SURGICAL PATIENTS

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INTRODUCTION: Cerebral oximetry based on near infrared spectroscopy (NIRS) measures regional cerebral tissue oxygen saturation ($SctO_2$). It is used intraoperatively as a continuous monitor for detection of cerebral ischemia and potential brain injury in cardiac surgical patients. Past research has shown that optimizing $SctO_2$ during cardiac surgery is associated with reduced incidence of major organ morbidity or mortality.[1] Several studies have shown an association between prolonged desaturations and postoperative cognitive decline.[2,3] We conducted a randomized controlled trial to determine if optimizing $SctO_2$ during cardiac surgery will lead to improved cerebral oxygen saturation and better neurocognitive outcomes.

METHODS: 125 adult (>18 yo) patients who underwent elective cardiac surgery requiring CPB were studied. Patients with severe preoperative cognitive impairment or end-stage organ failure were excluded. Patients were randomly assigned to either a treatment or a blinded control group. Data extracted from the medical record included: basic demographics, variables for computing Euroscores and Charlson Comorbidity Index scores, and NYHA classification. Cerebral oxygen saturation was monitored intraoperatively using the Fore-Sight® cerebral oximeter (CAS Medical Systems). In the treatment group, an intervention algorithm (Fig 1) was used to improve SctO2 if desaturation occurred <60 for >1min at either probe. In the control group, the SctO2 data were hidden from the perioperative team, unless a critical low value, SctO2 <40 for >1 min triggered an alarm. The SctO2 data were then revealed, and the intervention protocol was followed until SctO2 was restored to >60. Cognitive function was assessed using the Cognitive Stability Index® (CSI) HeadMinder computerized test battery, which assesses response speed, cognitive processing speed, attention, and memory. The test battery was administered preoperatively (n=125) and postoperatively at 3 (n=92) and 6 months (n=78). Data analysis was performed using $\chi 2$/Fischer's exact tests on categorical data and t-test/Wilcoxon rank sum on continuous variables. The level of statistical significance was set to 0.05.

RESULTS: The treatment and control groups were similar with respect to demographics, preoperative risk scores, baseline cognitive test scores, surgery duration, and CPB duration. The groups did not differ in incidence of desaturation episodes, mean time under threshold (TUT), or area under threshold (total time x depth under threshold). Of patients with desaturations, intervention was associated with less TUT and AUT (Table 1). Over all subjects, intervention was associated with better memory function postoperatively (Table 2).

CONCLUSIONS: NIRS-guided optimization of cerebral oxygenation during cardiac surgery is effective in reducing time and depth of intraoperative desaturation episodes in cardiac patients. In patients with desaturations, intervention is associated with better postoperative memory function.

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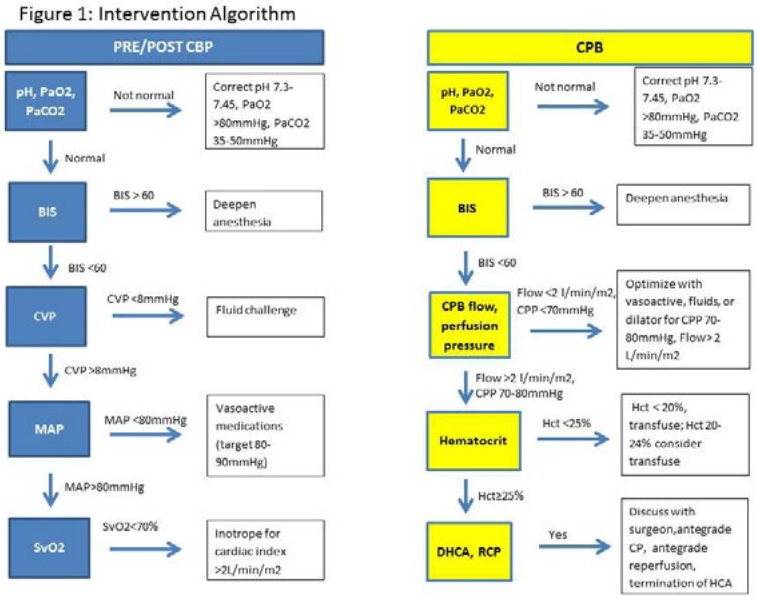
Figure 1: Intervention Algorithm



S-79 • CONTINUED ON NEXT PAGE

S-79 • continued

Table 1. Intraoperative characteristics and oxymetry data

	INTERVENTION GROUP			CONTROL GROUP			
Variable	**Group N**	**Mean Median N**	**(SD) [Interquartile range] %**	**Group N**	**Mean Median N**	**(SD) [Interquartile range]%**	**P-value**
OPERATIVE VARIABLES							
Surgery Duration	59	296	[263, 345]	66	308	[258, 371]	0.599 b
Surgery Duration	59	296	[263, 345]	66	308	[258, 371]	0.599 b
INTRAOPERATIVE OXIMETRY							
Desaturation Incidence	59	33	55.9%	66	31	47%	0.317 c
Group TUT	59	1.77	[0.17, 14.10]	66	0.95	[0.00, 16.27]	0.681 b
Group AUT	59	102.85	[9.70, 827.03]	66	54.99	[0.00, 935.87]	0.694 b
Desat Subgroup TUT	33	5.47	[2.40, 25.60]	31	21.33	[7.87, 53.33]	0.019 b
Desat Subgroup AUT	33	303.33	[135.68, 1351.57]	31	1247.62	[448.57, 3059.98]	0.017 b

P-values are based on a: t-test, b: Wilcoxon rank sum test, c: Chi-square test, d: Fisher's exact test.

Table 2: Cognitive outcome comparisons of the two groups.

	INTERVENTION			CONTROL			
Variable	**N**	**Mean**	**(SE)**	**N**	**Mean**	**(SE)**	**P-value**
NEUROCOGNITIVE OUTCOMES: TEST SCORES CHANGE FROM T1 to T2							
Processing Speed	38	0.909	0.533	52	0.718	0.487	0.3612
Reaction Time	37	0.036	0.038	54	0.025	0.029	0.6098
Attention	34	2.309	1.722	50	2.331	1.681	0.1702
Memory	38	0.442	0.246	54	0.075	0.254	0.0139
NEUROCOGNITIVE OUTCOMES: TEST SCORES CHANGE FROM T1 to T3							
Processing Speed	33	-1.067	0.549	44	-0.941	0.397	0.5153
Reaction Time	33	0.004	0.027	44	-0.018	0.037	0.2758
Attention	31	1.951	1.762	41	0.655	1.888	0.2114
Memory	34	0.603	0.299	44	-0.173	0.331	<.0001
Desat Subgroup AUT	33	303.33	[135.68, 1351.57]	31	1247.62	[448.57, 3059.98]	0.017 b

Change in cognitive test scores, adjusted for days, years of education, age and baseline test score. Means and (SE) are least squares means and standard errors.

S-80.

CEREBRAL HYPEREMIA FOLLOWING CIRCULATORY ARREST IN HUMANS

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INTRODUCTION: Deep hypothermic circulatory arrest (DHCA) is commonly employed to facilitate surgery on the aorta and great vessels. Although cooling dramatically reduces the cerebral metabolic rate, it does not prevent the occurrence of ischemia, which can be documented by electrophysiologic and metabolic markers after as little as 15 minutes.[1] The availability of non-invasive qualitative measures of relative changes in cerebral flow (cerebral flow index-CFI) allow the assessment of the hemodynamic effects of this ischemia.

METHODS: Eight patients undergoing DHCA were monitored for cerebral flow index (CFI) using c-FLOW monitors (Ornim, Inc.). CFI was recorded continuously and averaged in1 minute epochs throughout cardiopulmonary bypass (CPB) and DHCA. The pre-arrest baseline CFI was determined after cooling was complete and before beginning DHCA. The duration of DHCA was measured, and the time and value of the peak CFI after beginning reperfusion were recorded. Duration of hyperemia was measured from the beginning of reperfusion until CFI returned to pre-arrest baseline or began to increase due to rewarming. Duration of cooling prior to arrest and other aspects of case management were based on routine clinical care practices.

RESULTS: 6 patients had retrograde cerebral perfusion during the arrest period, one had "whole body retrograde", and one had no form of cerebral perfusion. One patient underwent 2 periods of circulatory arrest. The temperature at the start of DHCA averaged 20.4oC. The duration of DHCA averaged 29 minutes (range 20-56). On average, the peak CFI during reperfusion was 16% greater than the value before arrest (range 7-24), $P<0.01$. The time from the beginning of reperfusion to peak CFI ranged from 2 to 14 minutes, with an average of 6 minutes. The duration of hyperemia varied from 6 to 22 minutes with an average of 12.9 minutes.

CONCLUSIONS: These results demonstrate the occurrence of cerebral hyperperfusion following DHCA, even when retrograde perfusion is utilized. Hyperperfusion following ischemia has been associated with poor outcomes in both carotid endarterectomy and cardiac arrest[2,3], suggesting that this phenomenon should be avoided. Thus optimal management may require modifying perfusion parameters during the early stage of reperfusion in order to limit hyperperfusion.

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S-81.

SEDATION PRACTICE FOR TRANSTHORACIC ECHOCARDIOGRAPHY IN CHILDREN AGED 2-4 YEARS

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INTRODUCTION: Unlike young infants, most children aged 2 - 4 years are able to complete a detailed transthoracic echocardiogram (TTEcho) without sedation. A subset of these older children with neurologic or behavioral problems will obtain non-diagnostic quality echocardiograms due to motion artifact unless they are sedated or anesthetized. We hypothesized that the use of general anesthesia for TTEcho would decrease with the introduction of intranasal dexmedetomidine sedation.

METHODS: The study is a retrospective sedation log and chart review of patients aged 25 months – 48 months inclusive receiving sedation or anesthesia for transthoracic echocardiography. The first, historical cohort underwent sedation or anesthesia between July 2012 and Jun 2013. Intranasal dexmedetomidine was introduced in late 2013. The later cohort underwent sedation or anesthesia between July 2014 and June 2015. The primary variable was the method of sedation or anesthesia used for transthoracic echocardiography. The predominant techniques utilized were general anesthesia with sevoflurane with or without propofol infusion, enteral pentobarbital, or intranasal dexmedetomidine. A table of frequencies and percentages of the method of sedation or anesthesia was generated and we compared the proportions of general anesthesia with sevoflurance vs. other techniques in the two cohorts using a chi-square test.

RESULTS: During the 2012-2013 fiscal year, 161 children aged 25 - 48 months were sedated or anesthetized for TTEcho. During the 2014 - 2015 fiscal year, 125 children were sedated or anesthetized. The median age for patients presenting for possible sedation did not differ significantly between the two time periods (948 days and 937 days). There has been a 33% decrease in the use of sevoflurane anesthesia for TTEcho between fiscal year 2012 and 2014 ($P<0.0001$; 95%CI 22 -44) coincident with the adoption of intranasal dexmedetomidine sedation.

CONCLUSION: A previous report from our institution showed that sedation with oral pentobarbital for older children is less reliable and has lower family satisfaction than with infants.[1] Therefor, the predominant method of obtaining quality TTEcho scans in the 2 - 4 year age range children at our institution has been general anesthesia induction with sevoflurane with or without a subsequent propofol infusion. Since the introduction of intranasal dexmedetomidine to our practice, the proportion of these older children receiving sevoflurane general anesthesia for TTEcho has decreased from 70% to 37% and continues to decrease. Intranasal dexmedetomidine is utilized for sedation in at least 46% of these older children. The cost and charges for intranasal dexmedetomidine are significantly less than those for general anesthesia. Outcome data comparing sedation techniques will require a larger sample size and prospective data collection.

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S-82.

AN AUTOMATED CRITICAL CARE SYSTEM FOR PRESSOR AND FLUID TREATMENT OF HEMORRHAGE AND TRAUMATIC BRAIN INJURY IN SWINE

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INTRODUCTION: Severe bleeding associated with traumatic brain injury (TBI) requires stabilizing and minimizing secondary brain injury due to hypotension and hypoxemia. Hypotension occurring in the in the initial phase of resuscitation significantly increases mortality for patients with brain injury (Manley et al. 2001). We developed a prototype automated critical care system (PACCS) which titrates fluids and vasopressors to a target mean arterial pressure (MAP). Fluid therapy is the cornerstone strategy for treating hemorrhagic hypotension, but vasopressors can more quickly treat severe hypotension as shown in fig 1. Our two hypotheses are: 1) The PACCS can successfully resuscitate wine undergoing TBI + Hemorrhage. 2) Treating animals undergoing TBI + hemorrhage will require additional fluid and vasopressors compared to hemorrhage alone.

METHODS: Ten anesthetized swine were submitted to four separate bleeds at a rate of 1 ml/kg per minute. The first bleed lasted 10 minutes, after which the PACCS was activated and 3 more bleeds of 5 minutes each were administered at 15 minute intervals as shown in fig 2. Five animals received a contusion TBI prior to the hemorrhage protocol (HEM + TBI), while the other four underwent only hemorrhage (HEM-alone). Our PACCS is built with commercial off-the-shelf components including a vital sign transport monitor (Philips MP2), an intravenous drug pump (Body Guard), a rapid infusion fluid pump (Arcos Zoll PI) and a tablet PC (Panasonic Toughbook H2). The PACCS is functionally blind to the presence of TBI. The monitoring and treatment algorithms are identical in the two groups. The algorithms set infusion rates for IV fluids and phenylephrine (PHP) based on derivatives of arterial blood pressure. The fluid algorithm was a linear matrix based on MAP, and the PHP algorithm was a tuned proportional integral with anti-windup measures. Treatment objective was to maintain MAP at a target level of 80mmHg. Statistics were analyzed using Matlab, and Wilcoxon Rank-Sum was used for hypothesis testing.

RESULTS: The PACCS controlled MAP well for both groups of animals, system kept the MAP within 10 mmHg of the target 80% of the time in TBI+HEM animals and 83% of the time in HEM-Alone animals (p=0.79). The median MAPs of the two groups were 3 mmHg below target for HEM+TBI and 6 mmHg above target for Hem-Alone, showing a non-significant trend towards lower MAP in brain injured animals (p=0.14). The PACCS administered more PHP to the TBI+HEM group than to the HEM-Alone group (30.7 µg/kg vs 2.1 µg/kg, p=0.032). The PACCS also administered more IV fluids to the TBI+HEM group than the HEM-Alone group, but the difference between groups was not significant (35.6 ml/kg vs 23 ml/kg, p=0.15).

CONCLUSIONS: The PACCS maintained arterial pressure in animals impacted by both TBI and hemorrhage, but required more PHP to maintain MAP levels near the target level than for hemorrhage alone. The data suggest that a more aggressive pressor treatment may be needed in order to treat hemorrhagic hypotension with concurrent TBI.

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Fig. 1: Rapid Pressor Rescue With Fluid Support

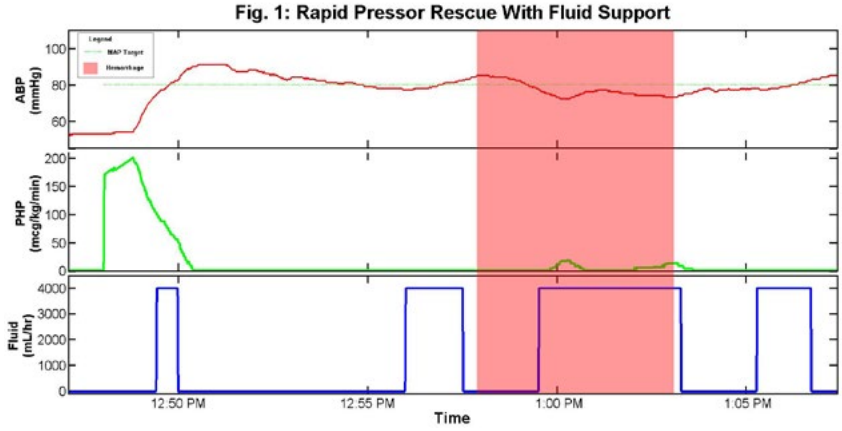
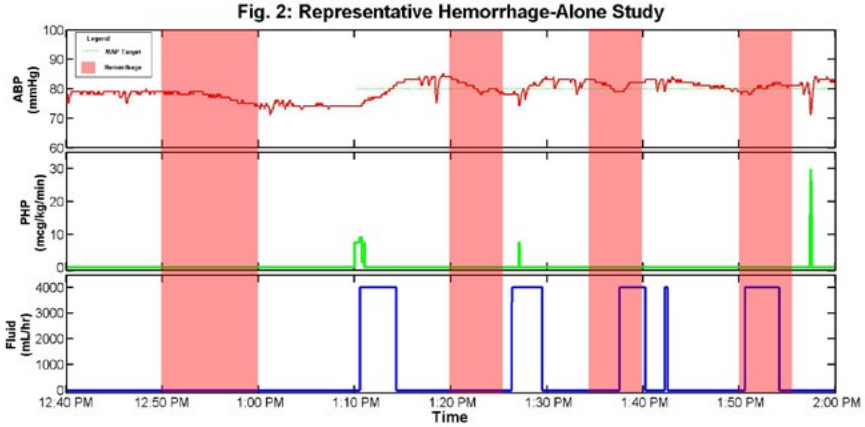


Fig. 2: Representative Hemorrhage-Alone Study



S-83.

A SYSTEMATIC REVIEW AND META-ANALYSIS OF INHALATION AGENTS FOR THE TREATMENT OF PULMONARY HYPERTENSION IN CARDIAC SURGICAL PATIENTS

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INTRODUCTION: In cardiac surgery, pulmonary hypertension (PH) is an important prognostic factor for which several treatments have been suggested over time. In this systematic review, we compared the efficacy of inhaled pulmonary vasodilators to placebo in the treatment of PH during cardiac surgery.

METHODS: We searched MEDLINE, CENTRAL, EMBASE, The Web of Science and clinicaltrials.gov databases up to October 2015 for randomized controlled trials comparing the efficacy of inhaled agents to placebo in cardiac surgical patients. Hemodynamic profile was assessed as the primary outcome. Secondary outcomes included mortality, length of stay in hospital and in intensive care unit, and mean dosage of inotropic and vasopressor agents.

RESULTS: Of the 2897 citations identified, 5 studies were included comprising a total of 211 patients.[1-5] No significant hemodynamically meaningful differences were observed between inhaled agents and placebo defined as heart rate, mean pulmonary artery pressure, mean arterial pressure, pulmonary vascular resistance, pulmonary capillary wedge pressure and central venous pressure (Table 1). Sensitivity analyses were consistent with these findings. Secondary outcomes could not be evaluated due to insufficient data.

CONCLUSIONS: A systematic review of the literature revealed that to date very few trials have reported on the efficacy of inhaled vasodilator agents compared to placebo. Furthermore, these are small trials with few participants. A meta-analysis of these studies reported no significant meaningful differences in hemodynamic variables between inhaled agents and placebo. Moreover, due to the limited number of studies reporting on the use of inhaled agents in cardiac surgical patients, the effect on clinically relevant end-points could not be assessed. Further research is therefore warranted in this area of research and should focus on clinically significant outcomes.

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Table 1. Outcome Measures, Hemodynamic Variables

Outcome	Studies	Study Reference No.	No Patients in Inhaled Treatment Group	No patients in Control (Placebo) Group	Mean Difference (95% CI)	I^2 (P value) %
Heart rate (beats/min)	3	2, 4-5	84	81	-3.16 (-8.56, 2.24)	16 (0.25)
Mean arterial pressure (mmHg)	4	1-2, 4-5	90	86	-2.56 (-10.51, 5.39)	55 (0.53)
Mean pulmonary artery pressure (mmHg)	4	1-2, 4-5	90	86	-1.24 (-5.87, 3.38)	44 (0.60)
Pulmonary vascular resistance (dyne.sec.cm-5)	4	3-5	88	86	-22.64 (80.80, 35.53)	61 (0.45)
Pulmonary capillary wedge pressure (mmHg)	4	2-5	98	96	0.09 (-2.51, 2.69)	48 (0.94)
Central venous pressure (mmHg)	4	2, 4-5	84	81	-0.80 (-2.30, 0.70)	0 (0.30)

Abbreviations: 95% CI, 95% confidence interval

Subspecialty Abstracts

Critical Care

S-84.

THE ROLE OF PDE4 IN IL-8-DEPENDENT INHIBITION OF CAMP-STIMULATED ALVEOLAR FLUID CLEARANCE IN A MURINE MODEL OF TRAUMA-HEMORRHAGE

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INTRODUCTION: Stimulation of the beta2-adrenergic receptor (β2-AR) can increase cAMP-mediated alveolar fluid clearance (AFC) in both animals and humans. However, in patients with acute respiratory distress syndrome (ARDS), treatment with β2-agonists has failed in two phase III clinical trials[1]. Multiple studies have determined that the β2-AR is heterologously phosphorylated and internalized after activation of the interleukin-8 (IL-8) receptor or transforming growth factor-beta receptor in respiratory syncytial virus infection or trauma-hemorrhage (TH)[2,3]. Inhibition of the β2-AR by these inflammatory mediators was phosphatidylinositol-3-kinase-dependent and led to decreased cAMP mobilization by β2-agonists. We hypothesized that inflammatory mediators induce β2-AR trafficking and signaling defects that can be reversed by rolipram, a phosphodiesterase (PDE) 4 inhibitor that increases cAMP levels. Roflumilast, a clinical PDE4 inhibitor, is used in chronic obstructive pulmonary disease and asthma as an adjunct to β2-agonist therapy.

METHODS: In alveolar epithelial cells after exposure to IL-8, we determined the internalization and recycling of the β2-AR and the spatiotemporal mobilization of specific cAMP pools in response to β2-agonists. Furthermore, we used a murine model of TH (in which IL-8 is increased in the lung) to determine β2-AR-mediated AFC. Rolipram was used to determine whether PDE4 inhibition could prevent or reverse IL-8-dependent effects. All studies were approved by the IACUC at UAB.

RESULTS: IL-8 exposure initiated internalization of the β2-AR and decreased β2-agonist-dependent cAMP mobilization in cytoplasmic pools. Furthermore, after internalization, the β2-AR did not recycle back to the cell surface. Pretreatment with rolipram prevents IL-8-mediated internalization of the β2-AR and altered mobilization of specific cAMP pools. Furthermore, after IL-8-dependent internalization of the β2-AR, treatment with rolipram restores recycling of the β2-AR. Finally, in a murine model of TH, treatment with rolipram after TH restores β2-AR-mediated AFC.

CONCLUSIONS: Our results provide a mechanism by which inflammatory mediators released during critical illness inhibit normal functioning of the β2-AR. Furthermore, we have revealed that pre- or post-treatment with a PDE4 inhibitor can reverse these effects. While this study focuses specifically on IL-8 effects and β2-AR-mediated AFC, these results are likely similar for other inflammatory mediators increased during critical illness and other organ systems in which β2-AR activation is vital for normal function such as the innate immune system and vascular smooth muscle.

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S-85.

ASSOCIATION BETWEEN PLASMA UCHL1 AND BDNF LEVELS AND DURATION OF DELIRIUM IN THE CRITICALLY ILL

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INTRODUCTION: Delirium is an acute form of brain dysfunction that is prevalent in the ICU, occurring in up to 80% of mechanically ventilated patients.1 It has significant short and long-term effects on morbidity and mortality but an incompletely understood pathogenesis.[1] One hypothesis is that critical illness such as sepsis leads to neuroinflammation, resulting in direct neuronal injury and altered neurotransmission.[2] Two plasma biomarkers associated with neuronal injury and repair include ubiquitin carboxyl-terminal esterase-L1 (UCHL1) and brain-derived neurotrophic factor (BDNF), but their associations with delirium in the critically ill are unknown. UCHL1 removes misfolded proteins in the brain, potentially preventing these damaged proteins from interfering with brain function.3 BDNF is involved in plasticity and protects the brain from injury by inhibiting apoptosis and stimulating neuronal repair.3 Due to their role in repairing organic brain pathology, we hypothesized that higher plasma levels of UCHL1 and BDNF would be associated with shorter duration of delirium in critically ill patients.

METHODS: We enrolled adult patients in respiratory failure and/or shock within 72 hours of being admitted to the medical or surgical ICU. Plasma concentrations of UCHL1 and BDNF were measured upon enrollment. Delirium was assessed twice daily by trained research personnel using the CAM-ICU. Negative binomial regression was used to examine the independent association between biomarker plasma concentrations and delirium, adjusting for severity of illness using cardiovascular SOFA score and APACHE II score, baseline cognition using the IQCODE score, comorbid disease using the Charlson score, Framingham stroke risk profile, presence of severe sepsis, and allowing for interactions with age and IL-6 plasma concentration.

RESULTS: In our cohort of 419 patients, median (interquartile range) age was 59 (48, 69), 50% were severely septic at enrollment, and the median APACHE II score was 25 (19, 30). 76% of patients developed delirium with a median duration of 3 days (2, 6.5). Higher plasma concentration of UCHL1 was independently associated with shorter duration of delirium (P = 0.036, Figure 1), and this association was not modified by age or IL-6 plasma concentration. There was no association between BDNF plasma concentration and duration of delirium (P = 0.51).

CONCLUSION: Higher plasma concentration of UCHL1, but not of BDNF, is independently associated with shorter duration of delirium in the critically ill. This suggests that increased proteasome pathway activity in the brain might have a protective effect on acute brain function during critical illness, potentially through increased ability to clear damaged protein aggregates. Further studies are needed, including studying UCHL1 plasma concentrations at multiple time points during critical illness to assess whether its association with delirium changes over time in response to disease progression and/or medical therapy.

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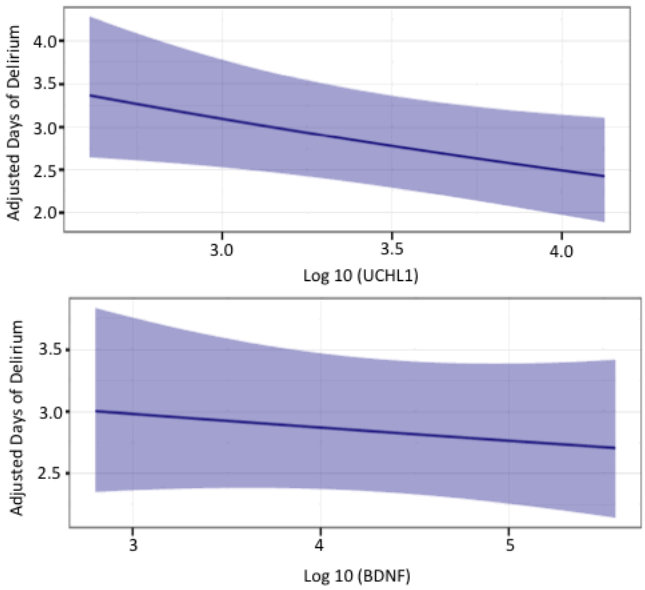
Figure 1: UCHL1 and BDNF vs Delirium Duration



S-86.

THE ENDOCANNABINOID *N*-ARACHIDONOYL DOPAMINE MODULATES TOLL-LIKE RECEPTOR AGONIST ACTIVATION OF INFLAMMATION IN MICE VIA TRPV1

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INTRODUCTION: Endocannabinoids are endogenous arachidonic acid-derived lipid mediators. We recently discovered that the endocannabinoid N-arachidonoyl dopamine (NADA) reduces human endothelial cell activation by microbial inflammatory agonists. NADA is known to activate TRPV1, an ion channel that has established roles in nociception and thermoregulation. TRPV1 has primarily been studied in the nervous system, but it is also expressed in non-neuronal tissues. Although TRPV1 has been reported to modulate immune responses, little is known about the role of TRPV1 in acute inflammation and sepsis. We hypothesized that NADA modulates inflammatory responses in mice challenged with microbial Toll-like receptor (TLR) agonists, and that NADA exerts its immunomodulatory effects via TRPV1.

METHODS: 8-wk old wild-type (C57BL/6, CD45.2) and TRPV1 KO mice (n = 4-6/group) were treated with NADA (IV) and then challenged IV with LPS (TLR4) or bacterial lipopeptide (Pam3Cys, TLR2). Cytokines, chemokines and plasminogen activator inhibitor-1 (PAI-1) were quantified in plasma, and blood oxygen saturation was non-invasively recorded 2h post-treatment. In bone marrow chimera studies 8-week old C57BL/6 (CD45.1) mice were irradiated and then transfused with hematopoietic stem cells from age-matched wild-type (CD45.2) or TRPV1 KO (CD45.2) mice. Nine weeks after reconstitution, mice were challenged with LPS in the presence and absence of NADA ($n \geq 5$/group), and plasma levels of inflammatory mediators and PAI-1 were quantified after 2h. Successful reconstitution was confirmed using flow cytometry for appropriate markers. Data were analyzed using Mann-Whitney tests; P values < 0.05 were considered significant. Studies were approved by our institution's IACUC.

RESULTS: Treatment with NADA reduced plasma levels of IL-6, TNF-alpha, and PAI-1 in wild-type mice challenged with LPS and Pam3Cys, whereas NADA augmented the production of the anti-inflammatory cytokine IL-10. These effects of NADA on LPS-induced inflammation and PAI-1 were absent in TRPV1 KO mice. NADA treatment also ameliorated the drop in oxygen saturation in endotoxemic wild-type mice. In contrast to the results with total TRPV1 KO mice, chimeric mice that exclusively express TRPV1 outside of the hematopoietic compartment remained just as responsive to NADA's effects as wild-type mice.

CONCLUSION: Our results indicate that the endocannabinoid NADA modulates inflammation and coagulopathy induced by endotoxin and bacterial lipopeptide, and that TRPV1 is required for NADA's immune modulating effects in vivo. Furthermore, the chimera study suggests that NADA's effects are entirely dependent upon non-hematopoietic TRPV1. Maladaptive responses in sepsis are believed to result in part from the failure to resolve inflammation, and pro-resolving lipid mediators such as resolvins have been implicated in the resolution of inflammation. Our study suggests that NADA may represent a novel endogenous lipid mediator that promotes the resolution of inflammation, and that the endocannabinoid system and TRPV1 may contribute to therapeutic strategies for sepsis.

S-87.

COMPARISON OF THE MULTIPLE COAGULATION TEST SYSTEM (MCTSTM) WITH EXISTING COAGULATION TESTS, IN FIVE IN-VITRO MODELS OF COAGULOPATHY

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INTRODUCTION: Coagulation tests are "diagnostic". They confirm abnormal coagulation, but do not guide treatment. The Multiple Coagulation Test System™ is a "theranostic". Rather than just indicating coagulation is abnormal, the MCTS is designed to indicate optimal therapy(ies) to improve hemostasis.

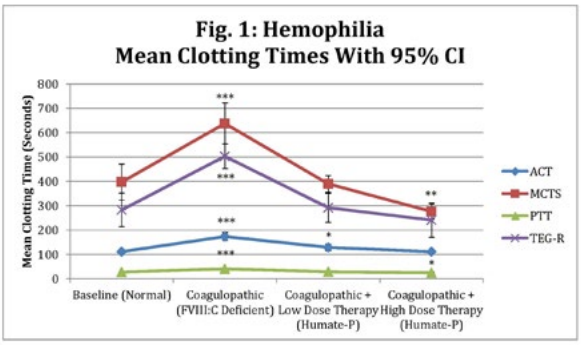
METHODS: With informed consent and IRB, blood of healthy volunteers was citrated. Coag tests were performed at steps A (normal blood); B (coagulopathic blood); C (coagulopathic blood + low-dose therapy); and D (coagulopathic blood + high-dose therapy). A, B, C, D steps were performed in 5 in-vitro models of coagulopathy: Hemophilia, von Willebrand Disease, Dilution, Hypofibrinogenemia, Factor VII deficiency. Coagulopathic blood was created by centrifuging whole blood, removing platelet-poor plasma, and replacing it with: Factor VIII-deficient plasma, VWF-deficient plasma, 5% albumin, fibrinogen-deficient plasma and F:VII-deficient plasma for the 5 experiments respectively. At A, B, C, D tests included: MCTS Clotting Time (MCTS-CT), ACT, PT, INR, PTT, TEG-R, TEG-K, TEG-α angle, and these factors for each coagulopathy: Hemophilia- F:VIII; VWD-VWF Antigen, Ristocetin cofactor and F:VIII; Dilution-Fibrinogen and F:VIII, as surrogate markers; Hypofibrinogenemia- Fibrinogen; Factor VII deficiency-F:VII. Ability of tests to differentiate coagulopathy (B) from normal (A), and return towards normal with therapy (C, D) was assessed with mixed model linear regression. In four experiments MCTS-CT was compared to ACT, PTT, TEG-R, TEG-K, TEG-α angle, and factors measured for coagulopathies with Pearson Correlation Coefficient. For F:VII deficiency, CC between MCTS-CT and PT/INR was also performed. $p < 0.05$ considered significant.

RESULTS: Multiple tests, including the MCTS, confirmed coagulopathy at B, and return towards normal at C and D in the first four experiments (See Figs. 1-4). F:VII deficiency did not display consistent prolongation of clotting at B, possibly due to activation of only intrinsic pathway with kaolin in the presence of platelets activated by centrifugation. Still, treatment with F:VII resulted in increased clot formation at C and D. The MCTS demonstrated good to excellent correlation with existing FDA-cleared tests in the five experiments (See Table 1).

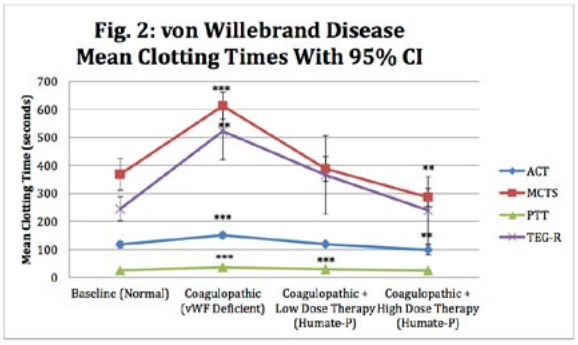
CONCLUSIONS: Evaluation of coagulopathies may require multiple diagnostic coag tests, with results in 0.5 – 2 hours, even days for some factor levels. TEG requires a trained user, 12-15 mins to obtain an initial tracing, longer to obtain a full tracing, and one sample does not guide treatment. If a fully automated MCTS, with 10 mins to results and treatment guidance is achieved, it would provide advantages over existing tests. Furthermore, use of MCTS cartridges pre-filled with reagents will eliminate the possibility of human error. In summary, the MCTS demonstrated good correlation with existing coagulation tests in blood with varying states of hemostasis, in five models of coagulopathy. Work is planned to assess efficacy of MCTS cartridges pre-filled with therapies.

Pearson Correlation Coefficient (p-value)

	MCTS Hemoph	MCTS VWD	MCTS Dilution	MCTS HypoFIB	MCTS FVII-Deficient
ACT	.84 (<.0001)	.72 (<.0001)	.996 (<.0001)	.98 (<.0001)	.76 (<.0001)
PTT	.81 (<.0001)	.86 (<.0001)	.94 (<.0001)	.98 (<.0001)	.74 (<.0001)
TEG-R	.92 (<.0001)	.70 (<.0001)	.51 (<.0001)	.64 (<.0001)	.88 (<.0001)
TEG-K	.53 (.0076)	.47 (.024)	-.12 (.60)	-.0043 (.98)	.31 (.086)
TEG-α angle	-67 (.0003)	-60 (.0024)	-.75 (<.0001)	-.48 (.001)	-46 (.008)
F:VIII	-65 (.0011)	-.63 (.0009)	-.63 (<.0001)	–	–
Ristocetin Cofactor	–	-.73 (<.0001)	–	–	–
Fibrinogen	–	–	-.63 (.0001)	-.27 (.073)	–
F:VII	–	–	–	–	-62 (.0001)



* = p < 0.05; ** = p < 0.01; *** = p < 0.001



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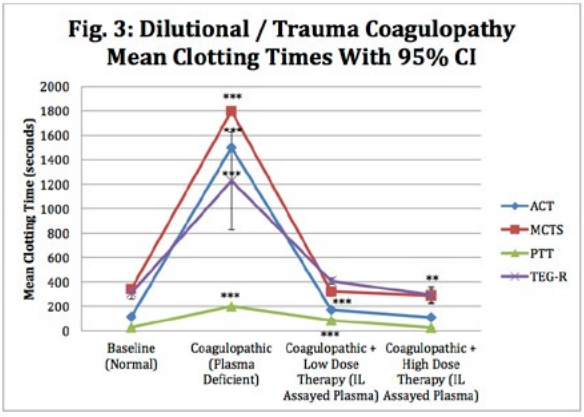

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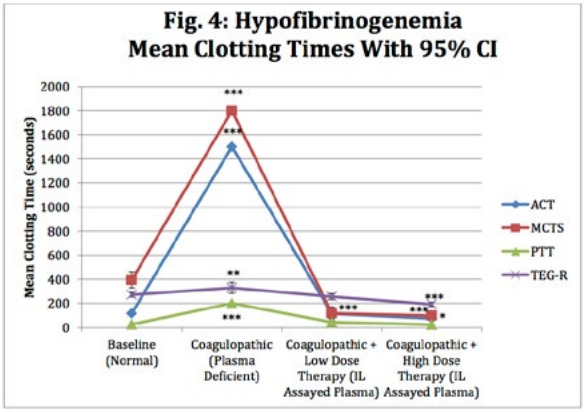

* = p < 0.05; ** = p < 0.01; *** = p < 0.001

S-88.

EFFECT OF IMMUNOGLOBULIN ON VIRULENCE OF PSEUDOMONAS AERUGINOSA IN VITRO CYTOTOXICITY ASSAY

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INTRODUCTION: *Pseudomonas aeruginosa* is an opportunistic pathogen that is associated with lethal systemic infections in immuno- compromised hosts, such as cystic fibrosis. In P. *aeruginosa* pneumonia, acute lung injury is associated with the virulence of the bacterial type III secretion system (TTSS). V-antigen (PcrV) is a trans-locational component of the P. *aeruginosa* TTSS. In the translocation process of TTSS, PcrV which is located at the tip of the secretory needle apparatus, is indispensable to toxication of the target eukaryotic cells. In our previous studies, we have reported that the specific antibodies against PcrV can inhibit the toxin translocation in animal models. In addition, we have recently also reported that commercially produced gamma-globulin solution (IVIG) had a significantly protective effect against lethal infection from virulent *P.aeruginosa* in a mouse model. In this study, we evaluated the effects of IVIG on the type III secretion-associated virulence in vitro cellular damage experiment.

METHOD: A macrophage-like cell line, J774 was cultured in RPMI1640 with 10% heat-inactivated fetal bovine serum with penicillin and streptomycin. When the cells reached confluence, they were transferred to 96 well tissue culture plates and incubated overnight. The next day, the J774 cells(2×10^4/well) pre-treated with IVIG or albumin(100ug/well) were then exposed to *P.aeruginosa* PA103 strain(1×10^7CFU/ml). (MOI=10) The strain was mixed with RPMI1640 with 25mM HEPES and applied to the cells. After a 3h incubation at 37°C with 5%CO_2, cytotoxicity was measured by the release of lactate dehydrogenase using a cytotoxicity assay kit (Cytotox 96non-radioactive cytotoxicity assay; Promega, USA)

RESULT: When IVIG was added to the culture medium of J774 cells, the cytotoxicity of PA103 strain fell (about 40% loss of viability). In contrast, the addition of albumin had no effect. That is to say the cytotoxicity levels remained completely the same and caused about 70% loss of viability. These results suggested that IVIG inhibited PA103 cytotoxicity for J774.

DISCUSSION: IVIGs are produced from the pooled plasma samples from around 1000 to 15000 healthy volunteers and have been proposed as an adjunctive therapy for severe infections and sepsis. However, MDR-PA (multi-drug resistant *P.aeruginosa*) has recently spread all over the world and *P.aeruginosa* strains displaying the cytotoxic phenotype are increasing. The results of our experiment have shown that IVIG has a potent TTSS neutralization ability and protects cells in culture from exotoxin mediated cytotoxicity. Since the PA103 strain secretes the ExoU exotoxin, which is highly cytotoxic, and the mechanism of cell killing is depend on TTSS, this shows that IVIG can be used to combat MDR-PA.

S-89.

MODES OF DEATH IN A JAPANESE PEDIATRIC INTENSIVE CARE UNIT

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INTRODUCTION: In previous studies, modes of death in pediatric intensive care units (PICUs) varied among countries, and 18-70% patients died after limitation of life-sustaining treatment (LST)[1,2]. Little is known about the end of life in Japanese PICUs. Our purpose was to examine modes of death in a Japanese PICU. The secondary purpose was to disclose the time to death after the decision of limiting LST and to describe what kinds of medical supports were provided at the end of life in patients whose LSTs were limited.

METHODS: This was a retrospective observational study, based on medical chart review at a single PICU from 2010 to 2014. All the patients who died in our PICU and those who were discharged from the PICU to general wards to receive terminal care were included. All deaths were classified into 1 of 3 groups; limitation of LST (limitation group, withholding or withdrawal of LST or do not resuscitate order), no limitation of LST (no-limitation group), or brain death. Data were collected from medical records and included age, sex, diagnosis, length of stay in the PICU, pediatric index of mortality 2, admission status (scheduled/emergent, postoperative, post- cardiopulmonary resuscitation). The time to death after the decision of limiting LST and LSTs provided at the end of life were also examined in the limitation group. The continuous numeric variables were compared using the Mann-Whitney's U test, and the categorical data were compared with Chi square test with Yates' correction. $P < 0.05$ was considered statistically significant.

RESULTS: There were 62 deaths (3.3%) in 1894 patients admitted to our PICU. The mode-of-death category distribution was as follows: limitation of LST 44(71%); no limitation of LST 18 (29%); there was no brain death. Demographic data were shown in Table 1.

The length of the PICU stay for the limitation group was longer than that for the no-limitation group (13.5vs 2.5 days; p=0.01), and the admission after cardiopulmonary resuscitation was less frequently observed in the limitation group than in the no-limitation group (6.8%vs 28% days; p=0.04). In the limitation group, the median time to death after the decision was shown in Figure1 (median; 2 days, interquartile range; 1 to 5.5 days).

LSTs provided at the end of life were described in Figure 2. Mechanical ventilation and vasopressor were continued more frequently than the previous study[3].

CONCLUSIONS: Limitation of LST was the most common mode of death in a Japanese PICU. The time to death after the decision of limiting LST was longer than that of the previous study 3, and not a few LSTs were provided at the end of life.

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Table1. Demographic data

	Total	limitation	no-limitation	p Value
N	62	44(71%)	18(29%)	
Age (mo): median	24	24	54	Ns
Male patients	32(52%)	19(43%)	13(72%)	Ns
Length of stay (days): median	8.5	13.5	2.5	0.01
Pediatric index of mortality 2	7.30%	9.20%	6.80%	Ns
Admission status				
Scheduled	22(35%)	14(32%)	8(44%)	Ns
Post- operative	22(35%)	15(34%)	7(39%)	Ns
Post- cardio pulmonary resuscitation	8(13%)	3(6.8%)	5(28%)	0.04
Diagnosis				
Cardiovascular	19(31%)	16(36%)	3(17%)	Ns
Respiratory	9(15%)	7(16%)	2(11%)	Ns
Hematologic	20(32%)	13(30%)	7(39%)	Ns
Neurologic	9(15%)	5(11%)	4(22%)	Ns
Others	5(8%)	3(6.8%)	2(11%)	Ns

Figure1. The time to death after the decision-making in the limitation group

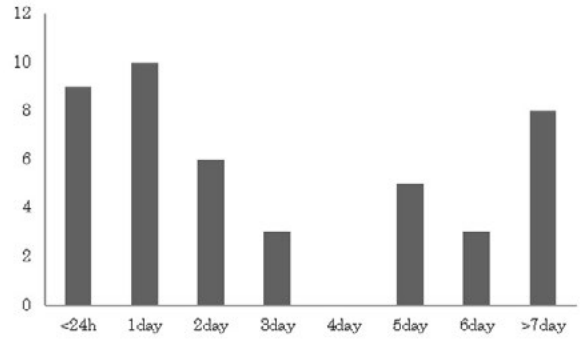
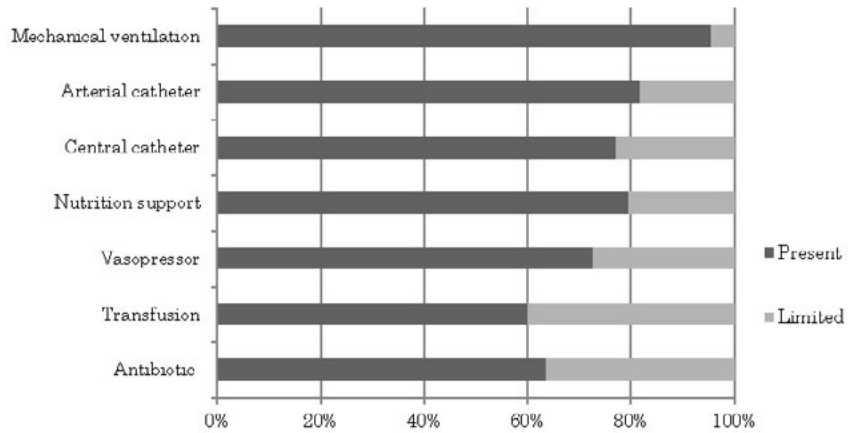


Figure2. LSTs provided at the end of life in the limitation group



S-90.

EVALUATION OF A NOVEL NON-INVASIVE VOLUME ASSESSMENT DEVICE CREATED TO OBSERVE THE EFFECTS OF INTRAVASCULAR VOLUME ON VASCULAR WAVEFORM HARMONICS OF HUMAN SUBJECTS: A PROOF OF CONCEPT PILOT STUDY

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Heart failure is projected to affect 8 million people by 2030.[1,2] Current recommendations of treatment focus on having patients monitor their symptoms and fluctuations in weight which suggest fluid retention.[3] Fluid status is difficult to monitor and current studies have shown promise with implantable monitors but these prove very invasive and expensive.[4,5] This study is a proof of concept pilot study of a novel Non-Invasive Volume Assessment (NIVA) device to observe the effects of intravascular volume on vascular waveform harmonics.

METHODS: Healthy controlled subjects (n=10) and patients with congestive heart failure (CHF) (n=8) were enrolled under an Institutional Review Board approved protocol. Using piezoeclectric sensors secured to the ventral side of the wrist of each subject, we obtained continuous, non-invasive, real-time data of their vascular waveform harmonics. Both arterial and venous waveforms were simultaneously measured and recorded (figure 1). The sensor was then interfaced with LabChart (ADInstruments, Colorado Springs, CO, USA) software analysis.

RESULTS: A significant signal power at higher harmonics was identified in patients with untreated CHF, and a general shift to lower harmonics in patients following diuretic therapy (figure 2). There was a significant change in vascular harmonics from a volume overload state, and at various treatment intervals of volume removal (figure 3). Notably, healthy control subjects had paucity of high frequency venous harmonics compared to CHF patients. Additionally, there was a significant change in the venous harmonics between patients with a urine output of 1000-1500mL versus >1500mL during diuresis (figure 4).

CONCLUSIONS: This piezoelectric evaluation of vascular harmonics could provide a real time measurement of intravascular volume status. This non-invasive information could prove valuable with the growing CHF population.

Funded by The National Science Foundation NSF 15-545 STTR Phase I

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Figure 1

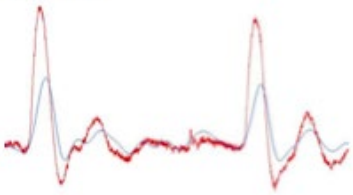

Figure 2

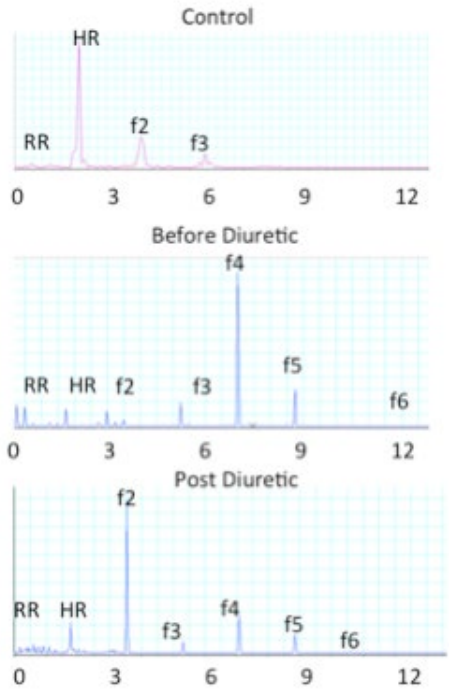

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Figure 3

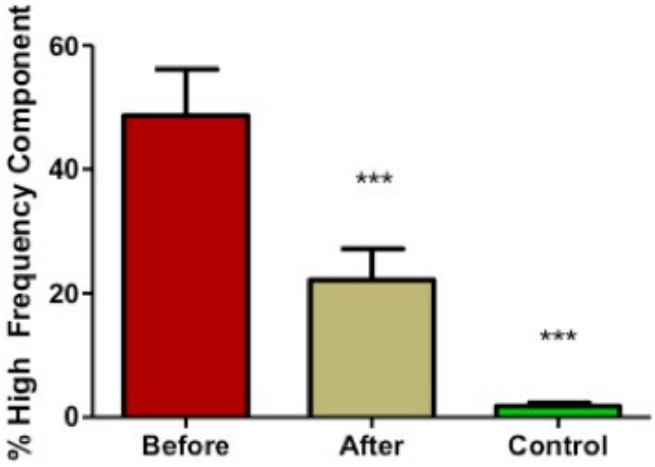
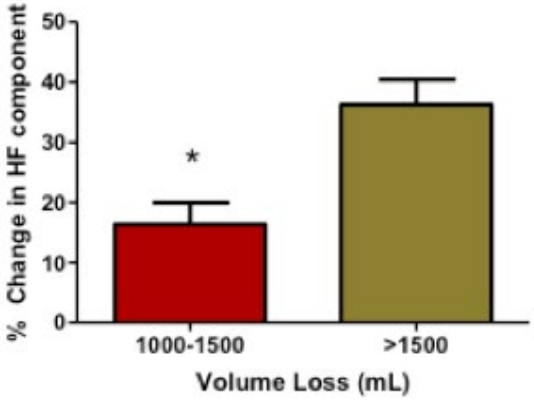


Figure 4



S-91.

A PROSPECTIVE OBSERVATIONAL PILOT STUDY OF ICU SEDATION VARIATION USING BISPECTRAL INDEX TO IDENTIFY DIURNAL PATTERNS RELATED TO CHANGE OF NURSING SHIFTS

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INTRODUCTION: The appropriate use and dosing of IV sedatives in mechanically ventilated intensive care unit (ICU) patients is key in preventing adverse effects[1] including prolonged mechanical ventilation[2] and delirium.[3] Intensivists often have the notion that patients may be oversedated in the nighttime hours despite protocol-based techniques. Although multiple sedation assessment scales are for sedation regimens, subjective differences have been found in the assessment of sedation levels between day and night caregivers, with night caregivers being less likely to judge patients as oversedated.[4] Bispectral index (BIS) for monitoring sedation in the ICU has been correlated with multiple clinical sedation scales[5,6] and can be useful for objective monitoring during deeper levels of sedation.[7] The objective of this study is to determine if shift time is associated with level of sedation. We hypothesized that patients during night shifts are maintained at deeper levels of sedation.

METHODS: We prospectively enrolled 34 trauma and acute care surgery ICU patients that were mechanically ventilated and sedated with continuous IV infusion of either propofol or midazolam along with fentanyl infusions for analgesia. The patients had BIS monitors placed and data collected for a period of 24 hours. BIS data was recorded every minute while the signal quality index (SQI) was above 80 indicating a good signal for each patient. The BIS values for each patient for day (0700-1900) and night (1900-0700) shift were separated and averaged. (Fig1) Paired T-tests were performed to detect differences between day shift and night shift BIS values. (Fig2)

RESULTS: The BIS values were averaged for each shift per patient demonstrating no significant difference between mean day and night shift BIS values (52±13.2 vs 50.6±14.6, p=0.27). (Fig 3)

CONCLUSIONS: Despite sentiment amongst critical care physicians that patients are oversedated during night shift as compared to the day, BIS values were no different between shifts. The data did demonstrate that patients were oversedated throughout the observation period as BIS values averaged 52 and 50.6, while values between 45 to 60 are consistent with general anesthesia. This data is consistent with findings that there is also loss of synchronized sleep-wake cycles in sedated ICU patients[8] as there was no diurnal BIS variation which is seen in physiologic sleep.[9,10] These findings suggest that although patients are oversedated in our ICU, no differences in sedation practices is evident based on objective BIS data between day and night shift.

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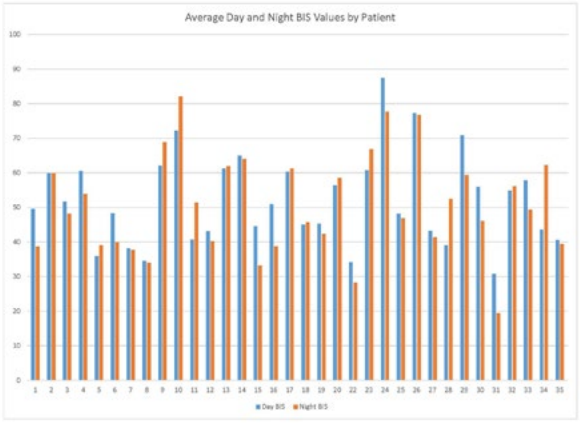


Paired t: Day, Night

Descriptive Statistics

Sample	N	Mean	StDev	SE Mean
Day	34	52.036	13.168	2.258
Night	34	50.610	14.603	2.504

Estimation for Paired Difference

Mean	StDev	SE Mean	95% CI for μ_d
1.426	7.554	1.295	(-1.209, 4.062)

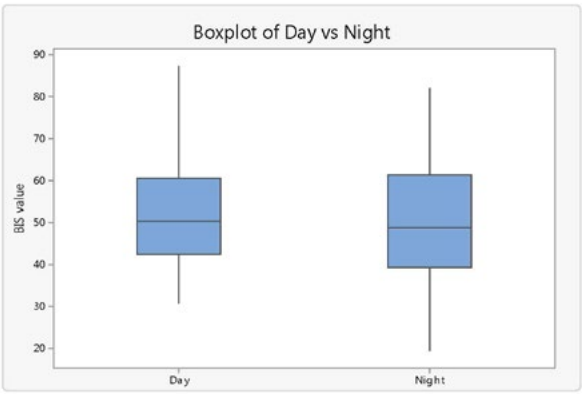
μ_d: mean of (Day - Night)

Test

Null hypothesis H_0: $\mu_d = 0$
Alternative hypothesis H_1: $\mu_d \neq 0$

T-Value	P-Value
1.10	0.2789

Boxplot of Day, Night



Summary Statistics

Variable	N	Minimum	Q1	Median	Q3	Maximum	95% Median CI
Day	34	30.730	42.448	50.265	60.623	87.360	(44.462, 58.059)
Night	34	19.410	39.288	48.760	61.380	82.040	(41.219, 58.598)

S-92.

LOW PULMONARY COMPLIANCE IS PREDICTIVE OF EXTUBATION FAILURE

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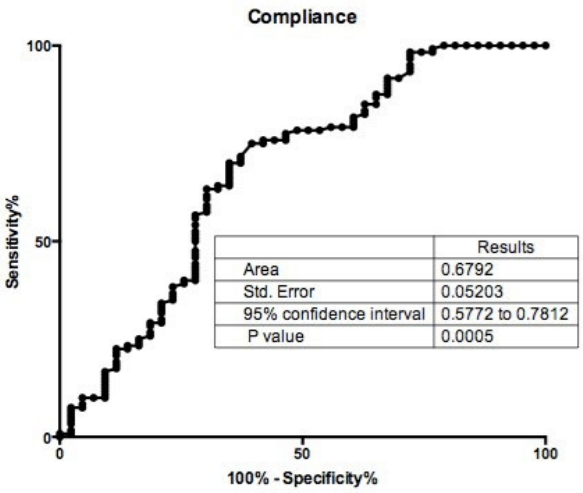
INTRODUCTION: Extubation failures are associated with a number of negative outcomes including pneumonia, prolonged mechanical ventilation and increased mortality. Pulmonary mechanics e.g., frequency to tidal volume ratio [F/TV < 100], maximum negative inspiratory pressure [-NIP < -20] and vital capacity [VC > 10 mL/kg] are commonly used along with other clinical assessments to predict the likelihood of a successful extubation. Pulmonary compliance (Cstat & Cdyn) is a critical component of respiratory mechanics and therefore likely impact extubation success. We hypothesized that a low pulmonary compliance would be associated with extubation failure.

METHOD: This retrospective analysis was conducted in patients intubated for 3 or 4 days in the Surgical Intensive Care Unit at our institution from January 2012 to December 2014. The exclusion criteria included presence of tracheostomy, withdrawal of care or death prior to extubation. Patients were stratified based on extubation disposition e.g., success versus failure if re-intubation was required within 7 days. Respiratory mechanics (F/TV, -NIP and VC) were performed within 12 hours of extubation using minimal CPAP. Static and dynamic [Cstat & Cdyn] compliance readings were calculated from ventilator data: TV/[(peak [Cstat] or plateau [Cdyn] pressure) - (PEEP)] one hour before CPAP trial.

RESULTS: Of the 223 patients that met criteria and analyzed, 170/223 (76%) extubated successfully whereas, 53/223 (24%) failed extubation and required re-intubation within 7 days. Failed extubation was associated with increased mortality (58% vs 85% for successful extubation). Traditional pulmonary mechanics favored the successful extubation group vs failed extubation group. Specifically, the F/T [56±2 vs 69±6 (p=0.003)], NIP [-33 ± 1 vs -27 ±2 mmHg (p=0.008)] and VC [945±65 vs 720 ±50 (p=0.06)] for successful vs failed, respectively. Pulmonary compliance: Cstat was 34±2 vs 28±3 (p=0.06) and Cdyn 46±3 vs 33±3 (p=0.007) were similarly discriminatory. Receiver operator characteristic curves were used to calculate the area under curve (AUC) with 95% confidence intervals [CI]. The AUC ranked from lowest to highest: F/T 0.59±0.05 [CI: 0.49 - 0.70], NIP 0.64±0.47 [CI:0.54 - 0.73], VC 0.65±0.05 [CI:0.54 - 0.75, Cstat 0.65±0.05 [CI:0.55 - 0.74] and Cdyn 0.68±0.05 [CI:0.57 - 0.78].

CONCLUSION: Our results show that although extubation criteria were in general met for both the successful and failed groups, the failed extubation group had lower static and dynamic pulmonary compliance. Further, reduced pulmonary compliance [Cdyn < 33] is a moderate indicator and increased likelihood (2-fold) of extubation failure. Although this data are descriptive, reduced compliance increases work of breathing, which likely contributes to extubation failure. Compliance values can be surveyed from ICU ventilators and could be used to judge adequacy of weaning. Further prospective studies are needed to determine if compliance can be used to predict extubation success. Research supported by US Army of DOD award #W81XWH-12-1-0598



Demographics and Pulmonary Mechanics (Mean± SEM)

	Success	Failed	Statistics
Male	103	29	
Female	67	24	
Age	53±2	59±3	0.012
Survival	85%	58%	<0.001
NIP	-33±1	-27±2	0.008
F/T	56±2	69±6	0.003
VC	945±65	720±50	0.06
Static Compliace	34±2	28±3	0.06
Dynamic Compliance	46±3	33±3	0.007

S-93.

WITHDRAWN.

S-94.

RAB8 GTPASE IS REQUIRED FOR MACROPHAGE EFFEROCYTOSIS AND RESOLUTION OF LUNG INFLAMMATION IN MICE

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INTRODUCTION: Efferocytosis, or phagocytosis of apoptotic cells by macrophages, is essential for resolution of inflammation and repair of damaged tissues,[1] however, the molecular mechanism involved remains elusive. After lung injury, recruited? neutrophils undergo apoptosis followed byand are subsequently phagocytizedosis by macrophages. The timely and efficient efferocytosis represents a critical step in tissue remodeling, level of (?) (what about??) modulation of immune responses, and resolution of lung inflammation. The impairment of efferocytosis is directly correlated with increased morbidity and mortality after lung inflammatory injury.[2,3] The small GTPase Rab8 has been shown to play an important role in the formation of lamellipodia, protrusions, and ruffles4 critical for phagocytosis. In the present study, we investigated the role of Rab8 GTPase in the regulation of macrophage efferocytosis and resolution of lung inflammatory injury.

METHODS: Neutrophil apoptosis was induced by ultraviolet light and then labeled with CellTracker™ Red. J774A.1 macrophages were transfected with control or Rab8A siRNA. At 48 h post-transfection, macrophages were labeled with CellTracker™ Green. Efferocytosis was assessed by fluorescence microscopy after co-incubation of macrophages with apoptotic neutrophils for 2 h. To examine the role of Rab8 expression in macrophages in resolution of lung inflammatory injury, mice were depleted of alveolar macrophages by intratracheal administration of clodronate liposomes and then challenged with lipopolysaccharide (LPS, 3.5 mg/kg i.p.). On day 3 following LPS challenge, saline or bone marrow-derived macrophages (BMDMs) transfected with control siRNA or Rab8A siRNA (2 × 106 cells, 200 µl total volume each) were given to alveolar macrophage-depleted mice via a jugular venous cannula. Resolution of lung inflammatory injury was assessed by analysis of bronchoalveolar lavage (BAL) fluid, lung wet/dry weight ratio, and biochemical/immunological analysis of lung tissue on day 5 after LPS challenge. Animal studies were approved by the Institutional Animal Care and Use Committee. All values were expressed as mean ± SD, and one-way ANOVA and Student Newman-Keuls test for post hoc comparisons were used to determine differences between control and experimental groups, with $p < 0.05$ regarded as significant.

RESULTS: Rab8A expression was reduced by >90% at 48 h posttransfection with a specific siRNA. Mouse PMNs were exposed to 15-min UV to induce apoptosis, and flow cytometric analysis showed that approximately 91% of PMNs were apoptotic as verified by annexin V-positive cells. Depletion of Rab8 in macrophages significantly inhibited the phagocytosis of apoptotic neutrophils compared with control siRNA-treated macrophages. Lavageable alveolar macrophage count was reduced by 95 % at 2 days following clodronate liposome nebulization. In vivo injection of BMDMs treated with a scrambled siRNA or Rab8A siRNA resulted in comparable reconstitution of macrophages in the lung. The total neutrophil count in BAL fluid increased by 8- fold and 5-fold after administration of LPS in control mice (without alveolar macrophage depletion) and alveolar macrophage-depleted mice, respectively. Mice depleted of alveolar macrophage before LPS challenge showed less PMN infiltration and lung edema formation. Alveolar macrophage-depleted mice receiving Rab8A siRNA-transfected BMDMs showed a significant increase in lung wet/dry weight ratio, neutrophil counts, and protein in BAL fluid compared with mice receiving control siRNA-transfected BMDMs on day 5 following LPS challenge. Importantly, a dramatic decrease in alveolar macrophages containing apoptotic bodies was found in macrophages obtained from BAL fluid of mice receiving Rab8A siRNA-transfected BMDMs.

CONCLUSIONS: We identified a crucial role for Rab8AGTPase in macrophage in the clearance of apoptotic neutrophils which in turn accelerates resolution of LPS-induced acute lung inflammation. Thus, modulation of Rab8A in lung macrophages may provide a promising strategy for the treatment of acute inflammatory injury and ARDS.

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S-95.

DELIRIUM RISK FACTORS IN CRITICALLY ILL CHILDREN

AUTHORS: H. A. Smith[1], M. Gangopadhyay[2], D. Fuchs[3], J. L. Thompson[4], R. Chandrasekhar[5], E. W. Ely[6], P. Pandharipande[7]

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INTRODUCTION: The recent validation of pediatric delirium monitoring tools, including the preschool Confusion Assessment Method for the Intensive Care Unit (psCAM-ICU) for use in children 6 months to 5 years of age, has demonstrated an alarming delirium prevalence of over 50% in critically ill infants and preschoolers during their ICU stay.[1] We undertook this prospective cohort study to elucidate possible risk factors for delirium in our most vulnerable patients.

METHODS: We enrolled critically ill patients aged 6 months to 5 years admitted to the pediatric medical ICU (PICU) and cardiac ICU (PCICU) of a tertiary medical center, and excluded those with hearing/visual impairments, those who were non-English speaking, moribund, or for whom the surrogates refused consent. Patients were evaluated for delirium using the psCAM-ICU for up to 14 daily assessments while in the ICU. Baseline demographic data and daily in-hospital information including medication exposure, presence of mechanical ventilation, and laboratory data were collected. Multivariable negative binomial regression was used to assess the associations of admission severity of illness (PRISM score), admission diagnosis of either sepsis or ARDS, history of cyanotic heart disease, exposure to benzodiazepines and opiates, cardiovascular SOFA score, mechanical ventilation, and hypoxia with delirium duration. Multinomial regression was used to investigate possible in-ICU risk factors for developing delirium on a given day versus having normal mental status or being comatose.

RESULTS: Our cohort of 300 patients had a median age of 20 months (IQR 11,37), 48% required mechanical ventilation, and 44% had at least one positive delirium assessment. Greater severity of illness [RR 1.04 (CI 1.01, 1.08, p=0.017)] and higher benzodiazepine exposure [RR 2.01 (CI 1.25, 3.24, p=0.002)] were both significantly associated with more days of delirium. In our multinomial models, higher benzodiazepine exposure (p=0.009) was significantly associated with a higher likelihood of being delirious the following day compared to having a normal mental status.

CONCLUSIONS: Delirium is prevalent among critically ill children. Higher severity of illness and, more importantly, benzodiazepine exposure are independent risk factors for increased delirium duration. Benzodiazepine administration is also significantly associated with the development of delirium the day following drug exposure. Studies targeting benzodiazepine exposure as a potentially modifiable target to reduce burden of delirium are warranted.

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S-96.

FILLING THE VOID - ADVANCE CARE PLANNING FOR INTENSIVE CARE

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INTRODUCTION: Most Canadians have not heard of Advance Care Planning (ACP)[1]. Less than 50% of Canadians have a designated substitute decision maker (SDM) and it is not known what kinds of discussions people have with them about their end-of-life (EOL) care. While 22% patients die in the Intensive Care Unit (ICU) in North America[2], it is not known what knowledge the average layperson has about life sustaining options in the ICU. Hence, we conducted a qualitative study to ascertain: 1) What is the state of knowledge about ICU interventions among healthy elderly laypersons in London, ON? 2) Do healthy elders have the necessary knowledge to formulate ACPs? 3) What barriers and opportunities exist for increasing ACP in the healthy elderly population?

METHODS: The study was approved by the local research ethics board, and all participants provided written consent. Using a qualitative research design informed by constructivist grounded theory[3], we conducted 20 semi-structured interviews with community-dwelling seniors in London, Ontario. Participants were included if they were 55 years or older, not housebound, in apparent good health and had the ability to make independent decisions about their health care. Data has been analyzed inductively using the constant comparative method.

RESULTS: Participants included 13 females and 7 males who were 65 ± 7.2 yrs (mean ± sd). Participants reported self-rated frailty scores were 2.5 ± 1.4 and they had lived in Canada for 51.8 ± 11 years. 19 out of 20 participants claimed to have made their ACP at the beginning of the interview. Participants had not really factored in ICU in their ACP and had limited knowledge of ICU interventions. They thought that outcomes from CPR were favorable and had misconceptions about Do Not Resuscitate (DNR) orders. However, participants expressed a keen interest in learning more about ICU interventions and ACP in general. Participants' wishes for EOL care were informed primarily by their conceptions about quality of life. In instances where participants had discussed EOL care with their SDM, they often provided descriptions of the conversations that were too vague to offer effective guidance to SDMs.

CONCLUSIONS: The participants interviewed in this study claimed to have completed their ACP, however they demonstrated limited knowledge of ICU interventions, and many expressed a desire to learn more in order to improve their ACP. Even among healthy elders who have engaged in ACP, there is still a need for more knowledge and explicit conversations about EOL care.

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S-97.

ASSOCIATION OF ENDOTHELIAL AND NEUROLOGIC INJURY BIOMARKERS WITH COGNITIVE IMPAIRMENT AFTER CRITICAL ILLNESS

AUTHORS: C. G. Hughes[1], T. D. Girard[2], J. Jackson[2], J. L. Thompson[3], R. Chandrasekhar[3], E. W. Ely[2], P. Pandharipande[1]

AFFILIATION: [1]Department of Anesthesiology, Vanderbilt University School of Medicine, Nashville, TN, [2]Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN, [3]Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, TN

INTRODUCTION: Delirium in the hospital is a predictor of cognitive impairment after critical illness.[1] Endothelial dysfunction may lead to delirium via perturbations in microvascular blood flow, release of biochemical mediators, or injury to the blood brain barrier (BBB).[2] Neuronal alterations from this acute insult may manifest as cognitive impairment in the long-term. We have shown that elevated plasma biomarker concentrations of endothelial activation, BBB, and brain injury are associated with prolonged delirium in ICU patients.[3] The relationship of these biomarkers with long-term cognitive impairment after critical illness has not been examined. We hypothesized that elevated plasma concentrations of endothelial activation (E-selectin, PAI-1), BBB injury (S100B), and brain injury (UCHL1, BDNF) biomarkers w ould be associated with worse cognitive impairment after critical illness.

METHODS: This prospective cohort study enrolled adult patients within 72 hours of respiratory failure or shock. At enrollment, we measured plasma concentrations of E-selectin, PAI-1, S100B, UCHL1, and BDNF. At 3 and 12 months after hospital discharge, global cognition was assessed with the Repeatable Battery for the Assessment of Neuropsychological Status.[4] We used multivariable linear regression to examine the independent associations of biomarker concentrations with global cognition. We adjusted for education, baseline cognition, comorbid disease, severity of illness, severe sepsis, delirium, and coma and examined interactions with age and systemic inflammation (IL-6 plasma concentration).

RESULTS: Our study included 392 survivors who underwent post-discharge cognitive assessment. The patients had a median age of 59 years and APACHE II score of 25, with 91% requiring mechanical ventilation, 65% having severe sepsis, and 76% developing delirium during the study. In general, higher S100B concentrations were associated with worse global cognition at both 3 and 12 months (overall P=0.057; P=0.005); these associations were modified by age and IL-6 such that the strongest associations were seen in younger patients and those with high inflammatory burden (Figure 1). Higher E-selectin (P=0.016) and UCHL1 (P=0.011) concentrations were associated with worse global cognition at 3 months but not 12 months (Figure 2) and not modified by age or IL-6. No significant associations were found between PAI-1 and BDNF concentrations with global cognition.

CONCLUSIONS: This study supports that BBB injury biomarkers are associated with long-term cognitive impairment after critical illness, particularly in younger patients and high inflammatory states. Endothelial activation and brain injury biomarkers are not consistently associated with long-term cognitive impairment. Further confirmatory studies are needed, including serial and post-ICU evaluations of biomarker concentrations to assess whether these associations change in response to disease progression or therapy.

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Figure 1. S100B versus Global Cognition by Age and Inflammation

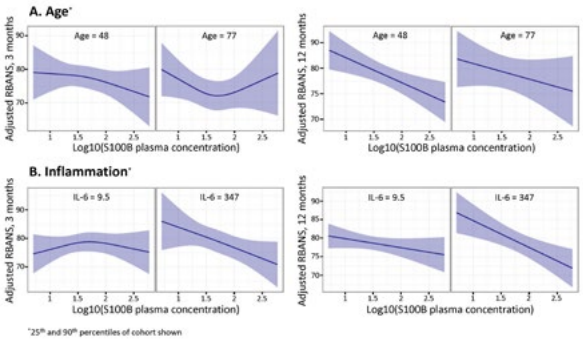
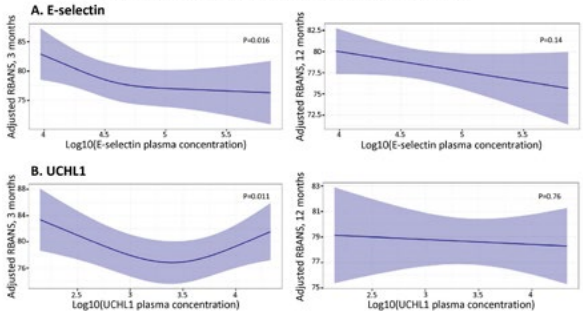


Figure 2. E-selectin and UCHL1 versus Global Cognition



S-98.

WITHDRAWN.

S-99.

DECOUPLING OF SODIUM AND POTASSIUM ION IS CORRELATED WITH POSTOPERATIVE RENAL FUNCTION AND RE-DIALYSIS RATE IN RENAL TRANSPLANTATION RECIPIENTS

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INTRODUCTION: The kidney is the major organ regulating the electrolyte balance of the body. Even though sodium and potassium ion are keenly manipulated by the kidney, the interaction of both ions is not popularly used to estimate the renal function. We developed the new scoring system to quantify the interaction of both ions. In this study, the relationship between decoupling of sodium and potassium ion and renal function in renal transplant recipients was investigated through retrospective chart review.

METHOD: After approval of local ethical committee, a retrospective study was performed on 197 patients who had undergone renal transplantation between Jan. 2011 and May 2012. The patients younger than 18 years old were excluded in this study, because estimated GFR could not be calculated. An electrical medical record review was performed to evaluate the serum electrolyte concentration (Sodium and potassium), eGFR, cause of renal failure, postoperative admission frequency, re-dialysis after transplantation and postoperative date. The coincidence score of Na-K was developed to quantify the coupling between two ions. The electrolyte values recorded during admission days for transplantation were used for calculation. The Na and K serum concentration measured in each day was subtracted from eGFR average. If newly calibrated Na and K concentration of the each day had same negative or positive values, “1” was assigned (coupling), but if they had opposite value, “o” was assigned (decoupling). The total sum of the assigned numbers was divided by the admission duration and multiplied by 100 to get the coincidence score of Na-K (CS Na-K). The CS Na-K was in high value range (above 44) if the trends of Na and K are same direction and coupled. But it was in low value range (below 44) if the trends of Na and K ions are inverse relationship. Independent t test, chi-square test, and Mann-Whitney U test was used for statistical comparison. Cox proportional hazard model was used to calculate the hazard ratio of the dialysis after graft failure between high and low CS Na-K group.

RESULTS: “43.4” was chosen as the cut-off value to divide the patients into two groups (High and Low CS Na-K group) from ROC curve. There was statistical difference in average eGFR during admission, eGFR at discharge between two groups, but not in GFR after 2 years later. Significant correlation was revealed between average eGFR during admission and CS Na-K by spearmann’s rank test (Spearmann’s correlation coefficient: -0.365, p=0.000). In Cox proportional hazard model, the patients with high CS Na-K group (10.38%) had a 345% increase in the hazard of re-dialysis after transplantation compared with low CS Na-K group (2.5%) (HR 4.45, 95% CI 1.173-16.876).

CONCLUSIONS: The newly developed coincidence score of Na-K has significant relationship with eGFR in renal transplant recipients. The decoupling ability of Na and K ion in kidney is associated with the renal function and re-dialysis rate in transplanted kidney.

S-100.

INTRAVASCULAR VOLUME STATUS ASSESSMENT IN CONGESTIVE HEART FAILURE PATIENTS USING PERIPHERAL INTRAVENOUS WAVEFORM ANALYSIS

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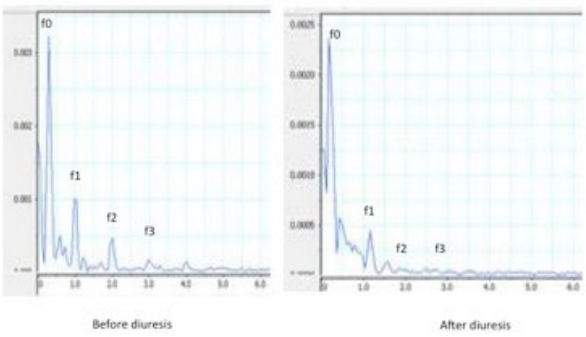
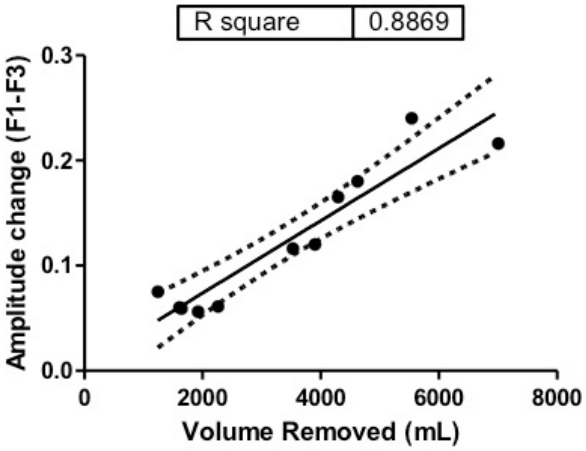
INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: The standard monitors that exist currently to monitor intravascular volume are inconsistent and often inaccurate.[1] Other methods used, such as pulse pressure variation (PPV) and transthoracic echo (TTE), have shown promise but have limitations; PPV requires an invasive line and specific tidal volumes[2] and TTE can be limited by patient anatomy, equipment or surgical interference and the evidence substantiating its utility is variable.[3] An excellent correlation between peripheral intravenous waveform analysis (PIVA) and early hemorrhage detection has previously been demonstrated.[4] In this study we use PIVA to measure volume status in hospitalized patients treated for congestive heart failure (CHF) in hopes of proving a less invasive and more reliable method for volume status assessment.

METHODS: In compliance with the IRB, patients admitted for CHF were enrolled just after the initiation of diuresis. A standard pressure transducer (Edwards LifeSciences, Irvine, CA), was attached directly to a peripheral intravenous catheter (Smiths Medical, Southington, CT) in the upper extremity. PIVA measurements were taken in 15 minute intervals every 12 hours until discharge. Peripheral venous data was recorded on an SD card reader and then interfaced with LabChart (ADInstruments, Colorado Springs, CO, USA) software analysis. Urine output, heart rate (HR), and blood pressure (BP) were recorded every 4 hours per standard monitoring procedures.

RESULTS: This study demonstrated the fidelity of the PIVA system. Once the peripheral venous data was transformed into the frequency domain, peaks representing the respiratory rate (f0), heart rate (f1), and harmonics of the heart rate (f2 and f3) were observed (figure 1). Heart rate and mean arterial pressure changes showed weak correlations to the change in volume status (n=11, R2= 0.0612 and R2= 0.0081 respectively). By calculating the change in amplitude across the sum of the three harmonics associated with heart rate (f1, f2, and f3), there was a strong correlation between amplitude change and volume removed (n=11, R2=0.8869, figure 2).





CONCLUSIONS: This study demonstrated the PIVA system is an accurate and reliable method for predicting fluid loss in CHF patients undergoing diuretic therapy than BP and HR.

Funded by Baxter Medical Investigator Initiated Research IIR

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S-102.

MITOCHONDRIAL DNA INDUCES STERILE TRACHEAL INJURY SECONDARY TO ENDOTRACHEAL INTUBATION: IMPACT ON NEUTROPHIL PHENOTYPES, ROS ACTIVITY AND TLR9 EXPRESSION

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INTRODUCTION: The pathophysiology of tracheal injury following endotracheal intubation is unknown. Excessive neutrophil activation due to bacterial or sterile factors will induce tissue damage. Previously we found minimal presence of bacteria in tracheal specimens of intubated patients. We aimed at investigating the presence of sterile factors such as damage associated molecular patterns (DAMPs) in human tracheal lavage fluids (TLFs).

METHODS: After approval by the IRB at Washington University St. Louis School of Medicine, we obtained consent from 45 healthy humans admitted for same-day surgery. Subglottic tracheal lavages of sore throat and no sore throat subjects were analyzed by flow cytometry for neutrophil phenotypes, ROS activity (DHR123) and TLR9 production, whereas qPCR was used for mitochondrial DNA (mtDNA) expression. Statistical analysis was done using student's t test, or Mann-Whitney U as appropriate and qPCR was analyzed with Welch two-sample t test. Data reported as SEM with *p<0.05; considered statistically significant.

RESULTS: Elevated mtDNA level (3.29±0.73µg/ml) detected in tracheal lavages of sore throat patients were several fold higher than no sore throat (0.037±0.015µg/ml) and serum of surgical patients (Fig. 1). A typical neutrophil phenotype CD66bhi/CD16 lo p<0.001 (Fig. 2) was documented and correlated with elevated levels of DHR 123 p<0.001 (Fig. 3), and TLR9 p<0.0001 (Fig. 4).

DISCUSSION: We confirmed that DAMPs (mtDNA) induced sterile inflammation locally and promote tracheal injury by increasing ROS and TLR9 activity. Excessive activity of ROS and TLR9 will delayed neutrophil apoptosis and enhance tissue destruction. There is need for therapeutic interventions aimed at modulating neutrophil activation.

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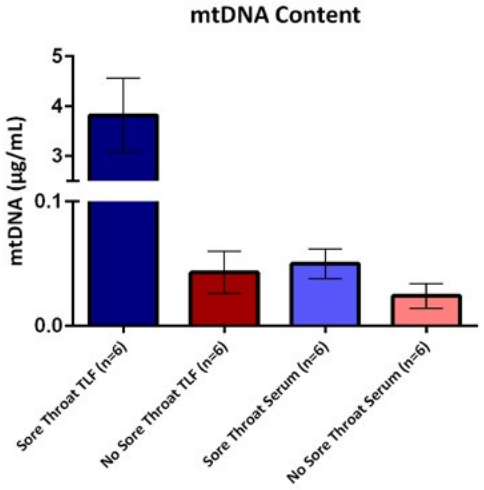

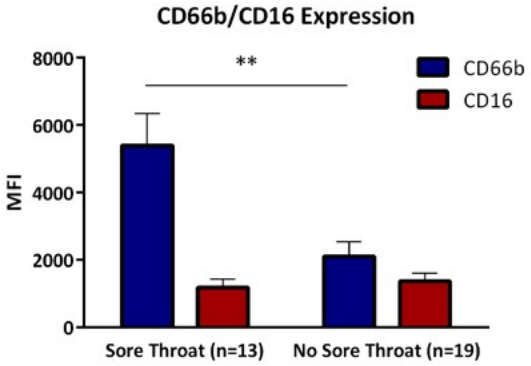

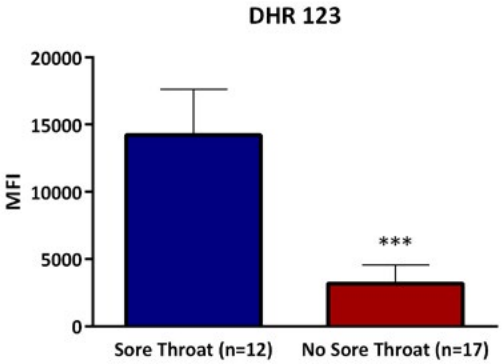

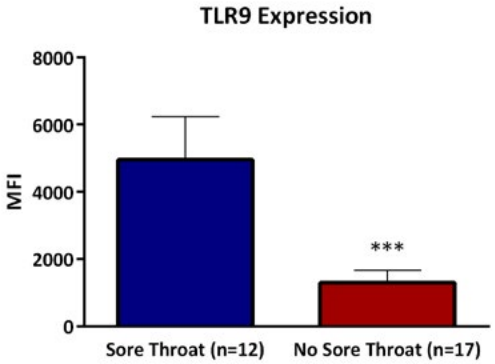

S-103.

NEUTROPHIL ACTIVATION IS AMELIORATED AFTER EXPOSURE TO DNASE I AND CHLOROQUINE IN A MODEL OF TRACHEAL INFLAMMATION

AUTHORS: C. Puyo[1], D. Peruzzi[2], A. Earhart[1], I. Mohsen[3], A. Gelman[3]

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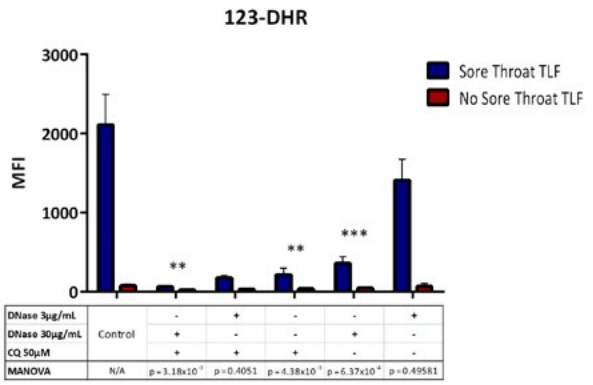
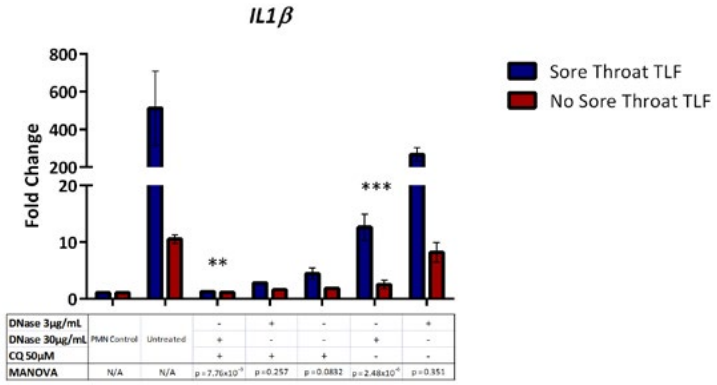
INTRODUCTION: Tracheal injury following endotracheal intubation results in neutrophil activation and sore throat. Excessive reactive oxygen species (ROS) activity promotes tissue damage and cytokine activity. No treatment is available for prevention of tracheal injury (sore throat, tracheo-malasia), and thus we studied the effects ex vivo of a single dose DNase I and chloroquine on neutrophil activation.

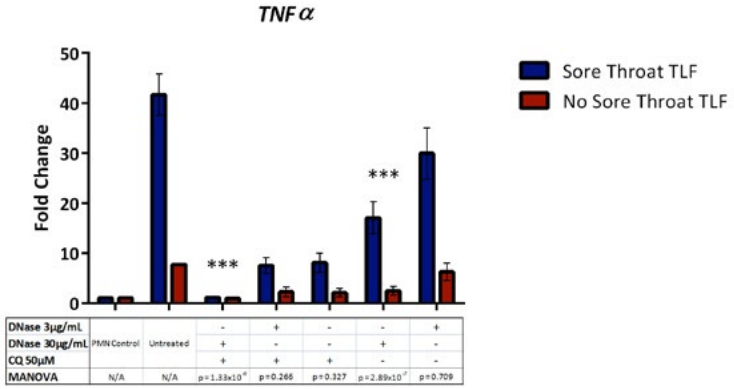
METHODS: After approval by the IRB at Washington University St. Louis School of Medicine, we obtained consent from healthy humans admitted for short-stay surgery. We cocultured supernatants of tracheal lavages of sore throat and no sore throat subjects with PMN of healthy volunteers. Neutrophils were identified by flow cytometry using mAb CD66b/CD16. The ROS probe (DHR123) was used for assessment of ROS activity. IL-1β, TNF-α and IL-8 activity were measured by qPCR. Analysis was conducted in 18 subjects (6 with sore throat, 6 without sore throat and 6 controls). Each specimen was exposed to different concentrations of DNase I (3-30μg/ml) and chloroquine 50μM. MANOVA was utilized for statistical analysis with *p<0.05; considered statistically significant.

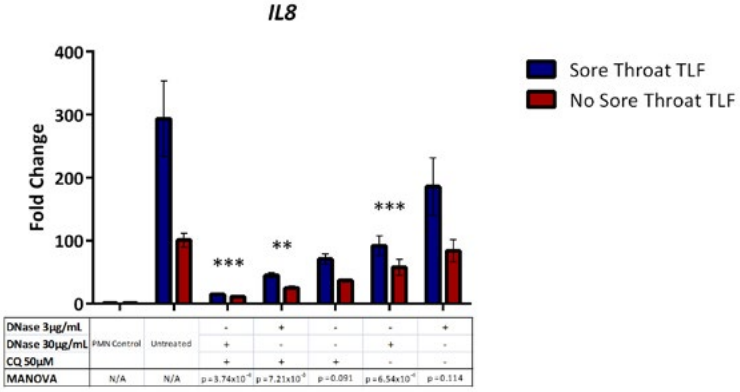
RESULTS: Compared to the no sore throat group the sore throat group showed higher DHR 123 activity and elevated IL-1β, TNF-α, and IL-8. DNase I and chloroquine (CQ) noticeable decrease all variables analyzed: DHR123 p<0.0003 (fig. 1), IL-1β p<0.007 (fig. 2), TNF-α p<0.0000001 (fig. 3), and IL-8 p<0.003 (fig.4).

DISCUSSION: A single dose of DNase I/CQ ameliorates neutrophil activation as determined by evaluation of DHR123, TNF-α, IL-1β and IL-8. Our results suggest potential benefit and possible tracheal protection with a single dose of DNase I/CQ. References: 1.J Innate Immun 2009;1:527-542. 2.Nat Rev. Rheumatol. 2012 8, 522-533









S-104.

INTRACRANIAL HEMORRHAGE OCCURING DURING ECMO SUPPORT

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INTRODUCTION: Hemorrhagic events have frequently been experienced during extracorporeal membrane oxygenation (ECMO) in critically ill patients due to exposure to anticoagulation (to prevent circuit clotting), making them susceptible to coagulopathy and platelet dysfunction[1]. Intracranial hemorrhage (ICH) during ECMO is associated with worse outcomes that significantly impacts patients' survival and quality of life[2]. We aim to determine the incidence and predictors of ICH occurring in adults during ECMO support in our Level 1 trauma hospital.

METHODS: An IRB-approved retrospective review was performed on adults >18 years who received ECMO from 2007-2013. The main outcome variable was the onset of imaging-confirmed ICH occurring during ECMO. Multivariate analysis was used to examine independent predictors for ICH during ECMO.

RESULTS: Out of 154 patients who received ECMO, 12 (7.8%) developed ICH. The majority of cases (98.1%) were on a heparin infusion during ECMO support to prevent circuit clotting. Patients with ICH had longer mean ECMO duration (10.3 vs. 5.3 days, P=0.029), a higher frequency of central ECMO cannulation (54.5% vs. 24.2%, P=0.039) and a higher mean ACT levels (629 vs. 444 seconds, P=0.027) -but no significant difference in aPTT, INR and platelet count (table 1). A longer ECMO duration was associated with a statistically significant difference in the frequency of ICH (e.g ECMO duration >5 days, P = 0.044, and with ECMO duration >9 days, P = 0.016). Patients who developed ICH also experienced a significantly higher frequency of other non-ICH bleeding episodes (75% vs. 36.6%, P=0.017), required more frequent RBC transfusions (58.2 vs. 28.5 units, P=0.03), platelet transfusions (143 vs. 40.5 units, P=0.001) and plasma transfusions (28.3 vs. 12.1 units, P=0.025) (table 2). Eleven out of the 12 cases with ICH died during index hospitalization and there was a trend towards higher in-hospital mortality compared to those without ICH (92% vs. 65%, P=0.091). In the multivariate model, a longer ECMO duration (OR=1.079, 95%CI 1.012-1.150, P=0.020) and central ECMO cannulation (OR=5.177, 95%CI 1.325-20.220, P=0.018) were independently associated with risk of ICH after controlling for patients' age, sex, and type of ECMO (whether venoarterial or venovenous).

CONCLUSION: We recommend more frequent neurological checks and monitoring of coagulation parameters in subjects who remain on ECMO for longer duration (>5 days) and to attempt earlier rather than later weaning from ECMO whenever feasible to avoid risk of ICH.

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Table 1: Type of ECMO cannulation and coagulation and bleeding parameters among cases with and without intracranial hemorrhage during ECMO support
ECMO: extracorporeal membrane oxygenation, aPTT: activated partial thromboplastin time, ACT: activated clotting time, INR: international normalized ratio. *We utilized the highest recorded values for aPTT, ACT and INR and the lowest recorded platelet count for each patient.

	All (n = 154)	Intracranial bleed (n =12)	No intracranial bleed (n=142)	P value
Type of ECMO cannulation				
Central ECMO cannulation % (n)	26.7% (35)	54.5% (6)	24.2% (29)	0.039
Axillary ECMO cannulation % (n)	14.5% (19)	27.3% (3)	13.3% (16)	0.221
Subclavian ECMO cannulation % (n)	13% (17)	9.1% (1)	13.3% (16)	0.691
Femoral ECMO cannulation % (n)	26% (34)	0% (0)	28.3% (34)	--
Coagulation and bleeding parameters during ECMO*				
aPTT (seconds, mean ±SD)	108±50	116±49	107±51	0.467
ACT (seconds, mean ±SD)	458±266	629±296	444±259	0.027
INR (mean ±SD)	2.3±1.1	2.25±0.85	2.29±1.1	0.676
Lowest platelet (k/cmm, mean ±SD)	47±31	38.8±21.1	47.8±32	0.188

S-104 • CONTINUED ON NEXT PAGE

S-104 • continued

Table 2: Baseline demographic, clinical and ECMO characteristics among cases with and without intracranial hemorrhage during ECMO support
ECMO: extracorporeal membrane oxygenation, BMI: body mass index, ESRD: end stage renal disease, CPR: cardiopulmonary resuscitation, VA: venoarterial, ECMO: extracorporeal membrane oxygenation, SD: standard deviation, AFib: atrial fibrillation, IABP: intra-aortic balloon pump, RBC: red blood cell, d: day, n: number.

	All (n = 154)	Intracranial bleed (n =12)	No intracranial bleed (n=142)	P value
Baseline demographics				
Age (years, mean ± SD)	51.3±15.7	48.3±17.6	51.6 ± 15.5	0.599
Male sex % (n)	75.3% (116)	75 % (9)	75.4% (107)	0.978
BMI (kg/m2, mean ±SD)	29.2±7.7	29±5.9	29.2 ± 7.9	0.970
Hypertension % (n)	62.3% (96)	66.7% (8)	62% (88)	0.748
Diabetes % (n)	36.4% (56)	33.3% (4)	36.6% (52)	0.820
Pre-ECMO ESRD % (n)	9.1% (14)	0% (0)	9.9% (14)	--
ECMO indications				
Cardiac arrest % (n)	10.1 % (15)	9.1% (1)	10.2 % (14)	0.905
Cardiogenic shock % (n)	40.5 % (60)	36.4% (4)	40.9% (56)	0.770
Cardiac surgery % (n)	12.8% (19)	18.2% (2)	12.4% (17)	0.585
Cardiac transplant % (n)	8.1 % (12)	0% (0)	8.8% (12)	--
Lung transplant % (n)	10.1% (15)	9.1% (1)	10.2% (14)	0.905
Respiratory failure % (n)	10.8% (16)	18.2% (2)	10.2 % (14)	0.421
Pulmonary embolism % (n)	4.1% (6)	0 % (0)	4.4 % (6)	--
ECMO characteristics				
VA ECMO % (n)	81.2 % (125)	83.3% (10)	81% (115)	0.842
IABP pre-ECMO % (n)	11.7% (18)	16.7% (2)	11.3% (16)	0.579
Pre-ECMO cardiac surgery % (n)	40.9 % (63)	25% (3)	42.3% (60)	0.253
ECMO for cardiac indication % (n)	74% (114)	66.7% (8)	74.6% (106)	0.547
ECMO duration (days, mean ±SD)	5.7±6.8	10.3±8.7	5.3±6.5	0.029
ECMO duration >5 days % (n)	31.2 % (48)	58.3% (7)	28.9% (41)	0.044
ECMO duration > 9 days % (n)	15.6 % (24)	41.7% (5)	13.4 % (19)	0.016
Blood products during ECMO				
Units of pRBC on ECMO (mean ±SD)	30.8±32	58.2±53	28.5 ± 28.7	0.03
Units of plasma on ECMO (mean ±SD)	13.3±16.7	28.3±26.9	12.1±15	0.025
Units of platelet on ECMO (mean ±SD)	48.5±79	143±159	40.5±62.8	0.001
Units of cryoprecipitate on ECMO (mean ±SD)	26.3±36.4	36.5±35.8	25.4± 36.4	0.198
ECMO complications				
Acute renal failure % (n)	51.9% (80)	41.7% (5)	52.8% (75)	0.461
Bleeding % (n)	39.6 % (61)	75% (9)	36.6% (52)	0.017
Hepatic dysfunction % (n)	41.6 % (64)	41.7% (5)	41.5% (59)	0.994
Sepsis % (n)	15.7% (24)	8.3% (1)	16.3% (23)	0.476
In-hospital mortality % (n)	66.9 % (103)	91.7% (11)	64.8% (92)	0.091

S-105.

THE IMPACT OF DEEP SEDATION ON THE INCIDENCE OF DELIRIUM IN MECHANICALLY VENTILATED, CRITICALLY ILL PATIENTS

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INTRODUCTION: Early deep sedation is an independent predictor for mortality in critically ill patients. There is high consistency about this finding among various studies[1-3]. The most typical syndromic form of brain dysfunction in critically ill patients is delirium[4]. Hypothesizing that early deep sedation injures the brain, there should be an association between early deep sedation and delirium, which is the most common presentation of acute brain injury in critically ill patients.

Primary aim of this retrospective cohort study was to investigate whether early deep sedation is independently associated with the occurrence of delirium in mechanically ventilated critically ill patients.

METHODS: Observational analysis of a clinical database (IRB: EA 1/126/08).

All patients admitted to our ICUs in seven consecutive years were screened for eligibility. Inclusion criteria were patient age ≥18 yrs, mechanical ventilation, and a minimum ICU stay of 48 hours. Patients with previous ICU stays within the same hospitalization period, external warming/cooling methods, ventricular assist devices, or less than three RASS assessments were excluded from analysis. The Richmond Agitation-Sedation Scale (RASS) was used to assess sedation depth (more than 85% of documented RASS-scores ≤ −3 during the first 48 hours were attributed to deep sedation group[3]). Delirium was assessed with the Confusion Assessment Method for the ICU (CAM-ICU) after an intensive staff training as described previously[5]. Non-parametric testing and multivariate logistic regression were applied to investigate the impact of early deep sedation with 48 hours after ICU admission on delirium.

RESULTS: Of 25,931 possible study-subjects, 1,884 met inclusion and exclusion criteria. 513 patients were deeply sedated, and 1,371 were not deeply sedated.

445 patients (32.5%) suffered from delirium in the not deeply sedated group and 216 patients in the deeply sedated group (42.1%), respectively (Table 1). Deep sedation during the first 48 hours was independently associated with a higher risk for delirium (OR 1.399, 95% CI 1.065-1.837, p=0.016). Other independent associations were higher age, a medical cause for admission, and high-doses of catecholamines (Table 2). Benzodiazepine based regimes (midazolam or midazolam+propofol) did not show a prodelirogenic effect in this setting.

CONCLUSION: Our data suggest that harmful effects of early deep sedation might even outweigh effects related to the sedative regime. Further trials are necessary to verify this hypothesis.

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Table 1: Basic patient characteristics and outcome

	Not deeply sedated N=1371	Deeply sedated N=513	p.overall
Patient characteristics:			
Age [y]	68.0 [59.0;75.0]	64.0 [50.0;73.0]	<0.001
Sex (male)	490 (35.7%)	150 (29.2%)	0.009
APACHE II on ICU admission	20.0 [16.0;26.0]	25.0 [18.0;31.0]	<0.001
Type of admission:			<0.001
Elective Surgery	697 (53.2%)	136 (27.6%)	
Emergergeny Surgery	348 (26.5%)	170 (34.5%)	
Medical	266 (20.3%)	187 (37.9%)	
Inotropics:			<0.001
None	267 (20.4%)	29 (5.73%)	
Dopamine ≤ 5	176 (13.5%)	6 (1.19%)	
Dopamine > 5 or E/NE ≤ 0.1	541 (41.4%)	115 (22.7%)	
Dopamine > 15 or E/NE > 0.1	324 (24.8%)	356 (70.4%)	
Sedatives:			<0.001
Propofol	1048 (76.4%)	191 (37.2%)	
Midazolam	26 (1.90%)	99 (19.3%)	
Both	129 (9.41%)	211 (41.1%)	
None of above	168 (12.3%)	12 (2.34%)	
VAS ≥ 5 or BPS ≥ 6 during first 48 hours	342 (24.9%)	42 (8.19%)	<0.001
Patient outcome:			
Delirium	445 (32.5%)	216 (42.1%)	<0.001

Table 2: Logistic regression

	p	OR	95% CI
Deep sedation during first 48h on ICU	0.016	1.399	1.065-1.837
Age	0.012	1.009	1.002-1.017
Gender (Female)	0.418	0.916	0.740-1.132
APACHE II on ICU admission	0.079	0.988	0.975-1.001
Admission			
Elective Surgery	Ref.		
Emergergeny Surgery	0.180	1.185	0.924-1.519
Medical	0.011	1.420	1.085-1.856
Inotropics			
No intropic drugs	Ref.		
Dopamine ≤ 5	0.890	0.969	0.621-1.505
Dopamine > 5 or E/NE ≤ 0.1	0.072	1.348	0.977-1.871
Dopamine > 15 or E/NE > 0.1	0.020	1.500	1.069-2.117
Sedativa			
Propofol	Ref.		
Midazolam	0.871	1.039	0.652-1.646
Both	0.432	1.125	0.838-1.506
None of above	0.970	1.007	0.682-1.471
VAS ≥ 5 or BPS ≥ 6 during first 48 hours	0.125	1.217	0.946-1.562

S-106.

ELEVATED BLOOD UREA NITROGEN INCREASE THE RISK OF MORTALITY INDEPENDENT OF ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY

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INTRODUCTION: Acute kidney injury (AKI) after cardiac surgery is a frequent complication that increases morbidity and mortality[1]. In critically ill patients uremia may worsen outcome even in the absence of acute kidney injury[2]. Furthermore the exact level of blood urea nitrogen (BUN) that requires the initiation of dialysis is not known. We aimed to determine if elevations of BUN after cardiac surgery are associated with worse outcome.

METHODS: This is a retrospective study of all cardiac surgery patients at one institution in 2011. BUN was measured and AKI was defined according to AKIN criteria as an increase in serum creatinine by more than 0.3 mg/dL within 48 hours of surgery. One-year mortality was determined using the US Social Security index. The effect of BUN on mortality independent of AKI was determined using a binary logistic regression model.

RESULTS: This study included 929 patients. 57 patients died within a year after surgery (6.1 %). Patients who died had higher level of BUN on postoperative days two to ten. Peak BUN during the first 10 days after surgery were 37.3 +/- 22.6 mg/dL in non-survivors compared to 31.1 +/- 29.6 mg/dL in survivors ($p<0.01$). 315 patient had AKI defined by AKIN criteria (33.9 %). Using a binary logistic regression model to predict one-year mortality elevated BUN levels were associated with increased mortality independent of the incidence of AKI.

DISCUSSION: Elevation of BUN was associated with higher mortality after cardiac surgery. This may indicate that high levels of BUN are harmful even if not associated with AKI. Further studies will have to be done to determine the level of BUN that should prompt initiation of dialysis.

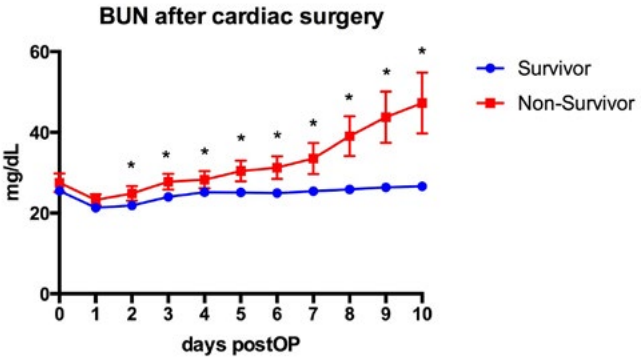

Figure 1: BUN after cardiac surgery

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S-107.

THE VALIDITY OF THE USE OF CEFMETAZOLE OR FLOMOXEF FOR THE PREVENTION OF SURGICAL SITE INFECTION (SSI) IN BILIARY TRACT PROCEDURES AND COLORECTAL PROCEDURES

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INTRODUCTION: The infections most commonly associated with biliary tract or colorectal surgical procedures include E.Coli, and Klebsiella species. Recently, the increases of antimicrobial resistance in these infections are noted, accounting for up to 40% of E.Coli isolates. Notably, an acquisition of an infection with extended-spectrum β-lactamase (ESBL) producing E.Coli and Klebsiella species has been reported to be associated with an initial treatment failure which results in high mortality rate. Additionally, an increase of such ESBL producers has been observed in outpatient settings, reducing the treatment options. Although ESBL producers are resistant to most of cephalosporins in addition to β-lactam/β-lactamase inhibitor combinations, fluoroquinolones, and aminoglycosides, the ESBL producers are often highly susceptible to cephamycins (i.e., cefmetazole(CMZ), flomoxef(FMOX)). We evaluated its efficacy for the ESBL isolates at a tertiary care hospital in Japan.

METHODS: The study was conducted in a retrospective fashion after an IRB approval was obtained. The samples consisted of 251 ESBL isolates from 173 individuals during the 5-year period from 2010 to 2015. All ESBL isolates were identified using the Clinical and Laboratory Standards Institute criteria. Minimal inhibitory concentrations (MICs) less than 8mg/L for CMZ and FMOX as well as other cephalosporins were considered to indicate susceptibility.

RESULTS: Of 251 isolates, 199 isolates were E.Coli, 37 isolates were Klebsiella pneumoniae, 2 were Klebsiella oxytoca, and the rest of 13 isolates were Proteus mirabilis. All the isolates were resistant to all the commercially available cephalosporins in addition to ampicillin and piperacillin. Similarly, 142 out of 251 isolates were resistant to fluoroquinolones (56%). By contrast, only 12 isolates were resistant to CMZ (4.7%) and 10 isolates were resistant to FMOX (3.9%). Similarly, resistance to carbapenems is rare (3 isolates, 1.1%).

CONCLUSIONS: Given the growing number of ESBL producers not only in the hospitalized patients but also in the outpatient settings, prevention of SSI by ESBL producers must be taken into consideration. Although recent guidelines suggest the use of carbapenems for the infection by ESBL producers, they are not appropriate for extensive use for the prevention of SSI, given the risks of outbreak of carbapenem resistant strain. In this respect, a relatively narrow spectrum of cephamycins makes it appropriate for the use of prevention of SSI for biliary tract and colorectal surgical procedures.

S-108.

EPIDEMIOLOGICAL ANALYSIS OF SERUM ANTI-PSEUDOMONAS AERUGINOSA PCRV TITERS IN ADULTS

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INTRODUCTION: Among various virulence mechanism of opportunistic pathogen Pseudomonas aeruginosa, the type III secretion system has been characterized as a major factor associated with acute lung injury, bacteremia and mortality. In addition, PcrV, a component protein of type III secretion system, has been characterized as a protective antigen against P. aeruginosa infections. This research performed epidemiological analysis of serum anti-PcrV titers in a fleet of adult patients.

METHODS: This study was approved by the Kyoto Prefectural University of Medicine Ethics Committee. From April 2012 to March 2013, serum anti-PcrV titers were measured in 198 volunteer participants (all non-Caucasian with Japanese nationality, from whom Written informed consents about the provision of medical information and the blood sample collection for serum titer measurement were obtained) who had a plan to have anesthesia management for the scheduled surgeries.

RESULTS: The median, the minimum, and the maximum values of serum anti-PcrV titers among 198 participants are 4.09 nM, 1.01 nM, and 113.81 nM, respectively. The anti-PcrV titer range of 2.00-4.99 nM includes a total of 115 participants (58.1%) with the maximum peak in the histogram. In 21 participants (10.6%), anti-PcrV titers were beyond the approximately 3-fold rise (exceeding 12 nM) in comparison with the median value. Among the factors analyzed in the binomial analysis, the increase in the age of every 10-year-old, traffic trauma treatment history, past surgical history demonstrated significant association with higher anti-PcrV titers above 10 nM.

CONCLUSIONS: This research revealed the variation of the anti-PcrV titers in adult patients without any obvious infection histories.

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S-109.

AUTOLOGOUS MYELOID CELLS TRANSPLANT RESTORES THE LONG-TERM POST SEPTSIS IMMUNE SYSTEM DECLINE IN HUMANIZED MICE

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INTRODUCTION: Recovery from a critical illness (CI) is a pivotal, yet poorly characterized, phenomenon. Here, we investigated the ability of peripheral blood monocytes (MO) to differentiate into immature dendritic cells (iDC; MOàiDC) in vitro after a clinically relevant model of a sepsis 28 days after the initial infection. We hypothesized that sepsis would induce a prolonged decline in ability of MO to differentiate into DC.

METHODS: The study was design as a longitudinal experimental study. We subjected humanized mice to cecal ligation and puncture (CLP) model of sepsis. Animals we sacrificed at 28 days (t+28day) after original surgery. Some animals received rescue from in vitro differentiated MO obtained from stem cells originally used for grafting two weeks after CLP. Isolated MO were differentiated into iDC in vitro with IL-4 and GM-CSF. Cytokine receptor expression and cytokine production was measured.

RESULTS: We found that 3 months after CLP a significant decline in % of DC was present after incubation of MO with IL-4&GM-CSF as compared to animals with sham surgery (31% vs 73%). This was accompanied by less favorable ability of IL-4&GM-CSF cells to trigger T cell proliferation or produce IL-12, a critical cytokine for DC function. The transplant of stem cells at two weeks recovered ability of MO to become DC. This process was partially dependent on exaggerated secretion of M-CSF.

CONCLUSIONS: Our data suggest a persistence of prolonged immunosuppression after sepsis in a novel model of humanized mice. This defect can be reversed by stem cells transplant or neutralization of M-CSF.

S-110.

SAFETY AND POSSIBLE BENEFITS OF SEVOFLURANE ON THE DAMAGED BLOOD BRAIN BARRIER IN A RAT MODEL OF SUBARACHNOID HEMORRHAGE

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INTRODUCTION: Volatile anesthetics have been proven protective in various vital organs. Sparse information is available with regard to safety and protective effects of sevoflurane in brain injury. The blood brain barrier (BBB) is of utmost importance to maintain brain homeostasis and is impaired upon injury such as subarachnoid hemorrhage (SAH). We assessed the safety profile of sevoflurane and its ability on brain protection in SAH.

MATERIAL AND METHODS: Adult male Wistar rats were assigned to SAH or sham operation. Animals were instrumented with an intracerebral and arterial pressure monitoring, a venous line and tracheotomy. SAH was induced using the intraluminal filament method via the carotid artery and animals underwent sedation for 4h with 0.5 mean alveolar concentrations (MAC) of sevoflurane or 5mg/kg/h propofol. Animals were sacrificed after 4h or allowed to wake up and were observed for 24h. Neurological function in these animals was assessed by the modified Garcia score. At the end of the experiment serum and brains were harvested and brain water content was determined. Statistical analysis was performed using ANOVA or student's T-test, $p<0.05$ was considered significant.

RESULTS: Hemodynamically all animal groups were similar. Animals undergoing SAH showed an accentuated rise in ICP (propofol vs. sevoflurane: 31.71+/-12.8 vs 36.9+/-16.0mmHg, p= 0.4) after successful induction of bleeding. Throughout the post-conditioning period SAH animals had an ICP of 14.9+/-1.0 vs 15.5+/-1.2mmHg (p=1.0) under propofol vs. sevoflurane sedation (baseline: 10.4 +/-5.1 vs 8.4 +/-3.4mmHg). Early brain water content (immediately after post-conditioning) was higher in animals sedated with propofol: 79.8+/-0.5 vs. 78.5 +/- 0.2% (p=0.047), after 24h brain water content was similar 80.0+/-0.6 vs. 80.1+/- 1.1% (p=1.0). Garcia scores (max. 20 points) were lower in animals suffering from SAH compared to the sham group, but there was no statistical significance different between propofol or sevoflurane sedation (15.3+/-1.1 vs. 13.5+/-2.0, p=0.06).

CONCLUSION: The use 0.5 MAC sevoflurane appears to be safe with respect to hemodynamic stability, ICP and neurological outcome of the animals. Our data suggest that early edema formation is less pronounced under sevoflurane sedation compared to propofol. The reason for a slower edema formation is unclear, in vitro data from our lab suggest that this may be a result of a protection of the ultrastructure of BBB-specific proteins.

S-111.

EFFECTS OF CANNABINOID RECEPTORS AND GPR55 MODULATION ON EXPERIMENTAL ENDOTOXEMIA IN MICE

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INTRODUCTION: Sepsis is the systemic inflammatory response to an infection and severe sepsis and septic shock are associated with tissue hypoperfusion, multi-organ dysfunction and high mortality. Accumulating evidence suggests that the endocannabinoid system is up-regulated in the pathogenesis of sepsis. In particular, cannabinoid 2 receptor, CB2, and GPR55, which are highly expressed on immune cells, are activated by endocannabinoids. Therefore, the endocannabinoid system represents a potential therapeutic target in sepsis. In the present study, we used a mice model of sepsis induced by lipopolysaccharide (LPS) and investigated the impact of CB2 and GPR55 modulation on leukocyte activation during endotoxemia using intravital microscopy (IVM) of the intestinal microvasculature, a key microcirculatorion in sepsis.

METHODS: Institutional Animal Care Committee approval was obtained for all experimental procedures used in this investigation. LPS (5 mg/kg) was administered intravenously (i.v.) to anesthetized male C57BL/6 mice (WT or $CB2^{-/-}$, 6-8 weeks old). Cannabinoid receptor and/or GPR55 modulation was studied post LPS administration using the following substances: endocannabinoid degradation enzyme (monoacylglycerol lipase, MAGL) inhibitor (JZL184, 16 mg/kg, i.v CB2 antagonist (AM630, 2.5 mg/kg, i.v.); GPR55 agonists (LPI, 5 mg/kg, O-1602, 5 mg/kg, i.v.); GPR55 antagonists (CID16020046, 20 mg/kg, O-1918, 5 mg/kg, i.v.); and cannabinoid 1 receptor (CB1) antagonist (AM281, 2.5 mg/kg, i.v.). For visualization of leukocytes and capillaries, Rhodamine-6G and FITC-labeled bovine serum albumin were administered i.v. 30 minutes prior to IVM. Intestinal leukocyte activation (rolling and adhesion) and capillary perfusion (functional capillary density – FCD) was evaluated two hours after LPS administration by IVM.

RESULTS: Inhibition of endocannabinoid degradation by JZL184 and antagonism of GPR55 by O-1918 or CID16020046, respectively, in WT mice showed beneficial effects on the intestinal microcirculation in experimental sepsis by significant reduction of leukocyte adhesion and improvement of FCD. In animals treated with the CB2 antagonist AM630 before JZL184 administration those effects were abolished. In contrary, inhibition of endocannabinoid degradation by JZL184 was still beneficial in CB2-/- mice. CB1 antagonism by AM281 was not sufficient to reverse decreased leukocyte adhesion.

CONCLUSION: Endocannabinoid degradation enzyme inhibition and GPR55 blockade reduced LPS-induced intestinal leukocyte activation and improved the microvascular blood supply in experimental sepsis in WT mice. Contradictory results found in the $CB2^{-/-}$ studies suggested alternative molecular targets of endocannabinoids to be further investigated.

S-112.

HIGH FLOW NASAL CANNULA VERSUS NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR THE TREATMENT OF RESPIRATORY FAILURE AFTER PEDIATRIC CARDIAC SURGERY: A RETROSPECTIVE STUDY

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INTRODUCTION: High flow nasal cannula (HFNC) is widely used as a respiratory support in children. There are a few studies about respiratory failure after pediatric cardiac surgery. The aim of this study is to compare the effect of HFNC with nasal continuous positive airway pressure (NCPAP) in patients with respiratory failure after pediatric cardiac surgery.

METHODS: This study is a retrospective matched control study approved by the institutional review board. Patients with respiratory failure after pediatric cardiac surgery, younger than 4 years old were included in this study. 37 patients who received HFNC from Jan 2014 to Dec 2015 were included as HFNC group. We recruited 37 patients as a NCPAP group from the patients who received NCPAP after pediatric cardiac surgery from Jan 2010 to Dec 2013. The matching parameters were body weight and Risk adjustment for congenital heart surgery 1 (RACHS-1) score. Body weight was taken priority. Primary outcome was reintubation rate. Secondary outcome was duration of ICU stay. We compered reintubation rate using Pearson's chi-square test and ICU duration in Wilcoxon rank sum test. We used multivariate regression analysis to adjust possible differences in baseline characteristics.

RESULTS: Body weight, RACHS-1 score had no difference between two groups. HFNC group was significantly younger than NCPAP group (3.0(1.0, 9.0) and 1.0(0, 5.0) month old, p=0.01). Duration of mechanical ventilation was significantly longer in NCPAP group than HFNC group (222(123, 511) and 75(7, 171) days, p<0.001). Median setting of each devises were fraction of inspiratory oxygen (FiO_2) 50 (21, 80)%, flow rate 2.1 (1.7, 2.3) L / kg / min in HFNC and FiO_2 50 (39, 52) %, positive end-expiratory pressure 10 (8, 10) cmH_2O in NCPAP. Nine patients in NCPAP group resulted in reintubation compared to one patient in HFNC group. Reintubation rate in HFNC group was significantly lower than NCPAP group (3 vs 28 %, p = 0.006). 70% of reintubation was performed within 24hours after HFNC or NCPAP was started. Duration of ICU stay in HFNC group was significantly shorter than NCPAP group (10 (7, 17) and 17 (11, 32) days, p = 0.005). We did multivariate analysis to investigate independent association of NCPAP therapy and reintubation. We analyzed differences in reintubation with multivariate logistic regression, adjusting for possible differences in baseline characteristics (Age, RACHS-1, Duration of mechanical ventilation). In multivariate analysis, NCPAP therapy was independent risk factor of reintubation (P = 0.03) (Table).

CONCLUSION: HFNC may prevent reintubation than NCPAP for respiratory failure after pediatric cardiac surgery.

Multivariate analysis to investigate independent association of NCPAP and reintubation

	Adjusted odd's ratio	P-value
Age (month old)	1.1 (1.0, 1.2)	0.28
Duration of mechanical ventilation (day)	1.0 (1.0, 1.0)	0.07
RACHS-1	1.5 (0.8, 2.9)	0.14
NCPAP	10.5 (1.2, 309.4)	0.03

S-113.

IMPACT OF INTRAOPERATIVE RIGHT VENTRICLE DYSFUNCTION ON ACUTE KIDNEY INJURY AND DELIRIUM FOLLOWING CARDIAC SURGERY

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Right ventricle (RV) dysfunction is common in patients undergoing cardiac surgery and, via reduced cardiac output and venous congestion, reduces perfusion to the kidneys and brain. Acute kidney injury (AKI) and delirium affect a large number of patients following cardiac surgery (30%1 and 26%,[2] respectively). We tested the hypothesis that RV dysfunction is associated with AKI or delirium following cardiac surgery.

We performed a post hoc analysis of a prospectively collected 615-patient cardiac surgery cohort. RV dysfunction was assessed using transesophageal echocardiography (TEE) by board certified TEE anesthesiologists, after induction of anesthesia (baseline) and after separation from cardiopulmonary bypass (CPB) or completion of off-pump bypass grafting (postoperative). RV dysfunction was defined as mild, moderate, or severe hypokinesis and AKI using AKIN criteria (0.3 mg/dl creatinine rise within 48h of surgery). Delirium was assessed by research personnel using the CAM-ICU exam twice daily during ICU hospitalization. We measured associations between RV dysfunction and brain and kidney injury, adjusted for confounders between these associations and risk factors for the outcomes. Covariates included age, Charlson index, congestive heart failure, LVEF, baseline eGFR (AKI models only), mini-mental state exam score (delirium models only), valve surgery, and duration of CPB.

Sixty-one of 615 participants (9.92%) had right ventricle dysfunction at baseline (7.48%, mild; 2.14%, moderate; 0.3%, severe) and sixty-one (9.92%) following surgery (7.64%,mild; 1.79%, moderate; 0.49%, severe). 28 participants (4.6%) had RV dysfunction both at baseline and postoperative. One hundred twenty-four of 615 patients (20.1%) developed AKI following surgery and 144 (23.4%) delirium. Baseline RV dysfunction was associated with a 100% increase in the odds of AKI (OR, 2.00 [95% CI 1.01-3.97]; P<0.05), but postoperative RV dysfunction was not associated with AKI (Table). On the contrary, baseline RV dysfunction was not associated with delirium but postoperative RV dysfunction correlated with a 109% increase in the odds of delirium (OR, 2.09 (1.04-4.22]; P=0.04).

Baseline but not postoperative RV dysfunction was associated with the development of AKI and postoperative but not baseline RV dysfunction was associated with development of delirium. While further studies are needed, preoperative assessment of RV dysfunction may improve AKI risk stratification and treatments to reduce postoperative RV dysfunction should be tested to reduce delirium following cardiac surgery.

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Table. Associations between baseline or postoperative right ventricular dysfunction and AKI (defined using AKIN criteria) or delirium (diagnosed by CAM-ICU) following cardiac surgery

Outcome	TEE exam	Covariate	Odds Ratio	95% CI	P value
AKI	**Baseline**	**RV Dysfunction**	**2.00**	**1.01 - 3.97**	**0.05**
		Age, years	1.02	0.99 - 1.04	0.14
		Charlson index, 1-24	1.35	1.15 - 1.63	0.002
		Congestive heart failure	1.29	0.68 - 2.44	0.43
		Left ventricle ejection fraction, %	1.01	0.98 - 1.04	0.39
		Preop eGFR, mL/min/1.73m^2	0.99	0.98 - 1.01	0.62
		Valve surgery	0.25	0.11 - 0.57	0.001
		Cardiopulmonary bypass time, minutes	4.70	1.79 - 12.35	0.002
	Postoperative	RV Dysfunction	1.46	0.72 - 2.98	0.29
		Age, years	1.03	0.99 - 1.05	0.06
		Charlson index, 1-24	1.32	1.09 - 1.61	0.005
		Congestive heart failure-	1.69	0.86 - 3.29	0.13
		Left ventricle ejection fraction, %	1.01	0.98 - 1.04	0.52
		Preop eGFR, mL/min/1.73m^2	1.00	0.99 - 1.02	0.93
		Valve surgery	0.21	0.09 - 0.51	0.001
		Cardiopulmonary bypass time, minutes	4.40	1.61 - 12.06	0.004
Delirium	Baseline	RV dysfunction	1.27	0.61 - 2.64	0.53
		Age, years	1.03	1.01 - 1.06	0.008
		Charlson index, 1-24	1.05	0.89 - 1.23	0.59
		Congestive heart failure-	0.79	0.41 - 1.50	0.47
		Left ventricle ejection fraction, %	0.99	0.96 - 1.01	0.38
		Mini-mental score, 1-30	0.84	0.73 - 0.96	0.009
		Valve surgery	0.80	0.32 - 2.01	0.64
		Cardiopulmonary bypass time, minutes	2.50	0.83 - 7.47	0.10
	Postoperative	**RV dysfunction**	**2.09**	**1.04 - 4.22**	**0.04**
		Age, years	1.04	1.01 - 1.07	0.004
		Charlson Index, 1-24	1.02	0.85 - 1.21	0.85
		Congestive heart failure	0.85	0.43 - 1.72	0.66
		Left ventricle ejection fraction, %	0.99	0.96 - 1.01	0.33
		Mini-mental score, 1-30	0.83	0.72 - 0.96	0.01
		Valve surgery	0.82	0.30 - 2.22	0.70
		Cardiopulmonary bypass time, minutes	2.49	0.73 - 8.54	0.15

Subspecialty Abstracts

Economics, Education & Policy

S-114.

ANESTHESIA RESIDENTS AWARENESS OF THE CLINICAL LEARNING ENVIRONMENT

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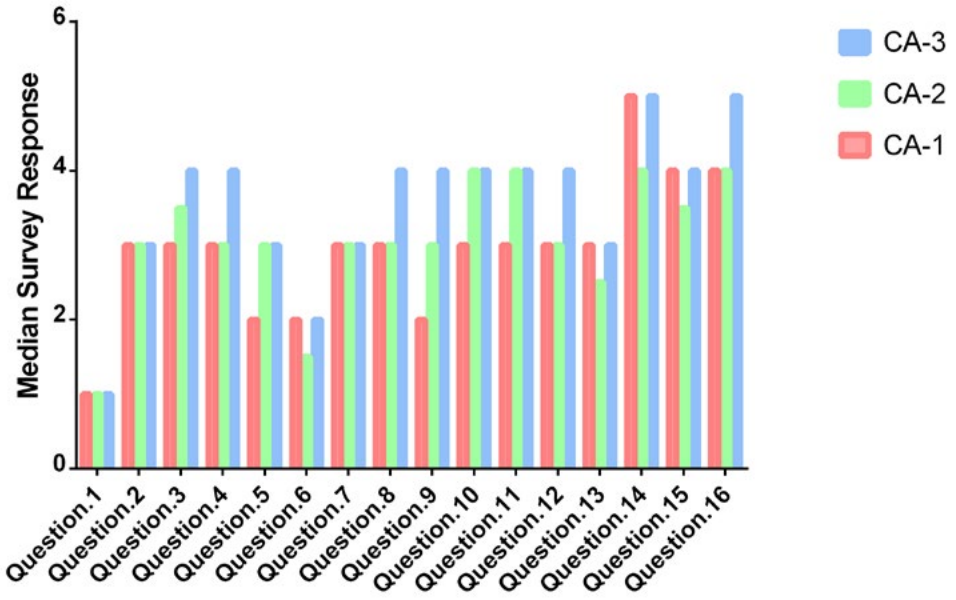
INTRODUCTION: The ACGME has developed a Next Accreditation System for residency programs that requires institutions to maintain a specific Clinical Learning Environment (CLE). The ACGME inspects institutions during the Clinical Learning Environment Review (CLER). The review consists of six focus areas: patient safety, quality improvement and healthcare disparities, transitions of care, supervision, professionalism and duty hour oversight with fatigue management and mitigation. During this review, peer selected residents are expected to participate in meetings and rounds with the inspectors. In addition, the residents complete an annual ACGME survey which addresses these elements. Resident's awareness to their CLE was tested in this study.

METHODS: With IRB approval, 21 CA-1's, 22 CA-2's and 21 CA-3's completed a questionnaire regarding their awareness of their CLE using a scale from 1 (never/unaware) to 5 (always/very aware). The following questions were answered: 1) Have you ever reported errors ? 2) Are you aware of the implications of reporting errors? 3) Have you received formal education regarding patient safety? 4) Are you aware of the quality and safety performance improvement plan? 5) Are you aware of the quality metrics such as readmission rates and hospital acquired infections? 6) Do you know where to find the quality metrics? 7) Have you had formal training in transitions of care? 8) Are you aware of the policies relating to transitions of care? 9) Are you aware of the resident supervision and escalation policy? 10) Are you comfortable escalating patient safety issues? 11) Are you aware of your scope of practice? 12) Are you aware of the steps to be taken if you are too fatigued to safely care for a patient? 13) Are you comfortable using the fatigue mitigation process? 14) Do you honestly report duty hours? 15) Are you aware how to report unprofessional behavior? 16) Are you aware of the code of conduct?

RESULTS: The questionnaire data was analyzed and compared across the CA classes using the Kruskal-Wallis test. The median answer for each CA level was calculated and significance across the classes was identified. Of particular note, all classes reported very rarely reporting errors or near misses using the site specific mechanisms. In addition all classes reported always honestly reporting their duty hours. Of significance across the classes were there awareness of quality metrics ($p<0.0085$), awareness of the resident supervision and escalation policy ($p<0.0047$), awareness of their scope of practice ($p<0.0032$), residents comfort with utilizing the fatigue mitigation process ($p<0.0093$) and their awareness of the code of conduct ($p<0.0045$). For all significant findings, the CA-3 class had more awareness than the CA-1 class.

CONCLUSIONS: Each program is annually monitored by the ACGME and the survey (with CLE questions) is one of their metrics. Moreover, the institution is inspected for their CLER where residents meet with the site visitors. Education on error reporting and their CLE is essential to the residents training and must begin early as the CA-1 residents have less awareness of their CLE then their senior residents.



S-115.

EVALUATING WORKFLOW UNDERSTANDING FOR PREOPERATIVE ULTRASOUND – A CONSENSUS PROCESS USING A MODIFIED DELPHI METHOD

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INTRODUCTION: Ultrasound (US) is rapidly becoming an essential component of perioperative management, and US education is being increasingly incorporated into residency curricula in anesthesiology. Proficiency in perioperative US can be understood as a composite of cognitive knowledge, manual skills, and workflow understanding. Although methods exist for objective evaluation of the cognitive knowledge and manual skills, there are no specific methods for evaluating workflow understanding. As part of a FAER grant funded project, the objective of this study was to develop a consensus list of essential procedural tasks to assess proficiency in perioperative US workflow by using the modified Delphi method.

METHODS: Three of the investigators compiled a preliminary list of general and modality-specific tasks for perioperative US workflow. This list was then edited through a four-stage process. The first stage consisted of a focus group of 10 members of our department that included experts in perioperative ultrasound modalities and anesthesia education. In this step, each item was evaluated for relevance and items were removed or added if deemed appropriate. On the second stage, the same group reevaluated the edited list through a similar process. For the third stage, each individual item was evaluated using a 5-point Likert scale (1= not at all important, 5= extremely important) by anesthesiologists from 133 hospitals around the United States using an anonymous, on-line survey tool (Survey Monkey, Palo Alto, CA). Raters could also include free text comments on each item and suggest removal or addition of items. Median scores and ranges for their responses were calculated. In the fourth stage, raters for the third stage were asked to reevaluate the item list with the median scores and confirm or change their scores. Participants were encouraged to insert comments, particularly if their scores deviated significantly from the median.

RESULTS: After the first stage, the preliminary list of 91 items was modified and reduced to 39 items. The list of tasks was edited and 6 items were added after the second stage (45 items total). A link to the survey was sent via email to a total of 257 attending anesthesiologists from over 133 national hospitals, including our institution, with a response rate of 28% (n=72). In the fourth stage, we asked the responders of the third stage to provide feedback, with 39 responses (54.1%). The final list is composed of 51 different tasks for perioperative US workflow distributed in 8 different categories.

CONCLUSION: A list of essential tasks for perioperative US workflow was constructed using a modified Delphi score. This workflow assessment could be used in addition to existing methods for evaluating psychomotor skills and cognitive knowledge to demonstrate proficiency in preoperative US.

Table 1. Essential tasks for perioperative ultrasound workflow assessment

General tasks	Modality-specific tasks
A. Pre-Procedural Questions: 1. Knows which procedure is being performed 2. Knows the indication for the procedure 3. Knows if the procedure is elective or an emergency 4. Knows the contraindications for the procedure 5. Adequately explains the procedure to the patient 6. Verify informed consent, when appropriate 7. Discusses the procedure with the surgical team 8. Selects appropriate machine 9. Selects an appropriate transducer 10. Prepares procedure-specific equipment **B. Procedural Questions:** 1. Connects machine to power and turns it on 2. Connects the probe 3. Correctly enters or verify demographic information 4. Positions the patient adequately 5. Operator and machine positioning 6. Correctly orients the probe (left/right, etc.) 7. Knows how to obtain adequate images 8. Knows how to store/save images **C. Post-Procedural Questions:** 1. Correctly archives the study and retrial for review 2. Writes a procedural note 3. Communicate clinical findings, when appropriate 4. Adequately clean the probe and machine after use	**D. Vascular Access (out of plane technique):** 1. Application of sterile sleeve 2. Differentiation of arterial and venous structures 3. Identification of target vessel. 4. Recognizes Vessel puncture 5. Ultrasound confirmation of adequate guide wire position **E. Regional Anesthesia:** 1. Application of sterile sleeve 2. Clear labelling of medication (local anesthetic vs iv medication) 3. Identifies the area to be blocked (from the patient, surgical team) 4. Pre-procedural general neurological function assessment of the to be blocked limb or area 5. Appropriate explanation to the patient regarding procedure, expectations from the block, post block care 6. Appropriate time out before the performance of the block with the team members 7. Adequate visualization of needle shaft throughout the procedure 8. Aspiration and incremental injection of local anesthetic 9. Ultrasound confirmation of appropriate local anesthetic spread 10. Checks for block onset **F. Transesophageal Echocardiography:** 1. Check if ECG is connected and an adequate signal is captured. 2. Performs suction of the stomach before probe insertion 3. Adequately inserts bite block for probe protection 4. Performs esophageal intubation. 5. Acquires echocardiographic images **G. Transthoracic Echocardiography:** 1. Check if ECG is connected and an adequate signal is captured. 2. Obtain the parasternal views: long axis, mid pap short axis 3. Obtain the apical views: 4 chamber 4. Obtain the subcostal views: 4 chamber, IVC **H. Abdominal/Chest Wall Examination:** 1. Adequately obtains abdominal and chest wall views 2. Identifies kidney 3. Identifies liver 4. Identifies lung 5. Identifies pleura 6. Identifies stomach 7. Identifies bladder

S-116.

IMPLIED IMPACTS ON ATMOSPHERIC RADIATIATIVE FORCING OF INHALED ANESTHETIC USE IN A COMMUNITY HOSPITAL

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INTRODUCTION: Inhalation anesthetics may alter the infrared (IR) absorption characteristics of the atmosphere.[1] While measurements of IR absorption spectra of inhalation anesthetics and models of their atmospheric kinetics are available, few data indicate the consumption of inhalation anesthetics in anesthetic practice or examine whether changes in anesthetic practice can alter the impact of inhalation anesthesia on the atmosphere.[2,3,4] We report consumption of inhalation anesthetics, in terms of potential to contribute to radiative forcing in the atmosphere over a period of 100 years, and assess whether education and a bundle of best practices can change patterns of inhalation anesthetic use.

METHODS: Inhalation anesthetic consumption, fresh gas use, induction technique (mask versus intravenous) and duration of anesthesia were recorded over five consecutive weekdays (week 1) for 12 operating rooms in a single hospital. After a 3 week interval, an educational session was held to describe the impact of inhalation anesthesia on atmospheric IR absorption, and offer a bundle of suggested best practices: use of sevoflurane in lieu of desflurane, avoidance of nitrous oxide, and use of low fresh gas flows. Data were again collected (week 2) in the same operating room suite. Anesthetics involving continuous infusion of intravenous agent were excluded. The radiative forcing potential of a given anesthetic was calculated relative to the effect of deposition of an equivalent mass of carbon dioxide in the atmosphere over 100 years (CDE 100).

RESULTS: Data were accumulated for 317 hours of anesthesia in week 1 and 248 hours in week 2. Sevoflurane anesthesia entailed an average CDE 100 of 4684 per hour (standard deviation 2637) versus 59779 per hour for desflurane (standard deviation 35306). For any given inhalation agent, atmospheric IR absorption potential expressed as CDE 100 did not differ significantly between weeks 1 and 2. However, total hourly CDE 100 for the 12 operating rooms decreased from 32,539/hour in week 1 to 11,034 in week 2 ($p=0.06$), reflecting primarily a decrease in the number of hours of desflurane anesthesia from 46 in week 1 to 5 in week 2.

CONCLUSION: Consistent with their physical properties, CDE 100 is higher for desflurane anesthesia than for sevoflurane. Education and a best-practice bundle did not significantly alter the CDE 100 of a given anesthetic technique, but did suggest the plausibility of decreasing CDE 100 for the operating room suite through a decrease in desflurane consumption.

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S-117.

RATING OBJECTIVE STRUCTURED CLINICAL EXAMS: IT MATTERS HOW (BUT NOT WHO)

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BACKGROUND: Objective structured clinical examinations (OSCE) are frequently used during residency to assess the resident skill level and have been proposed to become part of the primary certification process.[1] However, best practices for assessment are not well defined. We hypothesized that delayed, video-based scoring is superior to live scoring, and that raters' familiarity with examinees affects the OSCE evaluation process. The aim of this study is to compare live versus delayed (video review) OSCE scoring, and to compare internal (familiar) faculty evaluation with external (remote) faculty evaluation.

METHODS: At the training institution, 11 CA3 residents participated in a simulation event, consisting of several OSCE to assess the demonstrated competency level of several anesthesia milestones. Two OSCEs were video recorded and performance was rated by faculty using an anchored checklist. Two faculty members from the training institution were present at each OSCE and scored the encounter during the simulation (live score). The video recordings were reviewed by one independent faculty member from the training institution (delayed score) and one external faculty member [unaware of training level, non-familiar with resident] (remote score).

STATISTICAL ANALYSIS: Faculty scores from live raters, delayed rater and remote rater were compared using correlation of rater scores and percentage agreement in scoring group (based on the 5-point Global Score Rating Scale [GSRS]). Statistical significance was assessed using a 2-tailed t-test.

RESULTS: A total of 22 encounters were assessed by all raters. We found that there was no agreement (Table 1) between the live raters for both OSCEs (OSCE 1 r = 0.24; OSCE 2 r=0.31). The scores of delayed and remote raters showed a much better correlation (for 22 encounters r = 0.69, $p<0.0001$). If ratings were assessed in scoring groups based on the GSRS, there was agreement in 50% of observations (11 out of 22) amongst live raters, and 77% (17 out of 22) between delayed and remote raters.

CONCLUSIONS: 1) Delayed video-based scoring of an OSCE is superior to live scoring performed during the event. 2) Internal and external (remote) scores had high agreement, suggesting that familiarity with the resident did not bias the scoring.

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Table 1: Inter rater variability

	Live Score 1 (OSCE1)	Live score 1 (OSCE 2)	Delayed score	Remote Score
Live score 2 (OSCE 1)	0.237	-------	0.558	0.514
Live score 2 (OSCE 2)	-------	0.313	0.493	0.363
Delayed score	0.343	0.392	-------	**OSCE 1** 0.804
Remote score	0.473	0.384	**OSCE 2** 0.578	-------

The table shows the correlations between the scores obtained during the OSCE (live score) and the scores obtained delayed by reviewing the video recording (delayed score = faculty rater familiar with resident; remote score = faculty rater not familiar with resident).

S-118.

NORA TURNOVER TIMES: NEITHER HERE NOR THERE

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INTRODUCTION: For many hospitals, the non-operating room anesthesia (NORA) workload continues to expand.[1] NORA services tend to be poorly-utilized and highly variable. Current literature on the management of NORA tactical and operational decisions is scant. In this study, we hypothesized that turnover times are different between NORA and OR cases schedules.

METHODS: Using WiseOR® (Palo Alto, CA), we extracted the turnover times for all the anesthetics provided by the Department of Anesthesiology and Pain Medicine from January 1, 2015 to December 31, 2015. We studied a total of 9,463 turnover times and separated the times into the Main Campus/Minor Procedures (MPU) 1 and 2 (Main); Ambulatory (Amb); and Sedation/MPU 3-5 (NORA). At our institution, we use the minor procedure unit for both OR and NORA cases. We imported the data into RStudio (Boston, MA) and we used nonparametric tests because the data was not normally distributed.[2] We calculated the Brown-Forsythe test to assess the homogeneity of variance; Kruskal-Wallis H test to analyze the differences between means; and Nemenyi test to perform a post-hoc pairwise comparison.[3-5]

RESULTS: In Table 1, we show the data extracted from WiseOR®. Mean turnover times for the Main, Ambulatory and NORA cases were 35.9, 25.1, and 22.4 minutes, respectively. The Brown-Forsythe test ($p<0.0001$) showed that the group variances are significantly different. The Kruskal-Wallis H test ($p<0.0001$) showed that at least one group has a different distribution. Finally, the Nemenyi test shows that no two groups were identical ($p<0.0001$). Table 1. Raw data extracted from WiseOR® (Palo Alto, CA).

Group	n	Mean Turnover (min)	SD
Main	6134	35.9	12.9
Amb	2554	25.1	10.2
NORA	775	22.4	17.0

CONCLUSIONS: Previously, Macario commented that more efficient ORs had turnover times less than 25 minutes.[6] Although our turnover times for the cases in NORA are below this benchmark, we show that NORA turnover times are longer than their OR counterparts, both in the mixed, inpatient and outpatient settings. Future studies should elucidate the reasons underlying the longer turnover times (e.g. scheduling bias, lower utilization rates, availability of the anesthesia providers) and the possible differences between various NORA service lines. For instance, Luo et al showed that sequence-dependent differences exist for anesthesia-controlled times.[2] Similarly, the turnover times for our pediatric gastroenterology service averages 13 minutes, which is closer to the Main OR mean turnover times in this study (data not shown). As anesthesiology departments continue to expand their presence outside the OR, managers and administrators should understand the operational differences between NORA and OR sites.

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S-119.

SIMULATION-BASED ASSESSMENT OF IMPROVEMENTS IN COGNITIVE PERFORMANCE IN AN ANESTHESIOLOGY RESIDENCY TRAINING PROGRAM

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INTRODUCTION: Deficiencies in anesthesiology resident cognitive performance have previously been identified across three clinical domains (operating room, trauma, and cardiac resuscitation).1,2 We investigated if these deficiencies improved over time.

METHODS: Individual basic knowledge and cognition performance in simulation-based scenarios were assessed in 48 residents (PGY-3 and 4) using a 20- to 27-item scenario-specific checklist. Identical or similar scenarios were annually repeated by the same residents 18 times. For every scenario and item, we calculated: group error scenario rate (frequency) and individual (resident) item success. Grouped individuals' success rates are presented as mean ± SD and group error rates are presented as proportions. For all analyses, alpha was designated as 0.05.

RESULTS: Overall, PGY-4 residents' error rates were lower and success rates higher for the cognitive item compared to technical item performance in the operating room and cardiac resuscitation domains. In all three clinical domains, the cognitive error rate by PGY4 residents was fairly low (0.00-0.22) and the cognitive success rate by PGY4 residents was high (0.83-1.00) and significantly better compared to previous annual assessments (Tables 1 and 2). There was also an annual decrease in error rates, primarily driven by decreases in nontechnical errors. The differences between cognitive and technical errors were different between years, with this effect more predominant in trauma and cardiac resuscitation. The most common cognitive error types observed remained anchoring, availability bias, premature closure, and confirmation bias.

CONCLUSION: Simulation-based assessment continued to separate between higher-order and lower-order skills expected of a relatively experienced anesthesiology resident. Our evaluations demonstrated significant improvements in each domain compared to previous annual assessments, and in certain scenarios with previously identified learning gaps. Simulation-based assessments can highlight areas of relative strength and weakness in a resident cohort and can also guide modifications in the curriculum with regard to identified deficiencies in tasks requiring higher-order processing.

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Table 1. Error rate for all technical/nontechnical items according to the specific scenario and postgraduate year (PGY) level

Group Error Rate	Resuscitation		Trauma		OR	
Scenario	I	II	I	II	I	II
PGY Items						
PGY3 All			0.18	0.17	0.22	0.16
Tehcnical			0.14	0.13	0.24	0.17
Cognitive			0.26 ‡	0.22	0.19‡	0.15
PGY4 All	.29	0.11 †‡	0.15	0.06‡	0.15	0.19
Technical	0.34	0.13†	0.18	0.09‡	0.15	0.23
Cognitive	0.2*‡	0.08‡	0.11	0.00‡	0.14	0.14*‡

* P < 0.05 technical vs. cognitive (=nontechnical) value in the same group.
† P < 0.05 scenario 1 vs. scenario 2 success rate value.
‡ Value different from previous year annual assessment, same PGY level.

Table 2. Grouped success rates for all items according to the specific scenario and postgraduate year (PGY) level

Group Individual Success Rate	Resuscitation		Trauma		OR	
Scenario	I	II	I	II	I	II
PGY Items						
PGY3 All			0.80±0.11	0.84±0.07	0.77±0.06	0.82±0.09
Tehcnical			0.80±0.11	0.84±0.07	0.77±0.06	0.82±0.09
Cognitive			0.78±0.09‡	0.78±0.16	0.81±0.06*‡	0.74±0.26
PGY4 All	0.79±0.1	0.91±0.10‡	0.85±0.07	0.94±0.02‡	0.85±0.04	0.81±0.03
Technical	0.66±0.11	0.87±0.15†	0.82±0.06	0.91±0.04‡	0.85±0.06	0.75±0.03
Cognitive	0.83±0.11*‡	0.93±0.11*‡	0.88±0.11	1.0±0.0*‡	0.89±0.03	0.86±0.05

* P < 0.05 technical vs. cognitive (=nontechnical) value in the same group.
† P < 0.05 scenario 1 vs. scenario 2 success rate value.
‡ Value different from previous year annual assessment, same PGY level

S-120.

RACE EFFECT ON TYPE OF ANESTHESIA AND 30-DAYS POST-OPERATIVE OUTCOMES IN PRIMARY TOTAL KNEE AND HIP ARTHROPLASTY: NATIONAL DATABASE ANALYSIS

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INTRODUCTION: End-stage knee or hip osteoarthritis is a common disabling disease. Total joint arthroplasty (TJA) is an effective and generally safe procedure for osteoarthritis. Furthermore, a growing body of evidence supports the use of neuraxial anesthesia for TJA[1,2]. Previous studies have suggested a racial disparity in the utilization of these surgical procedures[3]. However, racial disparity in utilization of neuraxial blocks for TJA has not been evaluated. We utilized the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database[4] to study the effects of race on the type of anesthesia and the postoperative outcomes in elective TJA.

METHODS: We included African-American (AA) and White (W) adult patients undergoing elective primary total knee (TKA, CPT code 27447) and total hip arthroplasty (THA, CPT code 27130) receiving general or neuraxial (spinal and epidural) anesthesia from 2005 to 2013. Trauma, emergency surgery, other races and ethnic groups, cases done under other type of anesthesia were excluded. A 1:3 matched sample of African-American (AA) vs White patients was created based on propensity scores after adjusting for the patient's demographic characteristics, preoperative comorbidities, type of admission, and complexity of procedure. Conditional logistic regression analyses were used to evaluate the differences between the two groups in 30-days postoperative complications (composite of major postoperative complications) and type of anesthesia.

RESULTS: Total of 102,122 patients were included (THA 40% and TKA 60%). White patients utilized TJA more often than AA patients (ratio 1:12 in this sample vs 1:5 in US population). AA patients were younger (62 ±11years vs. 66 ±11, $p<0.001$) and had a higher ASA physical status score (OR 1.47, 95% CL 1.41-1.54, relative to ASA I-II, $p<0.001$), however, lower modified Charlson comorbidity index (CCI) score (OR 0.53, 95% CL 0.48-0.59, relative to CCI=1, $p<0.001$). General anesthesia was used more commonly in the AA patients group (OR 1.11, 95% CL 1.05-1.16, $p<0.001$). However, when the two groups were matched, the differences in the type of anesthesia disappeared (adjusted OR 0.96, 95% CL 0.85-1.08, $p=0.455$). AA patients had a higher rate of 30-days postoperative complications before matching (OR 1.41, 95% CL 1.24-1.62, $p<0.001$) and after matching (adjusted OR 1.58, 95% CL 1.13-2.21, $p=0.007$).

CONCLUSIONS: There is no difference in the type of anesthesia received for TJA between AA and White patients; however, there is a disparity in the postoperative outcomes in favor of the White patients. Further studies needed to explain these findings.

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S-121.

OUTCOME PREDICTABILITY AFFECTS ENGAGEMENT AND PERFORMANCE IN HIGH-STAKES SIMULATION

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INTRODUCTION: Recently in the field of anesthesiology, attention has been paid to learning theory and the influence of emotion on performance, especially as relating to simulation. It has been hypothesized that optimum learning and performance occurs within a discreet range of subjective emotional intensity, with very low and very high levels of emotion being less beneficial to performance.[1-3] In simulation, willingness of participants to "believe in" simulated scenarios, and thus to emotionally engage, may relate to perceived ability to predict the outcome of the scenario (i.e. "false security"). This study investigates whether unpredictability of outcome in simulated exercises could be correlated with objectively-scored performance.

METHODS: After IRB approval, anesthesia residents from our institution participated in a standardized series of weekly simulated operating room scenarios. Prior to participation, each resident was randomly assigned to one of three cohorts regarding patient outcome: in cohort 1, the patient always died during the simulation; in cohort 2, the patient always lived; and in cohort 3, the patient died approximately 50% of the time in no consistent order. Participants were not informed of their cohort assignment. After an acclimation period of eight weeks had passed, residents were scored on four subsequent scenarios using the Anesthesia Non-Technical Skills Scale (ANTS),[4] in which a higher score indicates a superior performance. Multivariate analysis was carried out to determine the effect of group assignment on performance.

RESULTS: 50 Anesthesiology residents were enrolled, of which 17 were assigned to the "patient never dies" cohort, 17 to the "patient always dies" cohort, and 16 to the "patient dies unpredictably" cohort. Inclusion in the "patient dies unpredictably" cohort was significantly associated with higher performance as measured by the ANTS ($p=0.01$). Inclusion in the "patient always dies" and "patient never dies" cohorts showed no correlation with objective performance.

DISCUSSION: In this study, residents who experienced patient death unpredictably in the simulated scenarios performed better in non-technical skills assessments as measured by the ANTS. Residents who experienced patient death in a consistent manner (never or always) performed neither better nor worse. While further investigation may clarify these results, it may be that the element of unpredictability encouraged sustained psychological engagement in the simulated exercises and led to improved performance.

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S-122.

ENHANCING FEEDBACK IN ANESTHESIA RESIDENCY PROGRAMS

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INTRODUCTION: Feedback from faculty is critical for enhancing resident performance.[1] In 1999, a survey of anesthesiology program directors demonstrated that only 20% of programs provided faculty development programs involving formal training in resident evaluation.[2] Interventions, including workshops and faculty development seminar series, have met with varied but incomplete success.[3] Our goal was to enhance feedback to residents from faculty using a video-based teaching tool at four institutions.

METHODS: We developed an educational program to teach faculty how to provide feedback. The program consisted of two video-based discussion sessions for faculty and one discussion session for residents. Faculty members were presented with techniques on how to provide feedback to residents on professionalism and communication. Residents were provided with information on how to ask for and receive feedback. We implemented the program at the four institutions, where faculty provide daily feedback to residents. Feedback records from three months prior to the intervention to three months after the intervention were rated by experts for quality (detailed, specific, behavior-focused, not harmful/destructive, and actionable), utility, whether it was related to professionalism/communication, and whether it had negative feedback. Pre-intervention feedback was compared to feedback during the intervention period and to post-intervention feedback using the Mann-Whitney U and chi-squared tests.

RESULTS: 1926 feedback records were rated (855 in the pre-intervention period, 175 in the intervention period, and 896 in the post-intervention period). Feedback had higher quality ($p = 0.04$) and utility ($p = 0.002$) from pre- to post-intervention at Institution 1 (Figures 1-2) but not overall. From pre-intervention to the intervention period, the institutions overall and Institution 2 had more feedback on professionalism/communication ($p = 0.01$ and $p < 0.001$, respectively; Figure 3); also, Institution 3 had more negative feedback ($p = 0.01$; Figure 4) and feedback with higher utility ($p = 0.04$).

CONCLUSIONS: We detected different changes at the institutions despite the identical intervention. The intervention may be more effective with new faculty and/or smaller discussion sessions as the discussion sessions at Institution 1 had fewer faculty who were all new staff at the time of the intervention. Future steps in this project include refining the rating system, exploring ways to sustain changes, and investigating other factors that may affect the quality and utility of feedback.

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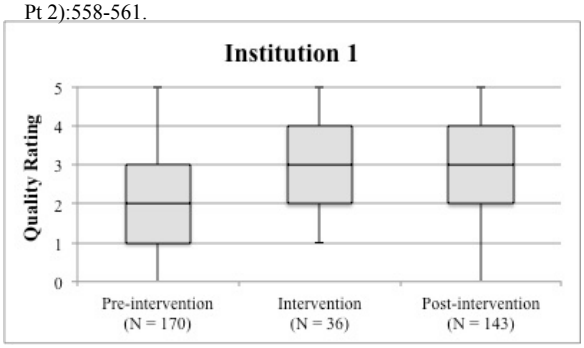

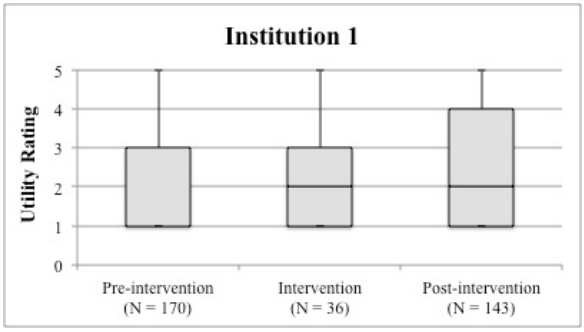

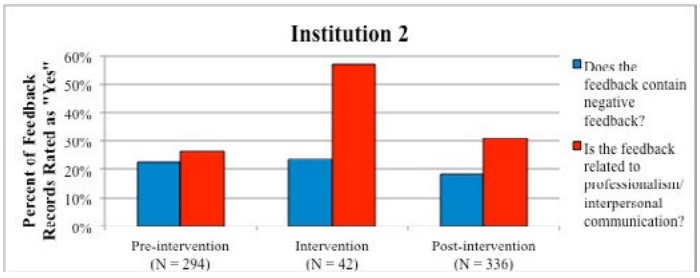

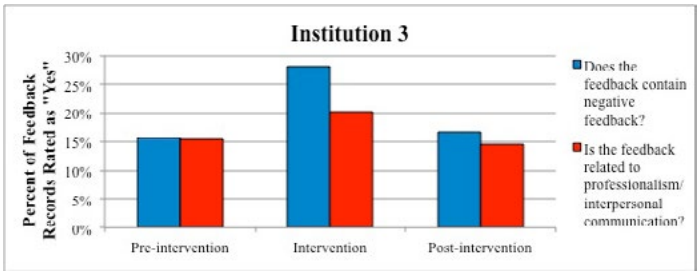

S-123.

THE UTILITY OF PRE-SPECIFIED MILESTONES IN THE PILOT PHASE OF A LARGE PRAGMATIC CLINICAL TRIAL

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INTRODUCTION: The 27-institute National Institutes of Health (NIH) invests 30.1 billion dollars in medical research annually. In 2015, one of its institutes, the National Institute on Aging (NIA),[1] invested $1.1 billion in research into human mechanism of aging and geriatric diseases[2]. It is important for the NIH to fund studies that are likely to yield scientific discovery and impact health care outcomes. Recently, the NIH began to fund studies through a phased mechanism where the initial pilot phase requires identification and achievement of study specific milestones as partial justification for continued funding during the subsequent expanded phase[3]. This phased mechanism hypothetically ensures that most funding is allocated to studies that are feasible, and are most likely to produce scientific discovery and improve health care delivery. We illustrate how such a phased approach translates to a large pragmatic study using the example of an the ongoing clinical trial, which hypothesizes that electroencephalography guidance of general anesthesia can decrease postoperative delirium and its downstream negative sequelae.

METHODS: Investigators at were awarded funding through a phased UH2/UH3 mechanism by the NIA for the trial. Five other studies were funded under this mechanism. The NIH simultaneously awarded an independent grant to an expert, independent research corporation (Westat, Rockville, MD) to help develop milestones and to evaluate progress during the pilot phase of these six trials. Collaborating with stakeholders, investigators established seven fundamental milestone categories covering regulatory documents, clearances, fidelity of outcome collection, recruitment, fidelity of study intervention, patient safety, and data collection. Using these categories, investigators established study specific milestones during the pilot UH2 phase (Table 1). Investigators evaluated progress monthly in collaboration with Westat, and prepared interim and final reports for the NIA.

RESULTS AND MAJOR FINDINGS: At the end of the pilot phase investigators were successful in completing all of the identified study milestones (Table 1).

CONCLUSION: While the NIH funds numerous large clinical trials each year, it is important for all stakeholders that the investigators determine early whether it is worthwhile to continue a trial beyond the pilot phase. Through the phased UH2/UH3 funding mechanism, with its structured milestone process, investigators are able to identify the challenges and barriers to success of a trial, as well as to collaborate effectively with the funding agency to increase the likelihood that the trial will meet expectations.

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S-124.

BLIND PALPATION VS ULTRASOUND GUIDED ARTERIAL LINE PLACEMENT

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INTRODUCTION: Arterial catheterization has become commonplace in OR to provide convenient and reliable access for frequent blood gas analysis, blood sampling, and real-time hemodynamic monitoring for critically ill patients and major surgeries. Several randomized controlled trials and meta-analyses have shown that use of ultrasound reduces complication and increases first-attempt success rate when compared with blind palpation technique. We hypothesized that ultrasound guidance for artery catheterization will improve placement time for arterial line in the OR.

METHODS: Following IRB approval, consented adult patients undergoing routine surgery were randomized to the conventional blind palpation or ultrasound guidance technique for artery catheterization. In this study we compared time required for placement of arterial line placement, number of sites, number of catheters used, and number of operators required to insert the arterial line. All catheterizations in both groups is performed by trained anesthesiology residents (CA-2 and CA-3 residents or staff anesthesiologist) who have similar level of experience in radial arterial catheterization with palpation technique and with US guided technique. In both groups, arterial catheterizations were performed after induction of general anesthesia. Start time was defined as the time when the ultrasound machine is turned on before gel is placed on the transducer. In the palpation technique, start time of the procedure is defined as the time when the operator's finger will be placed on the wrist to palpate the radial pulse. End time is recorded after successful arterial cannulation with appropriate pulsatile blood flow return.

RESULTS: A total of 298 subjects, 151 blind palpation group and 147 ultrasound group are currently enrolled for the study. Total time taken for successful arterial catheterization for blind palpation group vs ultrasound guidance group were 219 seconds and 187 seconds, respectively (p valve 0.63). Total number of the attempts, number of sites used, number of the catheter used and total number of operators were consistently higher in blind technique. Ultrasound rescue was required in 12 out of 151 patients in the blind palpation group. In contrast, only 1 out of 147 patient cross over to the palpation technique in ultrasound technique group.

CONCLUSION: Despite the frequency of arterial catheterization done in the OR, blind palpation technique continues to be a clinical challenge even for the most experienced anesthesiologist. At this time, time for successful arterial line placement for both blind and ultrasound guidance technique are similar, with ultrasound having slight advantage. Ultrasound technique also has the added benefit of using less sites and less number of catheters. This could be a potential deduction in complications and costs. Nevertheless, this is still on-going investigation. Our sample size of the study needed to complete the study is at least 210 patients in each group.

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S-125.

THE COST OF OPEN CARPAL TUNNEL RELEASE IN THE OPERATING ROOM VERSUS THE OUTPATIENT PROCEDURE ROOM: A TIME-DRIVEN ACTIVITY BASED COSTING APPROACH

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INTRODUCTION: Carpal tunnel release (CTR) is a common procedure performed over 400,000 times per year in the United States.[1] Open CTR can be performed in an operating room (OR) or an outpatient procedure room with considerable differences in time, labor and supplies for each setting. Time-driven activity based costing (TDABC) is a method that calculates the costs associated with supply and labor resources utilized as a patient moves along a care process.[2] We used TDABC to compare the costs of performing open CTR in the OR versus the outpatient procedure room.

METHODS: Using a TDABC model, we calculated the costs of open CTR in the OR and the procedure room. The model considered the following key variables: 1) the cost per clinical hour for each staff member, 2) the amount of time required of each staff member and 3) the supply costs. We determined labor costs per clinical hour using internal data. Similarly, we determined time and supply costs using one orthopedic surgeon's CTR cases performed in 2015. Of these, the surgeon performed 91 in the OR and 51 in the outpatient procedure room, respectively. We developed the model using Excel software (Microsoft Corporation, Redmond, WA). We provide data on our assumptions for calculating the costs of the two different CTR approaches in Table 1.

RESULTS: The cost of performing CTR in the OR was $577 per case compared to $386 per case in the procedure room, representing an absolute cost difference of $191. Labor costs were $399 in the OR compared to $208 in the procedure room while supply costs were $178 in both settings. The average time required to perform CTR in the OR was 52:30 minutes versus 48:06 minutes in the procedure room.

CONCLUSIONS: Performing open CTR in the procedure room costs 33.2% less per case than performing open CTR in the OR. A recent Canadian study found that use of the procedure room was more than twice as time efficient and cost 73.4% less per CTR case than the OR.[3] Value in health care can be defined by a given health outcome achieved per dollar spent.[4] Patients undergoing CTR in the procedure room have similar postoperative pain control, satisfaction scores and the same incidence of deep and superficial wound infection complications.[5,6] Given that open CTR in the OR and the procedure room produce comparable clinical outcomes, our analysis demonstrates that open CTR provides superior value when performed in an outpatient procedure room setting. In an era of declining reimbursements and operating room resource constraints the application of TDABC will help institutions optimize the use of surgical resources to maximize value and efficiency.

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Table 1 – Carpal Tunnel Release (CTR) Cost per Case in the OR and the Procedure Room

	CTR – Procedure Room				CTR – OR			
Personnel	No. of Staff	Cost per Clinical Hour	Total Time (mins)	Total Cost	No. of Staff	Cost per Clinical Hour	Total Time (mins)	Total Cost
Anesthesia								
Anesthesia Attending	0	$203	0	$0	1	$203	26.2	$89
Anesthesia CRNA	0	$93	0	$0	1	$93	52.5	$81
Surgery								
Orthopaedic Surgeon	1	$186	48.1	$149	1	$186	52.5	$163
Miscellaneous								
Circulator Nurse	1	$47	48.1	$38	1	$47	52.5	$41
Patient Care Tech	0	$19	0.0	$0	1	$19	10.0	$3
Surgical Technologist	1	$26	48.1	$21	1	$26	52.5	$23
Supplies				$178				$178
Totals	**3**			**$386**	**6**			**$577**
Absolute Cost Difference								**$191**
Absolute % Cost Difference								**33.2%**

S-126.

A DESCRIPTION OF THE LANDSCAPE OF ANESTHESIA CARE IN AN INTEGRATED NATIONAL HEALTH SYSTEM

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INTRODUCTION: The Veterans Affairs (VA) Administration is the largest integrated healthcare system in the U.S., serving over 8.7 million veterans per year. Surgical care for Veterans occurs primarily within the VA's 109 inpatient surgical hospitals and 27 ambulatory surgery centers. Anesthesia is a critical element of surgical care, and several models of anesthesia care delivery exist in U.S. healthcare system, including sole-provider models [physician or nurse anesthetist (CRNA) only] and team-based care (medical direction or supervision of a CRNA by a physician). Studies have been performed to determine if outcomes differences attributable to model of anesthesia care exist with mixed findings,[1-4] and the optimal model for anesthesia care remains an open question and a subject of debate among stakeholders. The purpose of this study is to understand and describe the landscape of anesthesia care across the nations largest integrated national health system.

METHODS: Data from the VA National Data Extract for Surgery package for all surgical procedures between October 1, 2013 and March 31, 2015 were utilized for this analysis. We created a 5-category model of anesthesia care classification system based on primary anesthetist and supervising anesthetist data fields (table 1). We next determined the prevalence for each of the five models of anesthesia care overall and by facility complexity (level 1a, 1b, 1c, 2, and 3). For each case we then cross-walked primary surgery CPT code to anesthesia CPT code with associated anesthesia base units. We used anesthesia CPT code base units to determine distribution of case complexity by model of anesthesia care, where 3-4 base units = low complexity, 5 base units = medium complexity, and 6 or more = high complexity.

RESULTS: Our analysis captured 726,706 unique case records, and 637,802 (88%) of these cases were confirmed to be surgical by verification of a valid corresponding primary surgical CPT code. The distribution of models of anesthesia care for all surgical cases appears in table 2. Anesthesiologist directing CRNA is the most prevalent model with just over half of surgical cases recording this model of care. Table 3 depicts the distribution of models of anesthesia care by facility complexity level. The team-based model of care is more prevalent at higher complexity facilities, while the CRNA alone model is only observed at lower complexity facilities. Finally, table 4 depicts the distribution of models of care by anesthesia case complexity.

CONCLUSIONS: Team-based anesthesia care is the model most commonly employed overall, and disproportionately so at higher complexity facilities and for higher complexity cases. The CRNA-alone model of care is utilized almost exclusively at smaller (level 2 and 3) facilities. Further investigation is needed to determine the drivers for the observed care model trends as well as to determine if model of care variations are associated with differing patient outcomes.

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Table 1: Models of anesthesia care classification

Model of Anesthesia Care	Description
0	No anesthesia providers documented
1	Anesthesiologist supervising/directing CRNA
2	Anesthesiologist supervising anesthesia resident
3	Anesthesiologist practicing alone
4	CRNA practicing alone

Table 2: Overall frequency for models of anesthesia care (n=540,145). Cases with missing anesthetist provider codes or non-surgical CPT codes were excluded.

Model of Anesthesia Care	Number	Percent
0	53,037	9.82
1	276,311	51.15
2	72,832	13.48
3	81,070	15.01
4	56,895	10.53

Table 3: Frequency of model of anesthesia care by facility complexity (n=539,394 cases). Cases with missing anesthetist provider codes, non-surgical CPT codes, or missing facility codes were excluded.

	Model 0		Model 1		Model 2		Model 3		Model 4	
Facility Complexity	N	%	N	%	N	%	N	%	N	%
1a	23,247	8.83	159,296	60.48	51,436	19.53	28,590	10.85	821	0.31
1b	11,789	12.22	49,511	51.33	15,768	16.35	16,071	16.66	3,324	3.45
1c	3,420	3.90	48,579	55.39	5,605	6.39	20,916	23.85	9,190	10.48
2	13,243	18.05	16,029	21.84	1	0.00	13,159	17.93	30,948	42.17
3	1,335	7.24	2,587	14.02	0	0.00	1,919	10.40	12,610	68.34

Table 4: Frequency of model of anesthesia care by case complexity (n=540,145 cases). Cases with missing anesthetist provider codes or non-surgical CPT codes were excluded.

	Model 0		Model 1		Model 2		Model 3		Model 4	
Case Complexity	N	%	N	%	N	%	N	%	N	%
Unknown	2,126	4.01	12,297	4.45	5,829	8.00	3,626	4.47	1,652	2.90
Low	22,915	43.21	132,735	48.04	23,833	32.72	40,022	49.37	26,922	47.32
Medium	18,327	34.56	65,420	23.68	13,793	18.94	20,170	24.88	20,626	36.25
High	9,669	18.23	65,859	23.84	29,377	40.34	17,252	21.28	7,695	13.52

S-127.

A NOVEL APPROACH TO RANDOMIZATION OF ACGME MILESTONES INTO DAILY ANESTHESIA RESIDENT EVALUATIONS

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: The goal of this study was to develop an assessment tool that implemented all 25 anesthesiology milestones and rotation specific EPAs over the course of a residency. In 2013, the ACGME and the American Board of Anesthesiology (ABA) published the Milestone Project with the charge to programs to use them as guidelines to track resident development and assess for graduation readiness. Our program desired to create an evaluation tool using all of the milestones over the course of residency as well as creating Entrustable Professional Activities (EPAs). We desired that this tool be "rotation specific" in that the document would maintain a single structure, but the content would be specific to each rotation's goals and objectives and only include those milestones thought to be appropriate for development on that rotation. We also desired to retrospectively examine our assessment tool for inclusion/exclusion of all milestones which we felt would lend some validity to the anesthesiology milestone project as an appropriate framework for our resident assessment.

METHODS: We have 30 rotations and 25 rotation directors. We requested that each RD create 8 EPAs, and pick 10 milestone subcompetencies that were applicable to their rotation. Each RD returned their EPAs and chosen milestones to us and a structurally identical assessment tool was created using New Innovations Evaluation Management System. After completion of all 30 evaluations, we mapped each evaluation and the chosen milestones to assess whether or not each milestone was utilized somewhere throughout the 30 rotations, at which point in training a particular milestone might be assessable, and to see which milestones were most and least commonly used.

RESULTS: All milestones were included by RDs in the 30 rotation evaluations. The most commonly used subcompetencies were SBP 1, PBLI 3, and ICS 2. The least commonly used subcompetencies were PROF 3 and PROF 5. We noted that the 6 core competencies were equally present between all three clinical anesthesia (CA) years; however, the MK competency was assessed the least. Between CA 1-3 years, the most frequently assessed subcompetency varied. SBP 1, PC 1, and PROF 1 were most commonly assessed in the CA-1 year, with no assessment of SBP 2, PROF 2, and PROF 5. In CA-2 year, PBLI 3, PROF 4, and ICS 2 were the most commonly assessed subcompetencies with gaps in assessment of SBP2 and PROF 3. During the CA-3 year, PC 1, SBP 1, PBLI 3, and ICS 2 were most frequently assessed and there was no assessment of PC 7.

CONCLUSIONS: We were able to incorporate the ACGME/ABA Anesthesiology Milestones into our assessments in a randomized way and evaluate both validity of the milestones for our program curriculum as well as identify gaps in our curriculum.

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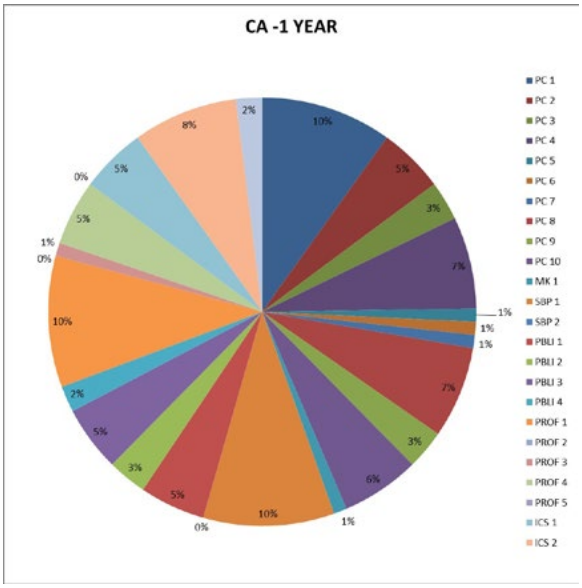

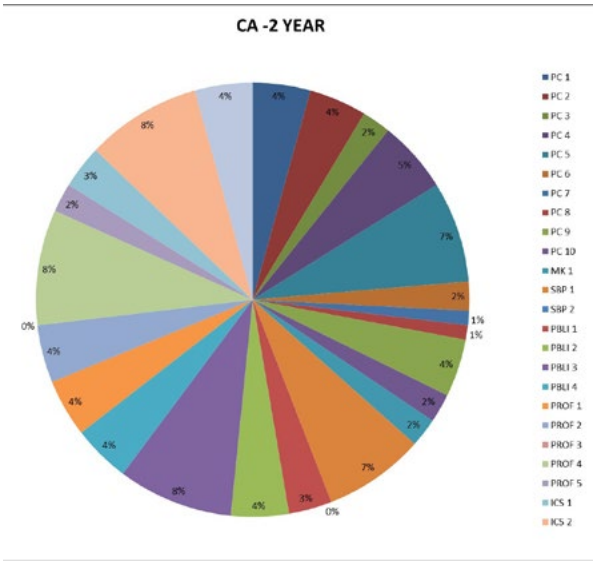

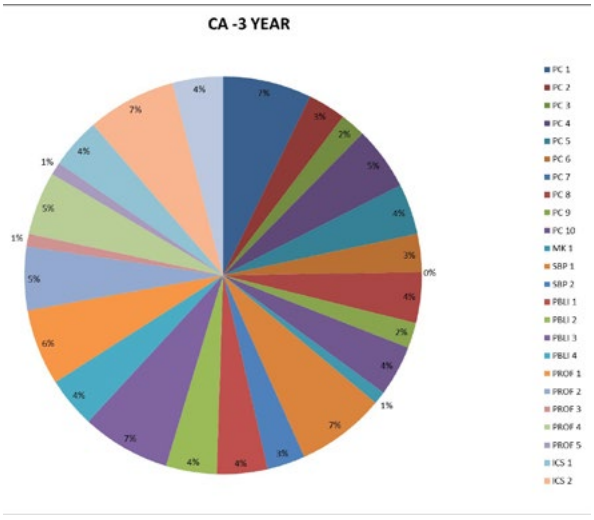

S-128.

TRAINING ANESTHESIOLOGY CLINICIANS IN EEG-BASED DETERMINATION OF ANESTHETIC DEPTH USING A SHORT MODULE

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INTRODUCTION: There is growing interest in the use of limited montage electroencephalogram (EEG) during general anesthesia. There is also evidence that EEG guidance of anesthesia improves patient outcomes.[1] Several processed EEG (pEEG) indices that utilize proprietary analysis algorithms have been developed as candidate depth of anesthesia monitors. However, current pEEG monitors have limitations including delays in response time, unreliable artifact filtration, poor performance with some anesthetic agents, and lack of accuracy in certain patient groups.[2,3] Importantly, when pEEG indices provide misleading information (e.g., provide a value suggesting general anesthesia when a patient is awake), clinicians trained in EEG interpretation can often discern this discrepancy from the EEG waveform. The purpose of this study is to test the hypothesis that anesthesia clinicians can demonstrate improvements in EEG waveform interpretation after completing a short, structured training module. Our primary objective was to show that, after training, clinicians could correctly identify whether EEG waveforms were consistent with wakefulness, general anesthesia, or deep general anesthesia.

METHODS: Clinicians (attending physicians, residents, medical students, and nurse anesthetists (CRNAs)) viewed a 30-minute training lecture (icetap.org Module 2). Prior to and after the lecture they completed tests consisting of ten EEG screen captures (Figure 1, 2) or videos with accompanying interpretation questions. They identified with which state (wakeful, anesthesia, deep anesthesia) each EEG waveform was consistent, and determined whether the EEG waveform was concordant or discordant with the displayed pEEG index.

RESULTS: Eighty-three clinicians took part in this study with 12 being excluded from analysis due to incomplete responses. Of the remaining 71 participants, 13 reported prior training in EEG-based anesthetic depth assessment. Clinicians showed improvement in interpreting EEG waveforms on the post-test compared to the pre-test (75.9% vs. 61.1% correct respectively), $t(68)=6.79$, $p<.001$. There was no significant difference in clinician performance for identifying concordance between the pre-test and post-test (63.9% vs. 63.4% respectively), $t(68)=.21$, $p=.83$. When comparing pre-test scores, trained clinicians scored higher than untrained (70.8% vs. 59.0% correct respectively), $t(69)=2.38$, $p=.02$. There was no significant difference however between trained and untrained participants' post-test scores (71.8% vs. 75.7% correct respectively), $t(69)=.95$, $p=.34$.

CONCLUSIONS: A brief, structured training session appears to improve the ability of untrained clinicians to interpret EEG waveforms during wakefulness and general anesthesia. While performance did not improve in identifying concordance vs. discordance, the subjective definition of concordance may have made this determination more difficult.

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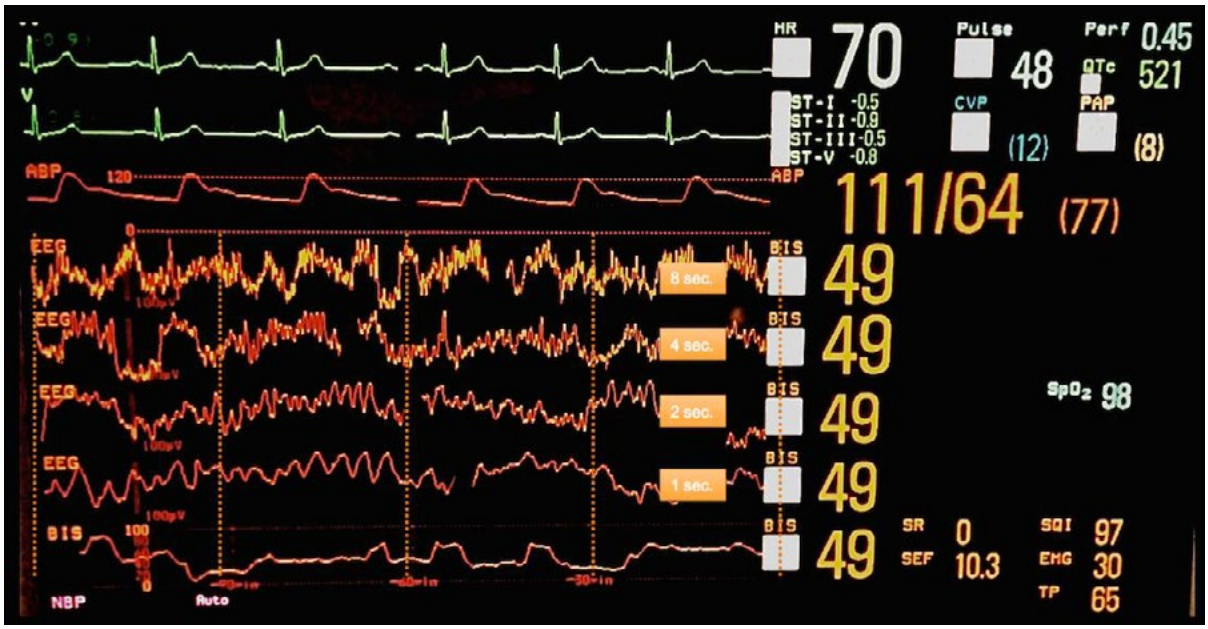

Figure 1.

S-128 • CONTINUED ON NEXT PAGE

S-128 • continued

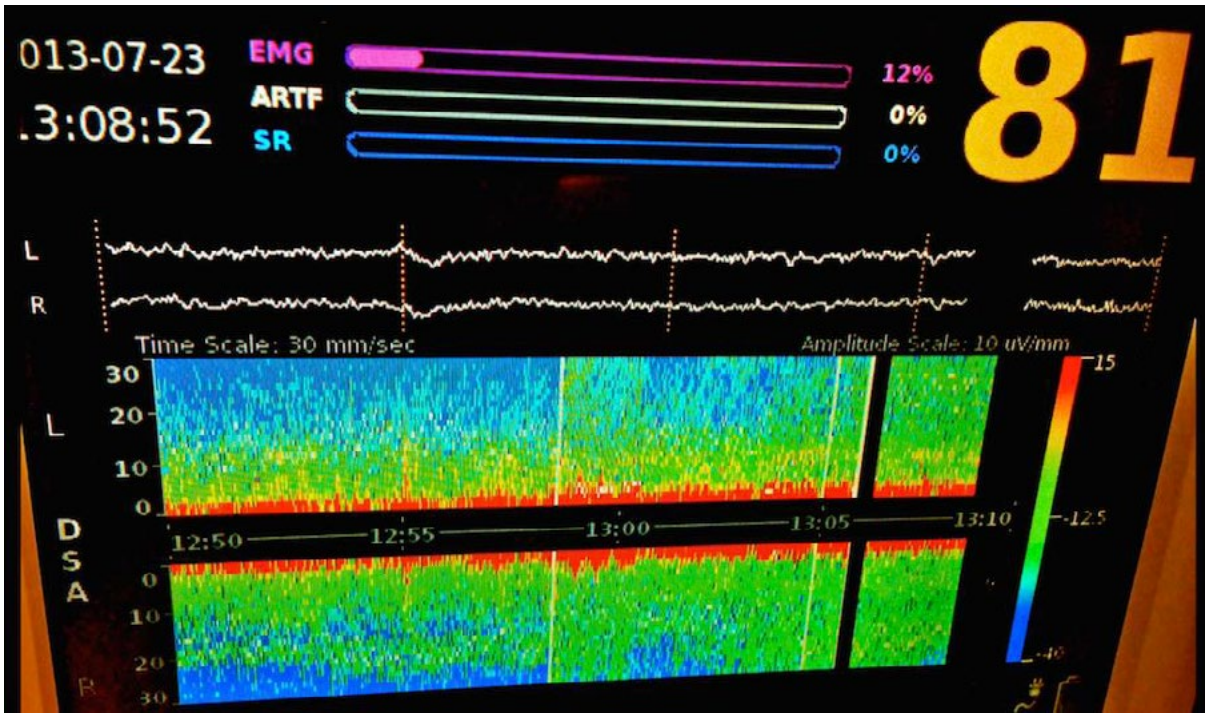

Figure 2.

S-129.

CASE CANCELLATIONS: AN UNAVOIDABLE AND COSTLY ISSUE

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INTRODUCTION: Operating rooms (ORs) are responsible for a major contribution margin to most hospitals. Impediments to OR efficiency can negatively impact finances. Cases cancelled on the day of surgery may result in financial costs (if equipment/supplies have been opened) and opportunity costs (if the time is not filled by another case). Although cancellations on the day of surgery are minimal on weekdays (Monday 0600 thru Friday 1900) we believed the cancellation rate of weekend cases in our institution was excessive.

METHODS: For this study, we looked at the number of cancelled cases on weekends (Friday 1900 - Monday 0600) from January 1, 2010 - December 31, 2015. During this time a reason must be listed for every cancelled case. Using a report generated by our scheduling software we determined the cause of cancellation for all cases that were cancelled on the scheduled day of surgery and aggregated them into causes related to the patient, the surgeon, resources and other. Cases that were cancelled for clerical reasons (e.g., cases posted twice, cases posted to test the scheduling program) were excluded from data analysis.

RESULTS: On the weekends during the study period 12,201 cases were posted, 2,585 cases were cancelled, producing a cancellation rate of 21% (Table 1). Data regarding the top causes of case cancellations are listed in Table 2. Data regarding the cause of cancellation related to surgeon, the patient, to resources (no equipment, no ICU beds avail, etc.) and to other is displayed in Figure 1.

CONCLUSIONS: Case cancellations have a significant impact on patient satisfaction, OR efficiency and hospital finances. Even though most family members do not have to take time off from work on weekends to be with their family members during the perioperative period they may still incur costs as a result of travel. In addition, frustration is likely when a scheduled procedure is cancelled. Cases cancelled at the last minute may also result in OR costs. Anesthesia costs occur as a result of time spent performing a preoperative evaluation. The cancellation rate for weekend cases exceeds that on weekdays. Since these cases are not planned in advance, the absence of a preoperative evaluation prior to the day of surgery likely contributes to the high cancellation rate. Other major contributors to cancellations are changes in the patient's medical or surgical condition. Surgical convenience also plays a role; our data demonstrate that multiple cases were cancelled by surgeons because it could not be done within the desired time frame. Cancellations were also reported because of lack of OR resources (e.g., lack of specific personnel, equipment or supplies). While hospital administration aims to limit case cancellations, due to the dynamic nature of the OR and its numerous working parts (anesthesia, surgeons, nursing, ever-changing patient conditions), cancellations will unfortunately always occur.

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Table 1

Cases Posted	12,201
Cases Cancelled	2585
% Cases Cancelled	21%

Table 2: Top Reasons For Cancellation in Order of Occurrences

Undefined
Surgeon changes order of cases for day
Patient's medical condition changed day of surgery
Case moved to another day
Patient's surgical condition changed day of surgery
Transplant posting-no match
Patient cancelled self
Patient not NPO
Surgeon incomplete work-up day of surgery

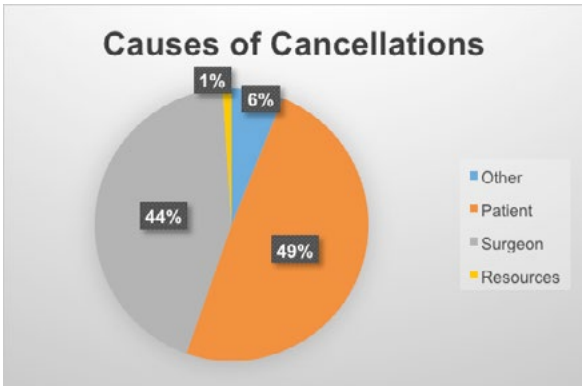

Figure 1.

S-130.

ANESTHESIOLOGISTS AND DISASTER MEDICINE: A NEEDS ASSESSMENT FOR EDUCATION AND TRAINING AND REPORTED WILLINGNESS TO RESPOND

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INTRODUCTION: Disaster medicine literature focuses primarily on the emergency department.[1-3] Anesthesiologists provide comprehensive healthcare, across the emergency department, the operating room, and intensive care unit. To date, the perspectives of anesthesiologists regarding disaster medicine and public health preparedness have not been fully described.

METHODS: Assessment of both resident and attending anesthesiologist thoughts and attitudes via a web-based survey occurred at three major U.S. anesthesiology residency programs. Specifically, frequencies, percentages, and odds ratios were used to assess self-reported perceptions of knowledge and skills as well as attitudes and beliefs regarding the following: education and training, employee development, professional obligation, safety, psychological readiness, efficacy, personal preparedness, and willingness to respond. Three representative disaster scenarios (natural disaster [ND], a radiological event [RE], and pandemic influenza [PI]) were investigated.

RESULTS: One hundred seventy-five anesthesiology attendings (AA) and 95 anesthesiology residents (AR) participated in the survey with a 47% and 51% response rate, respectively. Thirty-one percent and 40% of AA indicated that their hospital provides adequate pre-event preparation/training for ND and PI, respectively, while 14% responded the same for RE. Less than one-quarter of AR responded that their residency program provides them with adequate pre-event preparation/training for all-cause events (22%, 16%, and 17% for ND, RE, and PI, respectively). Subset analysis by specific residency program showed similar results. The majority of AA and AR believe their hospital or residency program should provide them with adequate pre-event preparation/training (89%, 88%, 87% of AA and 81%, 71%, 82% of AR for ND, RE, and PI, respectively). Approximately one-half of AA and AR are confident they would be safe at work during response to a natural disaster or influenza pandemic (55%, 58% of AA, 59%, 48% of AR, respectively), while approximately one-third responded the same regarding a radiological event (31% of AA, 28% of AR). Fewer than 40% of AA and AR have designated who would take care of their family obligations in the event they were called into work during a disaster. Regardless of severity, AA and AR indicated willingness to respond to a natural disaster or pandemic influenza (79%, 81% of AA and 73%, 70% of AR for ND and PI, respectively). Fewer were willing to respond to a radiological event (63% of AA, 52% of AR). Interestingly, both AA and AR were willing to respond in whatever capacity needed, not specifically to provide anesthesia.

CONCLUSIONS: Few anesthesiologists reported receiving sufficient education and training in disaster medicine. Providing education and training and enhancing related employee services may further bolster willingness to respond and actual response, thereby building a more capable and effective medical workforce for disaster response.

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S-131.

WITHDRAWN.

S-132.

INCIDENCES AND CAUSES OF CANCELLATION OF ELECTIVE SURGERY AT HRH PRINCESS MAHA CHAKRI SIRINDHRON MEDICAL CENTER

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INTRODUCTION: The cancellation of a surgical operation is a significant problem in many hospitals. This issue can cause serious consequences, especially patients' suffering and loss of healthcare resources and budgets. This study aimed to determine the incidence, causes and associated factors of elective surgical cancellation.

METHODS: A prospective study was performed at HRH Princess Maha Chakri Sirindhron Medical Center between May 2015 and October 2015. Data was collected from surgical schedules. The number of surgical cancellations and the reasons for cancellation recording from surgeons and anesthesiologists were collected and analyzed.

RESULTS: A total of 2,314 patients in the surgical schedules were enrolled. Males numbered 42.4%. Mean ± SD of age was 49.4 ± 20.2 years. Most patients were general surgery patients (27.7%). The incidences of elective surgical cancellation was 16.1%. The general surgery department had the highest percentage of incidences (28.4%). When comparing each department, the highest cancellation rate was cardiothoracic surgery (34.3%). The main causes of cancellation were n admitted patients not complying with scheduling (27.9%), excessive patients to operations' capacities (17.2%), and poor preoperative control of diseases (14.2%). The associated factors for surgical cancellation were higher age, no preoperative assessment and American Society of Anesthesiologist classification.

CONCLUSIONS: The elective surgical cancellation remains problematic in our hospital. The most common causes of cancellation were surgical planning and management. Therefore, a multidisciplinary approach for preoperative management is essential to prevent the cancellation of surgery. Further study is needed to verify to reduce this cancellation.

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S-133.

WITHDRAWN.

S-134.

PREJUDICE OR PERSPECTIVE? SUBJECTIVE VALUATION OF SIMULATION CORRELATES WITH OBJECTIVE PERFORMANCE

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AFFILIATION: [1]Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY, [2]Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY

INTRODUCTION: As simulation has been incorporated increasingly into the field of anesthesiology, heated debate has arisen regarding its value as a tool for teaching and assessment. Strong opinions are evident both for and against simulation, but the basis of these opinions at times seems based in emotion more than on facts. Previous studies have demonstrated that measurable benefit from simulation is not uniform among all participants.[1,2] This study seeks to determine if objectively scored performance on simulated exercises can be correlated with subjective assessment of the value of simulation.

METHODS: After IRB approval, anesthesia residents from our institution participated in a structured simulation-based curriculum consisting of a series of twelve standardized simulated operating room scenarios. During the final four scenarios, individual resident performance was assessed by blinded attending anesthesiologists using the Anesthesia Non-Technical Skills Scale (ANTS)[3] in which a higher score indicates a superior performance using benchmarks such as task management, situation awareness, and decisionmaking. After completion of the simulated curriculum, participants were asked to complete a simple Likert scale regarding how helpful they felt the simulated curriculum had been, with 1 indicating "Not at all helpful" and 5 indicating "Extremely helpful". Multivariate analysis was carried out to determine any correlation between ANTS scores (sum and average) and subjective assessment of simulation-associated benefit.

RESULTS: Fifty anesthesia residents participated in the twelve-scenario simulation series. All residents completed all scenarios and were scored by 2 of 3 participating attending anesthesiologists. Subjective assessment of benefit from the simulated curriculum was significantly associated with higher ANTS scores taken cumulatively ($p=0.05$) and as an average ($p=0.05$).

DISCUSSION: In this study, residents who scored better via objective assessment were more likely to report that they had found the simulated exercises beneficial. Though this may initially seem self-explanatory, it is surprising considering that participants who performed better (and thus had less opportunity to "improve") saw more value in the simulated curriculum they had just completed than those who had more room to grow. It may be that subjective assessment of the value of simulation is actually related to one's own ability to benefit from it, and hence rooted in fact rather than emotion. Further studies should be carried out to determine if pre-existing bias regarding simulation can be similarly correlated with performance.

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S-135.

CALM WITHIN THE STORM: EMOTIONAL SELF-REGULATION AFFECTS GRADED PERFORMANCE IN HIGH-STAKES SIMULATION

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BACKGROUND: In the field of simulation-based education and assessment, controversy persists regarding the role of emotional stress in augmenting or diminishing the benefit of simulation to participants.[1,2] In the heightened emotional environment of the simulator, it is unclear why some participants seem to thrive, while others suffer. Using validated measures from the field of psychology it is possible to quantitatively assess a person's skill at regulating their own emotions.[3] This study investigates whether skill at emotional self-regulation can be correlated with objectively assessed performance in a battery of simulated exercises.

METHODS: After IRB approval, PGY-2 anesthesia residents from our institution participated in a structured simulation-based curriculum consisting of a series of standardized simulated operating room scenarios designed to be progressively more "stressful". Prior to participating in these scenarios all residents completed the Difficulties in Emotional Regulation Scale (DERS), in which a higher score indicates greater difficulty with emotional self-regulation. For the final four scenarios, residents were assessed by blinded attending anesthesiologists using the Anesthesia Non-Technical Skills Scale (ANTS),[4] in which a higher score indicates a superior performance using benchmarks such as task management, situation awareness, and decisionmaking. ANTS scores over all four scenarios were 1) combined and 2) averaged and linear regression was carried out to determine any effect of DERS score on objectively-assessed performance.

RESULTS: Fifty anesthesia residents over two consecutive years were recruited to complete the simulation-based curriculum. All residents completed all scenarios. DERS score was strongly associated with ANTS cumulative score, with a higher DERS score correlating with poorer performance as measured by the ANTS ($p<0.0001$). This correlation persisted when ANTS score was taken as an average ($p<0.0001$).

DISCUSSION: Our study demonstrated that increasing difficulty with emotional self-regulation correlated significantly with poorer graded performance in a series of stressful operating room simulations. Future studies may determine whether an "optimum stress level" can be defined specific to individual participants in order to facilitate learning.

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S-136.

NORA FIRST CASE START DELAYS: A TALE OF TWO CITIES

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INTRODUCTION: For many hospitals, the non-operating room anesthesia (NORA) workload continues to expand.[1] Similar to the coverage expectations for capacity-based services, many anesthesia groups have sought subsidy payments to cover the expansion of services.[2,3] There is little literature on the optimization and management of NORA block allocations and NORA services tend to be poorly-utilized and highly variable. In this study, we hypothesized that the variability of first-case delays between NORA and OR cases are different.

METHODS: Using WiseOR® (Palo Alto, CA), we extracted the first case time delays for all the anesthetics provided by the department from November 1, 2014 to October 31, 2015. We separated the cases into the Main Campus, Ambulatory Center, and NORA. Using R v3.2.3 in R Studio v0.99.486 (RStudio, Inc., Boston, MA), packages BEST and rJAGS the differences between actual and scheduled start times between Main and NORA were examined.[5-7] This was done for all differentials (n = 3359 for Main, 319 for NORA) and for the cleaned dataset. Cleaning involved removing negative differences (arriving early) and removing delays greater than or equal to 100 minutes as visual examination of the distribution suggested these to be data entry errors rather than true delays. This resulted in a final sample size of 3262 for Main and 311 for NORA. MCMC estimation was performed using Gibbs sampling.[7] Prior distributions were minimally informative as per Kruschke.[6] 1,000 iterations x 3 chains were used for burn-in; 33,334 iterations x 3 chains for sampling. Convergence was achieved for all parameters in both models. Effective sample size for all parameters was greater than 20,000.

RESULTS: In Figure 1, we show that the means for the NORA cases are 21.68 (all) and 22.488 (cleaned). In Figure 2, we show that the means for the Main OR cases are 10.2 (all) and 10.5 (cleaned). In both scenarios, there is a significant difference because the 95% HDI (Highest Density Interval) is greater than 0. In Table 1, we show that the difference of standard deviations is significant (95% HDI > 0).

CONCLUSIONS: Previously, Macario published an OR dashboard to benchmark the efficiency of an OR.[8] Here, we show that there is significant variability in both the means and standard deviations comparing NORA to Main OR first start delays. We believe that the advantages of the Bayes estimator are two-fold. First, it is more robust to non-normality than the t-test. Second, we do not make assumptions about the means and confidence intervals when we graph the distributions of the first-case start delays for the NORA and Main OR cases. In short, NORA cases may have longer first-case start delays.

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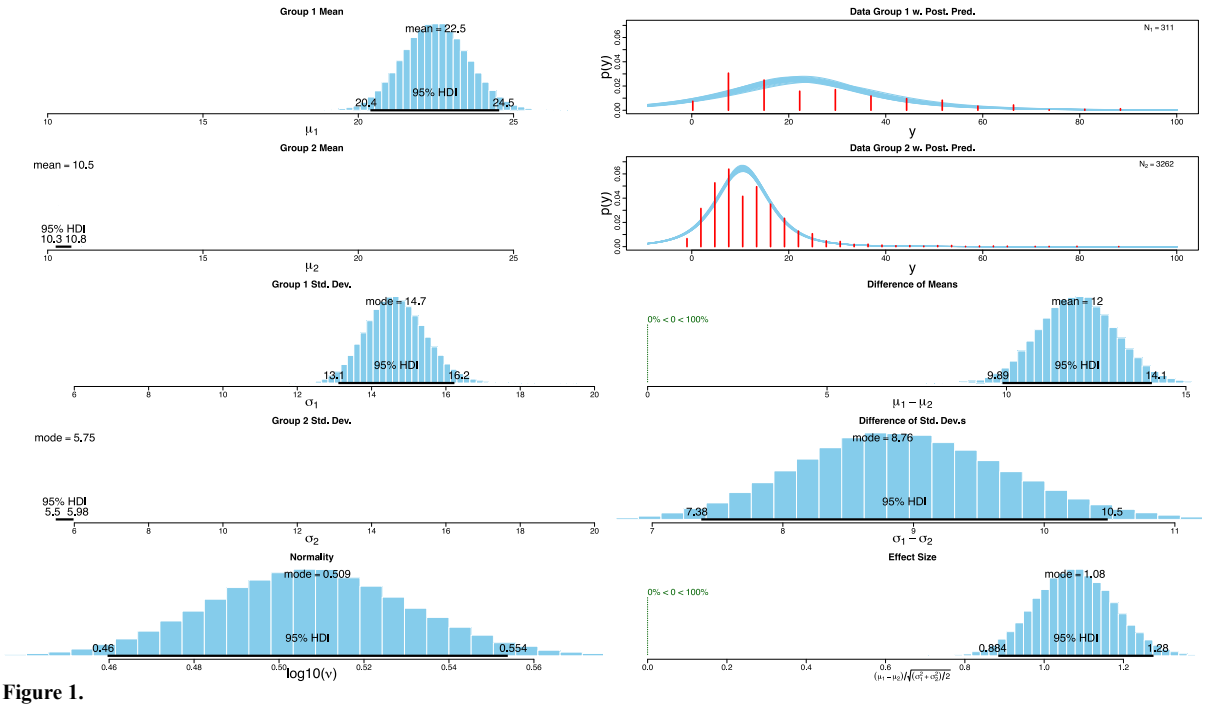

Figure 1.

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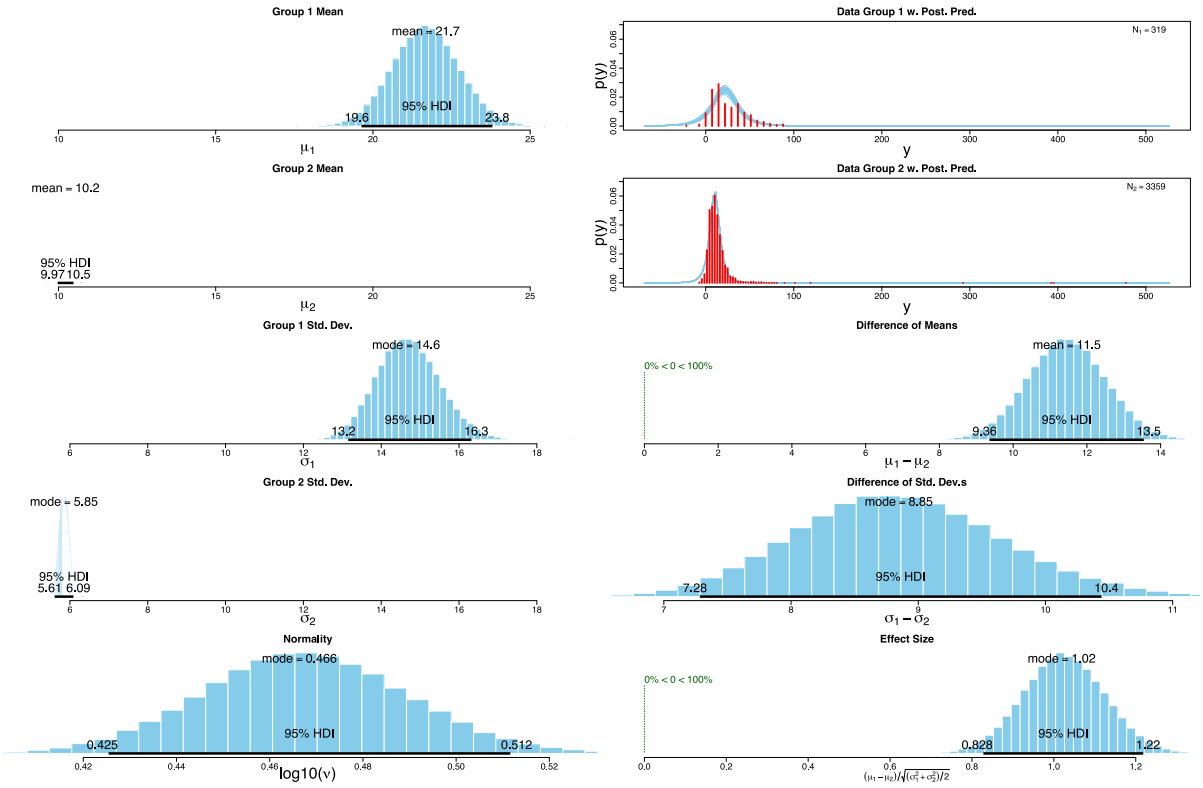

Figure 2.

Table 1: MCMC Model Parameter Posterior Distributions, NORA vs. Main: All

	Mean	SD	Median	HDIlo	HDIup	Rhat	n.eff
NORA Mean (μ_1)	21.680	1.0635	21.675	19.639	23.800	1	57,653
Main Mean (μ_2)	10.224	0.1291	10.223	9.973	10.477	1	50,215
Normality (ν)	2.939	0.1488	2.933	2.652	3.235	1	27,232
NORA SD (σ_1)	14.702	0.8117	14.676	13.153	16.318	1	50,802
Main SD (σ_2)	5.850	0.1235	5.849	5.609	6.091	1	29,462

Note: 100,002 simulations saved.
HDIlo and HDIup are the limits of a 95% HDI credible interval.
Rhat is the potential scale reduction factor (at convergence, Rhat=1).
n.eff is a crude measure of effective sample size.

S-137.

NON-OPERATING ROOM ANESTHESIA CANCELLATION RATES

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INTRODUCTION: Operating room (OR) managers use cancellation rates as a metric of efficiency for OR management dashboards.1 Outside of the OR, anesthesiologists typically control the tactical and operational resources for staffing non-operating room anesthesia cases. With the continued growth of NORA cases, anesthesiology groups have encountered a push and pull situation when it comes to expanded the breadth of coverage at their institution. In a similar vein to the coverage of obstetrics or other inefficient service lines, some anesthesiology groups have sought labor subsidies to cover the extension of NORA services. While there is scant literature on NORA metrics, we have previously published on the inaccuracies inherent in using OR management metrics for NORA management by showing that site utilization and physician efficiency is not always equivalent. In this study, we applied the concept of cancellation rates to the NORA services at one institution.

METHODS: Using WiseOR® (Palo Alto, CA), we extracted the sedation lists for pulmonary and gastroenterology NORA cases from September 1, 2014, to August 31, 2015. On a daily basis, WiseOR® pulls the tentative schedule for the next available workday. The next day, WiseOR® extracts data (date, actual room in, actual room out, anesthesiology staff members, proceduralist) for each corresponding scheduled case. We identified cases without real-time data to identify the cases which were not performed and we validated that no data was entered on OPTUM (Eden Prairie, WI) for these cases. We calculated cancellation rates (i.e. cases not staffed/total number of cases scheduled) for the year and by adult and pediatric service lines. We used Microsoft Excel (Redmond, WA) for database entry and Stata 13.1 (StataCorp LP, College Station, TX) to conduct the statistical analysis ($p < 0.05$ to test for significance).

RESULTS: For the study period, the pediatric cancellation rates were 0.88% and 5.1% for the pulmonary and gastroenterology divisions, respectively. The adult cancellation rates were 16.8% and 9.7% for the pulmonary and gastroenterology divisions, respectively. For the pediatric and adult NORA cases studied, the aggregated cancellations rates were 4.0% and 10.9%, respectively.

CONCLUSIONS: Anesthesiology groups should understand the labor efficiencies as anesthesia services continue to expand outside of the OR. Macario recommended a less than 5% cancellation rate for cases in the OR; however, the application of the metrics to NORA schedule lists is not known.[1] Here, we show that cancellation rates for NORA cases in pediatric pulmonary and gastroentereology fall within those recommendations. Similarly, Hoffman et al recently published an estimated cancellation rate of 4.5% for pediatric patients undergoing sedation for an MRI.2 By contrast, the cancellation raets for the NORA cases in adult pulmonary and gastroenterology are greater than recommended 5%. Future studies should expand the scope of this analysis and determine the underlying reasons behind the cancellations.

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Table 1. Cancellation Rates for Pediatric and Adult Pulmonary and Gastroenterology service lines with 95% confidence intervals. Aggregated for both pediatric and adult services

Department	Patient Group	Scheduled Cases	Cancelled Cases	Cancellation Rates	95% CI (lower)	95% CI (upper)
Pulmonary	Pediatric	113	1	0.88%	0.0002	0.0483
Pulmonary	Adult	250	42	16.8%	0.1238	0.2202
Gastroenterology	Pediatric	291	15	5.15%	0.0291	0.0836
Gastroenterology	Adult	1680	169	9.74%	0.0866	0.1160
Aggregate	Pediatric	404	16	4.00%	0.0228	0.0635
Aggregate	Adult	1930	211	10.93%	0.0957	0.1241

Subspecialty Abstracts

Geriatric Anesthesia

S-138.

CHANGES OF THE HEMODYNAMIC PROFILES DURING TRANSURETHRAL RESECTION OF PROSTATE IN ELDERLY PATIENTS UNDER SPINAL ANESTHESIA WITH LOW DOSE OF BUPIVACAINE: AN OBSERVATIONAL STUDY WITH NON-INVASIVE CARDIAC OUTPUT MONITORING

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INTRODUCTION: Transurethral resection of prostate (TURP) is associated with an increased risk of hemodynamic instability from irrigating fluid absorption during surgery.[1] Also, most patients undergoing TURP are elderly patients with multiple cardiovascular risk factors and they are vulnerable to fluid overload and hemodynamic instability during surgery. Spinal anesthesia with low-dose of bupivacaine has hemodynamic benefits.[2] The aim of this study was to evaluate the effect of irrigating fluid and spinal anesthesia with low dose of bupivacaine on hemodynamic profiles using non-invasive cardiac output monitoring (NICOM) based on bioreactance technique in elderly patients undergoing TURP.

METHODS: Thirteen consecutive patients were included. All patients were administrated with crystalloid 5 ml/kg before spinal anesthesia with 6 mg of hyperbaric bupivacaine. Hemodynamic profiles including cardiac index, stroke volume index, blood pressure, heart rate were obtained from NICOM at the following time points: before the spinal block, every 10 minutes after operation, and at the end of operation. Preoperative and postoperative electrolyte levels were measured and the amount of estimated irrigating fluid absorbed was calculated (fluid absorbed= % decrease in sodium x 0.2 x body weight).

RESULTS: All patients achieved peak sensory block between T10-T11. There was a significant decrease in mean blood pressure after spinal anesthesia compared to their baseline value (115 vs. 102-108 mmHg, $p < 0.05$), but cardiac index was well preserved without significant change throughout the study period (2.8 versus 2.6- 2.7 L · min-1· m-2, $p > 0.05$). Stroke volume index and heart rates were not changed after spinal anesthesia. Of the 10 patients, postoperative plasma sodium increased slightly compared to preoperative value. Irrigating fluid was not absorbed as the amount of estimated irrigating fluid absorbed was -0.20 [-0.27- 0.04] L. No patient had episodes of hypotension, and no patient required vasopressors or additional fluid administration.

CONCLUSIONS: Spinal anesthesia with low dose of bupivacaine was effective for elderly patients undergoing TURP without decrease in cardiac index. Irrigating fluid could be safely used without concern for accidental absorption.

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S-139.

RETROSPECTIVE ANALYSIS OF PERIOPERATIVE BLOOD TRANSFUSION IN GERIATRIC POPULATION UNDERGOING HIP FRACTURE SURGERY IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY

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INTRODUCTION: Hip fractures are a common injury in the elderly population that usually have significant preexisting co-morbidities. Hip fractures have in-hospital mortality rates up to 10 percent with a one-year mortality of 27.3% percent.

However, many studies have conflicting data in regards to post-operative morbidity and mortality following hip surgery in those receiving blood transfusions[1,2,3].

METHODS: This was an IRB approved retrospective analysis that was performed on data collected from 2008 to 2010 on 844 patients that underwent hip fracture repairs. The patients were broken down into groups, as having received pre-operative, intra-operative, post-operative, or peri-operative blood transfusion. Each subset was analyzed for the development of specific post-operative morbidities and mortality within 3 months.

The post-operative morbidity categories analyzed included cardiac (myocardial infarctions, MI), cerebral vascular events (CVA), acute renal failure (ARF), pulmonary embolism (PE) and pneumonia (PNA), and post-operative cognitive dysfunction or delirium (POCD). Statistical analysis was performed using a two tailed Pearson Chi-Square.

RESULTS: Perioperative transfusion (transfused either pre, intra or postoperatively) was correlated with increased incidence post-operative ARF ($p=0.009$). There was no statistical difference in patients that were transfused peri-operatively compared to non-transfused with respect to MI, CVA, PE, PNA or POCD. Intra-operative transfusion was correlated with increased incidence of post-operative ARF ($p = 0.006$) and PNA ($p = 0.008$). Post-operative transfusion was only associated with an increased incidence of post-operative ARF ($p = 0.034$), but not any other specific morbidities. Transfusion was associated with an increased the incidence of any post-operative complication (MI, CVA, PE, PNA, ARF, or POCD), $p=<0.0275$. Intra-operative transfusion was still significant ($p = 0.046$) for ARF after controlling for ASA ($p = 0.0013$). The choice of anesthetic technique (spinal vs. general) was not associated with an increase in morbidity.

Pre- and intra-operative transfusion, but not postoperative transfusion, were associated with an increased in mortality 10.2% vs. 31.3% ($p=0.02$), 9.5% vs. 19.5% ($p=0.09$), 10.5% vs. 10.6% ($p=1.00$), respectively. The choice of anesthetic technique was not associated with an increase in mortality.

CONCLUSION: Peri-operative transfusion was correlated with increased incidence of post-operative ARF and PNA. Peri-operative blood transfusion was not associated with increased incidence of MI, CVA, PE, or POCD. When accounting for ASA classification, transfusion increased the incidence of any post-operative complication (MI, CVA, PE, PNA, ARF, or POCD). Pre and intraoperative, but not postoperative, transfusions were associated with increased mortality.

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S-140.

INTERRATER RELIABILITY OF DELIRIUM ASSESSMENTS BETWEEN INVESTIGATORS AT MULTIPLE INTERNATIONAL CENTERSMONITORING

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INTRODUCTION: Delirium is a common postoperative complication.[1] There is a need to investigate delirium prevention in pragmatic, multi-center studies. In order to conduct such studies, it is necessary to demonstrate that delirium assessment can be consistent across multiple centers and between many independent researchers. The Confusion Assessment Method (CAM)[2] is based on the DSM diagnostic criteria for delirium, including acute onset or fluctuation, inattention, and disorganized thinking or altered level of consciousness.[3] The CAM, when administered by trained researchers, is sensitive (94%) and specific (89%) for delirium diagnosis, and is widely used in research studies.[4,5] This study seeks to determine the reliability of the CAM when used by trained researchers in multiple international sites.

METHODS: This is a sub-study of the randomized controlled PODCAST (NCT01690988) trial, which is investigating whether intraoperative administration of sub-anesthetic ketamine decreases the incidence of postoperative delirium. With IRB approval, patients consented to video recordings of delirium assessments and for these videos to be used for research purposes. Participants were researchers trained in CAM assessment. Training entailed either attending a one-day CAM training seminar or by completing the training protocol outlined in the PODCAST study guidelines.6 This requires attending a didactic training session and independent agreement with a trained researcher on the presence or absence of the twelve features of the CAM for two delirious and two non-delirious patients. Also, trained researchers participated in monthly conference calls to adjudicate difficult delirium assessments. Participants independently viewed nine video-recorded interviews of postsurgical patients and scored these according to CAM criteria. Inter-rater reliability was determined using Fleiss' kappa for delirium (delirious vs. non-delirious) and the presence or absence of the five CAM algorithm features.

RESULTS: Fifteen raters from five research centers completed the sub-study. Characteristics are detailed in Table 1. Agreement for overall delirium diagnosis was excellent, kappa = 0.92 (95% CI, 0.86-0.99). The five features of the CAM showed varying agreement, displayed in Figure 1.

CONCLUSION: Our results demonstrate that with appropriate training, researchers at multiple sites can reliably detect delirium in postsurgical patients. Suboptimal agreement of fluctuation may be attributed to the subjective nature of the feature; and altered level of consciousness may be attributed to the difficulty of observing subtleties in a video-recorded interview. These results provide conceptual support for the conduct of pragmatic, multicenter studies with delirium as the outcome of interest.

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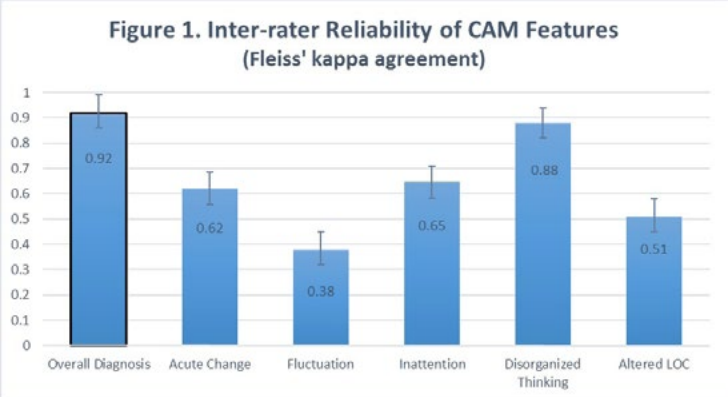
Table 1. Characteristics of Raters		(n=15)
Role:	Non-nurse research staff	8 (53%)
	Physician	4 (27%)
	Medical student	2 (13%)
	Nurse	1 (7%)
Primary language:	English	13 (87%)
	Other	2 (13%)
Highest level of education:	Graduate or professional degree	9 (60%)
	Bachelor's degree	6 (40%)



S-141.

VALIDATION OF A NURSE-BASED DELIRIUM SCREENING TOOL FOR HOSPITALIZED PATIENTS

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INTRODUCTION: Delirium affects up to 56% of hospitalized patients[1]. Its presence is associated with greater mortality and morbidity[2]. Yet, up to 50% of cases are undiagnosed[3]. *The Nursing Delirium Screening Scale* (NuDESC) was developed to improve detection. However, it has not been rigorously validated when used by nurses in diverse inpatient populations and settings. Furthermore, previous studies have excluded or had extremely limited numbers of patients with psychiatric or neurologic comorbiditie[4]. Therefore, the purpose of this study is to validate the NuDESC for broad use in medical, post-surgical and neurology inpatients.

METHODS: We conducted a blinded cross-sectional analysis to determine the test characteristics of the NuDESC as compared to delirium diagnoses using the gold standard *Diagnostic and Statistical Manual of Mental Disorders-V* (DSM-V) as part of a Quality Improvement initiative. We enrolled 315 consecutive patients on general medicine, neurology and post-surgical floors. NuDESC positive (threshold >1) patients were matched with an equal number of NuDESC negative patients with the same gender, age (+/-5 yrs) and hospital floor. All patients were assessed by a trained, NuDESC blinded, evaluator using a scripted interview and mental status examination on two consecutive days. Clinical vignettes documenting the assessment were then evaluated for delirium status using DSM-V criteria by a psychiatrist and neurologist for validation. Sensitivity, specificity and ROC curves were calculated with 95% confidence intervals (CI).

RESULTS: The sensitivity of the NuDESC (threshold >1) for diagnosing delirium was 82% (95% CI, 74-88%) and the specificity was 77% (95% CI, 70-84%). The Area Under the Receiver Operating Characteristics Curve (AUC) was 0.80 (95% CI, 0.70-0.84).

CONCLUSIONS: In a diverse inpatient population, the NuDESC is a sensitive screening tool for delirium detection that can be easily applied by nursing staff. However, due to a lower specificity relative to the sensitivity, delirium suggested by a positive NuDESC screen should be confirmed.

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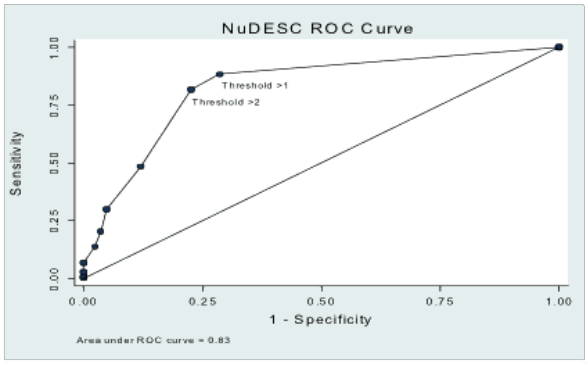

NuDESC Test Characteristics

	DSM-V Positive	DSM-V Negative	Total
NuDESC Positive	120	38	158
NuDESC Negative	27	130	157
Total	147	168	315
Sensitivity		**Specificity**	
82%		77%	

Subspecialty Abstracts

Liver

S-142.

THE SYSTEMIC-TO-PULMONARY ARTERY PRESSURE RATIO AS A PREDICTOR OF PATIENT OUTCOME FOLLOWING LIVER TRANSPLANTATION

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BACKGROUND: Outcomes following orthotopic liver transplant (OLT) are dependent on the ability of the patient's cardiovascular system to compensate for the physiological stress related to OLT. Right heart function appears to be a better predictor of survival after OLT than left ventricular function (LHF).[1] While the preoperative assessment usually focuses on the LHF, the contribution of the right ventricle is less commonly evaluated. However, the mean systemic-to-pulmonary artery pressure ratio (MAP/mPAP) has been shown to be a valuable predictor of outcomes following cardiac surgery.[2] The MAP/mPAP ratio as a predictor of patient outcome following OLT has not been investigated. Therefore the aim of this study was to assess the value of the MAP/mPAP ratio for predicting outcomes following OLT.

METHODS: After IRB approval, a retrospective data analysis was performed on OLT patients at a single University Hospital during a thirty-six month period. The following intraoperative data was collected: mean arterial blood pressure (MAP), mean pulmonary artery pressure (mPAP) and Cardiac Index (CI). These hemodynamic parameters were collected at several points during OLT: Baseline (A1, 30min after incision), preanhepatic (A2, 1hr before IVC cross clamp), anhepatic (A3, 15min before reperfusion), neohepatic (A4, 15min after reperfusion), and 1hr neohepatic (A5, 1hr after reperfusion). Outcomes evaluated were extubation time (ET; minutes after ICU arrival), length of ICU stay (LOS ICU) and total hospitalization (LOS Total). Statistical analysis was performed using a paired t-test (significance $p<0.05$).

RESULTS: A total of 100 patients were identified. Nine patients were excluded due to incomplete data collection. Based on the intraoperative course of the MAP/mPAP ratio, 2 hemodynamic responses were identified: Group 1 (MAP/mPAP ratio increase during anhepatic period with postreperfusion recovery, N=66); and Group 2 (MAP/mPAP with no change during anhepatic period or decreased without recovery, N=25). Surgery duration and intraoperative fluids were not different between the 2 groups. Group 1 ET, LOS ICU and LOS Total were significantly shorter than for Group 2 (Table 1). CI changes did not correlate with the MAP/mPAP ratio.

CONCLUSIONS: 1) The intraoperative pattern of MAP/mPAP ratio during OLT appears to be predictive of patient clinical outcomes. 2) Patients with an increased MAP/mPAP ratio during the anhepatic and neohepatic phases had an ICU stay 1/3 length of those who had no change or decreased MAP/mPAP. 3) An increased MAP/mPAP ratio during the anhepatic and neohepatic phases of OLT was associated with shorter ET and 2 week shorter LOS total. 4) Additional prospective studies are needed for more comprehensive risk stratification to explore the predictive value of this hemodynamic parameter.

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Table 1

	Group 1 anhepatic increase of MAP/mPAP ratio with postreperfusion recovery N=66	Group 2 no change or decrease of MAP/mPAP ratio during anhepatic/post reperfusion N=25	P-Value
MAP/mPAP baseline	3.32 ± 0.73	4.13 ± 1.19	0.19
% change preanhepatic	0.28 ± 1.28	0.18 ± 1.27	0.75
% change anhepatic	2.89 ± 1.83	-0.09 ± 1.14	*<0.01
% change neohepatic	0.21 ± 1.41	-0.69 ± 1.33	*<0.01
% change 1hr neohepatic	0.10 ± 0.83	0.61 ± 1.37	*<0.01
CI baseline	4.11 ± 1.23	4.21 ± 0.96	0.88
% change preanhepatic	0.04 ± 0.79	-0.20 ± 0.83	0.20
% change anhepatic	-1.61 ± 1.02	-1.19 ± 1.08	0.09
% change neohepatic	-0.33 ± 1.32	-0.06 ± 1.23	0.38
% change 1hr neohepatic	0.34 ± 1.11	0.45 ± 1.04	0.64
Surgery duration [min]	400.9 ± 43.5	427.9 ± 63.3	0.08
Crystalloid given [ml]	5804 ± 2824	6086 ± 3424	0.69
Colloid given [ml]	1440 ± 972	1607 ± 626	0.43
PRBC given [units]	3.3 ± 3.7	3.9 ± 3.1	0.47
FFP given [units]	2.8 ± 3.0	4.0 ± 4.6	0.15
Time to extubation [min]	967 ± 1361	1719 ± 1933	* 0.04
[hrs]	16.1 ± 22.7	28.7 ± 32.2	
LOS ICU [days]	3.9 ± 4.4	12.1 ± 19.2	* <0.01
Median [days]	2	6	
LOS hospital [days]	12.0 ± 12.5	26.3 ± 33.2	* <0.01
Median [days]	8	11	

MAP/mPAP = Mean Systemic-to-Pulmonary Artery Pressure Ratio, CI = Cardiac Index, Surgery duration = anesthesia time from induction to ICU transfer, Crystalloid = amount of intraoperative normal saline, Colloid = amount of intraoperative 5% Albumin, PRBC = packed red blood concentrate, FFP = Fresh frozen plasma, Extubation time = min from ICU arrival to extubation to supplemental oxygen, LOS ICU = length of stay in intensive care unit, LOS total = time from ICU arrival to hospital discharge.

Data are shown as mean ± SD. P value was obtained using paired t-test. * $p<0.05$

S-143.

FACTORS ASSOCIATED WITH POST-REPERFUSION SYNDROME IN PEDIATRIC PATIENTS UNDERGOING LIVER TRANSPLANTATION AT TWO ACADEMIC CENTERS

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INTRODUCTION: Pediatric orthotopic liver transplantations have become more common over the last decade. During liver reperfusion, a marked decrease in systemic blood pressure, systemic vascular resistance, and cardiac output frequently occurs, which is termed postreperfusion syndrome (PRS).[1] In adult liver transplantation, PRS occurs in approximately 30% of the recipients and is associated with an increase in morbidity and mortality.[1] Variables that are associated with PRS include cold ischemia time, total surgical time, total anhepatic time, and higher FFP requirements.[1-3] The purpose of this analysis is to identify demographic and intraoperative variables that were associated with PRS in pediatric liver transplantation patients.

METHODS: After IRB approval, we identified all patients who underwent orthotopic liver transplantation at Institution One from April 1st, 2014 to December 31st, 2015 and Institution Two from January 1st, 2010 to December 31st, 2015. Demographic, surgical, and other perioperative variables were then collected. For this analysis, PRS was defined as a reperfusion mean arterial blood pressure (MBP) that was at least 30% less than the averaged MBP over the ten minute interval immediately prior to reperfusion. This definition corresponds to previous literature.[1-3] All statistical analyses were performed using the R software package (version 2.15.1). Associations between selected demographic/intraoperative variables and PRS were first established utilizing only graphical methods to eliminate inflated type I error rates due to multiple comparisons. A logistic regression was then performed based on these results. P values less than 0.05 were considered statistically significant.

RESULTS: 67 patients were identified during this time period. The age range in this patient sample was 3 weeks to 17 years with a near 50:50 male to female ratio. Fifteen patients (22.4%: 95% CI 13.1 - 34.2%) had PRS in this cohort. Based on plots, only MELD/PELD score, cold ischemia time, and total surgical time appeared to be associated with reperfusion MAP changes and incidence of PRS. Of these variables, MELD/PELD score appeared most correlated (Figures 1 & 2). Utilizing logistic regression, only MELD/PELD was associated with PRS (P value = 0.01, Table 1).

DISCUSSION: The PRS rate in this pediatric group was similar to the rate noted for adult patients undergoing liver transplantation. Although many variables have been associated with PRS in the adult literature, these variables have been inconsistent across studies and point to a multifactorial process. Although MELD/PELD score was the only factor associated with PRS in this analysis, our next steps are to continue to discover other associations (especially with modifiable variables) and to establish any postoperative morbidity and mortality correlations in pediatric patients with PRS.

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Figure 1 - Pressure Change at Reperfusion

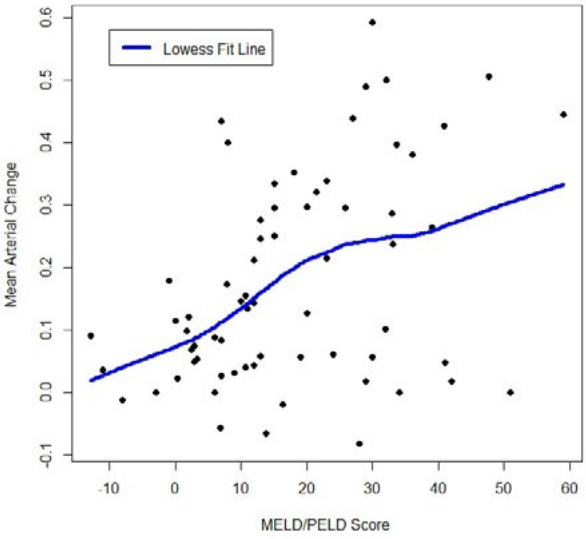

Figure 2 - MELD/PELD Scores in PRS Patients

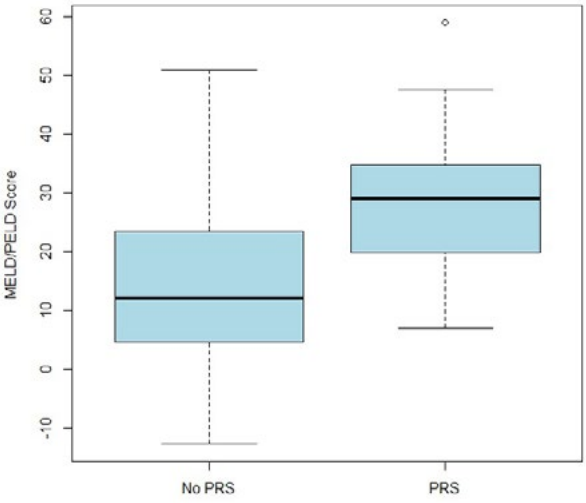

Table 1. Variables Associated with PRS in Pediatric Liver Transplant Patients*

Characteristic	OR	95% CI	P-value
MELD/PELD Score	1.07	1.02 to 1.13	0.010
Cold Ischemia Time	1.00	0.99 to 1.01	0.795
Total Surgical Time	1.00	0.99 to 1.01	0.263

S-144.

USE OF ELDERLY LIVER DONORS. RETROSPECTIVE SINGLE CENTER GRAFT AND PATIENT SURVIVAL

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INTRODUCTION: The demand for organs far exceeds the supply prompting the need to use organs previously not considered ideal for transplant, such as those from older donors. Many studies report higher 1-year and 3-year graft survival rates among recipients of hepatic allografts from donors between 60-70 years compared to those receiving organs from donors those >70 years[2]. There have been few reports of outcomes among recipients of liver grafts from donors >80[2,3].We present outcome data on liver transplant recipients who received grafts from donors above 70 and 80 years old.

METHODS: We reviewed liver transplants performed between January 2015 and December 2015 at our institution. We analyzed only recipients who received a liver graft from a deceased brain donor (DBD) aged 70 and above. Donor demographics and cause of death were tabulated. We recorded and analyzed liver function tests (AST/ALT) in the first 30 days post transplant as well as the incidence of surgical complications up to 5 years after post transplant. We compared this data to recipients from donors <70 years old. Re-transplants, split transplants, and multi-visceral transplants were not included.

RESULTS: Fifty nine donors who met our criteria for age (70-84) were identified. Of these, 7/59 (11.9%) grafts were exported out of the donor superfial area and 12/59 (20.3%) not accepted for liver transplant; 31/59 (52.5%) were transplanted at our center. Demographic data on local donors is presented in Table 1. Demographic and survival data on the 31 recipients are presented in Table 2. Recipients of donors above 70 years had 25.8% surgical complication rate, survival in the first year of 90.3% and 68.2% five year survival.

CONCLUSIONS: Our rate of surgical complication was superior to 20% of previous publications,[3] the survival rates are superior to the 1-year (83.9%) and 5-year (65.8%) patient survival among recipients with donor between 50-64 years of UNOS/OPTN database[4]. The objective suitability of the best receptor for grafts from elderly donor is field for future research.

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Table 1. Donor Characteristics

	Global (n=40)	70-79 years (n=37)	≥ 80 years (n=3)
Gender (F %)	45.0	43.2	66.6
Age years, mean ± SD	74.7 ± 3.5	74.0 ± 2.7	83.0 ± 1.0
BMI (kg/m^2), mean ± SD	25.5 ± 4.2	25.4 ±4.1	25.4 ± 5.8
Last AST (U/L), mean ± SD	50.6 ± 48.0	48.5 ± 49	76.0 ± 24.9
Last Total Bilirubin (mg/dL) mean ± SD	0.85 ± 0.54	0.88 ± 0.56	0.50 ± 0.17
Last Sodium (mEq/L) mean ± SD	146.2 ± 8.4	146.3 ± 8.5	148.3±8.0
History of Hypertension (n, %)	34 (85)	31 (83.8)	3 (100)
History of Diabetes (n, %)	13 (32.5)	10 (27)	3 (100)
History of Cardiac Disease (n, %)	21 (52.5)	19 (51.4)	2 (66.7)
History of Dyslipidemia (n, %)	26 (65)	23 (62.3)	3 (100)
History of Renal Disease (n, %)	1 (2.5)	1 (2.7)	0 (0)
Vasopressor Use (n, %)	39 (97.5)	36 (97.3)	3 (100)

Table 2. Recipient Characteristics

	Global (n= 31)	Donors of 70-79 years (n=28)	Donors above 80 years (n=3)
Gender (F %)	10 (32.2)	8 (28.6)	2 (66.7)
Age years, mean ± SD	59.4 ± 8.9	58.2 ± 9.0	64.0 ± 7.0
MELD score, mean ± SD	16.3 ± 5.1	16.8 ± 5.0	11.7 ± 4.5
Surgical Complications	8 (25.8)	8 (28.6)	
Primary Non Function	1 (3.22)	1 (3.6)	----
Hepatic Artery Thrombosis	1 (3.22)	1 (3.6)	----
Biliary Complications	5 (16.1)	5 (17.56)	----
Acute Rejection	1 (3.22)	1 (3.6)	----
Re-transplant	2 (6.4)	2 (7.1)	----
Patient 1-year survival	28 (90.3)	26 (92.9)	2 (66.7)
Patient 5-year survival * (n=22)	16 (72.7)	16 (72.7)	-----
Graft 1-year survival	28 (90.3)	26 (92.9)	2 (66.7)
Graft 5-years survival * (n=22)	15 (68.2)	15 (68.2)	-----
HCV Reactivation	7 (22.6)	5 (17.8)	2 (66.7)

* Nine patients have not completed 5 years post transplant

S-145.

THE PROTECTIVE EFFECT OF INSULIN AGAINST ISOFLURANE OR SEVOFLURANE INDUCED HEPATOCELLULAR APOPTOSIS IN LAPAROSCOPIC CHOLECYSTECTOMY PATIENTS

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INTRODUCTION: An alteration in control of cell death or survival is implicated in pathogenesis of a variety of human diseases including cancer and many other chronic diseases. Deficient apoptosis is associated with cancer, autoimmune disorders and viral infections, while excessive apoptosis is associated with ischemic injury , stroke, AIDS, neurodegenerative disease, sepsis and multiple organ dysfunction syndrome[1]. Anesthetic drugs influence the process of apoptosis in various human tissues so it is crucial to study thoroughly this role. This may explain why different anesthetic techniques have different postoperative outcome regarding postoperative decreased immunity, wound healing, postoperative stay and postoperative body organs dysfunction[2]. This study was designed in vivo to compare the apoptotic effect of isoflurane versus sevoflurane on human cells especially hepatocytes and to figure out the rule of insulin infusion as anti-apoptotic agent in modulation of such effect evidenced by immune-histochemical study of liver biopsy and serum apoptotic (caspase-3,and- 7) and (Bcl-xl, Akt) anti-apoptotic markers activity.

METHODS: Eighty (ASA I) patients who were scheduled for laparoscopic cholecystectomy surgery were randomly allocated into 4 groups (20 patients each). Forty patients were anesthetized with isoflurane (I groups) and the other forty received sevoflurane as an anesthetic agent (S groups). Both Isoflurane and sevoflurane groups were subdivided into control groups receiving Ringer infusion (Ic and Sc groups) and insulin groups received GIK infusion (Ii and Si). Both infusions were received 1 hr before anesthetic induction. For all patients in the four groups liver biopsy was taken before the umbilical port closure. Venous blood samples (3ml) were collected at (T0 before infusion), (T1 at the end of the surgery) and (T24 one day after) for the assessment of the apoptotic biomarkers. Serum K was investigated at T0 and T1 and blood glucose level was closely monitored.

RESULTS: At T1and T24, Serum AKt and Bcl-xl levels increased significantly in Ii and Si groups compared to Ic and Sc groups respectively ($p<0.01$). While in liver biopsy only AKt increased significantly in Ii group compared to Ic group ($p<0.05$).Caspase 3 level decreased significantly in both serum (at T1& T24) and liver biopsy of both Ii & Si groups compared to Ic & Sc groups respectively ($p<0.01$) as well as caspase 7 level which also decreased significantly in both serum (at T1& T24) and liver biopsy of Ii group compared to Ic group ($p<0.01$). In Sc group serum AKT level at T1 showed significant increase compared to Ic group ($p<0.05$).

CONCLUSIONS: Isoflurane induced more apoptotic changes than sevoflurane in the human hepatocytes and the whole body. Also we concluded that sevoflurane was more protective than isoflurane in the whole body most probably through activation of Akt pathway. Insulin has a protective effect against isoflurane and sevoflurane induced hepato-cellular and whole body apoptosis.

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S-146.

INTRAOPERATIVE PEAK BLOOD GLUCOSE AND EARLY GRAFT DYSFUNCTION: DOES DIABETES COMORBIDITY MATTER?

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INTRODUCTION: Intraoperative (IO) hyperglycemia is associated with worse outcomes in liver transplant (LT) recipients. Its effect on graft function and a possible influence of co-existing diabetes mellitus (DM) has not been well studied.

We examined the association of peak IO blood glucose (BG) and a history of DM with early graft dysfunction (EGD) in a deceased donor (DD) LT population.

METHODS: Data of all DDLT recipients over a 10 year period were reviewed. Combined liver/kidney, fulminant hepatic failure, re-transplantation, IO deaths, split LT, primary graft failure, and secondary graft dysfunction (vessel thrombosis or biliary stricture) were excluded. An EGD diagnosis required at least one of the following criteria: transaminases AST or ALT>2000 IU/L within the first week post LT, total bilirubin≥10mg/dL, or INR ≥ 1.6 at postoperative day 7. Data collection comprised demographics, DM comorbidity and peak IOBG. The two-sample Student t-test was used for calculations. The association between peak BG and EGD was examined for linearity and a cut-point of 300 mg/dL was selected for univariate and multivariate regression analyses. Variables for the multivariate model included MELD, IO insulin administration and DM comorbidity. Data are presented in means±SD, odds ratios (OR) and 95% confidence intervals (CI). $P<0.05$ is considered statistically significant.

RESULTS: Charts of 239 patients were analyzed; 86 (36%) met EGD criteria and 153 (64%) did not (N-EGD). DM was present in 26% (63/239) of recipients. In the full cohort the mean peak IOBG was 250±66 mg/dL.

The peak IOBG was significantly higher in DM than non-DM patients (268±62 mg/dL vs 244±67 mg/dL, $p=0.01$).

EGD occurred in 43% (27/63) diabetics and in 34% (59/179) non-diabetics, the difference was not statistically significant ($p=0.19$).

In diabetics, peak IOBG did not differ between EGD and N-EGD patients: 270±51 mg/dL vs 266±70 mg/dL ($p=0.82$). In non-diabetics, EGD patients had significantly higher peak IOBG than N-EGD subjects: 258±85 mg/dL vs 237±54 mg/dL ($p=0.048$).

Peak IOBG>300mg/dL was significantly associated with EGD as an outcome in univariate [OR=1.94 (95%CI 1.01-3.74); $p=0.047$] as well as in multivariate analyses [OR=2.17 (95%CI 1.05-4.49); $p=0.04$].

DISCUSSION: As may be expected, diabetics had significantly higher intraoperative BG levels compared to non-DM recipients, but no difference in peak IOBG between those with or without EGD. However, non-DM recipients with EGD had a significantly higher peak IOBG compared to those without EGD. Intraoperative peak BG>300 mg/dL was associated with worse graft function in both, univariate and multivariate, analyses. Intraoperative BG control is paramount for better graft outcome, particularly in non-diabetics, who are more likely to develop EGD when their peak BG is higher.

S-147.

OPTIC NERVE SHEATH DIAMETER AND PULSATILITY INDEX MEASUREMENTS AS MARKER OF POOR PROGNOSIS IN ACUTE LIVER FAILURE

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INTRODUCTION: Raised intracranial pressure accounts for significant morbidity and mortality (20-35%) in Acute Liver Failure (ALF) even with considerable improvement in critical care management.[1] Neurological monitoring along with measurement of intracranial tension (ICT) is thus desirable for both management and prognostication. Invasive intracranial pressure monitors though gold standard but are not be feasible in this subgroup of patients on account of coagulopathy, lack of expertise and inherent risk of complications. Optic nerve sheath diameter (ONSD) along with transcranial Doppler (TCD) is reliable, reproducible and bedside tool for intracranial pressure monitoring but has not been studied extensively in ALF.[2] There are limited studies to evaluate intracranial pressure with ONSD and TCD in ALF. This study intends to evaluate the role of serial measurement of ONSD and pulsatility index (P.I) over 24hr for early prognostication in ALF.

METHODS: We measured ONSD and P.I at the time of ICU admission and then sequentially in 4hr interval (T1-T6) for 24hr in ALF patients >12 yr of age. Ocular sonography with 10MHz linear probe was performed and ONSD measured at 3mm behind the globe. Transcranial Doppler was performed to insonate middle cerebral artery with 2MHz probe and P.I was noted.

RESULTS: Fifty one patients were enrolled in the study. Demographic profile is presented in Table 1. Trend for ONSD and PI over 24 hr in survivors and non-survivors was plotted in Table 2 and Table 3. At various time points the value of ONSD and P.I was able to differentiate between the two groups. Notably the baseline P.I (PI.B) value was not significantly different in two groups.

CONCLUSIONS: Cerebral edema and raised ICT had earlier been shown to be an important prognostic marker in ALF but quantification of the same has remained challenging.[3] This is even more important in the light of new evidence that invasive ICP monitors may even be detrimental in this setting.[4] Noninvasive parameters for ICP monitoring appear to be an important prognostic marker in ALF. We propose that ONSD and PI as an alternative for quantification of cerebral edema should also be taken into account while prognosticating along with indices like Ammonia, Lactate APACHE II, SOFA and King's college criteria. This can be critical in determining need for transplant in ALF.

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Table.1: Demographic profile

n=51	Mean±SD
Age (yr)	29.5±11.9
Gender (M:F)	21:30
APACHE	20.96±3.4
SOFA	11.3±2.9
ONSD Baseline	5.23±0.33
P.I Baseline	1.2±0.21

Table.2: Changes in ONSD seen in Survivors (at day 7) and Non-Survivors at different time intervals

	Survivors	Non-survivors	P value	95% C.I of difference
ONSD B	5.10±0.29	5.42±0.30	0.001	0.15-0.50
ONSD 1	5.12±0.28	5.42±0.32	0.002	0.12-0.47
ONSD 2	5.05±0.27	5.44±0.29	0.000	0.22-0.56
ONSD 3	5.02±0.26	5.42±0.27	0.000	0.22-0.57
ONSD 4	4.98±0.25	5.41±0.23	0.000	0.26-0.58
ONSD 5	4.98±0.25	5.41±0.22	0.000	0.26-0.59
ONSD 6	5±0.23	5.36±0.20	0.000	0.21-0.51

Table.3: Changes in P.I seen in Survivors (at day 7) and Non-Survivors at different time intervals

	Survivors	Non survivors	Pvalue	95% CI for difference
PI.B	1.18±0.19	1.22±0.21	0.45	-0.16-0.07
PI.1	1.38±0.25	1.10±0.18	.000	0.15-0.40
PI. 2	1.40±0.20	1.01±0.18	.000	0.21-0.44
PI. 3	1.36±0.26	1.05±0.17	.000	0.17-0.44
PI. 4	1.39±0.20	1.02±0.17	.000	0.24-0.49
PI. 5	1.26±0.16	1.01±0.17	.000	0.14-0.36
PI. 6	1.35±0.24	1.01±0.18	.000	0.19-0.47

Subspecialty Abstracts

Neuroscience in Anesthesiology and Perioperative Medicine

S-101.

IMAGING MITOCHONDRIAL REDOX STATUS FOLLOWING BRAIN INJURY USING DIFFUSE OPTICAL SPECTROSCOPY

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INTRODUCTION: Cellular metabolism is deranged following acute brain injury (ABI), and cytochrome c oxidase (CCO), complex IV in the mitochondrial respiratory chain, has been used to monitor cerebral energetic status[1]. Near infrared spectroscopy is a noninvasive technique that is used to monitor cerebral concentration changes of oxyhaemoglobin [HbO_2] and deoxy-haemoglobin [HHb] in a variety of clinical scenarios and, using an optimized broadband spectroscopy (BBS) system, simultaneous measurement of the oxidation status of CCO [oxCCO] is possible[2]. Knowledge of the spatial and temporal variation of [oxCCO] is necessary to understand metabolic disturbances following ABI. We describe, for the first time, the use of multi channel data BBS acquisition and optical modelling to resolve a tomographic image of Δ[oxCCO] in a patient following ABI.

METHODS: This case is one of a cohort recruited to an ongoing study investigating cerebral hemodynamics and metabolism in patients with ABI. Routine multimodal neuromonitoring was applied to direct clinical care and, following ethical approval and representative consent, optical data were collected as part of the study. The optode array from the BBS system was arranged as illustrated in Fig. 1, and time division multiplexing introduced by enabling light source switching as previously described[2]. Image reconstruction was performed with a multi-spectral multi-wavelength approach, directly reconstructing volumetric images of Δ[HbO_2], Δ[HHb] and Δ[oxCCO], which were then projected onto the cortical surface. Data at seventeen wavelengths were selected from the measured broadband spectrum (every 10nm from 740nm to 900nm) to perform the reconstruction[3].

RESULTS: Reconstructed images from a patient with a right frontal intracerebral haemorrhage are shown in Fig. 2. This demonstrates a time series of spontaneous slow oscillations of Δ[HbO_2], Δ[HHb] and Δ[oxCCO] at 4 time points over a 600 second window during which systemic physiology was stable. Changes in Δ[oxCCO] are demonstrated which are spatially and temporally distinct from those of haemoglobin.

CONCLUSION: This case demonstrates the feasibility of reconstructing Δ[oxCCO] images for the first time in a patient with ABI. The spatial and temporal variation of [oxCCO] is independent from that of [HbO_2] and [HHb], and therefore is not a result of 'crosstalk' between signals. Further it strongly suggests a brain origin of the signals, since changes of the three variables in extracerebral tissues would be expected to be uniform. Image reconstruction of Δ[oxCCO] in association with [HbO_2] and [HHb] has potential to delineate regional cerebral pathophysiology at the bedside, and to guide treatment after ABI.

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Figure 1.

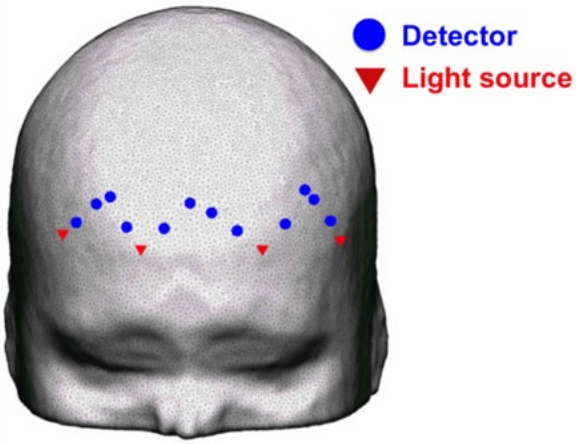
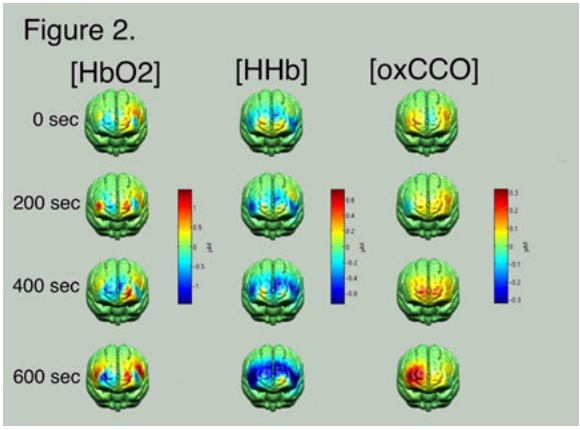


Figure 2.



S-148.

MICROGLIA ARE REQUIRED FOR THE DEVELOPMENT OF POSTOPERATIVE COGNITIVE DECLINE AFTER TIBIAL SURGERY IN MICE

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INTRODUCTION: The neuroinflammatory response to the aseptic trauma of peripheral surgery is responsible for the acute cognitive decline that is noted in preclinical models.[1] CCR2+ expressing bone-marrow derived circulating monocytes are attracted into the hippocampus through the elaboration of the chemokine MCP-1 and are necessary for surgery-induced cognitive decline.[2] Using a technique that antagonizes a crucial growth factor for microglia, the resident immunocompetent cells in the brain, we now show that microglia orchestrate the neuroinflammatory to surgery and can be considered a target for therapeutic intervention.

METHODS: All experimental procedures involving animals were approved by the University of California, San Francisco Institutional Animal Care and Use Committee, and conformed to National Institute of Health guidelines. Adult mice were fed with chow compounded with PLX5622 or control diet for 7 days before surgery (tibial fracture) till sacrifice. For the behavioral study, trace fear conditioning (TFC) training was performed 30 minutes before surgery, and TFC testing was performed on the 3rd day postoperatively. These groups were sacrificed to confirm the microglial depleting effect of PLX5622. In separate cohorts mice were sacrificed 24h postoperatively and hippocampal neuroinflammation was assessed.

RESULTS: PLX5622 depleted hippocampal microglia (Figure 1A&B). PLX5622 reversed postoperative cognitive decline (Figure 1C&D). PLX5622 prevented the neuroinflammatory response to surgery (Figure 2) and attenuated the MCP-1 signal in the hippocampus.

DISCUSSION: After depleting microglia from the hippocampus with PLX 5622, the neuroinflammatory and cognitive responses to peripheral surgery are abrogated. A key step appears to be the loss of the MCP-1 signal when microglia are depleted. Therefore, therapeutic strategies that disable microglial function can be considered for the prevention of postoperative cognitive decline.

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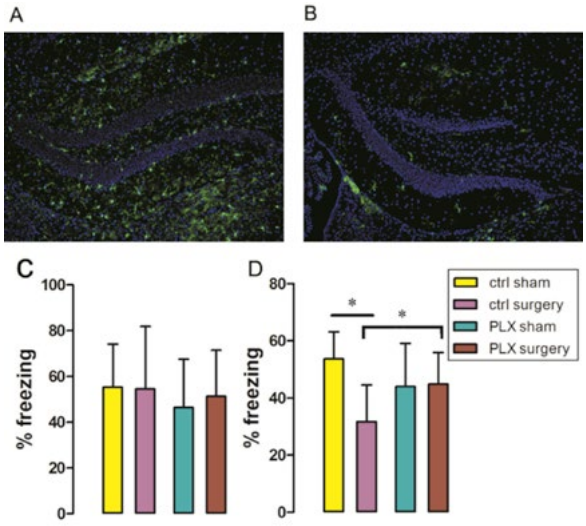

Figure 1. A&B: Staining for hippocampal microglia. Blue for DAPI, and green for Iba-1 stained the microglia **(A).** In the PLX 5622 exposed animals, microglia are depleted **(B)**. **C&D**: Trace fear conditioning (TFC). The freezing behavior during training for TFC is unaffected by PLX 5622 **(C)**. PLX 5622 prevented the decline in freezing behavior noted in the surgery animals **(D)**. * = $p<0.05$ (n=10/group)

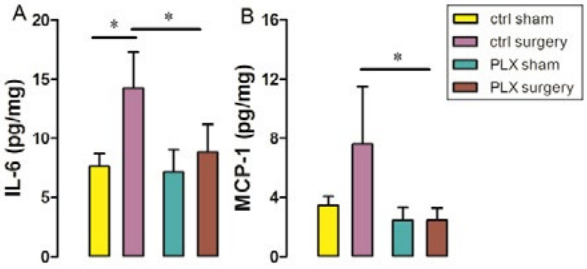

Figure 2. Neuroinflammation in the hippocampus 24 h postoperatively. PLX 5622 prevents the upregulation of the pro-inflammatory cytokine IL-6 **(A)** and the chemokine MCP-1 **(B)**.

S-149.

EXERCISE ATTENUATES THE PERSISTENT POSTOPERATIVE COGNITIVE DECLINE IN A RAT MODEL OF METABOLIC SYNDROME

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INTRODUCTION: In a rat model of Metabolic Syndrome (MetaS), deficiencies in the resolution of inflammation following aseptic trauma has been defined; these cause an exaggerated form of memory decline and a persistent form of learning and memory dysfunction.[1,2] Pre-operative exercise reversed the acute postoperative cognitive decline and normalized the dysregulated inflammation-resolution in MetaS rats. However, the effects of ore-operative exercise on long-term cognitive decline remain unknown. Therefore, this study was to investigate whether exercise attenuates the persistent form of postoperative cognitive decline in MetaS rats.

METHODS: All experimental procedures involving animals were approved by the University of California, San Francisco Institutional Animal Care and Use Committee, and conformed to National Institute of Health guidelines. Animals were handled in strict accordance with good animal practice. Male low capacity runners (LCR) and high capacity runners (HCR) rats were exercised five days/week for 6 weeks immediately prior to surgery. Following exercise, tibia fracture surgery was performed under isoflurane anesthesia, and non-operated rats were exposed to anesthesia and analgesia. Cognitive function was assessed postoperatively in Morris Water Maze 3 months after surgery. Group sizes were n=6.

RESULTS: Dwell-time in the target quadrant in a probe trial was shorter in the postoperative LCR compared to HCR rats (Figure 1). Dwell time in the target quadrant was significantly increased in exercised LCR rats as compared to un-exercised LCR rats. There was no difference between the exercised LCR and HCR rats for the dwell-time in the target quadrant. Swim speeds were similar in all groups (Figure 2) obviating this as a cause for any differences noted in the probe trial.

CONCLUSIONS: MetaS (LCR) rats exhibit acute exacerbation and persistent postoperative cognitive decline. Preoperative exercise prevented persistent cognitive decline in MetaS rats. This life-style change may be crucial for the well-being of surgical patients at risk for postoperative complications.

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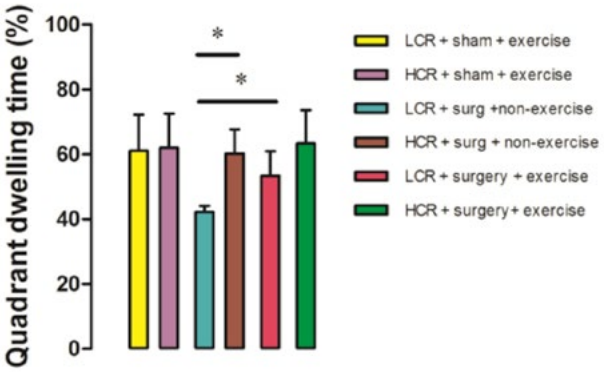

Figure 1. Dwelling time in target quadrant. Three months after surgery, immediately following the last session in the spatial reference test, rats were returned to the Morris Water Maze in which the submerged platform had been removed. The probe trial consisted of measuring the % of time spent within a 60s epoch, in the quadrant in which the platform formerly resided, and this is referred to as dwell time in target quadrant. *P<0.05, N=6.

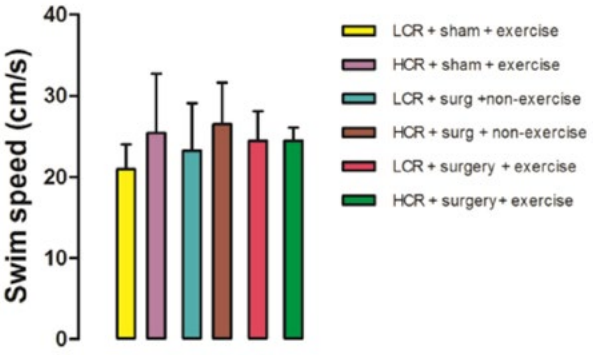

Figure 2. Three months after surgery, swim speed of the rats was measured for the probe trial session. Results are expressed as mean and SD. N=6.

S-150.

BENZODIAZEPINES MODULATE POST-TRAUMATIC BRAIN INJURY NEUROGENESIS IN MICE

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INTRODUCTION: Traumatic brain injury (TBI) affects millions of patients each year. Survivors can suffer from memory impairment, depression, seizures and loss of social independence. Previously, TBI was thought to result solely in neuronal loss. However, advancements in neuroscience have led to the discovery that certain regions of the brain possess some capacity to produce new neurons, known as neurogenesis. TBI has been shown to dramatically increase neurogenesis, specifically in the hippocampus. Because neurogenesis is modulated by GABAergic signalling, we investigated whether benzodiazepine administration would affect post-traumatic neurogenesis as it would have implications for the medical management of head injury patients.

METHODS: In accordance with IACUC-approved protocols, POMC-GFP transgenic mice were subjected to a controlled cortical impact (CCI) model of TBI vs. sham (non-injury), with subsequent implantation of an osmotic drug pump containing diazepam or vehicle. Pumps were removed after 1 week. Neurogenesis was quantified via immunohistochemistry (IHC) of cells in the dentate gyrus of the hippocampus. At 2 weeks post-CCI, neurogenesis was evaluated via counting of GFP-positive newborn neurons; at 3 weeks post-injury, doublecortin and BrdU expression was evaluated.

RESULTS:

2 week branch, POMC-GFP:

Comparing vehicle-only groups, CCI increased neurogenesis vs sham (1.00 vs 1.72, N=9 each, p=0.004). In mice receiving diazepam after CCI, there was no difference in neurogenesis compared to sham groups (diazepam or vehicle). Additionally, in non-injured (sham) mice, there was no difference in neurogenesis with diazepam exposure (1.00 vs 1.03, N=9&7).

3 week branch, doublecortin and BrdU:

In the vehicle-only groups, CCI again dramatically increased neurogenesis vs sham-injury (1.00 vs 7.11, N=6&8, p=0.005). In diazepam-treated groups, there was no difference in neurogenesis in CCI vs sham-injury. No difference in neurogenesis was observed between sham-vehicle and sham-diazepam mice.

CONCLUSIONS: CCI induces a robust neurogenic response in the dentate gyrus of the hippocampus, which appears to be profoundly inhibited by exposure to diazepam after injury. Possible mechanisms for this effect are related to GABAergic modulation of cell maturation or survival, or possibly via suppression of other post-TBI signalling. We are continuing to investigate this phenomenon to understand possible mechanisms underlying the effect of diazepam on post-traumatic neurogenesis.

S-151.

GENETICS OF ISOFLURANE-INDUCED NEUROTOXICITY IN C. ELEGANS

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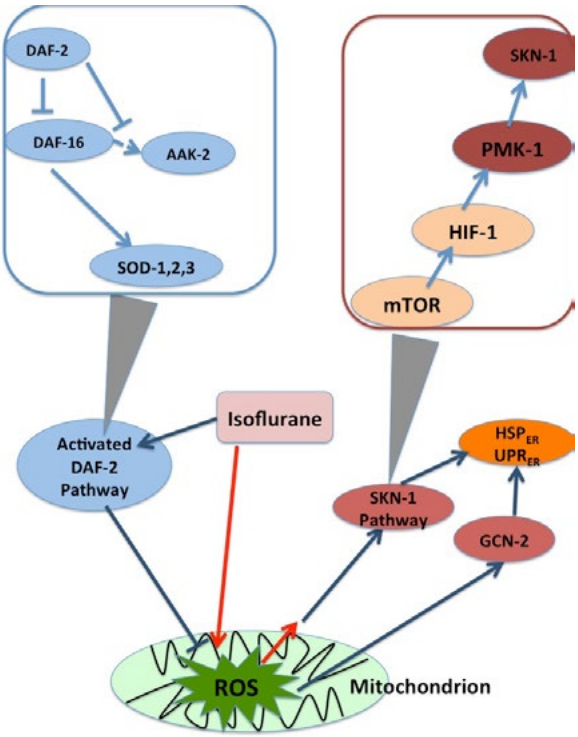
INTRODUCTION: Early developmental exposure to volatile anesthetics leads to anesthetic induced neurotoxicity (AIN) in nematodes, rodents, and primates[1-3]. The precise mechanisms by which anesthetics cause neurotoxicity are unknown. Using an array of genetic mutations, which affect neuronal development, we have taken a genetic approach in *C. elegans* to identify the molecular mechanisms underlying AIN. We have identified interacting pathways that control AIN and which may be useful to alleviate AIN.

METHODS: *Chemotaxis. C. elegans* L1 larvae were age synchronized and exposed to isoflurane at their EC95s from hours 4-8 after hatching. Larvae were removed from the anesthetic, and grown to adulthood. Chemotaxis on day one of adulthood (day 4 of life) was used as a measure of integrated neuronal function[1]. *Preconditioning (PC)*. Synchronized L1 larvae were exposed to isoflurane at their EC50s for hours 1-2 after hatching, followed by air for 3 hours and then exposure to isoflurane and chemotaxis studies as described above. *Rapamycin.* Rapamycin (LC laboratories) was dissolved in 100% DMSO at 50 mg/ml and added to plate agar to 100uM with final DMSO concentration of 0.2%. Nematodes were exposed to rapamycin for the first day of life then removed to regular plates and treated as above.

RESULTS: AIN was induced by exposure to the isoflurane at its EC50 for immobilization (6.5%) and a mammalian clinical concentration 2%). Mutations in the insulin-like receptor, DAF-2, induces a stress response and completely attenuates AIN in *C. elegans* (Figure 1A). Studying the downstream targets of DAf-2 identified a pathway (DAF-16, SOD-2, SOD-3, AAK-2) that controls AIN (Figure 1A). In addition, mutations blocking the ER-stress response also eliminated AIN. These included the kinase GCN-2, the heat shock protein HSP-4 and the transcription factors, SKN-1 and HIF-1. Both the target of DAF-2, DAF-16, and HSP-4 were activated by exposure to isoflurane. Preconditioning completely alleviated AIN in the wildtype N2. The DAF-2 pathway and ER-stress interact through the mechanistic target of rapamycin (mTOR). Inhibition of mTOR with rapamycin completely alleviated AIN.

DISCUSSION: The sum of our data earmark two pathways, highly conserved from nematodes to mammals, including mitochondrial dysfunction, ROS generation, and the ER-stress response as key regulators of AIN (Figure). The preconditioning results further indicate that a stress response can be induced by anesthetic pretreatment that protects against AIN. Since isoflurane exposure causes activation of the *daf-2* pathway that results in protection from ROS damage, we hypothesize that activation of that pathway leads to protection from AIN. A second pathway, ER-stress, is causative for AIN and inhibition of the pathway completely eliminates AIN. Inhibition of translation with rapamycin eliminates AIN. This suggests several testable mechanisms for potential alleviation of AIN in mammals.



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S-152.

TARGETED GENOTYPING IDENTIFIES TWO SUSCEPTIBILITY LOCI IN BDNF GENE FOR CHRONIC POSTSURGICAL PAIN

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INTRODUCTION: Chronic postsurgical pain is a well-recognized complication that affects at least 10% of patients undergoing common operations and adversely affects their quality of life. The purpose of this study was to evaluate the genetic association between single-nucleotide polymorphisms (SNPs) and chronic postsurgical pain.

METHODS: The Persistent Pain after Surgery study was approved by the Clinical Research Ethics Committee and all patients gave written informed consent. Adult patients undergoing a variety of surgical procedures that included a skin incision were recruited to the study. Patients were excluded if they underwent a pure endoscopic or radiologic procedure. Patients were contacted at 12 months after surgery and were asked to rate their experience of pain over the surgical site using the Brief Pain Inventory. The primary outcome was pain over the surgical site that had persisted for 12 months after the index surgery. Venous blood was collected before surgery. We genotyped 768 SNPs within 65 pain-related genes in 1,152 surgical patients using the GoldenGate genotyping assay. Genetic association was determined using PLINK software and was corrected for multiple testing by Bonferroni technique. A multivariate logistic regression model was also constructed to determine the predictors for chronic postoperative pain.

RESULTS: At one year follow-up, 246 patients reported persistent pain over the wound. A total of 40 SNPs from 10 candidate genes were found to be associated with chronic postsurgical pain. Following Bonferroni correction, only two SNPs (rs6265 and rs1491850) in BDNF gene remained significant. Patients carrying the allele A of rs6265 had a significantly lower risk but those with allele A in rs1491850 had a higher risk for chronic postsurgical pain (Table). Other clinical factors including age < 65 years, male gender, prior history of smoking, and pain syndrome were found to increase the risk of chronic postsurgical pain. The two SNPs had higher population attributable risk (6.25-12.3%) compared with clinical risk factors (3.71-8.76%).

CONCLUSIONS: Our data confirmed that genetic variations of BDNF play an important role in determining the susceptibility to chronic postsurgical pain. Genotyping of these two SNPs may help to identify patients that may require more intensive management of postsurgical pain.

Table: Multivariate regression model of predictors for chronic postsurgical pain.

Risk factors	Odds ratios (95%CI)	p value
Age ≤ 65	1.68 (1.12-2.52)	0.03
Male	2.31 (1.32-3.98)	0.01
Prior pain history	3.29 (2.09-5.19)	0.01
Smoker	1.43 (1.05-1.94)	0.03
BDNF polymorphism		
rs6265 A allele	0.51 (0.31-0.99)	0.03
rs1491850 A allele	1.83 (1.06-3.14)	0.03

S-153.

RESOLUTION OF EEG SLOWING MIRRORS RECOVERY FROM POSTOPERATIVE DELIRIUM

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INTRODUCTION: Delirium in the postoperative period is common, underdiagnosed, and linked with a greater risk of morbidity and mortality. Electroencephalography (EEG) may allow objective measures for predicting the incidence and course of delirium. In small case-control studies, slowing in the frontal-occipital EEG distinguishes delirious and non-delirious surgical patients[1]. It is not known whether this EEG slowing evolves as surgical patients recover from delirium. For this pilot study, we hypothesized that delirious patients would show EEG slowing compared to non-delirious patients, with a shift of power toward higher frequency bands during resolution of symptoms, as seen with metabolic encephalopathies[2].

METHODS: After HRPO approval, variants of the Confusion Assessment Method were used to assess the presence[3,4] of delirium. Two-channel EEG (F8 and O2, referenced to Cz) were recorded over 10 minute epochs of eyes open and eyes closed. Following multitaper spectral estimation, we calculated the proportion of power in the delta (1-4 Hz), theta (4-8 Hz), and alpha (8-13 Hz) frequency bands. Repeated measures analysis was implemented using a linear mixed model through SAS 9.3 Proc Mixed.

RESULTS: Forty-four recordings were obtained from 27 patients. Thirteen of these patients were delirious and followed with sequential recordings during their delirium recovery. Recordings associated with CAM+ assessments showed greater delta and theta power and lower alpha power (all $p < 10\text{-}4$, Figure 1). While the robustness of delta band power augmentation was similar in frontal and occipital EEG channels, modulation of theta and alpha band power was strongest in the O2-Cz channel. In patients with loss of theta and alpha power, recovery of delirium is associated with the progressive return of posterior dominant rhythm in theta and alpha bands (Figure 2).

Recovery from delirium was also associated with a return of visual reactivity in the alpha band ($p<0.01$, Figure 3).

CONCLUSIONS: A pragmatic sparse EEG montage is feasible for distinguishing recordings for delirious and non-delirious states. Consistent with other studies, lower frequency EEG power predominates during delirious states with occipital channels (delta and theta). These data suggest a shift of EEG power from delta, through theta, and alpha bands during the recovery from delirium, an evolution that may potentially be exploited for detection and tracking of delirium severity.

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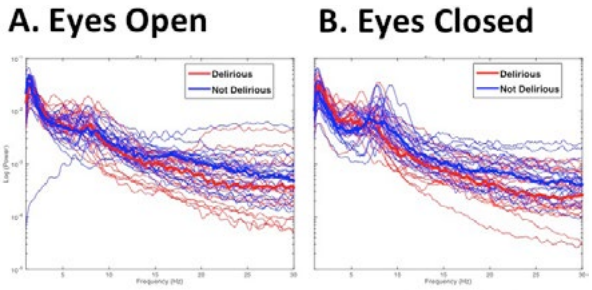

Figure 1. Power spectra for O2-Cz EEG. Individual spectra (light) and average power spectra (heavy) are shown for eyes open (A) and eyes closed (B) recordings.

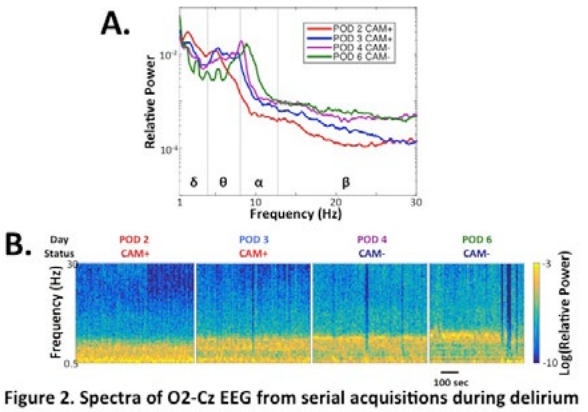

Figure 2. Spectra of O2-Cz EEG from serial acquisitions during delirium resolution. (A) Eyes Closed Spectra. (B) Eyes Closed Spectrogram.

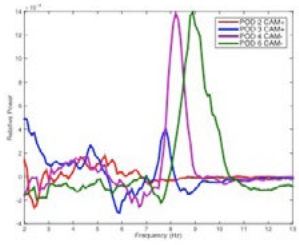

Figure 3. Visual Reactivity in the O2-Cz EEG during delirium resolution. Difference spectra (Eyes Closed – Eyes Open are shown.

S-154.

PERFORMANCE OF A TOUCHSCREEN-BASED VISUAL DISCRIMINATION TASK IS RESTORED WITH ELECTRICAL STIMULATION OF THE VENTRAL TEGMENTAL AREA (VTA) IN RATS SEDATED WITH ISOFLURANE

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INTRODUCTION: Electrical stimulation of the VTA restores righting in anesthetized rats[1]. It is unknown whether VTA stimulation also restores cognitive function. In this study rats were trained to perform a visual discrimination task to test if VTA stimulation restores performance during isoflurane (ISO) sedation. Methods: Male Sprague-Dawley rats (n=8) were first trained to perform a visual discrimination task. The chamber was in a sealed enclosure with ports for gas in/outflow and sampling. Two images were presented simultaneously on a touchscreen, and rats were trained to touch the correct image for a food reward. During each 30-minute session, rats were able to initiate a new trial 30 sec after completion of a previous trial. After reaching >85% correct responses for at least 3 consecutive days, the animals underwent stereotaxic implantation of bipolar stimulation electrodes in the VTA. The rats recovered for at least 7 days, and then were re-introduced to the testing chambers. Three weeks after surgery, the rats recovered to their baseline performance level. A dose-response was then performed by exposing them to steady-state ISO (0.1-0.5%) while performing the cognitive task. The rats were only exposed to one dose of ISO once per week. After establishing that 0.5% ISO reliably extinguished task performance, once a week (for 5 weeks) the rats underwent electrical VTA stimulation during steady-state 0.5% ISO sedation, and task performance was assessed. During week 3, the D1 dopamine receptor antagonist SCH-2330 was administered before VTA stimulation. Fig A shows the anesthesia protocol used to ensure steady-state ISO, while Fig B shows the waveform characteristics of electrical stimulation. Cognitive performance was assessed by: 1) number of trials completed per session, and 2) overall accuracy (percent correct). After completing all experiments, histological analysis of electrode placement was performed. The electrode tip was in the VTA in 5/8 animals. Only these animals were used for analysis.

RESULTS: The trials completed by each rat over time are shown in Fig C (black circles= correct responses, white=incorrect responses). At 0.5% ISO, all rats were heavily sedated, rarely moved, and performed no trials. However, during VTA stimulation 5/5 rats performed the task despite continuous 0.5% ISO (weeks 1,2,4,5). Administration of SCH-23390 prior to VTA simulation (week 3) reversibly abolished task performance. Figs D and E show number of trials and accuracy (mean with 95% CIs) for each week. Although VTA stimulation during ISO sedation restored task performance, mean accuracy was not restored to baseline.

CONCLUSIONS: At a dose of ISO insufficient to induce loss of righting (0.5%) the ability of rats to perform a visual discrimination task was reliably extinguished, suggesting that this many be a useful endpoint for loss of cognitive function. VTA stimulation restores task performance but not accuracy, and this effect is likely mediated by dopamine. Activation of this dopamine circuit may provide a novel target to treat POCD.

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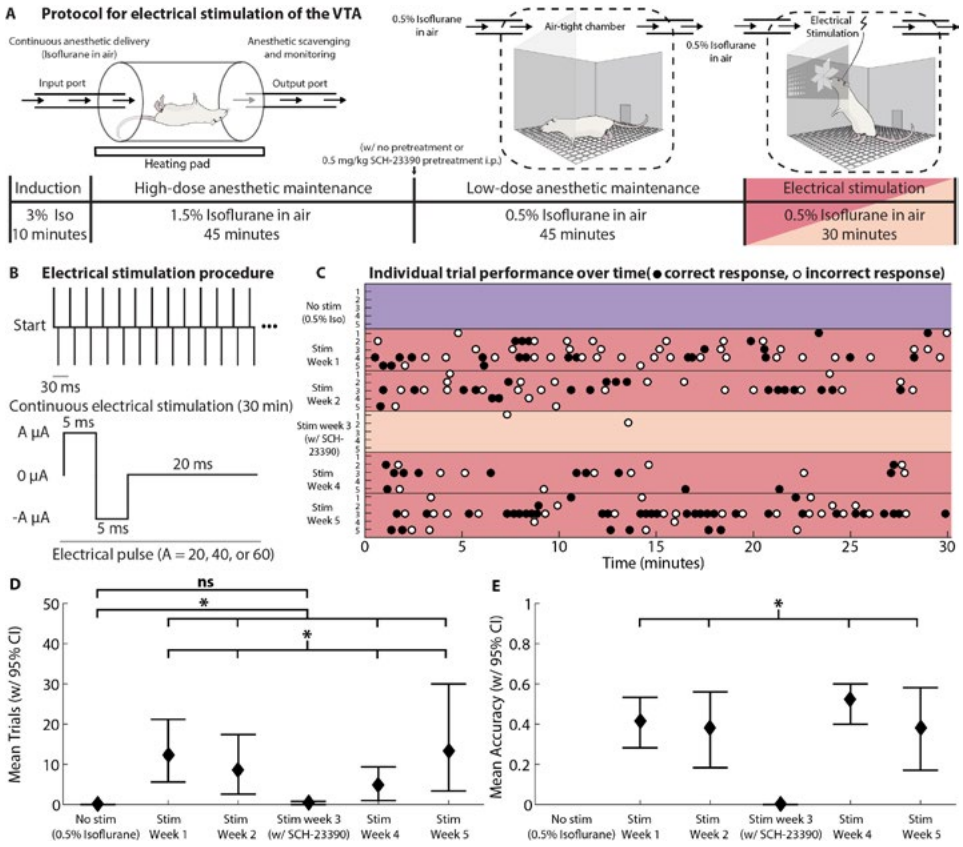

S-155.

GABAPENTIN RECRUITMENT OF δGABAA RECEPTORS TO THE CELL MEMBRANE CAUSES SEDATION AND ATAXIA IN MICE

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INTRODUCTION: The therapeutic properties of gabapentin have been widely attributed to blockade of the α2δ calcium channels[1]. However, gabapentin has both desired (analgesia, anxiolysis, sedation) and adverse effects (ataxia, confusion, prolonged emergence from anesthesia) that suggest it increases $GABA_A$ receptor activity. The mechanisms underlying the neurodepressive properties of gabapentin have remained elusive as it does not directly activate $GABA_A$ receptors. We previously showed that gabapentin increases a tonic inhibitory current generated by extrasynaptic $GABA_A$ receptors[2]. Here, we test the hypothesis that gabapentin increases cell-surface expression of extrasynaptic δ$GABA_A$ receptors and this action contributes to its behavioral effects.

METHODS: Studied were approved by the local animal ethics committee. Mice were treated with gabapentin (100 mg/kg, i.p.) or vehicle then sacrificed 2h later. Total and cell-surface expression of δ subunit protein was measured using biotinylation and Western blotting in cerebellum, thalamus and hippocampus. In behavioral studies, wild-type (WT) and δ$GABA_A$ receptor-deficient *(Gabrd-/-)* mice were treated with gabapentin or vehicle. Anxiolysis and ataxia were studied using the elevated plus maze and rotarod, respectively. Data are reported as mean ± SEM.

RESULTS: Gabapentin increased surface expression of δ subunit in cerebellum, thalamus and hippocampus. For example, in cerebellum it was increased by 36.3 % (control: 100.0 ± 4.8 %, GBP: 136.3 ± 5.4 %, n = 6, $P < 0.001$), whereas the total δ subunit expression was unchanged (control: 100.0 ± 4.0 %, GBP: 109.1 ± 4.4 %, n = 6, $P > 0.05$). Behavioral studies showed that gabapentin (GBP, 30 mg/kg) increased the percentage of time spent in the open arms of the elevated plus maze in WT mice (control: 1.0 ± 0.5 %, n = 9; GBP: 11.3 ± 3.2 %, n = 10, $P < 0.01$) but not in *Gabrd-/-* mice (control: 3.7 ± 2.0 %, GBP: 3.2 ± 1.1 %, n = 11, $P > 0.05$). In the rotarod test, gabapentin reduced the amount of time on the rod in WT mice (control: 298.4 ± 1.0 s, GBP 60 mg/kg: 139.3 ± 13.8 s, GBP: 100 mg/kg 111.5 ± 16.6 s, n = 6; $P < 0.0001$); but not in *Gabrd-/-* mice (control: 292.7 ± 3.2 s, GBP 60 mg/kg: 255.4 ± 18.0 s, GBP 100 mg/kg: 229.8 ± 34.9 s, n = 5, $P > 0.05$)

CONCLUSIONS: Gabapentin increases the cell-surface expression of δ$GABA_A$ receptors. The sedative and motor-impairing properties of gabapentin are mediated, at least in part, by δ$GABA_A$ receptors. We identified the first commercially-available drug that increases the accumulation of δ$GABA_A$ receptors on the cell surface. Given the increasing number of cognitive and mood disorders that are attributed to reduced δ$GABA_A$ receptor activity, the ability of δ$GABA_A$ receptors to increase neurogenesis, and adverse drug interactions associated with GABAergic drugs, these findings have broad therapeutic implications.

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S-156.

NEUROPROTECTIVE EFFECT OF AMIODARONE IN MOUSE MODEL OF ISCHEMIC STROKE

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INTRODUCTION: Ion channels play a crucial role in development of ischemic brain injury.[1-4] Recent studies have reported that the blockade of various types of ion channels improves outcome in experimental model of ischemic stroke.[1-4] Amiodarone, one of the most effective drugs in the treatment of life-threatening arrhythmia, works as a multiple channel blocker and its characteristics cover all four Vaughan-Williams classes.[5,6] Although it is known that amiodarone indirectly contributes to prevent ischemic stroke by maintaining sinus rhythm in patients with atrial fibrillation,[7] the direct neuroprotective effect of amiodarone has not been investigated. The purpose of this study is to investigate the direct effect of amiodarone on ischemic stroke in mice. Methods: Focal cerebral ischemia was induced by permanent distal middle cerebral artery occlusion (MCAO) in 24 adult male C57B6 mice under general anesthesia. Animals were randomized to two groups. Amiodarone group received single bolus intraperitoneal injection of amiodarone (50 mg/kg) one hour before the induction of ischemia; control group received 0.5 ml of normal saline. Heart rate and non-invasive blood pressure were monitored perioperatively. Mice were sacrificed 48 hours after MCAO followed by infarct volume analysis. The body asymmetry test and the corner test were used for neurological evaluation.

RESULTS: Single bolus intraperitoneal injection of 50 mg/kg amiodarone reduced the heart rate by 18.5 % at 1 hour and 8.0% at 49 hours after injection. No mice showed the toxicity or arrhythmia. There was no significant difference between two groups in the blood pressure. Amiodarone group showed smaller infarct volume (8.9 ± 2.1 % hemisphere (mean ± SD) vs. 11.2 ± 1.4 %, $P < 0.005$).[Fig. 1, 2] Amiodarone group also showed improved functional outcome (lower asymmetric body swing rate (52 ± 17 % vs. 70 ± 15%, $P < 0.05$) in the body asymmetry test and smaller number of left turns (8.0; 5-9 vs. 8.5; 6-10, (median; range), $P < 0.05$) in the corner test). [Fig. 2]

CONCLUSIONS: Amiodarone pretreatment attenuates ischemic brain injury and improves functional outcome without affecting the heart rhythm and the blood pressure. The neuroprotective property of amiodarone in this study may be explained by the blockade of multiple ion channels.

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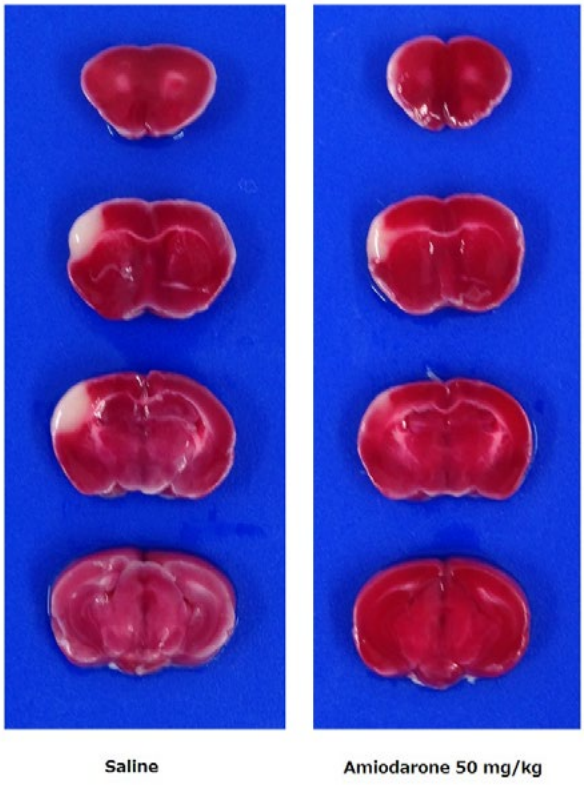

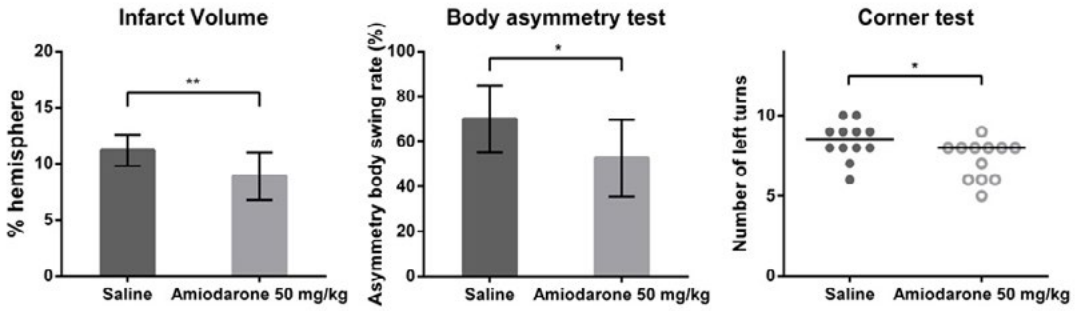

S-157.

CARBON MONOXIDE AND ISOFLURANE-INDUCED NEURODEGENERATION IN THE DEVELOPING MURINE BRAIN

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INTRODUCTION: The majority of commonly used general anesthetics activate the mitochondrial apoptosis pathway in the developing mammalian brain, resulting in widespread neurodegeneration and impaired cognition and behavioral disorders later in life. Carbon monoxide (CO), as a potential neuroprotectant, is of interest because infants and children are routinely exposed to CO during low-flow anesthesia. We have recently demonstrated that low concentrations of CO prevent isoflurane-induced lipid peroxidation and apoptosis in the forebrain of newborn mice in a dose-dependent manner. However, the effect of CO on anesthesia-induced neurodegeneration is unknown. We hypothesize that CO will prevent isoflurane-mediated effects on gross brain size and volume and will preserve neuronal content following a postnatal exposure.

METHODS: 7 day old C57Bl/6 mice underwent 1-hour exposure to 0 ppm (air), 5 ppm, or 100 ppm CO in air with or without isoflurane. A separate cohort of 7 day old mice served as unexposed controls. One week or 8 weeks after exposure, we measured body weight and brain weight and determined brain volume via Archimedes' principle. Neuronal content was then estimated in each cohort by performing immunoblot analysis for NeuN in forebrain homogenates. Densities were quantified with chemiluminescence. A total of 5 animals per exposure group per time point were evaluated in order to detect a 10% difference in brain weight with a power of 80%. Statistical significance was determined with two-way ANOVA and post-hoc Tukey's test and was set at $P < 0.05$.

RESULTS: Brain weight, brain volume, and body weight increased significantly overtime in each cohort as would be expected with normal development. However, there was no difference between cohorts at any time point with regard to gross brain weight and brain volume or with brain weight and brain volume normalized to body weight. On the other hand, steady-state levels of forebrain NeuN significantly decreased by 15% in animals exposed to isoflurane with air compared to air-exposed controls suggesting loss of neuronal content. In contrast, steady-state levels of NeuN were unchanged from control values in cohorts exposed to either concentration of CO with or without isoflurane.

CONCLUSIONS: Isoflurane exposure appears to induce neurodegeneration without affecting gross brain weight or volume. Furthermore, CO potentially limits isoflurane-induced effects on neuronal content. The lack of effect of isoflurane on overall brain size may be due to compensatory increases in other types of cells, an increase in non-cellular volume (such as CSF), or the lack of a gross effect seen with microscopic cellular loss. Future work will evaluate markers of other non-neuronal cell types and quantify region specific volumes in the developing murine brain following exposure. Our preliminary findings support the concept that low dose CO may protect the developing brain from isoflurane-induced neurodegeneration. These CO-mediated effects could have implications for the development of low-flow anesthesia in infants and children in order to prevent anesthesia-induced neurotoxicity.

S-158.

THE EFFECT OF DELAYED PRECONDITIONING INDUCED BY ISOFLURANE IN A RAT MODEL OF PROLONGED CARDIAC ARREST

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INTRODUCTION: Cardiac arrest is an important medical problem, with global brain injury a devastating complication in cardiac arrest survivors.[1] Isoflurane produces delayed phase preconditioning (PC) with proven pre-clinical protection in heart[2] and focal brain ischemia,[3] but is not well studied in cardiogenic global brain ischemia. We investigated the delayed preconditioning effect produced by isoflurane in a rat model of prolonged cardiac arrest (CA) induced by ventricular fibrillation (VF).

METHODS: The Loma Linda University Animal Health and Safety Committee approved all protocols. Sprague Dawley adult male rats (450-550g) were randomized into two groups (n=12/group): 1) Vehicle-PC +VF-CA and 2) Isoflurane-PC+VF-CA. Preconditioning was given at 24h prior to VF induction. Isoflurane-PC rats were put into a container continually flushed with 2% isoflurane in 30% O2 / 70% medical air for 1 hour; vehicle-PC was implemented in 30% O2 / 70% medical air mixture without isoflurane. VF was induced by a 60-Hz alternating current. After 8 minutes untreated VF, cardiopulmonary resuscitation was initiated with precordial compression using a pneumatically driven mechanical chest compressor, with coordinated mechanical ventilation for 8 minutes. Defibrillation was attempted with up to 3 anterior posterior, 2-J DC electrical shocks. Restoration of spontaneous circulation was defined as return of supraventricular rhythm with a mean aortic pressure of 60 mm Hg for ≥5 minutes. Mechanical ventilation with oxygen and hemodynamic monitoring were continued for 90 minutes after successful resuscitation. 24 hour survival was observed and neurological deficit scores 0 (no deficit) to 500 (total) were evaluated.

RESULTS: There were no significant differences in baseline characteristics before VF. Comparable perfusion pressures were maintained over 8 minutes of CPR. Isoflurane-PC tended to improve the success of resuscitation (9/12, 75%) compared to vehicle-PC (6/12, 50%). In resuscitated rats, post-resuscitation hemodynamics over 90 minutes did not significantly differ between the groups except for heart rate at 10 minutes after resuscitation (Fig 1). Similar 24h-survival was observed in isoflurane-PC rats (6 out of 9, 67%) and vehicle-PC group (4 out of 6, 67%). At 24h post-resuscitation, isoflurane-PC rats had lower neurological deficit scores than vehicle-PC rats (Fig 2), but there was no statistical significance.

CONCLUSIONS: One time isoflurane preconditioning 24h prior to cardiac arrest showed some benefit to overall resuscitability and post-resuscitation neurological deficit at 24h post-resuscitation. Future study is needed to investigate the protection efficacy of different isoflurane-PC regimens in the setting of global brain injury associated with prolonged cardiac arrest. Further exploration of the delayed preconditioning mechanisms induced by isoflurane may facilitate development of new specific target drugs to provide neuroprotection for cardiac arrest patients.

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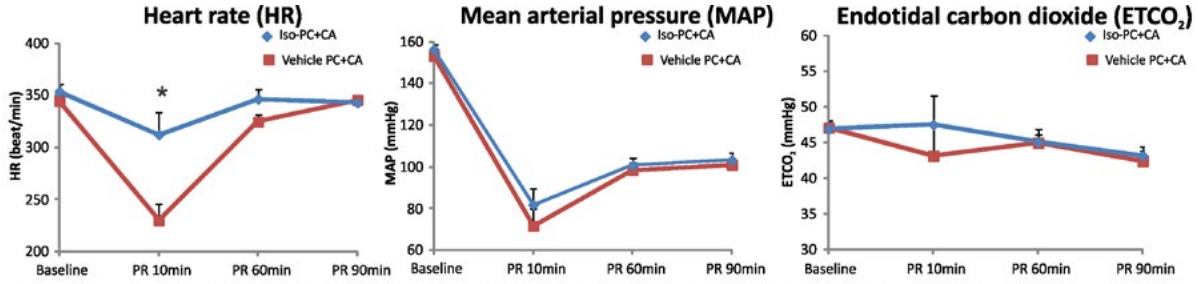

Figure 1 Hemodynamics at baseline (prior to VF induction), 10, 60 and 90 minutes post-resuscitation (PR). Data presented as Mean±Sem. *p<0.05 vs Vehicle-PC+CA.

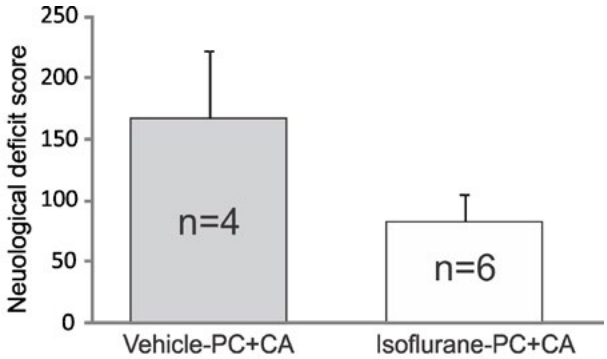

Figure 2 Neurological deficit at 24hours post-resuscitation. Isoflurane-PC reduced the neurological deficit scores compared to vehicle-PC rats subjected to cardiac arrest (CA). Data presented as Mean±Sem.

S-159.

LARGE SCALE NETWORK LEVEL ANALYSIS OF DEXMEDETOMIDINE INDUCED SEDATION

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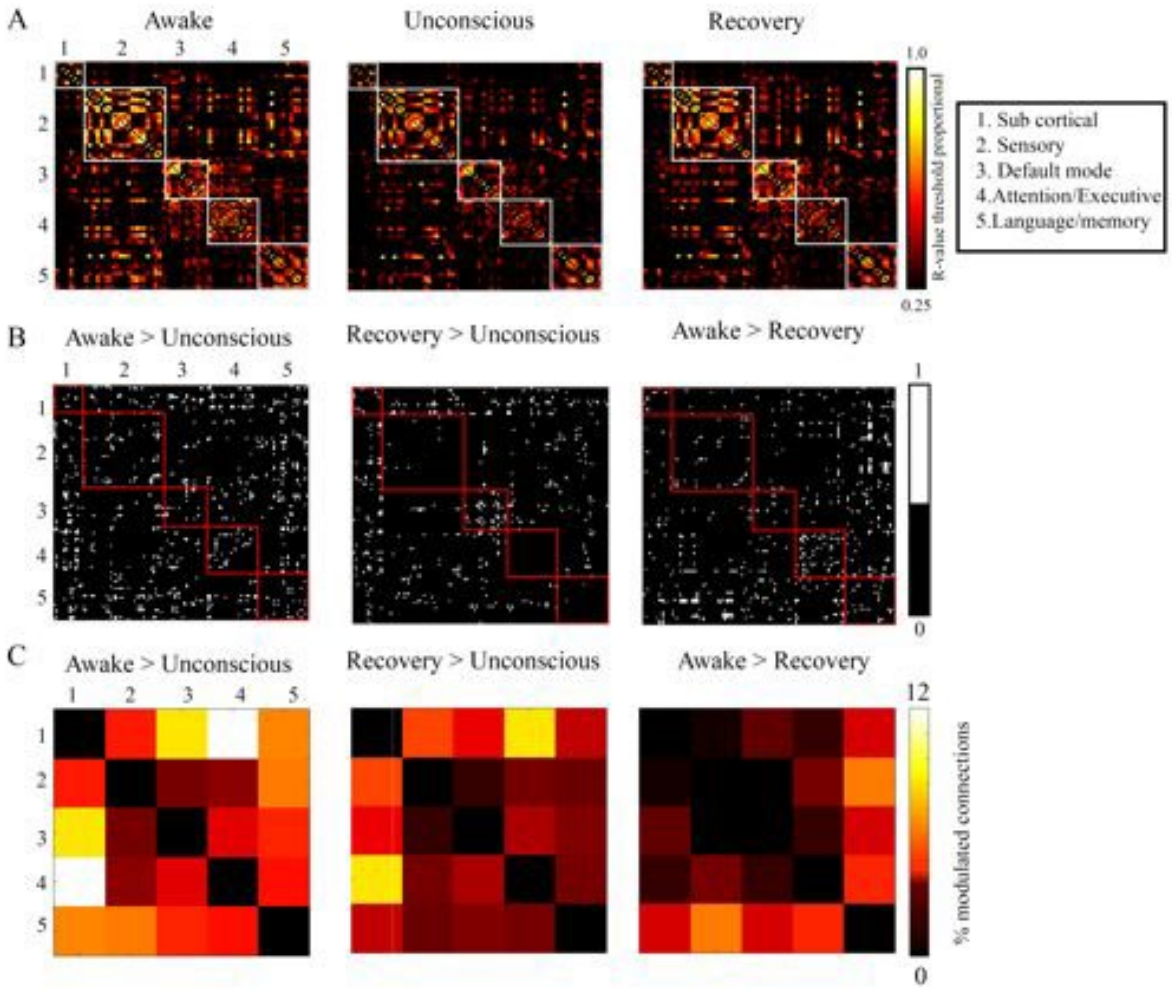
INTRODUCTION: Large-scale networks formed by synchronized fluctuations in functional MRI (fMRI) signals show a distinct architecture when observed from the vantage point of complex network analysis and graph theory. Local networks can be represented by clusters of connected brain regions formed by spatial correlations in fMRI signal. These local networks are in turn connected to each other to form a global network primarily though connections between hubs that have both intercluster and intracluster connections. The configuration of these networks is a putative mechanism to explain information dissemination in the brain. Here we studied the effects of dexmedetomidine on the capacity for efficient information transfer within local and global networks.

METHODS: Using resting state fMRI (rsfMRI), we imaged the brain of 14 healthy subjects during baseline (awake), dexmedetomidine-induced sedation, and recovery from dexmedetomidine. Using a whole brain network approach, networks were constructed at 6 different network density thresholds from a 131 parcellated brain regions. We used the Brain Connectivity Toolbox and custom codes written in MATLAB. Graph metrics were compared with paired t¬tests and results were corrected for multiple comparison using FDR ($p<0.05$).

RESULTS: We found significantly reduced capacity for efficient information transfer within the brain at both a local and a global level in weighted networks during the sedated state. The topological changes were associated with reduced strength of connections at a global mean level during the sedated state ($p<0.05$ for all network density thresholds). Importantly, we did not find significant changes in number of connections at a nodal level (degree distribution). As previously reported, we found reduced connectivity between the thalamus and the default mode network during the sedated state. However, our global network approach also showed reduced functional connectivity within and between all resting state networks. The most robust changes were observed for subcortical connections with multimodal networks, and for sensory connections with language/memory processing networks.

CONCLUSIONS: Our findings demonstrate that dexmedetomidine significantly disrupts the capacity for efficient information transfer at a local and a global scale. We found that the effects of dexmedetomidine were not specific to particular brain networks. Rather, connectivity was reduced both within and between several of the resting state networks.



S-160.

EEG BURST SUPPRESSION LEADS TO AN INCREASED AMPLITUDE OF THE MEDIAN NERVE SOMATOSENSORY EVOKED POTENTIAL UNDER PROPOFOL BUT NOT UNDER SEVOFLURANE

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INTRODUCTION: During general anesthesia, EEG "burst-suppression" indicates excessively "deep" anesthesia. During anesthesia, somatosensory evoked potential (SEP) can be used to detect brain ischemia. The early cortical response of the SEP (N20) is generated in the gray matter of gyrus postcentralis. Here, its correlation to the cerebral perfusion has already been shown, making the N20 a good potential to monitor the activity of the somatosensory cortex during anesthesia. Generally, increasing levels of anesthesia lead to a decrease of SSEP amplitudes. Still, in clinical practice it has been recommended that an increase of anesthesia may lead to an increase of the N20 amplitude. This study investigates median nerve SEP amplitues under clinical anesthesia and excessively deep anesthesia with EEG burst suppression induced by propofol or sevoflurane.

METHOD: The study was performed under two different anesthetig regimens, TIVA and Sevoflurane. Patients in the TIVA group received Propofol/Remifentanil infusion. After ten minutes of baseline (BL) recordings , the infusion rate was increased by 50%. Patients in the Sevoflurane group inhaled an increased concentration of the volatile drug after ten minutes of BL, which was maintained during the burst-suppression stage. In each group, the SEP of the left median nerve was monitored at electrode position CP4' and P4 for ten minutes during both the induction and burst-suppression stage. For statistical analysis, the paired sample t-test was applied to detect differences between BL and burst-suppression stage within each group

RESULTS: In the TIVA group, the N20 amplitudes were increased during EEG burst suppression (P4: p=0,039; C4': p=0,042), whereas such a difference was not detected in the Sevoflurane group (P4: p=0,101; C4' p=0,120).

DISCUSSION: The increase of SEP amplitues during propofol-induced EEG burst suppression may reflect suppression of non-stimulus related EEG activity by propofol (reduction of "noise"), or suppression of inhibitory pathways. SEP amplitudes in the Sevoflurane group did not increase. This may be due to widely spread, non-receptor specific and subcortical effects of the volatile anesthetics on the human brain. Because of the suppression of subcortical activity during general anesthesia, the volatile anesthetics could prevent an increase of the amplitude. In the next step, SEP will extracted either from EEG burst or from EEG suppression periods to clarify whether this increase of stimulus-responses occurs in periods of EEG bursts or during EEG suppression.

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S-161.

ACUTE AND SUBACUTE POSTOPERATIVE PAIN AFTER PARTIAL AND TOTAL MASTECTOMY: PROSPECTIVE ASSOCIATION WITH PYSCHOPHYSICAL AND PSYCHOSOCIAL PROCESSING OF PAIN

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INTRODUCTION: Breast cancer is the most common form of female cancer, the treatment of which often involves surgery. Previous reports cite persistent postmastectomy pain (PPMP) incidence around 30%, and putative risk factors include younger age, type of surgery, axillary dissection, anesthetic technique, genetics, negative affect (psychosocial factors) and increased pain sensitivity (psychophysical factors). However, most previous studies of PPMP have been retrospective and cross sectional in design.

METHODS: In the current study, a broad array of potential risk factors were assessed in women prospectively before surgery. Patients undergoing partial or total mastectomy were recruited and underwent preoperative assessment including validated psychosocial (anxiety, depression, catastrophizing, sleep disturbance etc) and psychophysical (quantitative sensory testing; pressure tolerance, pressure threshold, pinprick temporal summation and aftersensation pain) measures. Their degree of surgically related pain was then assessed using the Breast Cancer Pain Questionnaire, including frequency, severity and number of body areas assessments to determine a pain burden index (PBI) at several time points after surgery.

RESULTS: Patients undergoing more extensive surgery reported higher acute pain (postoperative day 0 and 1), with severity correlating with surgical extent (bilateral mastectomy> unilateral mastectomy> lumpectomy), as well as younger age, and higher preoperative psychosocial dysfunction (high catastrophizing, anxiety, depression). Subacute postoperative pain (postoperative day 14) also correlated with younger age and preoperative psychosocial dysfunction, but not surgical extent and duration. By 90 days after surgery, PBI was no longer associated with age or surgical factors, but remained correlated with preoperative psychosocial factors, as well as heightened baseline sensory processing (higher temporal summation of pain and painful aftersensations).

CONCLUSIONS: These findings suggest that the factors influencing acute pain after surgery may differ somewhat from those that predict more persistent pain. By more extensively phenotyping individual differences in pain processing in the preoperative period, we may differentially identify those at greater risk of acute vs chronic postsurgical pain, and design preventive therapies accordingly.

S-162.

ISOFLURANE REDUCES CEREBROVASCULAR DEPRESSION-INDUCED BY SINUSOIDAL GALVANIC STIMULATION IN A RAT MODEL OF VASOVAGAL SYNCOPE

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Vasovagal syncope (VVS) is the transient loss of consciousness due to decreased cerebral perfusion and is a major part of elderly falls (da Silva 2014). VVS is characterized by hypotension, bradycardia, and reduced cerebral blood flow. Current therapies for VVS have been unsatisfactory, therefore novel treatments are needed. Until recently there was no animal model of VVS. We have utilized sinusoidal galvanic stimulation (sGVS) in rats to mimic human VVS. The purpose of this study is to investigate isoflurane preconditioning as a potential therapy to reduce VVS pathophysiology.

METHODS: Male Sprague-Dawley rats were subjected to either sGVS or sham surgery. In adequately anesthetized animals, sGVS was induced by a 4 mA current at 0.05 Hz delivered for 3 minutes through two electrodes placed into the skin over the mastoids (Cohen et al. 2011). Blood pressure, heart rate, and cerebral blood flow were monitored before, during, and post-sGVS. Sham animals were subjected to all surgical procedures, but no current was delivered. A cohort of rats was subjected to 5 days of isoflurane preconditioning: 90 minutes of isoflurane exposure. Five days after completing the preconditioning regimen, rats were subjected to sGVS. All procedures were approved by the Loma Linda University IACUC.

RESULTS: sGVS results in hypotension, bradycardia, and decreased cerebral blood flow (Figure 1). The reduction in mean arterial pressure (10% reduction) and heart rate (10% reduction) recovers following sGVS while cerebral blood flow (30% reduction) continues to decrease over 30 minutes post-sGVS (50% reduction). Isoflurane preconditioning has no effect on either sGVS-induced hypotension or bradycardia. However, isoflurane preconditioning significantly reduces the cerebrovascular depression caused by sGVS resulting in a 10% reduction in cerebral blood flow for animals preconditioned with isoflurane compared to a 30% reduction in cerebral blood flow for rats subjected to sGVS only.

CONCLUSIONS: Herein isoflurane preconditioning attenuates the cerebrovascular depression caused by sinusoidal galvanic stimulation, but not either the hypotension or bradycardia induced by sGVS. The mechanism by which isoflurane conditions the cerebrovasculature against sGVS and VVS sequelae is unknown but is currently under investigation. This study indicates that isoflurane preconditioning may provide insight into potential therapies that can decrease syncopal episodes and reduce the injuries associated with syncopal falls.

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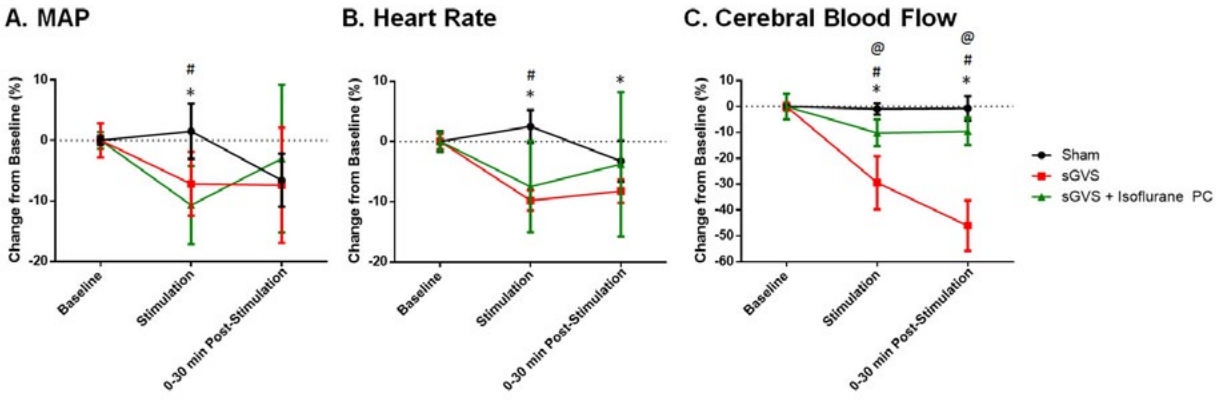

Figure 1. sGVS-induced changes in mean arterial pressure (MAP) (**A**), heart rate (**B**), and cerebral blood flow (**C**). Isoflurane preconditioning (sGVS + Isoflurane PC) reduces the cerebrovascular depression induced by sGVS. Isoflurane preconditioning does not affect MAP or heart rate during sGVS in rats subjected to only sGVS (sGVS). n=8/group. Mean ± SD. Two way ANOVA, Tukey post-hoc. * p<0.05 Sham vs sGVS, # p<0.05 Sham vs sGVS + Isoflurane PC, @ p<0.05 sGVS vs sGVS + Isoflurane PC.

S-163.

THE EFFECT OF ANESTHETIC AGENTS ON MARKERS OF NEUROLOGIC INJURY IN JUVENILE RATS

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INTRODUCTION: Experimentally, common anesthetic agents induce neuronal apoptosis and long-term behavioral deficits when administered to a developing rat brain.[1,2] This was documented in post-natal day seven rats (PND7, ~ neonate) but not in PND17 rats (~ 3-5 year old infant). Multiple mechanisms were implied to mediate such deficits. Specifically, propofol was linked to tumor necrosis factor alpha (TNFa) signaling.[3,4] In our pilot study we analyzed the effect of clinically relevant anesthetics in immature rodents with the goal of determining the mechanism and identifying potential therapies for anesthetic-induced neurodegeneration. We hypothesized that PND17 rats subjected to different anesthetic protocols will not exhibit neurological damage.

METHODS: Male Sprague-Dawley PND17 rats were anesthetized, intubated and mechanically ventilated (FiO_2 0.5). Left femoral artery and vein were cannulated for blood pressure monitoring and for drug administration, respectively. According to randomization, five groups (n=4/group) were studied: 1) naïve; 2) fentanyl (10 mcg/kg + 50 mcg/kg/h); 3) isoflurane (isoflurane 1%); 4) isoflurane + fentanyl (isoflurane 1%, fentanyl 10 mcg/kg + 50 mcg/kg/h); 5) propofol (20 mg/kg/h). Anesthesia was maintained for 6 h. Hemodynamic and biochemical parameters were assessed at baseline (BL) and at 1, 3 and 6 h. At 24 h, rats were sacrificed and plasma and brain tissue samples were obtained for analysis of neuron-specific enolase (NSE, marker of neuronal injury), soluble protein 100-b (S100b, marker of astroglial injury) and TNF-a (pivotal pro-inflammatory cytokine) by ELISA. TNFa was evaluated separately for cortex, cerebellum and brain homogenate. Hemodynamic parameters were assessed by repeated measures analysis of variance (ANOVA) with post-hoc Bonferroni correction. Biochemical parameters were assessed by one-way ANOVA. $p<0.05$ was considered statistically significant.

RESULTS: Significant differences in heart rate (Fig. 1) and mean arterial pressure (Fig. 2) existed between groups. No differences over time in individual groups were observed. Biochemical values showed differences between groups (Table 1). No differences in plasma NSE, plasma S100b or brain S100b were detected. Brain tissue NSE levels were highest in naives, and lowest in the propofol group ($p<0.05$). (Fig. 3) TNFa was not detected in any brain region.

CONCLUSIONS: In this small-size exploratory pilot study, we report previously undescribed changes in brain tissue NSE after propofol anesthesia. This could be suggestive of neuronal injury. (5) Our preliminary findings are of importance since no neurotoxic effects of anesthetics were previously reported in rats at this developmental stage. These effects do not seem to be mediated via TNFa signaling. Histological damage and neurobehavioral deficits need to be assessed in future experiments.

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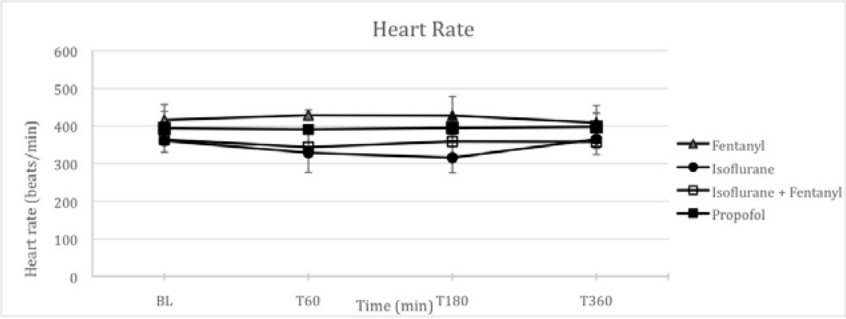

Figure 1. Heart rate at baseline and 60, 180 and 360 minutes after induction of anesthesia. $p<0.01$ fentanyl vs. Isoflurane; $p<0.05$ fentanyl vs. isoflurane + fentanyl.

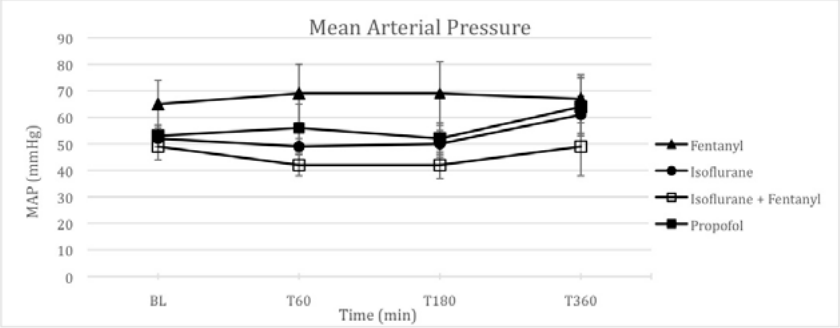

Figure 2. Mean arterial pressure at baseline and 60, 180 and 360 minutes after induction of anesthesia. $p<0.05$ fentanyl vs. isoflurane; $p<0.01$ fentanyl vs. isoflurane + fentanyl.

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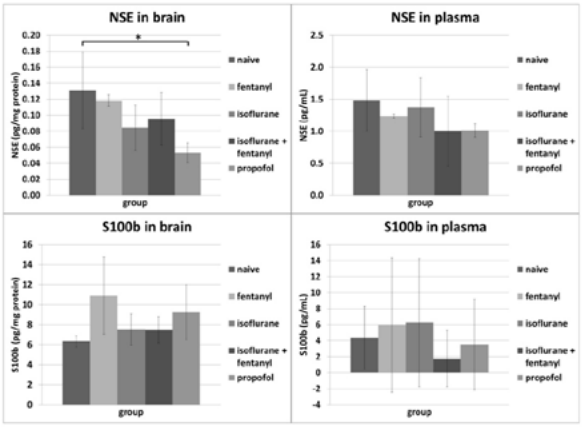

Figure 3. NSE and S100b levels in brain and plasma, respectively. * p<0.05

Table 1. Hemodynamic and biochemical data during anesthesia.

	BL	T60	T180	T360
Temp (°C)				
F	37.5 ± 0.6	37.2 ± 0.2	37.2 ± 0.2	37.2 ± 0.2
I	37.1 ± 0.2[a]	37.2 ± 0.2	37.1 ± 0.2	37.0 ± 0.1
I+F	37.3 ± 0.2	37.4 ± 0.1	37.3 ± 0.2	37.2 ± 0.2
P	37.2 ± 0.2[a]	37.3 ± 0.2	37.3 ± 0.2	37.3 ± 0.3
HR (beats/min)				
F	416 ± 41	429 ± 43[b,c]	428 ± 51[b,c,d]	409 ± 26[c]
I	361 ± 31	329 ± 52[a]	316 ± 40[a]	365 ± 41
I+F	364 ± 14	344 ± 15[a,d]	359 ± 21[a]	358 ± 18[a]
P	394 ± 45	391 ± 7[c]	395 ± 33[b]	398 ± 57
MAP (mmHg)				
F	65 ± 9[b,c,d]	69 ± 11[b,c]	69 ± 12[b,d]	67 ± 9
I	52 ± 5[a]	49 ± 3[a,c]	50 ± 5[a]	61 ± 7
I+F	49 ± 5[a]	42 ± 4[a,b,d]	42 ± 5[a,d]	49 ± 11[a]
P	53 ± 4[a]	56 ± 9[c]	52 ± 6[c]	64 ± 11
pH				
F	7.35 ± 0.06	7.32 ± 0.02[d]	7.33 ± 0.02	7.33 ± 0.10
I	7.42 ± 0.05	7.34 ± 0.05	7.34 ± 0.04	7.33 ± 0.00[c]
I+F	7.40 ± 0.01	7.32 ± 0.03[d]	7.31 ± 0.03	7.27 ± 0.03[b]
P	7.39 ± 0.02	7.39 ± 0.03[a,c]	7.34 ± 0.01[c]	7.31 ± 0.07
PCO2 (mmHg)				
F	42 ± 6	42 ± 1[d]	40 ± 3	36 ± 8
I	35 ± 4	40 ± 4	36 ± 3	37 ± 2
I+F	36 ± 2	40 ± 2	38 ± 2	40 ± 2
P	37 ± 3	36 ± 3[a]	38 ± 3	42 ± 6
PO2 (mmHg)				
F	201 ± 21	209 ± 5[b,d]	205 ± 8	210 ± 36
I	251 ± 40[d]	247 ± 28[a,d]	250 ± 42	232 ± 24
I+F	210 ± 10	213 ± 7	202 ± 15	206 ± 10
P	190 ± 18[b]	192 ± 21[b]	190 ± 26	208 ± 27
HCO3 (mmol/l)				
F	23.4 ± 1.0	21.8 ± 1.0	21.0 ± 1.1[c]	19.9 ± 1.7
I	22.6 ± 1.1	21.3 ± 0.8	19.5 ± 1.3	19.8 ± 1.1
I+F	22.3 ± 0.6	20.5 ± 0.6	19.3 ± 0.9[a]	19.3 ± 0.9
P	22.3 ± 1.0	22.2 ± 2.1	20.1 ± 1.5	21.0 ± 2.8
BE (mmol/l)				
F	-2.0 ± 1.5	-3.9 ± 1.1	-4.5 ± 1.1	-5.3 ± 0.6
I	-1.7 ± 1.2	-4.1 ± 1.5	-5.7 ± 1.5	-5.7 ± 1.1
I+F	-2.3 ± 0.3	-5.1 ± 0.7	-6.4 ± 1.2	-7.4 ± 1.6[a]
P	-2.5 ± 0.7	-2.5 ± 2.2	-4.5 ± 2.0	-4.9 ± 3.2
Na (mmol/l)				
F	140 ± 2[b,d]	144 ± 2[b]	147 ± 1[b]	149 ± 2[b,d]
I	136 ± 2[a]	138 ± 1[a]	141 ± 2[a]	142 ± 2[a]
I+F	138 ± 3[d]	141 ± 3	145 ± 3	146 ± 4
P	134 ± 1[a,c]	141 ± 5	143 ± 6	139 ± 5[a]
K (mmol/l)				
F	5.1 ± 0.4	4.7 ± 0.3[b]	4.4 ± 0.4[c]	4.0 ± 0.5[c]
I	5.2 ± 0.2	5.2 ± 0.3[a]	4.9 ± 0.3	4.5 ± 0.2
I+F	5.3 ± 0.5	5.3 ± 0.3	5.3 ± 0.4[a,d]	4.7 ± 0.3[a]
P	5.1 ± 0.4	4.8 ± 0.5	4.4 ± 0.6[c]	4.2 ± 0.5
Cl (mmol/l)				
F	108 ± 1[b,d]	112 ± 3[b]	117 ± 2[b,d]	121 ± 1[b,d]
I	104 ± 2[a,c]	107 ± 1[a,c]	112 ± 2[a,c]	115 ± 3[a]
I+F	107 ± 2[b]	111 ± 2[b]	116 ± 2[b,d]	119 ± 6
P	105 ± 2[a]	108 ± 2	110 ± 3[a,c]	111 ± 4[a]
Ca (mmol/l)				
F	1.23 ± 0.04	1.27 ± 0.02	1.23 ± 0.05[d]	1.19 ± 0.08
I	1.25 ± 0.05	1.29 ± 0.02[c]	1.25 ± 0.05[d]	1.19 ± 0.04
I+F	1.21 ± 0.05	1.22 ± 0.05[b]	1.26 ± 0.05[d]	1.19 ± 0.06
P	1.22 ± 0.3	1.30 ± 0.07	1.34 ± 0.02[a,b,c]	1.20 ± 0.09
Lactate (mmol/l)				
F	1.2 ± 0.6[b,d]	0.8 ± 0.2[b,c]	0.8 ± 0.2[b,c]	1.0 ± 0.5[c]
I	2.3 ± 0.6[a]	1.8 ± 0.5[a,d]	1.7 ± 0.2[a,d]	1.5 ± 0.1
I+F	2.2 ± 0.7	1.8 ± 0.5[a,d]	1.8 ± 0.6[a,d]	1.6 ± 0.1[a]
P	3.4 ± 1.1[a]	0.8 ± 0.2[b,c]	0.8 ± 0.1[b,c]	1.9 ± 1.3
Glucose (mg/dL)				
F	148 ± 11[d]	123 ± 5[b]	121 ± 5[b]	132 ± 21
I	172 ± 18	176 ± 15[a,d]	175 ± 11[a,c,d]	157 ± 5[c]
I+F	163 ± 38	148 ± 24	123 ± 12[b]	112 ± 14[b]
P	185 ± 9[a]	139 ± 10[b]	120 ± 8.7[b]	150 ± 31

Values given as mean ± SD. BL, baseline; T60, T180, and T360 represent 60, 180, and 360 minutes after induction of anesthesia, respectively. Groups: F, fentanyl; I, isoflurane; I+F, isoflurane + fentanyl; P, propofol. [a] p<0.05 vs. fentanyl; [b] p<0.05 vs. isoflurane; [c] p<0.05 vs. isoflurane + fentanyl; [d] p<0.05 vs. propofol. HR, heart rate; MAP, mean arterial pressure; BE, base excess.

S-164.

INSUFFICIENT ASTROCYTE-DERIVED BDNF CONTRIBUTES TO PROPOFOL-INDUCED NEURON DEATH THROUGH AKT/GSK3β/MITOCHONDRIAL FISSION PATHWAY IN RATS

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Increasing numbers of animal studies demonstrate that prolonged exposure to propofol during brain development induces widespread neuronal cell death, but there is little information on the role of astrocytes. Astrocytes can release neurotropic growth factors, such as brain-derived neurotropic factor (BDNF), which can exert a protective effect on neurons. We hypothesize that during propofol anesthesia, BDNF released from developing astrocytes may not be sufficient to prevent propofol-induced neurotoxicity. Hippocampal astrocytes and neurons isolated from neonatal Sprague Dawley rats were exposed to propofol at a clinically relevant dose of 30 μM, or dimethyl sulfoxide as a control, for 6 hours. Propofol-induced cell death was determined by propidium iodide staining in astrocyte-alone cultures, neuron-alone cultures, or co-cultures with either low or high density of astrocytes [1:9 or 1:1 astrocyte to neuron ratio (ANR), respectively]. The astrocyte-conditioned medium was collected 12 hours following propofol exposure, and measured by a protein array assay. BDNF concentration in astrocyte-conditioned medium was quantified by ELISA. Neuron-alone cultures were treated with BDNF, tyrosine receptor kinase B (TrkB) inhibitor Cyclotraxin-B, glycogen synthase kinase 3β (GSK3β) inhibitor CHIR99021, or mitochondrial fission inhibitor Mdivi-1 prior to propofol exposure. Western blots were performed for quantification of Akt and GSK3β levels. Mitochondrial shape was visualized through TOM20 staining. Propofol increased cell death in neurons, but did not influence astrocyte viability. The neuronal death was attenuated by the co-culture with a high ANR, but not with a low ANR. Astrocytes secreted BDNF in a cell density-dependent manner, and propofol decreased BDNF secretion from astrocytes. Administration of BDNF, CHIR99021, or Mdivi-1 significantly attenuated the propofol-induced neuron death and aberrant mitochondria in neuron-alone cultures and in co-cultures with a low ANR. Blockage of the BDNF receptor or Akt activity abolished astrocyte-induced neuroprotection in the co-cultures with a high ANR. The results indicate that astrocytes attenuate propofol neurotoxicity partially through BDNF-mediated cell survival pathways, suggesting multiple neuroprotective strategies, including administration of BDNF, astrocyte-conditioned medium, decreasing mitochondrial fission, or inhibiting GSK3β.

S-165.

ANESTHESIOLOGISTS CONTRIBUTION TO THE GENERAL VS LOCAL ANESTHESIA CONTROVERSY IN ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE

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INTRODUCTION: Endovascular treatment of acute ischemic stroke (AIS) has been performed since 2004, when the FDA approved the first generation mechanical cerebral clot retrieval device, the Merci retriever. In 2015, 5 RCTs have proven that endovascular mechanical thrombectomy is superior to iv t-PA alone in AIS caused by large anterior cerebral circulation vessel occlusion, establishing a new standard of care. In 2010, 3 retrospective studies reported worse outcomes when General Anesthesia was used in AIS. In June 2015, the AHA/ASA has issued a focused update to its 2013 guidelines on the early management of patients with AIS, including a new recommendation (No. 16, Class IIb, Level of Evidence C) that "it might be reasonable to favor conscious sedation over general anesthesia during endovascular therapy for AIS"[1]. The recommendation lists 3 references: 1 original study, 1 review and 1 meta-analysis. The contribution of anesthesiologists to the data, on which it is based, is not known.

METHODS: A Pubmed literature search, using the terms Stroke AND Anesthesia, Intubation AND Stroke, with filters: human studies, clinical trial, full text in English from 2010 through 2015 was performed. References from papers cited by ASA/ASA in 2015 and the 2014 SNACC Expert Consensus Statement: Anesthetic Management of Endovascular Treatment for Acute Ischemic Stroke[2] were reviewed as well. The affiliation with an anesthesiology department of the authors of the 21 papers in the final list was sought.

RESULTS: Using the specified criteria, 25 papers were identified. 4 were reviews, with 2 co-authored by an anesthesiologist (2012 both). There was 1 meta-analysis (no anesthesiologist); 20 papers were original contributions, of which the specialty affiliation of 1 was not specified. Of the remaining 19 – 7 were authored or co-authored by anesthesiologists. Of those, 1 was published in 2010 (practice survey), 1 in 2012, 1 in 2014 and 5 in 2015. All 7 analyzed under 100 patients.

CONCLUSION: The most influential literature on anesthetic technique and outcome in endovascular thrombectomy in AIS includes 1 paper published by an anesthesiologist in Anesthesiology[3]. The AHA/ASA recommendation to avoid general anesthesia in AIS is based on studies published by non-anesthesiologists. The SNACC Expert Consensus opinion states there are no data relating anesthesia provider presence to outcome. The documented contribution of anesthesiologists to the body of literature on the subject and the influential AHA/ASA recommendation indicates weak engagement of academic Neuroanesthesiologists in the management of interventional treatment for AIS.

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S-166.

MORPHINE EFFECTS ON ADULT RAT BRAIN RESTING-STATE NETWORKS: DOES PREVIOUS INFANT EXPOSURE TO MORPHINE MATTER?

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INTRODUCTION: Opioids, including morphine, remain a mainstream therapy for pain treatment and sedation of newborns. Although such treatment is considered standard care, little is known about possible long-term effects of early, prolonged exposure to opioids on the network dynamics. We hypothesized that prolonged morphine administration during infancy will be associated with long-term alterations in rat resting-state networks both in the absence and presence of subsequent administration of morphine in adulthood.

METHODS: We used functional magnetic resonance imaging and independent component analysis to map patterns of resting-state brain activity in 4 different groups of lightly anesthetized adult rats as approved by the Institutional IRB: (1) saline-saline adult (SSA) that received saline as infants and adults (N=12); (2) saline-morphine adult (SMA) that received saline as infants and morphine as adults (N=11); (3) morphine-saline adult (MSA) that received morphine as infants and saline as adults (N=12); and (4) morphine-morphine adult (MMA) that received morphine at both ages (N=12).

RESULTS: A total of 7 robust resting-state networks were identified in adult rats that include: Default Mode, Sensory (Exteroceptive), Salience (Interoceptive), Basal Ganglia-Thalamic-Hippocampal, Autonomic, Cerebellar, and Thalamic-Brainstem Networks. We report discrete changes in all adult resting-state networks as a result of early infant morphine exposure both in the absence (MSA vs. SSA) and the presence of subsequent adult morphine exposure (MMA vs. SMA).

CONCLUSIONS: Presented results suggest that prolonged morphine treatment in a developing rat model is associated with long-term changes in resting-state networks. These observations demonstrate the need for further research into the consequences of early opioid exposure on brain development.

S-167.

BEYOND KETAMINE FOR PSYCHIATRIC DISEASE: UNRAVELING THE MURINE NEURAL MECHANISMS OF THE EMPATHOGEN MDMA, A NOVEL, RAPID-ONSET SINGLE-SHOT CLINICAL THERAPY FOR POST-TRAUMATIC STRESS DISORDER

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INTRODUCTION: The commonly used anesthetics ketamine, N_2O and isoflurane have drawn increasing interest for their rapid-onset antidepressant effects. These compounds have multiple pharmacological targets, limiting insight into their mechanism. In contrast, the only other established rapid-onset, single-shot therapy for psychiatric disease, MDMA, an empathogen used to assist therapy for post-traumatic stress disorder (PTSD), has clearer pharmacology. Its major target is the serotonin (5-HT) transporter, SERT, and MDMA has an easily translated acute pro-social effect in mice. Several lines of evidence implicate oxytocin (OT) release in MDMA's pro-social effect. These attributes of MDMA provide crucial traction for studying the neural circuit-based mechanism of this therapy, and may allow broader insights into how neural systems mediate rapid-onset therapeutic effects for psychiatric disease.

METHODS: Behavioral experiments and electrophysiology were done in male and female adult C57 wild-type mice. To restrict knockout of OT receptors (OTR) to either 5-HTergic (SERT) or dopaminergic (DAT) neurons, SERT•$Cre^{+/-}$ or DAT•$Cre^{+/-}$ x Flx[OTR]+/+ mice were used. Affiliative behavior was assayed by the "3-chamber test", and rewarding properties were tested by conditioned place preference (CPP). Mice were given intraperitoneal (IP) injection of saline or MDMA (3-15 mg/kg). Some mice were pre-treated with OTR antagonist or 5-HT-selective reuptake inhibitor (SSRI) delivered IP or via intracranial microinjection (ICM). *Electrophysiology:* After terminal anesthesia, mouse brain was removed into chilled artificial cerebrospinal fluid, bubbled with 95% O2/5% CO_2, and 300um slices containing nucleus accumbens (NAc) were cut. Excitatory postsynaptic currents (EPSCs) were obtained by stimulating afferents with a bipolar electrode and recording from NAc neurons in whole-cell mode.

RESULTS: We show for the first time that MDMA produces a robust dose-dependent increase in a validated measure of sociability in male and female mice. This effect occurred at doses that were not rewarding as measured by CPP. A SERT inhibitor, the SSRI citalopram, significantly attenuates this effect when given IP, and when delivered specifically to the NAc via ICM, indicating 5-HT release in the NAc is required for MDMA's pro-social effect. This effect also requires OT release onto DAT+, but not SERT+, neurons, as mice lacking the OTR on DAT+ neurons show no MDMA-enhanced pro-social behavior. NAc-containing brain slices exposed to MDMA show a robust long-term depression of excitatory synaptic transmission, suggesting a possible mechanism for MDMA"s behavioral effect.

CONCLUSIONS: We have recapitulated several core features of MDMA's pro-social effect using a behavioral paradigm in mice, a species with tremendous genetic tractability. Our data indicate that SERT in the NAc and the OTR on DAT+ neurons is required for MDMA's pro-social effect. MDMA-induced alterations in NAc synaptic physiology lay the groundwork for future studies to identify a synaptic mechanism sufficient to produce this complex behavior.

S-168.

WITHDRAWN.

S-169.

THE CORRELATION BETWEEN REGIONAL CEREBRAL OXIMETRY AND MEAN ARTERIAL BLOOD PRESSURE IN THE BEACH CHAIR POSITION: A SECONDARY ANALYSIS OF A PROSPECTIVE INTERVENTIONAL STUDY

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INTRODUCTION: Cerebral autoregulation is better preserved with propofol compared to inhalational anesthesia[1] potentially conferring advantage for the use of propofol for patients anesthetized in beach chair position (BCP). Here, we conduct a secondary analysis of a previously published study[2] to evaluate the influence of anesthetic choice on the relationship between regional cerebral oxygenation (rSO_2) and mean arterial pressure (MAP) as proxy for cerebral autoregulation in patients anesthetized in BCP.

METHODS: The primary study[2] was a prospective interventional within-group study of patients undergoing shoulder surgery in the BCP that incorporated a randomized comparison between desflurane and TIVA with propofol; we demonstrated that increasing inspired oxygen fraction (FIO_2) and end tidal carbon dioxide ($PETCO_2$) results in an increase in rSO_2 that was independent of anesthetic choice. Following approval by the IRB and written informed consent, 56 patients were randomized. After induction of anesthesia FIO_2 and minute ventilation were sequentially adjusted for all patients. rSO_2 was recorded along with blood pressure (noninvasive cuff) at each of 5 ventilation set points: 1) FIO_2 0.3 and $PETCO_2$ 30mmHg - supine position, 2) FIO_2 0.3 and $PETCO_2$ 30mmHg - BCP, 3) FIO2 1.0 and $PETCO_2$ 30mmHg - BCP, 4) FIO_2 1.0 and $PETCO_2$ 45mmHg - BCP, 5) FIO_2 0.3 and $PETCO_2$ 30mmHg - BCP. rSO_2 was measured using the INVOS 5100C monitor. Depth of anesthesia was measured using Bispectral Index and targeted to the range 40-60. Blood pressure was maintained within 20% of preoperative MAP using either intravenous ephedrine (5mg) and/or phenylephrine (50-100mcg). In this secondary analysis, the correlation between MAP and rSO_2 was investigated as a proxy for cerebral autoregualtion;[3,4] for the entire study population and for each randomized anesthetic group. Furthermore, the influence of anesthetic choice, FIO_2, $PETCO_2$ and position on the relationship between blood pressure and rSO_2 was assessed in a mixed linear regression model controlling for age, body mass index, ASA physical status, and variation between time points between subjects (using a spline of continuous time measure).

RESULTS: No significant correlation was observed between MAP and rSO_2 in the BCP for the entire study population or for either anesthetic group (Table 1; Figure 1). Based on the mixed linear regression model, FIO_2, $PETCO_2$ and position did not significantly influence the relationship between MAP and rSO_2 (all p-values>0.05; AIC=1596.11). As expected, due to the sequential interventions of the primary study, there was variability between time and rSO_2 (figure 2).

CONCLUSION: With blood pressure controlled within 20% baseline it appears that cerebral autoregulation is maintained in patients anesthetized in the BCP. Anesthetic choice, FIO_2 and $PETCO_2$ do not appear to have a major influence on this physiology.

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Table 1

MAP*rSO2	Correlation Coefficient (p-value)
Combined Drugs (n=55)	0.03762 (05789)
Propofol (n=28)	0.13710 (0.1495)
Desflurane (n=27)	-0.04606 (0.6360)

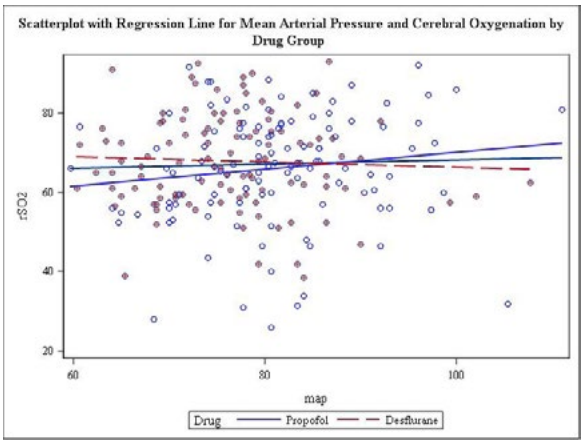

Figure 1.

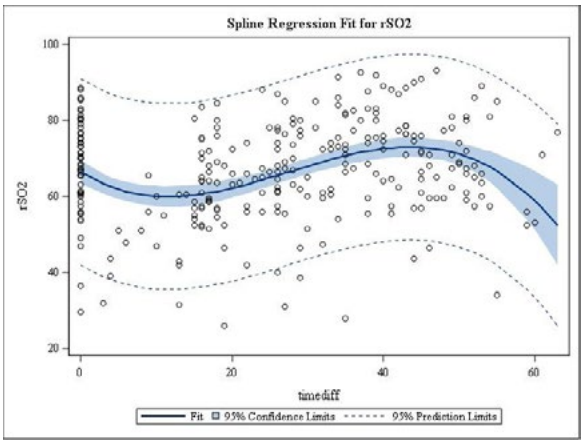

Figure 2.

S-170.

CLOSED LOOP CONTROL OF TOTAL INTRAVENOUS ANESTHESIA DURING SIGNIFICANT INTRAOPERATIVE BLOOD LOSS

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INTRODUCTION: During closed-loop control of anesthesia, drugs are titrated automatically according to a measure of clinical effect such as processed electroencephalography (pEEG). As a result, drug dosing is individualized, and constantly optimized to dynamic clinical circumstances[1]. Furthermore, the controller can act at a higher frequency and without distraction, allowing the anesthesiologist to dedicate their mental efforts to more challenging tasks[2]. Thus, the benefits of closed-loop may become evident during extreme circumstances, in which distraction-free thinking and prompt actions are required[3]. We describe a case of closed-loop controlled anesthesia in which a sudden, significant loss of blood volume required immediate intervention.

CASE REPORT: This case was part of a larger study of closed-loop anesthesia, conducted with local ethics board and Health Canada approval [ClinicalTrials# NCT01771263]. Consent was obtained for participation in the study and again for this report. A 79 yr old male with obesity (BMI 35) and hypertension presented for sigmoid tumor resection with loop ileostomy, and right radical nephrectomy with inferior vena cava (IVC) tumor embolectomy.Induction and maintenance of anesthesia were controlled in closed-loop[4]: propofol and remifentanil infusions were automatically adjusted based on feedback from bilateral frontal pEEG data (WAVCNS) acquired from the NeuroSENSE NS-701 monitor [NeuroWave, Cleveland, USA;[5] A case summary is shown in Figure 1. The default WAVCNS target was 50, with a remifentanil baseline infusion of 0.1 mcg/kg/min. Upon IVC tumor mobilization, a rapid loss of blood volume with concurrent hypotension occurred. Packed red blood cell (pRBC) and fluid transfusions were initiated. The patient received 6 units of pRBC before hemodynamic stability was re-established. During this episode, burst suppression (alternating isoelectric suppression and high-voltage bursts in the pEEG signal[6]) was detected primarily in the right hemisphere. The WAVCNS remained ±10 units of the target for 91% of maintenance of anesthesia. On postoperative day (POD) 1, the patient had proximal muscle weakness, dysarthria and an upgoing plantar reflex on the left side. A head CT scan on POD 4 revealed several subcortical white matter hypodensities in the right posterior middle cerebral artery territory, consistent with ischemia. An MRI on POD 20 confirmed the presence of subacute ischemic infarct, with no evidence of prior infarct, considered related to watershed effect[7] of hypotension during surgery (Figure 2).

CONCLUSION: This case illustrates that 1) closed-loop control maintained an appropriate depth of hypnosis in a rapidly changing surgical situation, allowing the anesthesiologist to focus on other tasks, and 2) pEEG may be useful as an indicator of cerebral hypoperfusion.

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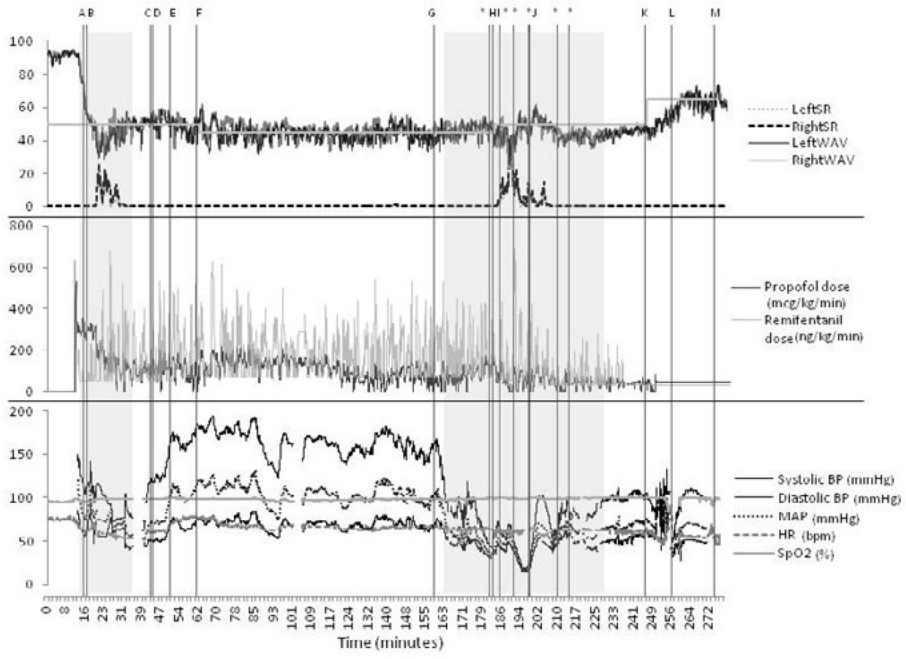

Figure 1: Case summary. Top: suppression ratio (SR) and bilateral WAV_{CNS} indices relative to WAV_{CNS} target (horizontal line); Middle : propofol and remifentanil dose; Bottom: vital signs. **A:** Induction complete (WAV_{CNS} < 60 for 30 seconds); **B:** endotrachial tube inserted; **C:** remifentanil bolus (53 mcg) given; **D:** procedure start (skin incision); **E:** remifentanil baseline infusion rate increased to 0.14 mcg/kg/min; **F:** WAV_{CNS} target decreased to 45; **G:** surgeon advised to prepare for blood loss; **H:** WAV_{CNS} target increased to 50; **I:** remifentanil baseline infusion rate decreased to 0.1 mcg/kg/min; **J:** remifentanil baseline infusion rate decreased to 0.06mcg/kg/min; **K:** WAV_{CNS} target increased to 65; **L:** patient opened eyes; **M:** endotrachial tube extracted. Each infusion of 1 unit of packed red blood cells marked by an asterisks (*).

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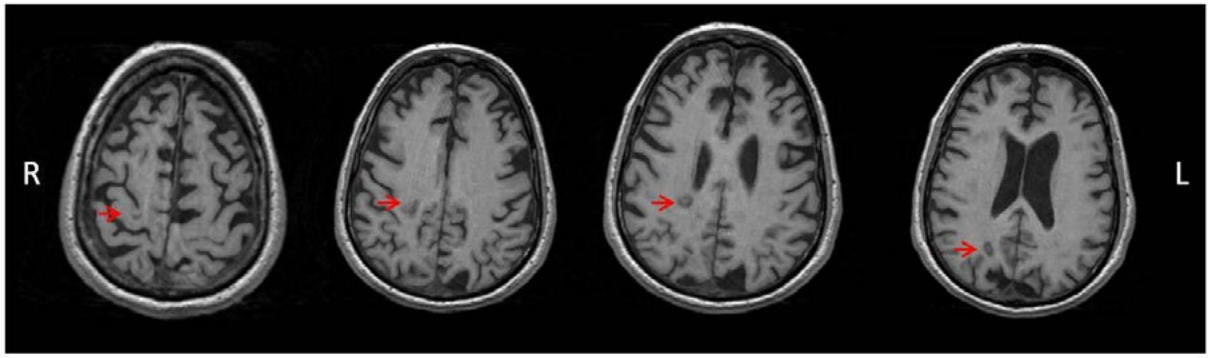

Figure 2: MRI taken on post-operative day 20. Subacute ischemic infarct in the posterior right middle cerebral artery territory shown by red arrows.

S-171.

CLOSED-LOOP CONTROL OF REMIFENTANIL AND PROPOFOL ANESTHESIA: EFFECTS ON PERFORMANCE AND BURST SUPPRESSION

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INTRODUCTION: Closed-loop control of anesthesia involves the continual adjustment of drug infusion rates according to measured clinical effect[1]. Processed electroencephalographic measures[2] can provide feedback for closed-loop infusion of propofol to control the Depth of Hypnosis (DoH)[3], but variations in surgical stimuli suggest the need for extending closed-loop control to the administration of analgesia. This is expected to improve stability of the DoH[4]. The purpose of this study was: in phase 1, to collect data for the design of a controller to automatically adjust both remifentanil and propofol infusion rates based on the WAVCNS index (NeuroWave, Cleveland, OH); in phase 2, to evaluate the system's performance. We hypothesized that closed-loop administration of remifentanil would improve DoH stability. Our controller design also increases remifentanil infusion in the presence of burst suppression (BS). We hypothesized that this would reduce closed-loop propofol administration and consequently the degree of BS observed. We present complete results from both phases.

METHODS: With Health Canada and REB approval and informed consent, ASA I-III adults, requiring general anesthesia for elective surgical procedures, were enrolled. In both phases, the propofol infusion was controlled by a closed-loop system during induction and maintenance of anesthesia. The WAVCNS provided continual feedback, with an initial setpoint of 50 used in all cases. In phase 1, remifentanil was administered by target controlled infusion[5]. Collected data was used to model the effects of varying remifentanil levels on the WAVCNS, and to design an automated remifentanil controller. In phase 2, remifentanil was automatically titrated to counteract rapid increases in the WAVCNS, assumed to be a result of nociceptive stimulation, with propofol continuing to target the overall DoH setpoint.

Results: 138 patients were recruited. Cases that were not completely run in closed-loop were excluded from this analysis (5 in phase 1, 6 in phase 2; Table 1). In Phase 2, higher doses of remifentanil were administered (Table 2) and the controller performance improved (Table 3), compared with Phase 1. However, there was no change in the percentage time during maintenance of anesthesia with BS ratio >10%, which was median [IQR] 6.74 [0, 15.5] in Phase 1 and 7.30 [0.71, 24.6] in Phase 2 (p=0.25).

CONCLUSIONS: Adding closed-loop control of remifentanil to closed-loop propofol infusion improved the DoH stability. Overall, remifentanil consumption was significantly increased in phase 2. However, the consequent reduction in propofol administration was not statistically significant and this did not reduce BS. Further studies are required to establish the clinical significance of BS during propofol anesthesia and to determine optimal closed-loop control of propofol and remifentanil in the presence of BS.

Table 1. Patient characteristics

	Phase I (n=58)	**Phase II** (n=80)
Gender (F: M)	24:34	35:45
Age (years)	**63** [51, 69]	**64** [55, 69]
BMI (kg/m^2)	**28.5** [25.7, 32.5]	**27.8** [24.9, 31.1]
ASA	I: 8%, II: 53%, III: 39%	I: 8%, II: 48%, III: 44%
Exclusions	1 propofol switched to manual mode to reduce dose; 1 propofol switched to TCI mode to increase dose; 3 propofol switched to TCI due to unreliable WAV_{CNS}	1 lost data due to technical failure; 1 remifentanil switched to TCI to reduce dose; 4 propofol switched to TCI due to unreliable WAV_{CNS}

Table 2. Procedure and drug summary

	Phase I (n=53)	**Phase II** (n=74)	**P-value** (2-tailed)
Length of procedure (min)	**97.0** [56.6, 159.4]	**107.8** [80.9, 160]	0.06
Time to induction (min)	**3.77** [3.23, 4.65]	**4.08** [3.20, 5.18]	0.23
Mean propofol dose (mcg/kg/min)	**106** [85.7, 133]	**96.4** [77.3, 116]	0.07
Mean remifentanil dose (mcg/kg/min)	**0.100** [0.0783, 0.127]	**0.150** [0.133, 0.166]	**<0.001**

Values are median [IQR], measured during maintenance phase.
P-value from Wilcoxon rank sum test.

Table 3. Controller performance measures

	Phase I (n=53)	**Phase II** (n=74)	**P-value** (2-tailed)
% time WAV_{CNS} within 10 of setpoint	**84.8** [73.9, 91.2]	**88.3** [83.3, 93.4]	0.06
Wobble	**7.20** [5.30, 8.84]	**6.00** [4.80, 7.51]	**0.05**
Global Score	**18.1** [13.8, 27.2]	**14.6** [11.6, 20.4]	**0.03**

Values are median [IQR], measured during maintenance phase.
Wobble: Measure of the DoH variability; Global Score = (MDAPE + Wobble)/Time WAV_{CNS} within 10 of setpoint, with MDAPE: Median absolute performance error during maintenance of anesthesia; lower values reflect better control performance.
P-values from Wilcoxon rank sum test.

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S-172.

POSTOPERATIVE COGNITIVE DYSFUNCTION: THE IMPACT OF STROKE AND SILENT ISCHEMIC LESIONS FOLLOWING AORTIC VALVE REPLACEMENT FOR AORTIC STENOSIS

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INTRODUCTION: Aortic valve replacement (AVR) for calcific aortic stenosis (AS) is associated with high rates of perioperative clinical stroke and "silent" cerebral ischemic lesions on diffusion-weighted MRI. Cognitive outcomes have been understudied, particularly in older adults.

METHODS: 185 participants undergoing AVR (Mage= 766 yr) and 198 non-surgical controls with cardiovascular disease (Mage=746 yr) were prospectively evaluated using a comprehensive cognitive protocol at baseline, 4-6 weeks, and 1 year post-surgery. Postoperative cognitive decline (POCD) was defined based on reliable change index scores. Predictors of POCD, including clinical stroke and ischemic lesions identified through serial neurologic exams and MRI, were examined using logistic regression.

RESULTS: In the surgery group 12.4% met criteria for POCD at 4-6 weeks and 7.5% showed POCD at 1 year. Relative to the control group, surgery participants showed lower scores on tests of working memory/inhibition and less improvement from baseline on tests of language at 4-6 weeks; at 1 year the groups did not differ. POCD at 4-6 weeks was significantly associated with advanced age, but at 1 year POCD was significantly associated with larger acute ischemic lesion volume/clinical stroke. Silent infarcts without overt clinical symptoms did not significantly affect cognitive outcome.

CONCLUSIONS: The overall impact of AVR for AS upon cognition in this aged sample largely manifested as only diminished practice effects relative to non-surgical controls and resolved by one year. High rates of stroke and acute ischemic lesions were noted in the surgical group, with large perioperative lesions (Mean total lesion volume = 6,500mm3) associated with poorer long-term cognitive outcomes.

S-173.

ELECTROENCEPHALOGRAPHIC CORRELATES OF HYPNOSIS INDEPENDENT OF DRUG EFFECT IN MICE

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INTRODUCTION: In the continuing effort to develop a method to independently assess consciousness and unconsciousness, a number of novel electroencephalographic (EEG) correlates of hypnosis have been proposed in human and animal models. These correlates have been shown to correlate well with behavioral markers of hypnosis, but whether these metrics are a direct reflections of changes in arousability or are instead changes from direct drug concentration effect is unknown. Here, we employ an engineered mouse, lacking dopamine-beta-hydroxylase *(Dbh -/-)* with increased anesthetic sensitivity to decouple drug concentration from arousal state in order to evaluate the validity of specific EEG correlates of hypnosis.

METHODS: Mice were implanted with 28 transcranial electrodes spaced from 3 mm anterior to bregma to 4.5 mm posterior to bregma, spanning 2.3 mm laterally in either direction, 2 cervical EMGs, and 2 thoracic EMGs. After a 2 week recovery, mice were tethered to head caps and placed in a sealed, temperature-controlled chamber. Isoflurane was ramped from 0 to 1.0% and back to 0% in 0.2% increments, 40 minutes per step, while continuously recording EEG and EMG. Data was acquired using 32 channel headstages (Intan Technologies, Los Angeles, CA) through an acquisition board based on open source designs provided by Open-Ephys (openephys.org) and imported for analysis into Matlab (Mathworks. Natick, Massachusettes.)

RESULTS: Mutant mice (n=5) and heterozygote littermates (n=5) displayed divergent EEG responses to identical concentrations of isoflurane, reflective of previously described differences in behavioral responses between the two genotypes (Hu).[1] Differences were noted in delta power between the two groups at multiple concentrations of isoflurane during induction and emergence. These changes, as well as the previously published behavioral responses to given concentrations of isoflurane, were analyzed in parallel to each genotype's global coherence (Cimenser),[2] stability (Solovey),[3] and frontal-parietal feedback (Ku),[4] per published protocols.

CONCLUSIONS: Patterns of behavioral divergence between mutant and heterozygote littermates at a given anesthetic concentration held for EEG analysis, suggesting such differences are true divergences in hypnosis, rather than a behavioral confound.

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S-174.

INTRAVENOUS ACETAMINOPHEN SIGNIFICANTLY REDUCES PAIN AFTER CRANIOTOMY : A RANDOMIZED CONTROL TRIAL

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INTRODUCTION: Intravenous acetaminophen has been shown to reduce post-operative pain and/or opioid consumption after a wide variety of surgical procedures[1-3]. However, its analgesic and opioid sparing effects have not been studied after craniotomy. We sought to determine if intravenous acetaminophen could reduce post-operative pain and/or opioid requirements in patients having sequential bilateral extracranial to intracranial bypass operations for moyamoya disease.

METHODS: Twelve patients undergoing bilateral extracranial to intracranial bypass graft procedures for moyamoya disease (typical duration of ~ 6 hrs) were included. Each patient served as their own control. At the time of their first surgery, patients were randomized to receive either 2 doses of saline placebo, or two doses of 1 g IV acetaminophen. One dose was given after induction, the other dose during closing of the surgical wound. When a patient returned for their contralateral surgery they received either acetaminophen or saline control as appropriate. Anesthesiologists were not blinded, but patients and ICU nurses who assigned pain scores and administered analgesics were blinded. All patients were given a similar intraoperative anesthetic. Induction consisted of midazolam 2 mg IV, fentanyl 500-1000 mcg IV, propofol 40-80 mg IV. Rocuronium 0.6 mg/kg or succinylcholine 1 mg/kg was given for paralysis. Maintenance with 50% nitrous oxide and 50% oxygen and a half MAC of isoflurane or sevoflurane was given to all patients except those with a history of PONV who received propofol 50 mcg/kg/min as a substitute for nitrous oxide. All patients were run on a remifentanil infusion (0.05 - 0.2 mcg/kg/min) intraoperatively for analgesia. No other opioids were given. Nurses were instructed upon arrival to the ICU to administer opioids at their discretion.

RESULTS: Data were analyzed using fentanyl consumption and reported pain scores on a 10-point scale in the ICU after each operation and compared using a paired t-test. Postoperative fentanyl consumption was reduced after IV acetaminophen administration compared to placebo in the first 6 hours (p=0.05), 12 hours (p=0.045) and 18 hours (p=0.025) postoperatively (Table 1). Pain scores were not significantly different at 6 hours (p=0.52), 12 hours (p=0.36) or 18 hours (p=0.33) postoperatively (Table 2).

CONCLUSION: The data demonstrate that IV acetaminophen significantly decreases post-operative opioid consumption in patients having bilateral extracranial to intracranial bypass surgery for the first 18 hours after surgery. This opioid-sparing effect increased over time, while pain scores were not significantly different across the entire 18 hour study period. These results show that two doses of IV acetaminophen had a significant opioid sparing effect which is advantageous after neurosurgical operations to facilitate timely neurological examinations and decrease opioid related side effects such as respiratory depression, excessive sedation and PONV.

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Table 1: Average Postoperative Fentanyl Consumption Per Patient (mcg)

	Hours 0-6	Hours 0-12	Hours 0-18
Tylenol	45.8	83	91.7
Placebo	143.8	239.6	300

Table 2: Average Postoperative Pain Score Per Patient (0-10)

	Hours 0-6	Hours 0-12	Hours 0-18
Tylenol	2.7	2.4	2.2
Placebo	3.2	3.3	3.1

S-175.

ACTIGRAPHY FOR DIAGNOSING AND PREDICTING HYPOACTIVE POSTOPERATIVE DELIRIUM

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INTRODUCTION: Postoperative delirium is common, underdiagnosed, and linked with poor outcomes. Wrist actigraphy can measure altered perioperative circadian patterns of motor activity[1] that may be associated with delirium risk[2-3]. It remains unclear whether actigraphy may predict or diagnose hypoactive delirium, the predominant subtype characterized by psychomotor retardation or impaired level of consciousness[4]. The goal of this pilot study is to evaluate the diagnostic utility of motor measures acquired on the day and night of surgery. We hypothesized that (1) patients with hypoactive delirium have low levels of activity during both epochs and that (2) patients who later develop delirium lack a circadian pattern of motor activity.

METHODS: Actigraphy bracelets were placed on the non-dominant wrist of surgical patients immediately following their procedure. Counts of activity were compiled in 1-minute epochs and combined across all three accelerometer axes. For each patient, the mean motor activity was calculated within the first day (1600-2300) and night (2300-0600) after surgery[2]. Delirium was assessed using variants of the Confusion Assessment Method[5-6].

RESULTS: Of 146 patients followed in the study, 75 (51%), 123 (84%), and 139 (95%) were assessed for delirium on POD 0, POD 1, and POD 2-5, respectively. Hypoactive delirium was observed in 70%, 68%, and 60% of delirious patients on POD 0, POD 1, and POD 2-5 (Table 1). Contrary to expectations, the group with hypoactive delirium on POD 0 or 1 (N = 21) had the largest median motor activity. Patients who experienced delirium during POD 2-5 (N = 23) had the lowest median motor activity, while those who did not experience delirium (N = 68) had an intermediate population median. These population medians were not significantly different for either day or night (Wilcoxon Rank-Sum test, all $p > 0.05$).

Among non-delirious patients, motor activity was greater during the day than at night (Wilcoxon Signed-rank test, $p < 0.01$). Delirious patients did not differ in their activity between night and day (Wilcoxon Signed-rank test, $p > 0.05$).

DISCUSSION: Our results show feasibility of within-patient comparison of motor activity during first 24 hours after surgery. Loss of day-night differences in motor activity in this period may reflect disruption of circadian patterns associated with concurrent or subsequent delirium. Early postoperative actigraphy may assist in the diagnosis and prediction of delirium.

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Table 1.

	POD 0	POD 1	POD 2-5
Proportion of patients assessed for delirium	75/146 (51%)	123/146 (84%)	139/146 (95%)
Proportion of patients positive for delirium	23/75 (31%)	25/123 (20%)	35/139 (25%)
Proportion of delirious patients with hypoactive subtype	16/23 (70%)	17/25 (68%)	21/35 (60%)
Proportion of delirious patients with hyperactive subtype	3/23 (13%)	4/25 (16%)	2/35 (7%)
Proportion of delirious patients with mixed subtype	4/23 (7%)	1/25 (4%)	7/35 (20%)
Proportion of delirious patients with other subtype	0/23 (0%)	3/25 (12%)	5/35 (14%)

S-176.

PLASMA NITRITE CHANGES DURING EC-IC BYPASS SURGERY IN MOYAMOYA PATIENTS

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INTRODUCTION: Plasma nitrite is elevated during acute ischemic events in animals[i]. This study was to determine if nitrite is elevated during a known and controlled cerebral ischemic event in humans. Six adult female moyamoya patients undergoing extracranial/intracranial (EC/IC) bypass surgery at Stanford Hospital were enrolled. During surgery a branch of the middle cerebral artery (MCA) is temporarily occluded to permit anastomosis with a branch of the superficial temporal artery (STA). This ischemic event is not consistently detected using cerebral oximetry, evoked potentials or EEG.

METHODS: The protocol was approved by the Stanford IRB. Patients provided informed, written consent prior to enrollment. During surgery, blood was sampled from a central venous line. Samples were immediately analyzed for nitrite as describedi. Each patient served as their own control, with nitrite measured near the beginning of the procedure (prior to arterial occlusion) and again before, during and after arterial occlusion. As part of the anesthetic protocol, patients were cooled to ~ 33°C, and administered a burst-suppression bolus of propofol approximately one minute prior to cross-clamp. To compensate for the expected decrease in blood pressure following propofol administration, patients received phenylephrine and ephedrine, which resulted in a slight elevation of mean arterial pressure.

RESULTS: Nitrite was elevated in 5 of 6 patients immediately following arterial occlusion. Nitrite was significantly elevated ($p=0.01$) 12 minutes after cross-clamp as compared to baseline. Patients were cross-clamped for 17.3 ± 2.5 (range 14-21) minutes while the STA was anastomosed to an M4 branch of the MCA. Nitrite decreased slowly after clamp release but did not achieve a statistically significant decrease within 12 ± 9 minutes of clamp release. This may be due to the half-life of nitrite, which may be 45 minutes[ii].

CONCLUSIONS: Plasma nitrite is significantly elevated during cerebral artery occlusion as compared to baseline within individuals. The fact that nitrite was not elevated in all patients suggests that this is due to ischemia, rather than propofol, phenylephrine or ephedrine since all patients received these drugs. Due to variations in collateral circulation, it was not expected that ischemia would occur in all patients. Propofol is a cerebrovascular vasoconstrictor and a peripheral vasodilator[iii]. Work remains to clarify the potentially confounding effects of propofol on central venous nitrite levels.

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S-177.

WITHDRAWN.

S-178.

WITHDRAWN.

S-179.

CONSCIOUSNESS, CONNECTEDNESS AND INTRAOPERATIVE UNRESPONSIVENESS STUDY (CONSCIOUS): A PROSPECTIVE INTERNATIONAL MULTICENTER COHORT STUDY OF THE ISOLATED FOREARM TECHNIQUE FOLLOWING INTUBATION

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BACKGROUND: Prior data from the isolated forearm technique (IFT) following noxious stimuli suggest that the incidence of response to command may approach 40% under anesthesia[1,2]. We conducted an international, multicenter, pragmatic study of the IFT to establish the incidence of responsiveness following intubation in current practice (NCT02248623). Methods: Following IRB approval at six sites, 260 adult patients were recruited from six centers into a prospective observational cohort study of the IFT during induction of anesthesia. Univariate comparisons were made with Student's t-test assuming equal variances, and Pearson's $\chi 2$ test. Bivariate models were constructed using logistic regression.

RESULTS: The incidence of IFT responsiveness following intubation was 4.6% (12/260). Responders were younger than non-responders ([mean±standard deviation] 39±17 vs. 51±16 years old; p=0.009) and had a higher incidence of observer rated signs of distress (50% vs. 2.4%; p=0.027) with 5 out of 12 responders reporting pain through a second hand squeeze. No subject reported explicit recall of intraoperative events when questioned after surgery (n=253). Depth of anesthesia monitoring values showed a wide range in both groups; however mean values were higher for responders before (53±19 vs. 42±14; p=0.032) and after (55±24 vs. 43±16; p=0.032) intubation. In patients not receiving total intravenous anesthesia, exposure to volatile anesthetics prior to intubation reduced the odds of responding (OR 0.2 (0.1 - 0.8); p=0.022) following adjustment for age.

CONCLUSIONS: An incidence rate of 4.6% suggests that intraoperative connected consciousness may occur frequently but this rate is lower than predicted from previous studies. Larger studies are required to identify risk factors for, and long-term consequences of, IFT responsiveness.

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S-180.

CB2R ACTIVITY INHIBITION LINKED TO CIDS REVERSAL IN MICE

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INTRODUCTION: One of the most frequently occurring medical complications after acute CNS injury is infection due to the post-injury disturbance of the normally well-balanced interplay between the immune system and the CNS. This dysregulation has been termed CNS injury-induced immunodeficiency syndrome (CIDS)[1]. The underlying mechanisms that are responsible for CIDS are still not elucidated but are hypothesized to be promoted by the injured brain. The endocannabinoid system (ECS) is composed of cannabinoid receptors, endocannabinoids and enzymes - all responsible for key homeostatic functions in the CNS and the immune system. It is suggested that local upregulation of the ECS occurs following CNS injury and represents an adaptive mechanism. CB2R is expressed in higher levels on microglia and immune cells and is shown to have an immunosuppressive role, suggesting that the activation of CB2R contributes to the immunosuppression in CIDS. Our study investigates if the immunosuppression can be reversed by inhibiting CB2Rs on immune cells using the CB2R antagonist, AM630.

METHODS: The study was conducted in accordance with the guidelines and standards set forth by the National Council on Animal Care and approved by the University Committee on Laboratory Animals at local University. CNS injury was induced in C57Bl/6 mice (male, 6-8 weeks) via an intracerebral injection of the vasoconstrictor peptide, endothelin-1 (ET-1, 2µg/µl). Immune activation by the TLR-4 agonist lipopolysaccharide (LPS) was assessed 24 hr later using intravital microscopy to monitor leukocyte adhesion and rolling within the intestinal microvasculature, a key microcirculation in systemic inflammation such as sepsis. The brain tissue was extracted and stained with triphenyl tetrazolium chloride (TTC) to confirm the presence of CNS injury and to calculate the infarct volume. The effect of genetic CB2R knockout on the severity of CNS injury, as well as the severity of CIDS was investigated in CB2R -/- C57Bl6 mice.

RESULTS: Consistent with the induction of CIDS, intravital microscopy confirmed that immunochallenged animals with CNS injury have a reduced count of activated leukocytes within the intestinal microcirculation when compared to immunochallenged animals without CNS injury. AM630 (2.5 mg/kg, i.v.) administration 15 min prior to LPS challenge, reversed this measure of suppressed immune function and did not have any detrimental impact on the infarct size. Genetic knockout of CB2R revealed that the CIDS was not induced after an acute CNS injury, confirming the involvement of the ECS in CIDS.

CONCLUSIONS: Our current findings suggest that inhibition of the CB2R pathway after an acute CNS injury reverses CIDS without exacerbating the brain injury. Further studies will focus on investigating various time points in order to identify the optimal treatment window for CB2R inhibition.

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S-181.

THE EFFECT OF REMIFENTANIL INFUSION ON SUCCESSFUL CORTICAL MAPPING DURING AWAKE CRANIOTOMY

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INTRODUCTION: Many studies have been published regarding anesthetic management during awake craniotomies. The study protocols generally have discontinued sedation during cortical mapping, out of concern for compromising mapping integrity. Even with adequate surgical block, patients may experience positional and emotional discomfort. In this observational crossover study, we assessed whether a steady state concentration of remifentanil would compromise cortical mapping.

METHODS: Upon arrival, all consented patients received scalp blocks with lidocaine and tetracaine during light sedation and after placing standard monitors. A sedation regimen of remifentanil 0.03-0.18 mcg/kg/min and propofol 5-25 mcg/kg/min titrated to a respiratory rate of 8-12 breaths per minute was started. Infusions of remifentanil and propofol were discontinued for at least 15 minutes prior to mapping to allow washout. After completion of cortical mapping, remifentanil was restarted for five minutes at a dose of 0.1 mcg/kg/min, if the dose of the previous maintenance infusion was 0.1 mcg/kg/min or higher. If the maintenance infusion dose was less than 0.1 mcg/kg/min, the infusion was restarted at the same dose. After five minutes, the dose was decreased by half for five more minutes to achieve a patient-specific steady state concentration. The neurosurgeon then repeated sensory, motor, and speech mapping to the previously labeled areas. We assessed the ability to obtain the same responses with the steady state remifentanil concentration.

RESULTS: Twenty-one subjects successfully completed the study, with a total of 172 stimulations that were repeated after the remifentanil infusion was restarted. Three patients were dropped from the study due to intraoperative complications (seizure or dysphagia) prior to commencement of the study. Sensory mapping was unaffected by remifentanil in 77% of cases, while motor mapping was unaffected by remifentanil in 80% of cases. Speech mapping was unaffected 89.2% of the time (see Table 1). Of note, in five patients (nine total stimulations – 2 sensory, 5 motor, and 2 speech) when a response was not replicated during the study, the surgeon increased the intensity of the stimulus by 0.5 mA or 1 mA. In eight of these nine stimulations, the original response was reproducible. The only response that was not able to be replicated was one motor response. No patients endured any complications from increased stimulus intensity.

DISCUSSION: Remifentanil is frequently administered for sedation and analgesia in awake craniotomies. This study demonstrates that it may be used during cortical mapping in the majority of cases without affecting mapping fidelity. If there is concern for compromise, the stimulation intensity could be increased by 0.5 to 1 mA. It appears that doing so greatly increases the ability to reproduce the responses without additional complications.

Table 1

	Number of Stimulations	Number of Stimulations Unchanged with Remifentanil	Number of Stimulations Altered with Remifentanil
Sensory	74	57 (77.0%)	17 (23.0%)
Motor	70	56 (80.0%)	14 (20.0%)
Speech	28	25 (89.2%)	3 (10.8%)

Subspecialty Abstracts

Obstetric Anesthesiology

S-182.

WITHDRAWN.

S-183.

WITHDRAWN.

S-184.

INCIDENCE OF PRURITIS IN PREGNANT WOMEN UNDERGOING LOWER SEGEMENT CESAREAN SECTION UNDER SPINAL ANAESTHESIA WITH FENTANYL ADDED TO BUPIVACAINE

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Regional anesthesia and analgesia isbeing widely used now days especially for lower segment cesarean sections (LSCS). Till date, only few studies have reported the incidence of pruritus in pregnant women afterspinal anesthesia with added fentanyl[1,2]. Our observation suggests that there is a higher incidence of pruritus in pregnant women who receive intrathecal fentanyl in comparison to non-pregnant candidates. In this study we hypothesize that pregnancy is a risk factor of pruritus after intrathecal fentanyl. Many treatments have been tried, but to date, the data are conflicting and only limited studies have confirmed their efficacy[2,3]. In this trial we aimed to observe the efficacy of lidocaine to treat pruritus caused by intrathecal fentanyl owing to its cell wall stabilization property.

METHODS: Following approval by Hospital Ethical Issues committee, 160 ASA I and II female patients between 18-45 of age who gave consent for spinal anesthesia were included in this trial. They were divided into two groups of 80 patients each. Pregnant group underwent LSCS while non-pregnant patients underwent lower limb orthopedic surgery. A fixed dose of 20 mcg of Fentanyl was added to bupivicaine for spinal anesthesia. Times of intrathecal injection versus development of pruritus, severity of pruritus, and type of treatment were recorded in the data collection form by a blinded observer. The patient using visual analog scale determined the severity of pruritis (mild= 1-3, moderate 4-6, severe >6). Patients who developed pruritis were treated with either Naloxone 0.1mg IV two doses 5 minutes apart, or Propofol 10mg IV two doses 5 minutes apart, or a single dose of Lidocaine 1mg/kg IV, which were chosen by sealed envelope. Failure to abolish pruritis by the above treatment was followed by management decided by the attending anesthetist. Statistical analysis of the data was done using Chi-square test and Logistic regression by using SPSS version 22.p value< 0.05 was considered significant.

RESULT: The incidence of pruritus in pregnant women is 25%, which is significantly higher than in the non-pregnant patients (3.8%).The total success rate of treatment was nearly comparable between propofol and lidocaine (75 vs 77.8) with a better success of lidocaine than propofol in moderate pruritus (100% vs 66.7). Although the success rate of Naloxone was 100% in both mild and moderate pruritus, there was no severe case treated with it, therefore the success rate of Naloxone in severe pruritus is unknown.

CONCLUSIONS: -Pregnancy is a risk factor for pruritus after the injection of intrathecal fentanyl. -Lidocaine can be used to treat pruritus caused by intrathecal fentanyl. -Propofol and lidocaine is useful in mild and moderate, but not in severe pruritus.

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Incidence of Pruritus	Severity of Pruritus in pregnant women	Success rate with different treatment agent						
Group	%	Grade	%	Drug	Total success Rate %	Mild Pruritus %	Moderate Pruritus %	Severe Pruritus %
Pregnant	25	Mild	55	Propofol	75	100	66.7	0
Non-pregnant	3.8	Moderate	30	Lidocaine	77.8	100	100	0
P value	< 0.05	Severe	15	Naloxone	100	100	100	No case

S-185.

ANALYSIS AND COMPARISON BETWEEN TERM VAGINAL DELIVERY AND TERM CESAREAN DELIVERY NEONATAL TEG ASSAYS WITH ESTABLISHMENT OF NORMATIVE DATA

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INTRODUCTION: Thromboelastography (TEG) is utilized for point of care monitoring of coagulation. Normal adult values, patterns and various abnormalities are well described. However, immediate newborn TEG information is poorly documented. TEG changes throughout the later weeks of gestation has not been documented nor has the influence of mode of delivery been measured on this coagulation function. In this investigation, we looked at describing normative term delivery TEG and the influence that vaginal and cesarean delivery methods have.

METHODS: Venous umbilical blood was obtained within ten minutes of stage 3 delivery of the placenta. Citrated-kaolin sampling and analysis were conducted. Cesarean samples were collected for scheduled cases, and cases that were converted to cesarean delivery for failure of cervical progression of labor prior to stage 2. TEG values with corresponding images were obtained. A total of 50 vaginal delivery and 50 cesarean delivery samples were collected.

RESULTS: Total numbers of samples for neonate venous cord blood were 49 vaginal deliveries and 34 cesarean deliveries in each group. One vaginal neonatal sample was excluded for poor fetal well-being in the setting of low APGAR scores and not included in analysis. A total of 16 cesarean samples were excluded (6 for poor fetal heart rate tracing and 10 for insufficient sample volume). Vaginal term deliveries in which no known previous abnormalities were documented resulted in neonatal, infant and adult TEG study values: R: 5.4 ± 1.4 (mean ± SD) minutes, K: 1.6 ± 0.8 minutes; α-angle: 65.3 ± 8.8 degrees, MA: 65.9 ± 5.8 mm, and LY30: 1.3 ± 1.1 percent. Results of the cesarean deliveries showed: R: 5.9 ± 1.8 (mean ± SD) minutes, K: 1.6 ± 0.5 minutes; α-angle: 62.3 ± 9.9 degrees, MA: 64.4 ± 3.6 mm, and LY30: 1.2 ± 1.1 percent. Statistical differences were only significant for MA ($p=0.036$). Comparison data analysis is described in Table 1.

CONCLUSION: We found that observing TEG samples from term gestation overall mimics adult values when delivery was normal. There appeared to be a tendency to a more pro-thrombotic state however, parameters were neither statistically nor clinically significant. This we speculate to be favorable to the baby in order to not have a neonate at risk for bleeding while immediately delivered. More likely, factors to affect neonatal TEG assays appear to be the clinical state of mother and fetus without being inherent to the delivery type or age of the neonate.

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Comparison Data between Neonatal TEG assays of Vaginal and Cesarean Deliveries

Delivery Type	Statistic	R	k	alpha	MA	LY30
Vaginal	Mean	5.42	1.62	65.34	65.94	1.33
	N	49	49	49	49	49
	Std. Deviation	1.35	.758	8.85	5.84	1.10
	Median	5.60	1.40	8.45	5.84	1.1
Cesarean	Mean	5.88	1.60	62.27	64.41	1.21
	N	34	34	34	34	34
	Std. Deviation	1.83	.53	9.90	3.62	1.11
	Median	5.85	1.55	66.45	64.40	.95

S-186.

COMPARISON OF CONTINUOUS IV PHENYLEPHRINE VS. NOREPINEPHRINE INFUSION IN PREVENTION OF SPINAL HYPOTENSION DURING CAESAREAN DELIVERY: ASSESSMENT OF HEMODYNAMIC PARAMETERS AND MATERNAL OUTCOMES

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BACKGROUND: Hypotension is common under spinal anesthesia for caesarean delivery (CD) which may consequently lead to maternal nausea and vomiting. Phenylephrine is currently the vasopressor of choice for treatment of maternal hypotension. However, phenylephrine can have clinically significant side effects such as a baroreceptor-mediated bradycardia. The aim of this study is to compare the efficacy of continuous intravenous phenylephrine infusion to continuous norepinephrine infusion regarding maternal hemodynamic stability and maternal outcomes (nausea and vomiting) for elective caesarean delivery under spinal anesthesia.

METHODS: In this prospective randomized clinical trial, 85 parturients scheduled for elective CD under standard spinal anesthesia were randomized to Group P (continuous phenylephrine infusion 0.1 mcg/kg/min) or Group N (continuous norepinephrine infusion 0.05 mcg/kg/min) to maintain systolic blood pressure (SBP) within 100-120% of baseline. Measured variables included Blood Pressure (BP), number and type of provider interventions to control blood pressure, Heart Rate (HR), Cardiac Output (CO), Cardiac Index (CI), Stroke Volume (SV), Systemic Vascular Resistance (SVR) as measured by a continuous noninvasive hemodynamic monitor, newborn APGAR scores at 1 and 5 minutes, and intraoperative maternal nausea and emesis.

RESULTS: No differences were noted between groups in duration of continuous vasopressor infusion (69.24 ± 18.56 min Group P vs. 66.65 ± 21.57 min Group N; *P*=0.57), incidence of hypotension (63.2% Group P vs. 51.2% Group N, *P*=0.53), bolus interventions (24 Group P vs. 22 Group N, *P*=0.28), total bolus dose of phenylephrine (146.05 ± 200.47 µg Group P vs. 163.95 ± 207.69 µg, *P*=0.31), multivariate analysis of variance of measured hemodynamic parameters (SBP *P*=0.25, DBP *P*=0.15, HR *P*=0.17, CO *P*=0.5, CI *P*=0.84, SV *P*=0.5, and SVR *P*=0.54), incidence of maternal nausea episodes (63.2% Group P vs. 51.2% Group N, *P*=0.53), incidence of maternal emesis episodes (26.3% Group P vs. 16.3% Group N, *P*=0.53), incidence of bradycardia (13.2% Group P vs. 18.6% Group N, *P*=0.71), and 1 minute Apgar scores (*P*=0.20). More total bolus dose of ephedrine to treat maternal hypotension was required in Group P (5.39 ± 15.5 mg) compared to Group N (0.70 ± 4.57mg, *P*=0.01) and 5 minute Apgar scores were statistically better in Group P (*P*=0.05) but most likely not clinically significant.

CONCLUSIONS: Both medications are equally efficacious as prophylactic continuous infusions for the prevention of maternal hypotension under spinal anesthesia. If continuous phenylephrine is used, more intermittent ephedrine may be required as a bolus secondary to reflex bradycardia.

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Table1. Demographic, Maternal and Fetal Outcome Data

	Group P (n=38)	**Group N** (n=43)	*P* value
Age (years)	29.05 ± 5.59 (27.27-30.83)	30.16 ± 6.75 (28.14-32.18)	0.43
BMI (kg/m^2)	33.57 ± 6.63 (31.46-35.68)	35.04 ± 7.01 (32.94-37.14)	0.34
Gravidity	3 (1-5)	2 (1-8)	0.14
Parity	1 (0-4)	1 (0-2)	0.08
Gestation (weeks)	37.63 ± 1.95 (37.01-38.25)	38.07 ± 1.61 (37.59-38.55)	0.27
Infusion duration (minutes)	69.24 ± 18.56 (63.34-75.14)	66.65 ± 21.57 (60.20-73.10)	0.57
Incidence of hypotension (%)	63.2% (47.87%-78.53%)	51.2% (36.26%-66.14%)	0.53
Number of bolus Intervention (Yes/No)	24	22	0.28
Total phenylephrine bolus dose (µg)	146.05 ± 200.47 (82.31-209.79)	163.95 ± 207.69 (101.87-226.03)	0.31
Total ephedrine bolus dose (mg)	5.39 ± 15.53 (0.45-10.33)	0.70 ± 4.57 (-0.67-2.07)	**0.01**
Nausea (%)	63.2% (47.87%-78.53%)	51.2% (36.26%-66.14%)	0.53
Emesis (%)	26.3% (12.3%-40.3%)	16.3% (5.26%-27.34%)	0.53
Incidence of bradycardia (%)	13.2% (2.44%-23.96%)	18.6% (6.97%-30.23%)	0.71
APGAR score 1 min	8 (3-9)	8 (1-9)	0.20
APGAR score 5 min	9 (5-9)	9 (4-9)	**0.05**

Data is presented as mean ± SD with 95% CI, median with range in parenthesis, or percentage with 95% CI for proportions.

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Figure 1. Study CONSORT diagram showing patient recruitment and flow.

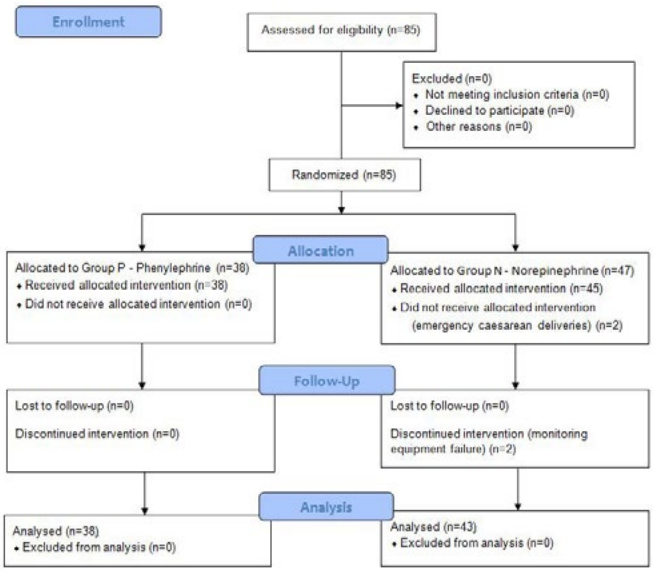
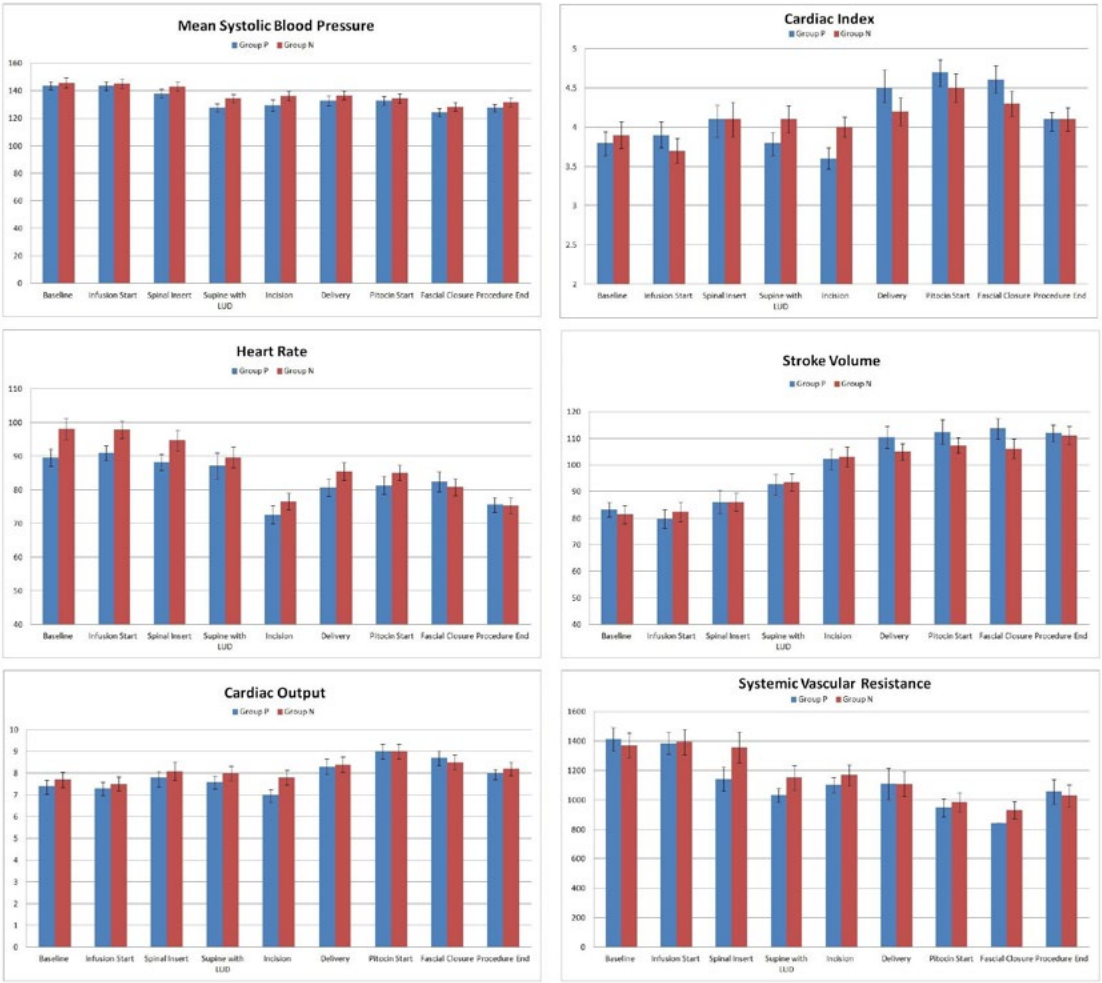


Figure 2. Haemodynamic parameters Multiple Analyses of Variance (MANOVA) at each of the recorded time intervals.



S-187.

KETOROLAC PREVENTS NAUSEA AND VOMITING RELATED TO UTERINE EXTERIORIZATION DURING CESAREAN SECTION: A RANDOMIZED, CONTROLLED DOUBLE-BLINDED STUDY

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INTRODUCTION: Exteriorization of the uterus to facilitate closure during cesarean section (CS) may result in increased nausea, vomiting and hypotension compared with in-situ repair[1]. These symptoms may impact patient satisfaction and smooth surgical closure. Returning the uterus to the abdominal cavity is a potent trigger of these symptoms which have been attributed to pain, vagal stimulus and vena caval compression[2]. Another possible mechanism is the release of prostacyclin from the mesentery which accompanies re-positioning the uterus[3]. Elevated levels of prostacyclin may cause vasodilatation and hypotension and result in nausea, vomiting, flushing and headache (HA). In the vascular literature this has been referred to as "mesenteric traction syndrome"[4].

Ketorolac is a non-steroidal agent routinely used for post operative pain relief. As a cyclooxygenase inhibitor, it may also aid in reducing prostacyclin-associated side effects. The purpose of this randomized, controlled, double blinded study was to determine if ketorolac reduces the symptoms associated with returning the uterus to the abdominal cavity if given immediately after delivery, prior to re-positioning the uterus.

METHODS: With IRB approval and informed consent, 168 patients undergoing elective CS with uterine exteriorization for repair, were randomized to a study (n=86) or control (n=82) group. Following prehydration, spinal anesthesia was administered using 12 mg hyperbaric bupivacaine, with fentanyl 10 mcg and morphine 0.15mg. Immediately after delivery, a one ml vial from our pharmacy (labeled "A") containing either ketorolac 30mg or saline was given IV. A second vial (labeled "B") containing the other solution was given at the conclusion of the procedure. Both groups received an oxytocin infusion and ondansetron 4 mg IV after delivery. Phenylephrine and/or ephedrine were used at the clinician's discretion to treat hypotension. Outcomes studied were the incidence of nausea, vomiting, headache, vasopressor use and 15% drops in systolic blood pressure during the ten minutes following the return of the uterus to the peritoneal cavity.

RESULTS: Age, height, weight, baseline BP and sensory levels were similar in both groups. The ketorolac group showed significant reductions in nausea (.05% vs. 32%, P<.0001), vomiting (.02% vs 23%, P<.0001), HA(0 vs. 10%, P=.0012), the number of patients with at least one 15% drop in systolic blood pressure (10% vs. 40%, P<.0001), and the number requiring rescue vasopressor use (38% vs. 81%, P<.0001). Estimated blood loss was similar in both groups (873.4 vs. 873.7 ml).

CONCLUSIONS: This study demonstrates that the use of ketorolac during CS reduces the incidence of nausea, vomiting, hypotension and headache after repositioning the exteriorized uterus, without increasing blood loss. These results seem to confirm the role played by prostacyclin in the development of these symptoms and the ability to reduce their occurrence using cyclooxygenase inhibitors.

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Subspecialty Abstracts

Pain Mechanisms

S-188.

EFFECTS OF PREGABALIN ON THE HYPERPOLARIZATION-ACTIVATED MIXED CATION CURRENT, I(H), IN HCN2-EXPRESSING CHO CELLS AND RAT THALAMOCORTICAL NEURONS

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BACKGROUND: Pregabalin is FDA-approved and widely used for the treatment of fibromyalgia, a potentially incapacitating chronic condition characterized by body-wide musculoskeletal pain, allodynia, fatigue, and sleep disturbances.[1] The pathophysiology of fibromyalgia involves abnormalities within the thalamus, the brain's major somatosensory relay station, which plays a significant role in nociceptive signal transmission.[2,3] A critical component of thalamic signalling is the hyperpolarization-activated mixed Na^+/K^+ current, I_h, which serves as a "cerebral pacemaker current" in the generation of the different physiologic states of consciousness and sleep,[4] which are abnormal in fibromyalgia patients. However, the actions of pregabalin on I_h specifically and on thalamic neurons in general are unknown. We conduced an *in vitro* electrophysiological study to test the hypothesis that pregabalin's actions involve I_h in thalamocortical (TC) neurons.

METHODS: The approach to research included (1) direct study in a mammalian expression system (transfected Chinese hamster ovarian [CHO] cells) of pregabalin's actions on the HCN2 channel isoform that is dominant in TC neurons and underlies I_h in the thalamus, and (2) study in a higher complexity, physiologically relevant system of pregabalin's effects on TC neurons in rat brain slices.[5] We performed whole-cell patch-clamp recordings in both current- and voltage-clamp modes; all of the animal experiments were approved by the institutional animal care committee.

RESULTS: In CHO cells, pregabalin at a supratherapeutic concentration (200 μM) did not alter the magnitude of HCN2-mediated I_h. Pregabalin delayed activation of the conductance underlying I_h, G_h, by shifting its half-activation voltage from −97.2 ± 3.6 mV to −108.3 ± 2.4 mV (n = 7; P = 0.02). Further pregabalin concentration increases (up to 1000 μM) did not produce I_h activation property changes. Pregabalin (200 μM) produced no significant effects on I_h activation or deactivation. In TC neurons, pregabalin did not alter membrane electrical properties of neurons (resting membrane potential, input resistance, or capacitance), firing properties, or current-voltage relationships. In the neurons, pregabalin did not affect I_h conductance, activation, or deactivation.

CONCLUSIONS: The only identified significant effect of pregabalin in these studies was a concentration-dependent shift to more hyperpolarized potentials of the half-activation voltage of the conductance underlying I_h, G_h, in CHO cells expressing HCN2 channels. Otherwise, we found no effects on I_h magnitude, activation, or deactivation. Hence, the present studies provide little evidence that the mechanisms of pregabalin in fibromyalgia and chronic pain significantly involve HCN2 channels or I_h in the thalamus.

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S-189.

AMITRIPTYLINE REVERSES THE ATTENUATION OF NOXIOUS STIMULUS-INDUCED ANALGESIA AFTER NERVE INJURY IN RATS

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INTRODUCTION: Noxious stimulus-induced analgesia (NSIA) is a type of conditioned pain modulation in rats that has been used to assess endogenous pain control systems. The descending noradrenergic system is involved in the NSIA, and nerve injury induces plastic changes of descending noradrenergic neurons. Thus, we hypothesized that nerve injury would affect NSIA strength, and that amitriptyline and pregabalin, frequently used for treatment of neuropathic pain, might further modulate the NSIA through effects on the descending noradrenergic system.

METHODS: We examined the change in NSIA over time after right L5 spinal nerve ligation (SNL) in rats by measuring the contralateral hind paw withdrawal threshold after left forepaw capsaicin injection. In addition, we examined NSIA after 5 daily intraperitoneal injection of amitriptyline or pregabalin. Microdialysis studies were performed to measure noradrenaline levels after left forepaw capsaicin injection in the left spinal dorsal horn in non-injured rats, SNL rats and rats after 5 daily intraperitoneal injection of amytriptyline or pegabalin.

RESULTS: NSIA was dramatically attenuated 5 and 6 w after SNL ($P < 0.001$). The noradrenaline level in the lumbar spinal cord was significantly increased in non-injured rats receiving forepaw injection of capsaicin compared to vehicle injection ($P < 0.001$), but not in rats 6 w after SNL surgery. Five daily intraperitoneal injections of amitriptyline (10 mg/kg) or pregabalin (10 mg/kg) at 5 w after SNL gradually increased the ipsilateral hindpaw withdrawal threshold ($P < 0.001$). At 6 w after SNL, amitriptyline, but not pregabalin, reversed the attenuation of NSIA by SNL ($P < 0.001$), and increased the spinal noradrenaline level after forepaw injection of capsaicin ($P < 0.01$).

CONCLUSIONS: These data suggest that endogenous analgesia in neuropathic pain state is strongly decreased from a certain time after nerve injury, and amitriptyline reverses the attenuation of endogenous analgesia through effects on the descending noradrenergic system.

S-190.

THE MECHANISM OF NICOTINE ANALGESIA AND THE EFFECTS OF NICOTINE-INDUCED HYPERALGESIA IN RATS AFTER PERIPHERAL NERVE INJURY

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INTRODUCTION: Studies have demonstrated that opioid requirements of postoperative patients are greater in smokers than non-smokers[1-2]. Our previous research has demonstrated that discontinuation of nicotine causes hyperalgesia in animals (Figure 1).[3] We now use peripheral nerve injury to explore the mechanisms of smoking-induced hyperalgesia and to compare the pain sensitivities of smokers and non-smokers.

METHODS: IACUC approval was obtained. 4-week male Sprague-Dawley rats were divided into 4 groups: Control (CTR, n=8),Nicotine treatment (NIC, n=8), CTR rats with chronic constriction injury (CCI) of sciatic nerve (CTR+CCI, n=8), and NIC rat with CCI (NIC+CCI, n=8). NIC rats had an oral sweetened nicotine solution as drinking water, 10 mg/kg/day for 4 weeks. Nicotine levels were monitored by urine cotinine. Urine cotinine conc. >1000 ng/ml were considered similar to smokers4. Cotinine levels in all NIC rats reached 1000 ng/ml. The CTR rats were provided sweetened drinking water. Mechanical sensitivity was measured using von Frey filaments, and thermal sensitivity was measured using a Plantar Test Apparatus. Temperature was set at 52°C, cut-off time was 20 sec. CCI of the sciatic nerve was performed in CTR and NIC rats after 4 weeks of treatment. Spinal cord samples were taken at the end of the behavior tests (12 days post-CCI). Levels of proinflammatory factors (IL-1β, IL-6 and CCL2) and β-endorphin were measured. Data are presented as means±SEMs. T-test of $p<0.05$ was considered significant.

RESULTS:

1. Nicotine increased mechanical thresholds and thermal latencies in normal conditions (Figure 2, * $p<0.05$ in mechanical test, ** $p<0.01$ in thermal test, CTR vs. NIC)
2. Nicotine decreased mechanical thresholds, but not thermal latencies after CCI (days 3 to 9 post-CCI) (Figure 2, **P<0.01, ***P<0.001, CTR vs. NIC)
3. The expression levels of IL-1β, IL-6 and CCL2 were increased after CCI in both the nicotine treated and control rats. IL-1β and CCL2 increases were greater in the nicotine treated rats (Figure 3A, B, C, * $p<0.05$, ** $p<0.01$, and *** $p<0.001$, compared to CTR; # $p<0.05$, CTR+CCI vs. NIC+CCI)
4. Both groups demonstrated a decrease in β-endorphin after CCI. The expression level of β-endorphin in nicotine treated rats was lower than in CTR before and after CCI (Figure 3D, * $p<0.05$ compared to CTR group; ## $p<0.01$, CTR+CCI vs. NIC+CCI).

CONCLUSION: Nicotine appears to decrease pain sensitivities at baseline as measured by mechanical and thermal stimuli. Sensitivity to mechanical and thermal stimuli was increased in both groups after CCI. An increase in sensitivity to mechanical stimuli was greater in the nicotine treated group. This correlated with altered levels of proinflammatory factors and β-endorphin in the nicotine group. It remains to be determined how nicotine induces hyposensitivity in a normal state, but produces hyperalgesia in the presence of injury.

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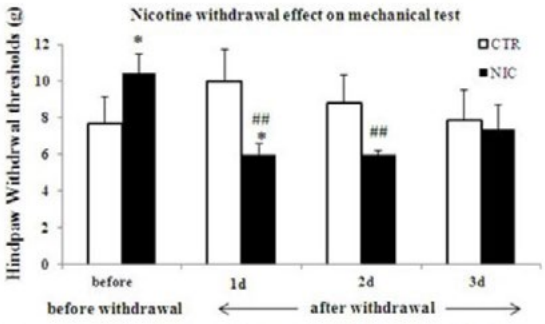

Figure 1. Nicotine and nicotine-withdrawal effects on mechanical test. *p<0.05, CTR vs. NIC in the same time point. ## p<0.01, compared to NIC before withdrawal point.

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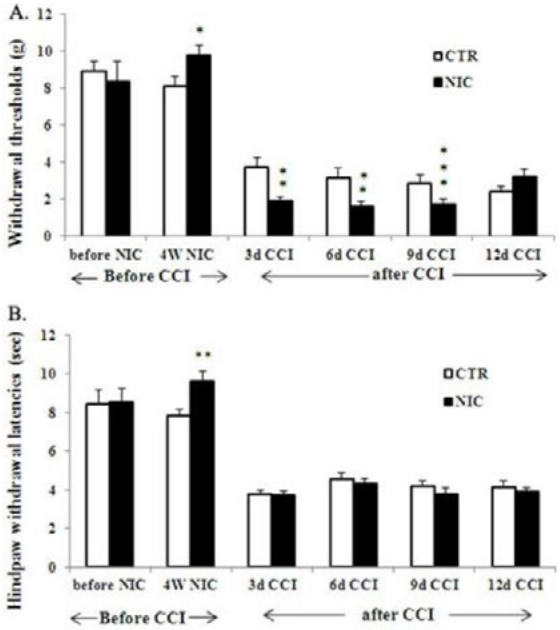

Figure 2. Mechanical (A) and thermal test (B). ** p<0.01, *** p<0.001, CTR vs. NIC in the same time point.

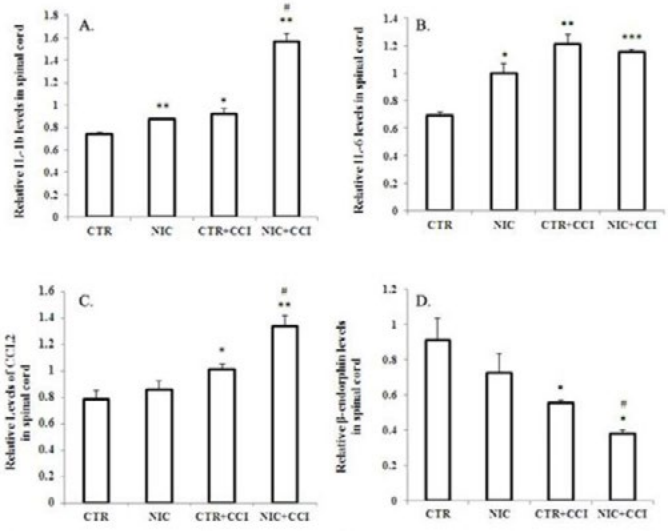

Figure 3. Western Blot analysis of the expression levels of IL-1β, IL-6, CCL2 and β-endorphine. * p<0.05, ** p<0.01, and *** p<0.001, compared to CTR group; # p<0.05, CTR+CCI vs. NIC+CCI.

S-191.

THE PHARMACOKINETICS AND ANTI-HYPERALGESIC EFFICACY OF THE ORALLY ADMINISTERED MGLU5 ANTAGONIST FENOBAM IN A HUMAN EXPERIMENTAL PAIN MODEL

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INTRODUCTION: Metabotropic glutamate receptor 5 (mGlu5) has been shown to modulate nociception in mice[1,2]. The investigational drug fenobam [N-(3-chlorophenyl)-N'-(4,5-dihydro-1-methyl-4-oxo-1H-imidazole- 2-yl)urea] is a selective mglu5 antagonist. Preclinical data suggest that fenobam is analgesic in rodent pain models[3], and that neither analgesic tolerance nor significant side effects develop with repeated dosing[4]. Following IRB approval and obtaining Investigational New Drug (IND) status with the FDA, we tested the hypothesis that fenobam (150 mg) reduces measures of hyperalgesia in the heat-capsaicin test, a human model of central sensitization[5].

METHODS: The effects of fenobam on hyperalgesia were evaluated in a randomized, double-blinded, placebo-controlled, balanced, two-way cross-over trial with 32 healthy volunteers who received either 150 mg fenobam or placebo and were then exposed to the heat/capsaicin model of cutaneous sensitization (Fig. 1). Two sessions were conducted (placebo or fenobam, balanced order) one week apart. Blood samples were collected hourly for 7 hours after administration of fenobam and fenobam plasma concentrations were determined by mass spectrometry. Measures of hyperalgesia and hypersensitivity were taken at regular time points during each study session, and included the area of cutaneous sensitivity to Von Frey filament (VF) stimulation and Heat Pain Detection Thresholds (HPDTs). A mixed within-between subject linear model approach using SAS Proc Mixed procedure was used to analyze the data. Type III tests of fixed effects were used to evaluate the main effects of treatment group, time and interaction of treatment group with time.

RESULTS: *Fenobam disposition:* Plasma concentrations of fenobam peak 2-4 hours following oral administration and demonstrate large inter-individual variability (Fig. 2). Peak concentrations ranged from 1.8 to 187 ng/ml.

Antihyperalgesic data: A carry-over effect of the drug and sensitization procedure from session 1 could not be excluded in a post-hoc analysis. Therefore, data from sessions 1 and 2 were examined separately. In the first session, after controlling for age, alcohol use, and wrist circumference, mean VF area in the fenobam group was 22.8 cm^2 smaller (CI: 4.3 to 41.3) than the placebo group. Main effect of treatment on VF area was significant $F(1,111) = 594$; $p=0.016$ (Fig. 3). Mean HPDT in the fenobam group was 1.17 degrees C higher (95% CI: -0.15 to 2.48) than the placebo group, however main effect of treatment was not significant $F(1,140)=3.05$; $p=0.0828$ (Fig 4.).

CONCLUSIONS: Fenobam reaches peak plasma concentration 2 to 4 hours after oral administration with marked inter-individual differences. Initial antihyperalgesic data obtained in human subjects showed a reduction in the size of VF areas in patients who received oral fenobam compared to placebo, but no differences in HPDT.

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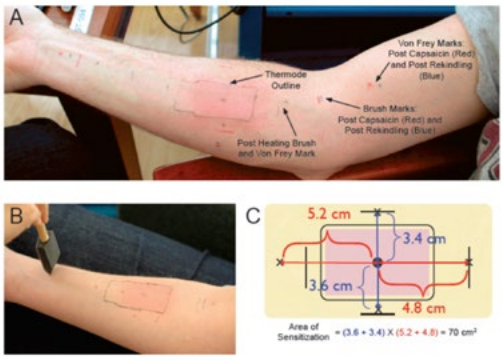

Figure 1. The Heat/Capsaicin sensitization model

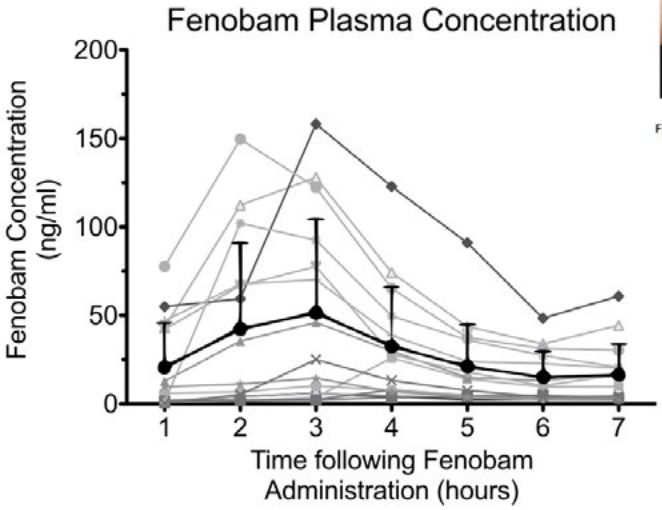

Figure 2: Plasma fenobam concentration following oral dosing. Individual subjects are plotted in gray. Mean and standard deviation for all subjects are plotted in black. Peak concentrations for each subject ranged from 1.8 to 187 ng/ml.

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S-191 • continued

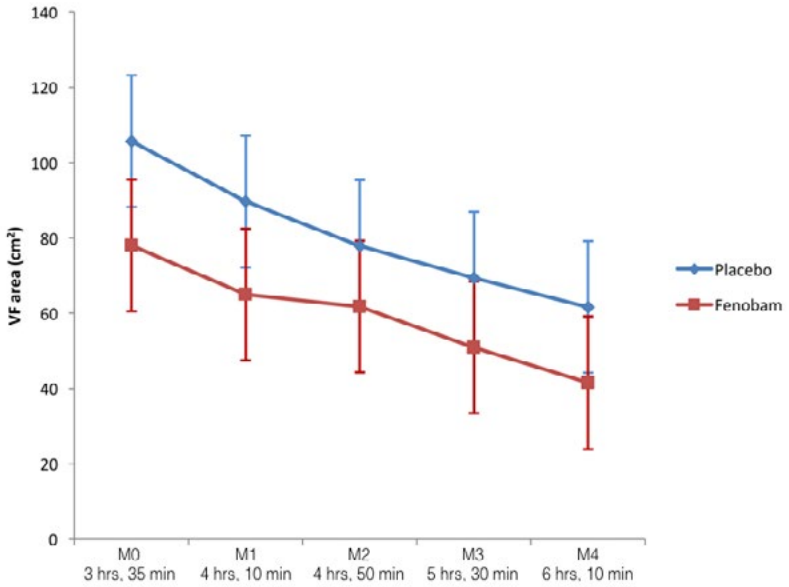

Figure 3: Von Frey measurements were taken immediately following heat capsaicin induced central sensitization (M0) and at 4 subsequent time points (M0 to M4) that correlated with 4 separate applications of heat rekindling to the initial site of central sensitization. The time following fenobam administration is listed under each time point. The lines graphs presented are mean with SD error bars at each time point. After controlling for age, alcohol use in the last 6 months, and wrist circumference, VF area in the fenobam group was 22.8 cm^2 smaller (95% CI: 4.3-41.3) than the placebo group by main effects analysis F(1,111)=594; p=0.016.

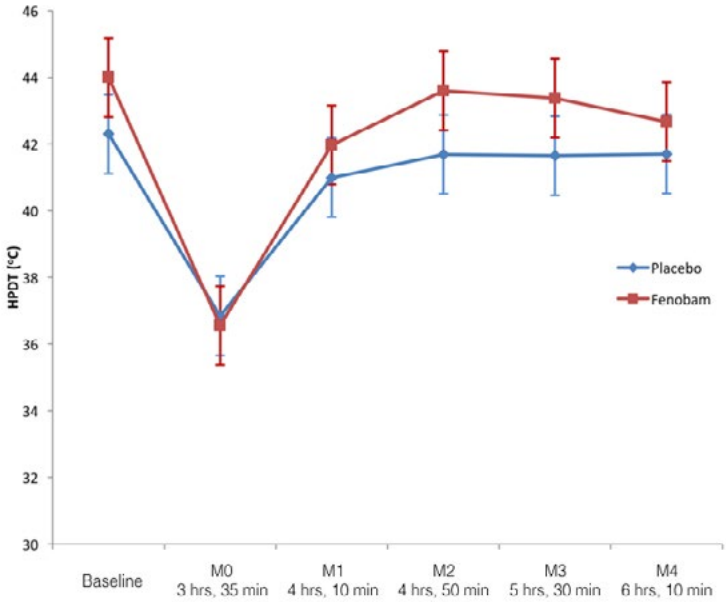

Figure 4: Heat Pain Detection Thresholds were taken at baseline (15 minutes prior to fenobam administration), immediately following heat capsaicin induced central sensitization (M0), and at 4 subsequent time points (M0 to M4) that correlated with 4 separate applications of heat rekindling to the initial site of central sensitization. The time following fenobam administration is listed under each time point. The lines graphs presented are mean with SD error bars at each time point. Mean HPDT in the fenobam group was 1.17 degrees C higher (95% CI: -0.15 to 2.48) than the placebo group, however main effect of treatment was not significant F(1,140)=3.05; p=0.0828.

Subspecialty Abstracts

Pain Medicine

S-192.

THE EFFECT OF CURRENT LOW BACK PAIN ON VOLITIONAL PREEMPTIVE ABDOMINAL ACTIVATION DURING A LOADED FUNCTIONAL REACH ACTIVITY

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INTRODUCTION: A volitional preemptive abdominal contraction (VPAC) supports trunk stability during functional activity. Pain-free individuals can sustain VPAC during function, but such has not been reported for individuals with current low back pain (cLBP). The purposes of this study were to examine whether cLBP affects VPAC performance during a loaded functional-reach (LFR) activity.

METHODS: A crossover mixed design examined the effects of the LFR activity (with 4.6kg load) and VPAC using the abdominal drawing-in maneuver (ADIM) on TrA activation. Setting was in a laboratory. Participants were 18 Controls and 17 cLBP subjects with pain ratings of 1-7/10. Interventions were blinded TrA thickness measurements were recorded from M-mode ultrasound imaging during 4 conditions (Figure 1-A&B): (1) Quiet standing (QS) without ADIM; (2) QS with ADIM; (3) LFR without ADIM; and (4) LFR with ADIM. A physical therapist with 29 years of experience collected historical and examination data. Main Outcome Measures were TrA muscle thickness (mm) representing muscle activation and selected examination data.

RESULTS: A 2(Group) x 2(Contraction) x 2(Reach) Analysis of Variance (ANOVA) demonstrated a significant Group x Contraction interaction [F (1, 31) = 4.499, p = 0.042]; ADIM produced greater TrA thickness increases in PLBP subjects (2.18mm) versus Controls (1.36mm). We observed a significant main effect for Reach [F (1, 31) = 14.989, p = 0.001] (Figure 2-Activity mean-mm). Post-hoc comparisons demonstrated that LFR activity produced a greater TrA thickness (6.15 ± 2.48mm) versus quiet standing (5.30 ± 2.12mm).

CONCLUSIONS: While subjects with cLBP demonstrated slightly less abdominal activation during every condition, they exhibit a greater increase in TrA activation during ADIM versus controls. Individuals can utilize the ADIM strategy as a protective VPAC response during a LFR.

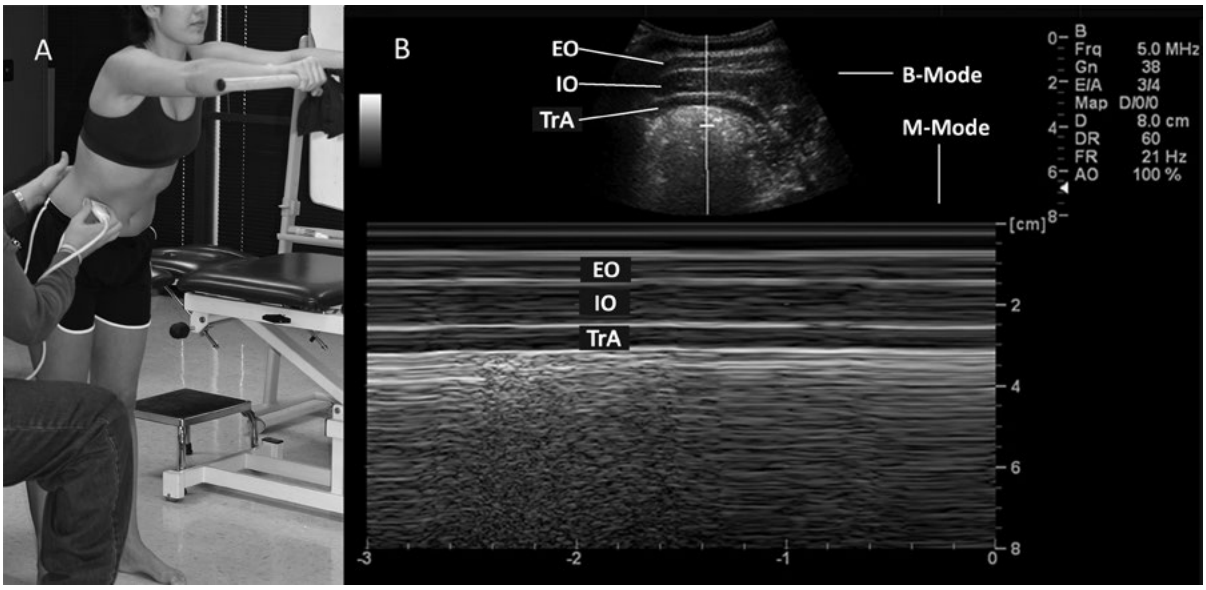

Figure 1.

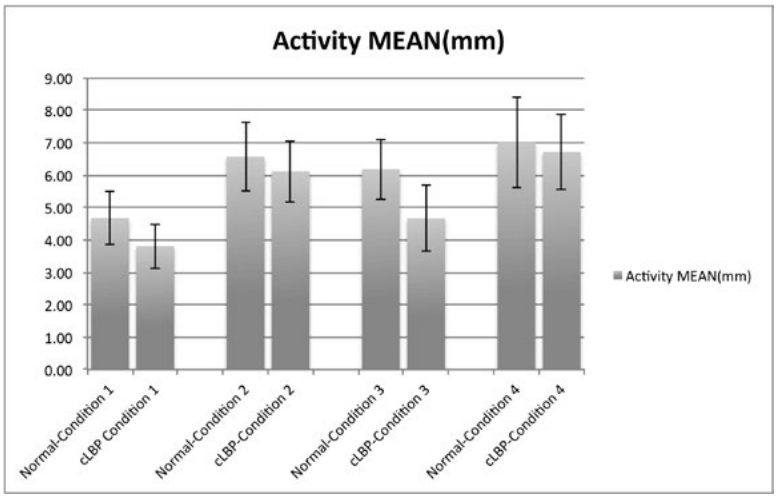

Figure 2.

S-193.

REMIFENTANIL INDUCED HYPERALGESIA ON POSTOPERATIVE DAY ONE - A PROPENSITY SCORE MATCHED ANALYSIS FROM THE PAIN OUT REGISTRY

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INTRODUCTION: Remifentanil is suspected to cause opioid induced hyperalgesia (OIH). Clinical trials studying OIH mostly have small sample sizes with contradictory results. A meta-analysis[1] found small but significantly elevated pain for remifentanil. To investigate the clinical impact of remifentanil associated increase in postoperative pain levels the PAIN OUT registry[2] was analyzed for different qualities of pain on the 1st postoperative day.

METHODS: The study protocol was approved by the responsible ethics committee of the coordinating center (University of Jena; Germany) and registered (NCT02083835). The 21 most performed surgeries were identified and grouped by means of anatomical and surgical issues. The individual groups were divided into intraoperative remifentanil or other opiods and propensity score matched regarding relevant comorbidities. Mean values and standard deviations of pain perceptions, satisfaction of pain treatment (numeric rating scale 1-10) and opioid consumption were calculated. Mann-Whitney-U-test was performed to detect differences between the groups. A p-value < 0.05 was considered significant.

RESULTS: The registry included 42,815 cases. Six groups were built: thyroid (n=317 cases after matching), laparoscopic (n=499), laparotomy (n=148), hysterectomy (n=189), mastectomy (n=208) and spine surgery (n=201). The overall opioid consumption in all surgical groups except thyroid surgery was significantly increased in patients receiving remifentanil. Worst pain was significantly elevated in remifentanil treated patients for laparoscopy, and significantly reduced for hysterectomy, and mastectomy (figure 1). Satisfaction was only significantly different for the spine surgery and laparotomy with higher scores in patients receiving remifentanil (figure 2).

CONCLUSIONS: There is a difference in worst pain perception on the first postoperative day for some surgical procedures. These results are heterogeneous. The use of remifentanil seems to have no influence on patients' satisfaction with pain treatment.

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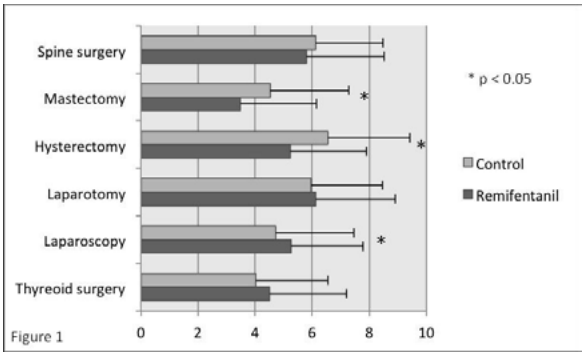

Figure 1

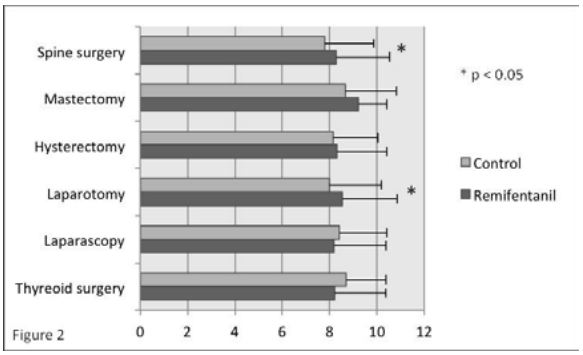

Figure 2

S-194.

SYSTEMATIC REVIEW OF YOGA FOR LOW BACK PAIN

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INTRODUCTION: With increasing trends to decrease overall opiate use for analgesia[1], recent contamination issues in steroid manufacturing for spinal injections and subsequent outbreaks of fungal meningitis[2], and more recent emphasis on cost-effective therapie[s3,4], yoga has become an attractive therapeutic option for CLBP. The goal of this study was to provide an updated systematic review examining the therapeutic effect of yoga on CLBP.

METHOD: Literature was sought from a query of 4 major databases (Medline, Embase, Cochrane Library, PsycINFO) from their inception to June 2015 (See Figure 1). Studies were deemed appropriate for inclusion if the following criteria were met: (1) a randomized control trial design, (2) focused on patients with low back pain, (3) sought to study any physically active form of Yoga, and (4) reported the measurement of patient specific outcome measures (i.e. pain, functional status, disability score, quality of life measure). RCTs that met criteria were analyzed for methodological quality using the JADAD scoring scale. RCTs that met a score of 3 or more were included for quantitative analysis.

RESULTS: Seventeen full text articles (15 study cohorts) were included in the systematic review. The methodological strength of these studies ranged between a 1 and 4 on the Jadad scoring scale. Of the 17 grouped trials, 15 individually reported author's conclusions supporting improvement in patient reported outcome measures in patients receiving Yoga therapy as compared with other usual treatments, education, and other non-invasive comparators. 8 studies with a JADAD score > 3 of which 7 were utilized for group analysis. An analysis of grouped VAS scores yielded a finding consistent with the majority of the studies included in the review. Mean baseline VAS score before yoga therapy is 5.45 with range between 4.06 and 6.73 (n>30 across the 7 RCTs). Mean pain score improvements compared to baseline following yoga-therapy showed 38.3% reduction at 1-2 weeks; a 35.1% reduction at 4-6 weeks; 52.8% reduction at 10-12 weeks; a 56.2% reduction at 24 to 26 weeks; and a 49.2% reduction at 48 weeks. Plot of yoga's effect on VAS scores over timeshows the best fit line follows an exponential decay model with the parameter of 0.396 (the inverse rate constant of 2.5 weeks) with a 95% confidence interval of [-0.75, 0.867] and a p-value close to significance ($p<0.1$).

CONCLUSION: Current body of evidence is of mixed quality and requires filtering for high quality RCTs. Despite adequate numbers of high quality RCTs and the heterogeneity in yoga forms across different populations, the effect of yoga seems consistent in reducing VAS scores according to an exponential decay model. Due to lack of adequate studies examining the immediate and long term effects of yoga on CLBP, future RCTs examining VAS scores to fill in existing data gaps are needed to provide a clearer picture of the time-dependence of yoga's effect. Functional aspect of pain was not assessed in this review.

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S-195.

COMPARISON OF MINUTE VENTILATION TO RESPIRATORY RATE MEASUREMENTS IN THE POST-OPERATIVE PERIOD

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AFFILIATION: [1]Outcomes Research, Anesthesiology Institute, Cleveland Clinic Foundation, Cleveland, OH, [2]Research, Respiratory Motion, Inc., Waltham, MA

INTRODUCTION: Opioids are commonly used for postoperative pain management but decrease respiratory drive and can cause opioid-induced respiratory depression. Current respiratory monitoring in non-intubated patients relies on late indicators of respiratory depression, such as pulse oximetry or capnography, or on measurements of respiratory rate (RR)[1,2]. However, ventilation is dependent on both tidal volume (TV) and RR. Thus, RR is not a complete or adequate solution. Here, we assess the effectiveness of RR alone to detect respiratory depression by using a non-invasive respiratory volume monitor (RVM) which accurately measures minute ventilation (MV), TV, and RR[3].

METHODS: Impedance-based RVM (ExSpiron, Respiratory Motion, Waltham MA) was used to non-invasively collect MV, TV and RR measurements from 104 patients (55 males, BMI: 27.2 ± 5.0 kg/m2) recovering from elective major abdominal surgery. MV, TV and RR were calculated from 30-second respiratory segments for up to 48 hours following surgery. Post-operative pain was managed initially with boluses of hydromorphone or fentanyl followed by PCA hydromorphone with and without IV acetaminophen. Predicted MV (MVPRED) was calculated for each patient based on body surface area. LowMV was defined as MV < 40% MVPRED and LowRR was defined as RR < 6 breaths/min (bpm). RR values were compared to MV measurements, and the sensitivity and specificity of LowRR as a predictor of LowMV were calculated.

RESULTS: Patients were monitored for an average of 34.5 ± 14.7 (mean ± SD) hours in the PACU and general hospital floor. Analysis of all 417,850 paired MV and RR measurements revealed that although MV is a function of RR (MV=TV*RR), there was poor correlation between a given MV measurement and its corresponding RR measurement (r=0.35, fig 1). A variety of RR alarm conditions (4-8 bpm) were explored which showed that the majority of LowMV measurements remain undetected. Specifically, with a RR cutoff of 6 bpm, 85% of LowMV measurements would be missed. With a RR cutoff of 8 bpm, 74% of LowMV would be missed and decreasing the RR cutoff to 4 bpm would result in 93% of LowMV being missed (fig 2). Overall, LowRR was a poor predictor of LowMV with a sensitivity of 15.0% and specificity of 98.6% (fig 3). Furthermore, 29% of all LowRR measurements were associated with adequate MV, indicating that patients were often adequately ventilated even in the presence of LowRR.

DISCUSSION: Our data suggest that LowRR alone does not accurately reflect episodes of LowMV for postoperative patients in the PACU and on the general hospital floor. Measurement of TV is also required for accurate assessment of ventilation. Continuous MV measurement provides a more complete reflection of respiratory status, which is critical to avoid respiratory depression.

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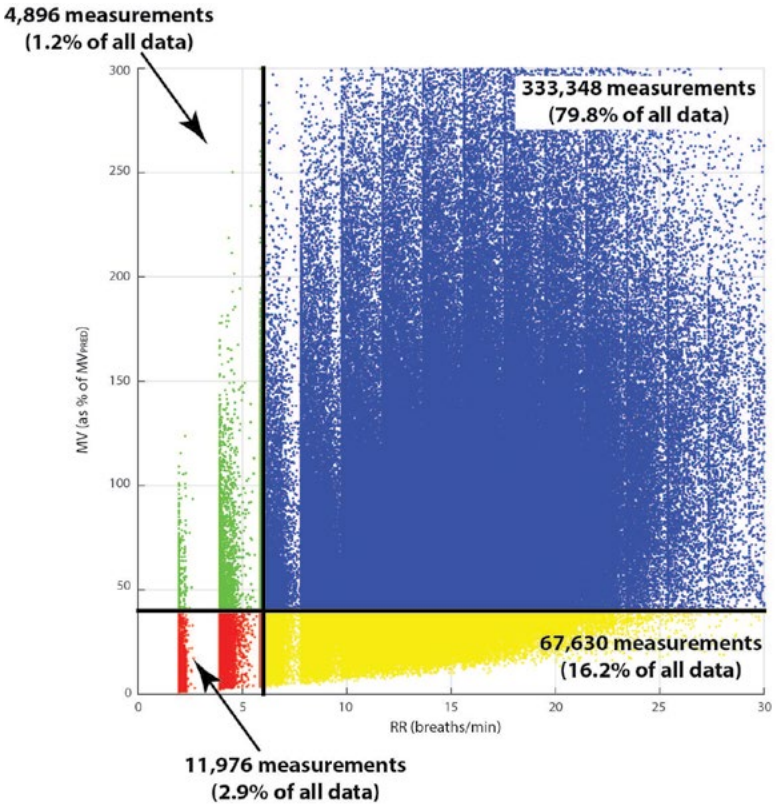

Figure 1: Analysis on all measurements collected (417,850) reveals a weak correlation between any particular MV measurement and its corresponding RR measurement (r = 0.35). Specifically, with a RR cutoff of 6 breaths/min, 85% of all MV measurements below 40% MVPRED would be missed. This suggests that RR is not an adequate proxy for respiratory performance.

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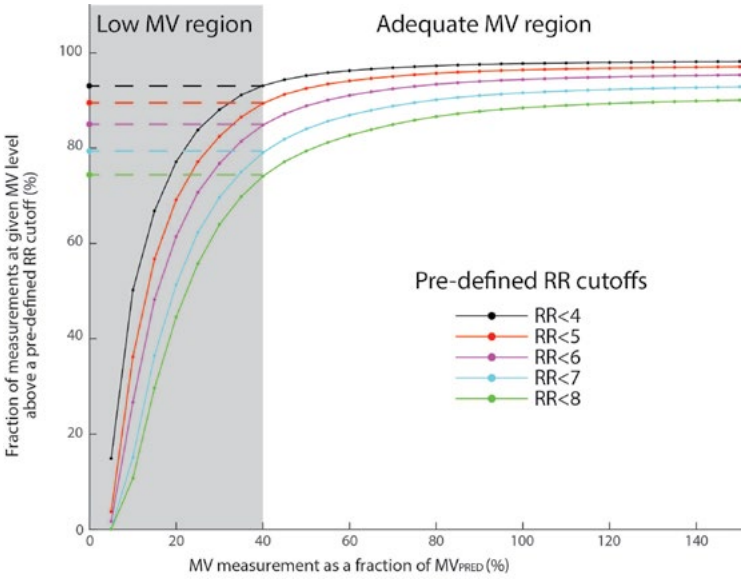

Figure 2: A simulation of a variety of potential RR alarm conditions and the probability they correspond to MV measurements below 40% MV_{PRED}. Varying RR cutoff from 4 breaths/min (black line) to 8 breaths/min (green line) increases the fraction of MV measurements below 40% MV_{PRED} captured by the RR alarm. However, a substantial fraction remains undetected in all conditions. Specifically, with a RR cutoff of 8 breaths/min (green line), 74.1% of all MV measurements below 40% MV_{PRED} level would be missed. Decreasing the RR cutoff to 4 breaths/min misses 93.1% of MV measurements below 40% MV_{PRED} (black line).

417,850 measurements in 104 patients

		Low MV (MV < 40% $MV_{BASELINE}$) positive	Low MV (MV < 40% $MV_{BASELINE}$) negative	
Low RR (RR < 6 b/min)	positive	True Positive TP = 11,976	False Positive FP = 4,896	PPV 71.0%
	negative	False Negative FN = 67,630	True Negative TN = 333,348	NPV 83.1%
		Sensitivity 15.0%	Specificity 98.6%	

Figure 3: LowRR (RR < 6 b/min) as a predictor of LowMV (MV < 40% MVPRED). Analysis of 417,850 RR measurements from 104 patients showed that RR was a poor predictor MV < 40% of MVPRED with a sensitivity of 15.0%, specificity of 98.6%, positive predictive value (PPV) of 71.0% and negative predictive value (NPV) of 83.1%.

S-196.

EFFECT OF CHRONIC PAIN AND NSAIDS ON COGNITIVE PERFORMANCE IN THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE DATABASE

AUTHORS: R. P. Kline[1], D. Choi[1], L. Doan[2]

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INTRODUCTION: Chronic pain may have far-reaching effects on cognition. Several studies have used neuropsychological testing to assess cognition in subjects with chronic pain. These studies found impairments in memory, executive function, and psychomotor performance in subjects with pain compared to those without[1,2]. Patients with chronic pain often take analgesic medications which may also affect cognitive function. Most studies on the impact of chronic pain on cognitive function have been cross-sectional in nature and have excluded patients with pre-existing cognitive impairment. We used the longitudinal Alzheimer's Disease Neuroimaging Initiative (ADNI) database to examine the interaction of chronic pain, baseline cognitive status, and medication use on cognitive function. We hypothesized chronic pain would be associated with a decline in cognitive function.

METHODS: Putative patients with chronic pain were selected by searching the "Concurrent Medications Log" for analgesic medications. Patients taking medications for a painful condition were considered to have chronic pain if the start date of medication use occurred prior to enrollment in ADNI and continued throughout the study. All subjects underwent neuropsychological assessment. Composite scores for executive function, (ADNI-EF), as well as memory, (ADNI-MEM), have been developed and validated in ADNI participants. Values were available for baseline, 6 month, 1 yr, and 2 yr time points.

RESULTS: Our first result showed a dependence of ADNI-EF on age ($p<0.001$), baseline cognitive status ($p<0.001$), and presence of chronic pain ($p=0.008$). However, the dependence was such that the presence of pain led to increased ADNI-EF performance. We hypothesized this effect was due to the NSAID use which often accompanied pain symptoms. Repeated measures ANOVA revealed that over 4 time points (factor; $p<0.001$) the group pain/NSAID use versus control (no pain/no NSAID) had a positive impact ($p= 0.027$), with performance showing significant dependence also on baseline cognitive status ($p<0.001$) and age ($p=0.019$). For cognitively normal (NL) subjects, there was a slight increase in performance over time consistent with rehearsal effects. For subjects with mild cognitive impairment (MCI) and AD, there was a drop in performance over time, with marked deterioration for AD. Repeating this analysis with ADNI-MEM, we found that an effect of pain/NSAID group was only apparent in NL subjects where pain/NSAID presence lead to increased ADNI-MEM at all 4 time points ($p = 0.025$). Examining pain in a repeated measures analysis for subjects without NSAIDs did not show a significant pain effect.

CONCLUSION: Whereas it has been shown that chronic pain can lead to changes in cognitive performance, we show here this effect is complicated by the impact of medication use. Since there are numerous medications used to treat pain which may have differing impacts on the brain, it may become increasingly important in the future to consider the secondary effects when choosing a regimen of pain treatment.

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S-197.

EFFECTS OF A LIDOCAINE-LOADED POLOXAMER/ ALGINATE/CACL2 MIXTURE ON POSTOPERATIVE PAIN AND ADHESION IN A RAT MODEL OF INCISIONAL PAIN

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INTRODUCTION: Pain and adhesion are problematic issues after surgery. A novel combination of lidocaine with analgesic and anti-inflammatory properties and poloxamer/alginate/$CaCl_2$ (PACM) as known anti-adhesive agent would be an effective strategy for reduction in postoperative pain and adhesion. We purposed to identify the effect of a lidocaine-loaded PACM in a rat model of incisional pain.

METHODS: Ninety male Sprague-Dawley rats were evenly allocated in six groups: sham group S; control group C; four groups applied PACM combined with lidocaine of different concentrations. After plantar incision and adhesion formation, PACM in group C and 0.5%, 1%, 2%, and 4% lidocaine-loaded PACMs in groups L0.5, L1, L2, and L4, respectively, were applied at the incision site. Mechanical withdrawal threshold (MWT) was measured using a von Frey filament. Serum levels of tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, and high-sensitivity C-reactive protein (hs-CRP) were measured. Rats were sacrificed two weeks after surgery, and inflammation and fibrosis were assessed using microscopy.

RESULTS: MWT was significantly increased in group L4 compared to: group S at 1, 2, 4, 6, and 8 hours after surgery; group C at 1, 2, 4, and 6 hours after surgery (Figure 1). Inflammation and fibrosis showed a significant reduction in groups L2 and L4 compared to group S (Figure 2). Serum levels of TNF-α, IL-1β, IL-6, and hs-CRP were decreased in lidocaine-loaded groups compared to group S or C at 1, 2, 48, and 2 hours after surgery, respectively.

CONCLUSIONS: Lidocaine-loaded PACM reduces postoperative pain, and lidocaine strengthens the anti-adhesive effect of PACM.

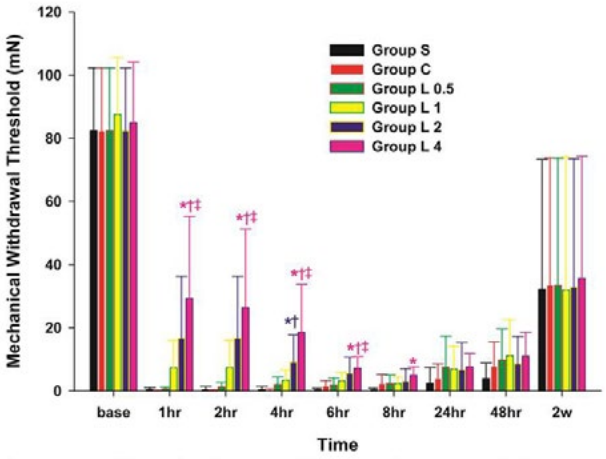

Figure 1. Effects of lidocaine-loaded poloxamer/alginate/CaCl2 mixtures on mechanical hyperalgesia

* P<0.05 compared to Group S, † P<0.05 compared to Group C, ‡P<0.05 compared to Group L0.5

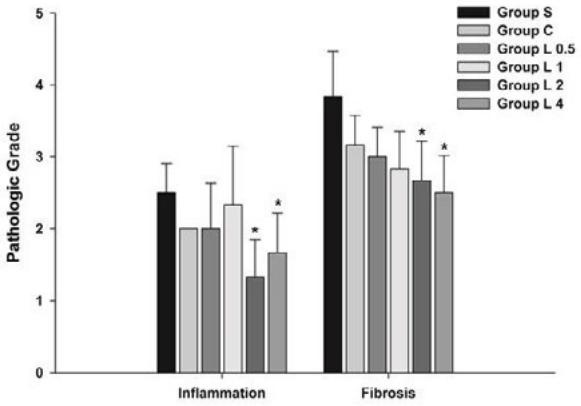

Figure 2. Microscopic assessments of inflammation and fibrosis.

*P<0.05 compared to Group S

S-198.

WITHDRAWN.

S-199.

KETAMINE INFUSION FOR POSTOPERATIVE PAIN CONTROL AFTER MAJOR OPEN ABDOMINAL SURGERY: A RETROSPECTIVE COHORT PILOT STUDY

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INTRODUCTION: Adequate pain control after major open abdominal surgery continues to be an area of acute post-surgical pain management that is inadequately treated. Epidural or paravertebral techniques are the best option for pain control. However, there are many instances when an epidural is not utilized due to contraindications prohibiting placement, or due to the surgeon's preference to not have it placed. The objective of this study was to compare patients who were not candidates for an epidural due to surgeon preference and were instead given ketamine intraoperatively along with opioids to patients who only received opioids preoperatively.

METHODS: Retrospective, case control analysis of hospital patients and pharmacy data. Patients over the age of 18 who underwent major open abdominal procedures with a laparotomy incision from 2008-2014 were reviewed. 25 patient charts were reviewed in each of the two groups. The Ketamine group (N=25) underwent an open laparotomy and was treated with an intravenous ketamine bolus during induction followed by a low dose ketamine infusion (0.05-0.2 mg/kg/hr) for multiple days (2-5) in the perioperative period. The Control group (N=25) consisted of patients that only received opioids in the preoperative period until hospital discharge.

RESULTS: The primary outcome of total opioids consumed, measured as IV Morphine equivalents, was not significantly different in Ketamine (K) vs. No Ketamine (No K) groups with a median of 212.3 and 173.5 and an interquartile (IQ) range Q1-Q3 of 82-584 and 116-341 respectively (p=0.91). VAS pain scores pre-operatively, in PACU, and on post-op days 1-3 were examined. Analysis of variance showed there was no significant interaction (p=0.23) and thus no significant effect on overall VAS scores. Days to ambulation were not significantly different for K vs. No K; median of 1 day for both groups (p=0.41).

CONCLUSION: Optimizing pain control after laparotomy procedures is vital to patient recovery and discharge. At times when a neuraxial or paravertebral technique is not offered to a patient due to surgeon preference or due to a contraindication, an alternative therapy is desired. In our study, we found that total opioid consumption, time to ambulation and pain scores were no different with exposure to ketamine in the perioperative period compared to patients who only received opioids. Despite its clinical advantage with previously demonstrated opioid sparing and analgesic effects, ketamine did not reveal such properties in our study for this particular patient population.

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S-200.

COMPARISIOIN OF PREGABALLIN AND TRAMADOL FOR PREMPTIVE ANALGESIA AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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INTRODUCTION: This study was undertaken to evaluate analgesic efficacy of oral pregabalin in comparison to tramadol for postoperative analgesia in elective surgical laparoscopic cholecystectomy patients.

METHODS: After taking informed consent ninety patients posted for elective laparoscopic cholecystectomy were randomly allocated to three groups of 30 patients each. Along with premedication of ranitidine and lorazepam they received pregabalin 150 mg, tramadol 100 mg or placebo orally.

A standardized anaesthesia of lignocaine, midazolam, fentanyl, propofol, vecuronium and sevoflurane was used in all patients. Residual muscle paralysis was reversed using neostigmine and atropine at termination of anaesthesia.

VAS scores were collected at 0, 6, 12 and 24 hr after surgery in postoperative ward. Rescue analgesia was provided by IM diclofenac sodium 25 mg at VAS score of 5 or higher.

RESULTS: Patients in pregabalin group had lower mean VAS scores at all time points compared to those of tramadol group as were their requirements of diclofenac. Patients of pregabalin group had higher incidence of side effects; they were more sedated though none developed respiratory depression.

CONCLUSIONS:

1. Patients in pregabalin group showed a reduced analgesic requirement in the first 24 hr after surgery compared to tramadol group
2. The VAS scores in pregabalin group were lower than those in tramadol group at 0, 6, 12 and 24 hr after surgery.
3. There was higher incidence of somnolence in patients of pregabalin group compared to tramadol group though none required any medical intervention.

S-201.

COLLABORATIVE HEALTH OUTCOMES INFORMATION REGISTRY (CHOIR): OPEN SOURCE PLATFORM FOR LEARNING HEALTH SYSTEMS

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INTRODUCTION: The Institute of Medicine (IOM) and the National Pain Strategy called for the development of national patient registries for patients with pain. Several efforts have answered this call and developed pain registries that further serve as platforms for Learning Healthcare Systems (LHS). As envisioned by the IOM, LHS leverages an integrated digital infrastructure to provide data-based and coordinated care that is available just-in-time to the clinician and that is centered on the patient.

METHODS: In answer to the call from the IOM, we developed the Collaborative Health Outcomes Information Registry (CHOIR), an open-source web application to assess patients and to support clinic staff with integrating the pain registry into the clinic workflow. On the back-end, patient assessment included integrated NIH PROMIS (Patient Reported Outcome Information Measurement Systems) item-response theory computer adaptive testing engine. On the front-end, assessments are designed for use on mobile devices with touch interfaces (smart phones and tablets), while also supporting desktop web browsers. Key technologies used include Java, Oracle database, Google Web Toolkit, jQuery Mobile, AngularJS, and Bootstrap.

RESULTS: Since roll-out in August 2012 and the subsequent slow ramp-up, over 7,500 unique patients have completed surveys, with over 210,000 NIH PROMIS assessments including Global Health (Physical and Mental), Mood (Depression, Anxiety, Anger), Function (Fatigue, Physical Function), Sleep (Sleep Disturbance, Sleep-Related Impairment), Social (Emotional Support, Instrumental Support, Satisfaction with Roles and Activities, Social Isolation, and Ability to Participate in Social Activities). Surveys were completed at home via email link, or at the Pain Clinic, using computers, iPads, Android tablets, and Chrome notebooks.

CONCLUSIONS: In conclusion, we have created an open source, extensible platform CHOIR (Collaborative Health Outcomes Information Registry) that enables rapid definition and deployment of data capture tools. This represents a successful partnership between the NIH and Stanford with funding from most of the NIH Institute Directors. Future works include the expansion of survey items, into additional disease areas, dissemination of code, as well as networked registry build-out.

S-203.

PREVALENCE AND CHARACTERISTIC OF OPIOID USE PRIOR TO ADMISSION BASED ON GENDER, AGE, AND ETHNICITY

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INTRODUCTION: The use of prescription opioids to treat pain has skyrocketed in the last 25 years[1]. This has led to an increasing proportion of our population that is 'opioid tolerant' (OT), per the FDA defined as taking 60mg oral morphine equivalence (OME) for 7 days. These patients have significantly longer LOS and greater all causes 30-day readmission rates[2]. In spite of this overall increase, gender disparities in pain care appear to be an ongoing issue. Pain in women is purportedly less aggressively managed compared to men despite increased incidence, and longer duration of pain[3]. Our study reviews the prevalence and characteristics of opioid use prior to admission based on the gender of the patient.

METHOD: A retrospective analysis of all patients admitted to University of California, Irvine (UCI) was conducted from 2011 to 2015. Pediatric and emergency room admissions were excluded. These admissions were then grouped by gender per admission year. The data was then analyzed to identify the OT patients in each group. Patients were further stratified as surgical or medical admissions based on the records and then grouped as Hispanic or Non-Hispanic. (Fig 1)

RESULTS: Of the 103,297 admissions during the 5-year study period, 52.8% were females and the rest were males and OT patients increased from 16.7% to 22%. Opioid tolerant females increased from 18% in 2011 to 22% in 2015 (p = 4.2E-13). Amongst males, 15% were OT in 2011 and 22% were OT in 2015 (p = 5.39E-27). About 30% of OT females were medical admissions compared to about 70% surgical admissions and 40% of males were medicine admissions compared to 60% surgical admissions. Non-Hispanic patients outnumbered Hispanic patients almost 2 times amongst the surgical and medical patients and amongst both OT males and females in each year (Table 1). The average age increased in each category every year. The average age amongst OT males was 46 in 2011 and 48 in 2015 (p = 1.5E-5) and amongst OT females was 44 in 2011 and 47 in 2015 (p = 1.6E-9) (Table 2).

CONCLUSION: In keeping with the exponential use of prescription opioids in the nation, the percentage of patients on significant opioids prior to admission increased steadily over the study period to 1 in 5 admissions in 2015. While there was a statistically significant increase in OT patients in the female group, the rate of increase in males over the study period was even higher. Limitations of this study include the single center nature of the analysis. In both male and female groups, non-Hispanic patients appear to be predominant. The average age of OT patients in both groups appears to be increasing over the study period. At this point, the prevalence of opioid use prior to admission appears to be similar in males and females while in the recent past a higher percentage of female patients were opioid tolerant.

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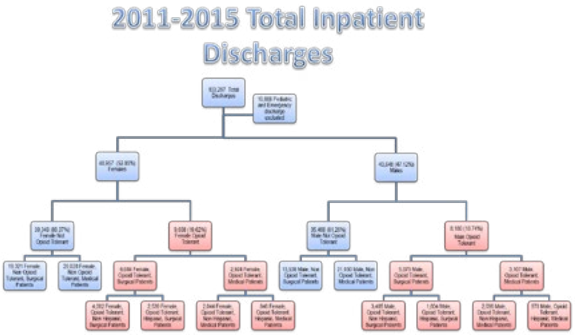

Figure 1.

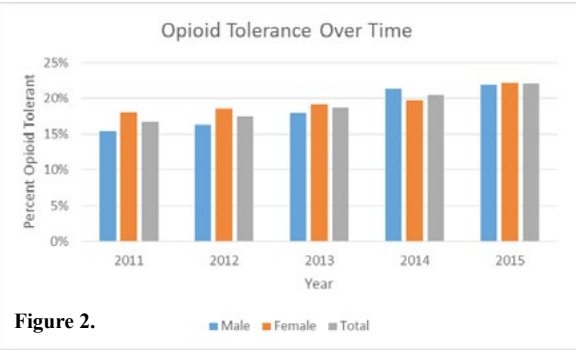

Figure 2.

TABLE 1	2011	2012	2013	2014	2015
Female	8669	9607	9842	10201	10638
Male	7835	8366	8986	9073	9388
Total	16504	17973	18828	19274	20026
Female OT	1560	1779	1896	2010	2363
% of OT female	18%	19%	19%	20%	22%
Male OT	1211	1362	1614	1937	2056
% of OT male	15%	16%	18%	21%	22%
Total OT	2771	3141	3510	3947	4419
% of OT Total	17%	17%	19%	20%	22%
Medicine female	465	513	557	652	737
% of female	30%	29%	29%	32%	31%
Surgical fem	1095	1266	1339	1358	1626
% of female	70%	71%	71%	68%	69%
Medical Male	465	542	658	684	758
% of male	38%	40%	41%	35%	37%
Surgical Male	746	820	956	1253	1298
% of male	62%	60%	59%	65%	63%

TABLE 2 AGE and 95% Confidence Interval					
Opioid Tolerant Male	2011	2012	2013	2014	2015
Total Male	46.7 (0.9)	46.0(0.9)	47.1 (0.8)	48.1 (0.8)	48.3 (0.7)
Medical Service	48.3 (1.3)	48.2 (1.2)	49.1 (1.1)	51.5 (1.1)	50.8 (1.1)
Hispanic	45.0 (2.5)	44.8 (1.9)	46.5 (1.9)	47.8 (1.9)	46.6 (1.7)
Non-Hispanic	49.4 (1.6)	49.9 (1.5)	50.2 (1.4)	53.2 (1.4)	52.9 (1.5)
Surgical Service	44.1 (1.2)	44.5 (1.2)	45.6 (1.1)	46.3 (1.0)	47.0 (1.0)
Hispanic	37.4 (2.0)	36.4 (1.9)	38.0 (1.9)	38.4 (1.6)	39.9 (1.5)
Non-Hispanic	47.4 (1.5)	48.4 (1.5)	48.9 (1.3)	50.1 (1.2)	50.3 (1.2)
Opioid Tolerant Female					
Total Female	43.8 (0.8)	42.5 (0.8)	45.0 (0.8)	46.6 (0.7)	47.1 (0.7)
Medical Service	47.9 (1.4)	47.6 (1.5)	49.7 (1.4)	48.8 (1.2)	52.9 (1.2)
Hispanic	42.8 (2.4)	41.5 (2.5)	44.5 (2.3)	43.8 (2.0)	48.4 (2.1)
Non-Hispanic	49.5 (1.7)	49.9 (1.8)	51.7 (1.8)	51.0 (1.5)	55.0 (1.4)
Surgical Service	42.0 (1.0)	40.4 (0.9)	43.0 (1.0)	45.5 (0.9)	44.5 (0.8)
Hispanic	35.0 (1.3)	33.1 (1.1)	35.3 (1.2)	37.3 (1.3)	37.7 (1.2)
Non-Hispanic	45.9 (1.3)	45.7 (1.3)	48.0 (1.2)	50.1 (1.1)	48.6 (1.1)

S-204.

PATIENTS RECEIVING PCA OPIOIDS WHO EXPERIENCE LOW MINUTE VENTILATION SPEND 70% LONGER IN THE PACU

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INTRODUCTION: Respiratory monitoring is vital for patient care. Unfortunately, respiratory monitoring in non-intubated patients often hinges on subjective assessments and secondary indicators. Clinicians struggle to identify patients at-risk for respiratory complications and tend to err on the side of caution by reducing opiates or extending the period of monitoring in a higher acuity setting. Such behavior may decrease patient satisfaction due to sub-optimal pain management and put strain on hospital staff and resources. A non-invasive real-time respiratory volume monitor (RVM) can identify at-risk patients. This could allow clinicians to alter therapy in time to prevent more serious complications, while increasing PACU throughput.

METHODS: 259 patients (140 females, mean age: 67 (range: 28-91) yrs; BMI 29.8 (19.0-49.1) kg/m^2) were enrolled and RVM data were collected in the pre-op area, during surgery and until PACU discharge. For each patient, predicted Minute Ventilation (MVPRED, expected MV during quiet respiration) was calculated based on body surface area & gender. MV measurements were expressed as %MVPRED (MVMEASURED/MVPRED x100%). Low MV (LMV) was defined as MV <40% MVPRED for ≥1-min. The criteria for Low MV <40% MVPRED was based on the ARDSnet protocol for successful extubation. Low MV <40% MVPRED was subsequently used to risk-stratify patients in the PACU.[1] LMVs within a 10-min period were considered part of the same event. Patients were stratified based on opioid use in the PACU. Unpaired two-sided t-tests compared length of stay (LOS) across groups (with and w/o opioids and with & w/o LMV).

RESULTS: Patients were monitored for 2.7 ± 0.1 hrs in the PACU. 198/259 patients (76%) experienced ≥1 LMV event (2.3 ± 0.1 Low MV events per hour) and the remaining 61 (24%) patients maintained adequate MV throughout their entire PACU stay. LOS in the PACU for patients experiencing LMV was significantly longer than those who maintained adequate MV (2.8 ± 0.1 hr vs 2.4 ± 0.1 hr respectively, $p < 0.001$). Patients were also stratified by opioid use in the PACU, with 166/259 (64%) receiving opioids. Patients receiving opioids had an increased likelihood of LMV (80% vs 69%, $p < 0.05$) and a significant increase in LOS (2.9 ± 0.1 hr vs 2.3 ± 0.1 hr, $p<0.001$) vs those without opioids. Among the patients receiving opioids, the presence of LMV was coupled with a significant increase in LOS. The 133 (80%) of 166 patients on opioids with LMV spent 75% longer in the PACU than the 33 (20%) patients on opioids without LMV (3.0 ± 0.1 hr vs 1.7 ± 0.2 hr, $p< 0.001$).

CONCLUSIONS: While generally undetected, intermittent respiratory depression is strongly correlated with increased PACU LOS, particularly for patients receiving opioids. Repeated Low MV events, while not directly quantified by clinical staff, are likely causing intermittent desaturations or a less specific clinical concern, leading to longer observation in the PACU. RVM can help clinicians individualize patient care, adjust opioid dosing and increase PACU throughput. Similar benefits may translate to the general care floor and pre- and post-hospital environments.

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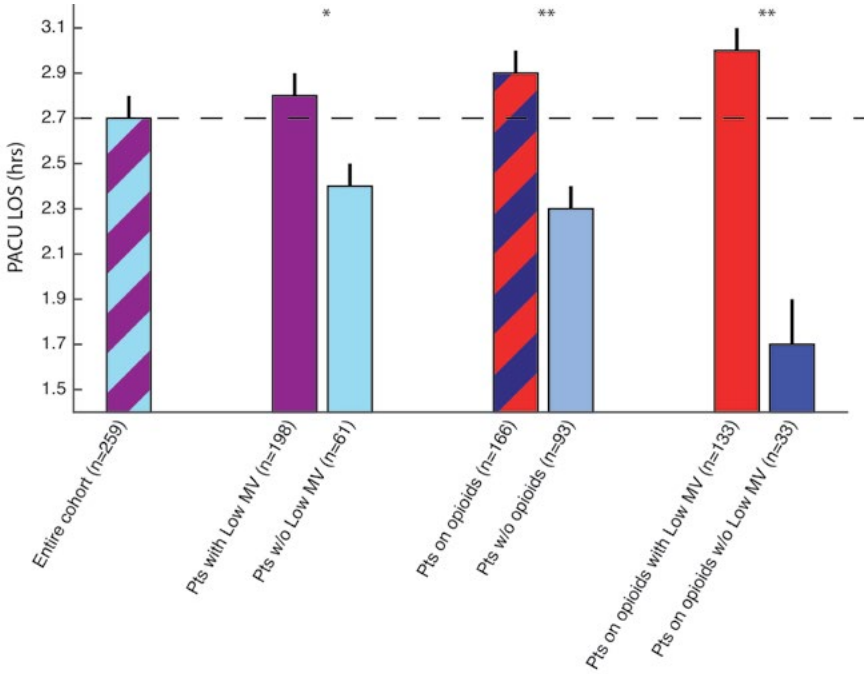

Figure 1: Length of stay in the PACU, stratified by the presence or absence of Low MV events and the use of PCA opioids in the PACU.

S-205.

INTRATHECAL MORPHINE REDUCES CIRCULATING ENDOCANNABINOID LEVELS IN COMPARISON TO PLACEBO IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY

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INTRODUCTION: The endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) serve as agonists at cannabinoid receptors and mitigate pain and inflammation. The structurally related lipids, palmitoylethanolamide (PEA) and oleoylethanolamide (OEA), are ligands at nuclear peroxisome proliferator-activated receptors and likewise exert anti-inflammatory and antinociceptive effects. Previous studies have demonstrated that the opioid and cannabinoid systems may work synergistically to regulate nociception; but it is currently unknown if opioid receptor agonists influence systemic levels of endogenous endocannabinoids. The goal of this study was to examine whether or not administration of intrathecal morphine influences the pre- and postoperative circulating levels of AEA, 2-AG, PEA, OEA, and cortisol. An additional goal was to determine to what extent intrathecal morphine reduces postoperative pain and opioid intake after total knee arthroplasty (TKA).

METHODS: The experiments were approved by the institutional review board and written consent was obtained from each patient. Intrathecal vehicle or morphine (200micrograms) was administered at the time of the spinal anesthesia with isobaric bupivacaine (12-15mg) and immediately prior to the preoperative blood draw. An additional blood draw occurred at 4 hrs after TKA. Postoperative pain was quantified using a verbal 0-10 numerical rating scale. Endocannabinoid quantification was performed as described[1].

RESULTS: Our results indicate that administration of intrathecal morphine significantly attenuated postoperative pain after TKA. At baseline, morphine administration led to a significant reduction in circulating levels of OEA, AEA, and 2-AG. In patients administered intrathecal placebo, 2-AG levels were elevated 4 hrs after surgery. In contrast, patients administered intrathecal morphine exhibited highly significant reductions in PEA, OEA, and 2-AG when compared to placebo. At baseline, cortisol levels were similar between the groups but at 4 hrs were significantly elevated and reduced in the placebo and morphine groups, respectively.

CONCLUSIONS: These results indicate that therapeutically effective levels of intrathecal morphine reduce pain and concomitantly lower circulating levels of endocannabinoids and related lipids. This may suggest that the strong analgesic effects of morphine may supplant the necessity for and consequently attenuate the recruitment of analgesic endocannabinoids. This study is the first to document the existence of rapid communication between the endogenous cannabinoid and opioid systems in humans.

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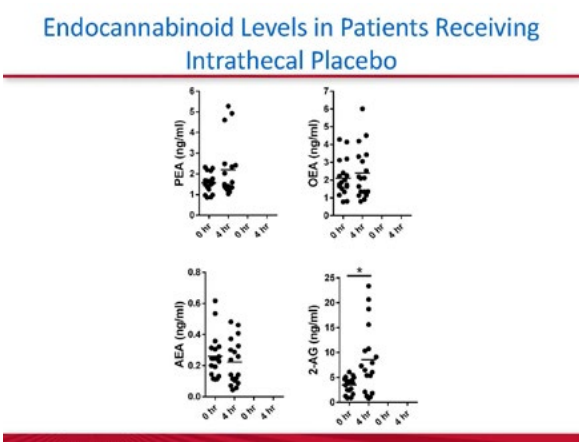

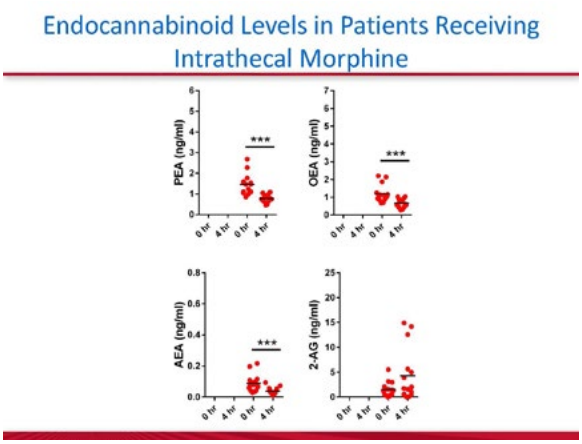

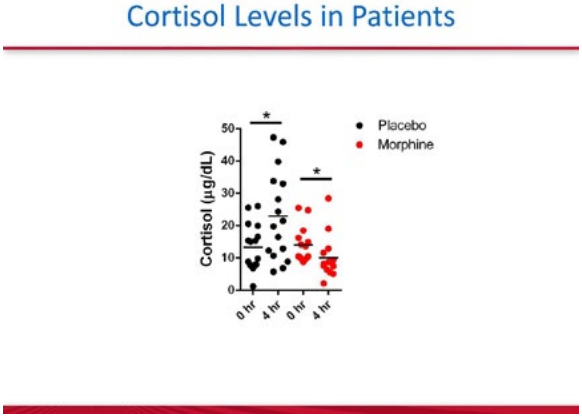

S-206.

OPIOID USE IN CHRONIC PAIN PATIENTS WITH CHRONIC KIDNEY DISEASE- A SYSTEMATIC REVIEW

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INTRODUCTION: Chronic pain is a common and disabling symptom among patients with chronic kidney disease (CKD).[1] Very few reviews with rigorous methodological quality assessment criteria have analyzed the prevalence of pain with CKD; type, dose and reason for opioid use; effectiveness of pain control and associated adverse effects of opioids in patients with CKD. Therefore, the objective of this study was to investigate the prevalence of chronic pain and current opioid management among patients with CKD.

METHODS: A systematic literature search was performed for English papers, including citations from 1960 to May 2015. The studies providing appropriate study design, statistical evaluations and outcome evaluations were analyzed.[2,3] The quality of each individual article was assessed by the Cochrane Review Criteria for randomized trials, and the Newcastle-Ottawa Scale for cohort studies. Main outcome measures were prevalence of opioid use, opioid dose, effectiveness of symptom control, and associated adverse events.

RESULTS: Twelve of 131 papers met inclusion criteria. There were no randomized controlled trials (RCT) evaluable, and 12 were observational studies (Figure 1). Out of these 12 studies, 4 were of high quality, 6 were of moderate quality, and the remaining 2 were low quality studies. The studies were from different countries with a sample size ranging from 10 to 12,782. Several studies showed a high prevalence (47% to72%) of chronic uncontrolled pain. The use of opioids for the treatment of chronic pain with CKD ranged between 18-36%. The effectiveness of different categories of opioids, dose, duration and commonly prescribed opioids varied across studies. No clear guidelines or RCTs were found regarding the management of chronic pain with opioids in CKD. It is possible, based on knowledge of opioid pharmacodynamics and pharmacokinetics, to suggest caution with certain opioids in the treatment of patients with CKD (Figure 2).

CONCLUSIONS: 1) Based on a systematic review of the current literature there is fair evidence for the high prevalence of chronic pain among patients with CKD. 2) There is fair evidence for the inadequate use of opioid therapy for the treatment of CKD patients with chronic pain. 3) Clinicians are in need of additional and well-designed RCTs that focus on the indications for opioid therapy, appropriate opioid doses and dosing intervals, outcomes with adequacy of symptom control, and reporting on the incidence of adverse side-effects. 4) Fentanyl and buprenorphine transdermal are perhaps the most safe opioids to treat chronic pain in patients with CKD.

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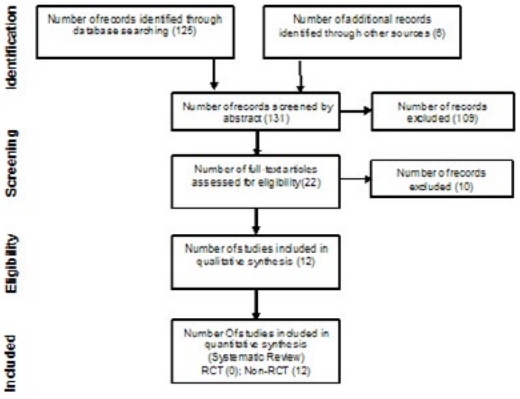
FIGURE 1



The flowchart based on study selection recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) search strategy. Possibly relevant (discussed to arrive at a consensus), and relevant (included). After discussion, there was a 100% final consensus between the 3 researchers.

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Figure2

Opioid	Metabolism	T1/2	T1/2 metabolite	Clinical Outcomes	Dosage consideration based on available evidence
Buprenorphine TD (Davis MP 2012, Filitz J 2006, Hand 1990)	• Plasma protein binding of about 96%, but not to the albumin fraction like most drugs, only to the a- and b-globulin fractions; • Primarily metabolized to norbuprenorphine and N-dealkylbuprenorphine• 2/3 of metabolites are excreted via the faeces, only 1/3 is renally excreted• Evidence of enterohepatic recirculation in non-human studies• Low plasma levels of buprenorphine during transdermal analgesic therapy	=	=	Two main inactive metabolites renally excreted; parent drug eliminated mainly via biliary system. Not dialyzable.	**Patch considered safe** (Niscola P 2010)
Codeine (Dean 2004; Gasche 2004).	Codeine is metabolized via CYP2D6 to codeine-6-glucuronide (C6G,81%), morphine (10%), normorphine (2%), M6G, and M3G, as well as other metabolites in negligible amounts. Both codeine and C6G are renally excreted, and renal clearance of codeine and its metabolites are significantly decreased in patients with moderate to severe renal failure	↑	↑	Metabolites can accumulate causing adverse effects.	**Adjustment of dosage** may be required in some patients with uremia receiving multiple doses, or do not use (Guay 1988).
Fentanyl TD (Joh J 1998; Sloan PA 1998; Pergolizzi J 2008)	• Primarily oxidized to norfentanyl• 75% excreted within 72 hours mostly as metabolites, 10% excreted unchanged	=/↑	=/↑	No active metabolites, but use caution because fentanyl is poorly dialyzable	**Appears safe**, monitor with long term use, and consider a dose reduction (Niscola P 2010).
Hydrocodone (Lurcott 1998; Singla A 2013)	• Hydrocodone is metabolized to hydromorphone by CYP2D6. Poor metabolizers experience little or no analgesia	↑	↑↑	3-glucuronide metabolite can accumulate and can cause neuro excitatory effects.	**Dosage ↓** and use cautiously (Dean 2004)
Hydromorphone (Dean 2004; Boeger RH 2006)	• Metabolized to active metabolites hydromorphone-3-glucoronide, hydromorphone-3-glucoside, and dihydroisomorphine-6-glucoside	↑	↑↑	Accumulation of metabolites described causing neuroexcitatory effects (Smith MT 2000)	**Dosage ↓** and use cautiously by careful symptom monitoring (Razaq M 2007)
Meperidine (Hassan et al. 2000; O'Connor AB 2005)	•Meperidine is metabolized in the liver to various metabolites, primarily normeperidine, which is the most toxic and long-lasting. •Meperidine and its metabolites are excreted by the kidney. •Metabolites can accumulate causing an increased risk of adverse effects	↑↑	↑↑	Effects of normeperidine are more profound in uremic patients due to its excessive accumulation; Normependine decreases seizure threshold and may induce seizures	**Do not use** (Niscola 2010)
Methadone (Furlan V 1999; Fredheim OM 2008; Sloan PA 2015)	• Converted to 2-ethylidene-1, 5-dimethyl-3, 3-diphenylpyrrolidene and 2-ethyl-5-methyl-3, 3-diphenylpyraline• Methadone is poorly removed by hemodialysis. • Metabolites are inactive.	↑	↑	Careful monitoring with long-term use due to risk of hypoxemia as well as hypercapnic ventilatory responses; QTc interval prolongation	**Dosage ↓** even though appears relatively safe. A specialist setting by a skilled and experienced team is required (Pergolizzi J 2008).
Morphine (Pergolizzi J 2008; Hanlon JT 2009)	• Large presystemic elimination (in gut wall and liver)• Only about 40% of dose reaches central compartment	↑	↑↑	Increased active metabolites M3G and M6G may lead to long-lasting respiratory depression	**Dosage ↓**, use with high caution, or do not use (Mercadante S 2002)
Oxycodone (Pergolizzi J 2008; Niscola 2010)	• Oxycodone hydrochloride is extensively metabolized to active noroxycodone, oxymorphone, and their glucuronides• Oxycodone and its metabolites are excreted primarily via the kidney• The plasma concentrations of oxycodone are 15% greater in the elderly	↑	↑	Parent drug and its multiple active metabolites can accumulate causing toxic and CNS depressant effects.	**Dosage ↓**, adjust interval of administration, or do not use (Foral PA 2007)
Oxymorphone (Sloan PA 2008; Chamberlin KW 2007)	Renally impaired patients may have a 57-65% increase in bioavailability	↑	↑	Need careful monitoring for side effects	**Dosage ↓** and use cautiously by careful symptom monitoring (Sloan PA 2008)
Propoxyphene (Baillie GR 2002; Kurella 2003)	•Propoxyphene is not dialyzed. •Metabolites can accumulate causing increased risk of hypoglycemia, cardiac conduction problems, and CNS and respiratory depression	↑↑	↑↑	Metabolites can accumulate causing adverse effects.	**Do not use** (Niscola 2010)
Tramadol (Gardner JS 2000; Barnung SK 1997; Izzedine H 2002)	•Extensive hepatic metabolism via demethylation,glucuronidation, and sulfation; •Active metabolites formed by CYP2D6 (M1; O-desmethyl tramadol); •30% of unchanged tramadol is renally excreted, active metabolite is predominantly renally excreted	↑↑	↑↑	Parent drug & metabolite undergo renal excretion, with approximately 90% of oral dose excreted by the kidneys, HD removes 7% of a tramadol dose in 4hr. accumulation increases risk of adverse effects	**Dosage ↓**, increase dose interval, and careful patient monitoring (Niscola 2010)

S-207.

THE INFLUENCE OF PHANTOM LIMB PAIN ON FUNCTIONAL IMPROVEMENT IN LOWER LIMB AMPUTATION PATIENTS DURING ACUTE INPATIENT REHABILITATION

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INTRODUCTION: The purpose of this study was to examine whether phantom limb pain appropriately treated with pain management affects functional performance of lower extremity amputation patients during acute inpatient rehabilitation in a free-standing rehabilitation hospital.

METHODS: Retrospective review of patients admitted for acute inpatient rehabilitation after lower extremity amputation at a free-standing rehabilitation hospital from 01/2013 to 5/2015 (29-month period) was investigated. The phantom limb pain patients were treated with one or combination of the following medications, Tylenol, Gabapentin, Pregabalin, Tricyclic antidepressant, Opioids, Selective serotonin reuptake inhibitors, Selective serotonin/norepinephrine reuptake inhibitor and Nonsteroidal anti-inflammatory drugs. Functional performance was defined by total Functional Independence Measure (FIM) scores as well as motor and cognitive subset scores.

RESULTS: A 2 (pain) X 2 (rehabilitation status) mixed design analysis of variance (ANOVA) for all patients for total, motor, or cognitive FIM scores did not demonstrate significant interactions. Regarding total FIM scores, a significant main effect was observed for rehabilitation status ($F [1, 1] = 434.44$, $P = <0.05$), where the scores were greater at discharge (87.61 ± 16.84) versus admission (58.08 ± 14.66) (Figure 1). Regarding motor FIM scores, a significant main effect was observed for rehabilitation status ($F [1, 1] = 358.71$, $P = <0.05$), where scores were greater at discharge (57.12 ± 13.49) versus admission (36.19 ± 10.87). Regarding cognitive FIM scores, a significant main effect was found for rehabilitation status ($F [1, 1] = 297.47$, $P = <0.05$), where scores were greater at discharge (30.48 ± 5.34) versus admission (21.89 ± 5.90). A 2 (pain) x 2 (type of amputation) between-subjects ANOVA did not demonstrate any significant interactions or main effects for FIM efficiency scores (FIM gain/length of stay).

CONCLUSIONS: Effective pain management in phantom limb pain patients improves functional recovery similarly to non-phantom limb pain patients during acute inpatient rehabilitation for lower extremity amputation. Future studies investigating pain, quality of life and patient satisfaction in lower extremity amputation patients are warranted. Inpatient rehabilitation with appropriate pain management appears crucial for achieving favorable functional outcomes in lower extremity amputation patients.

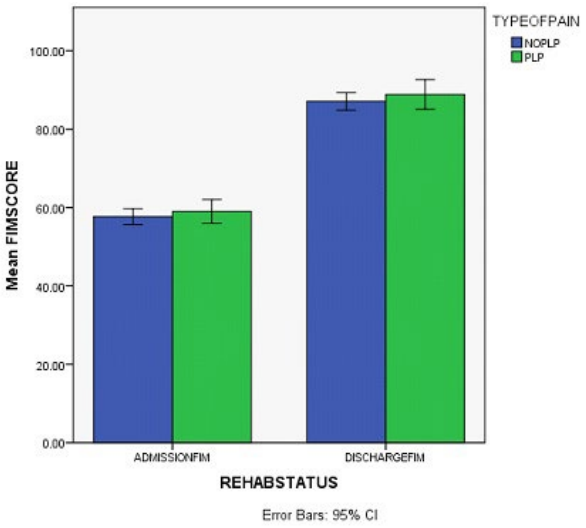

FIGURE 1: Total Functional Independence Measure (FIM) Score Change from Admission to Discharge. PLP- Phantom Limb Pain; NOPLP- No Phantom Limb Pain; CI- Confidence Interval.

S-208.

RESULTS OF THE ZALVISO SUBLINGUAL SUFENTANIL TABLET SYSTEM VERIFICATION TESTING

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BACKGROUND AND GOAL: The sufentanil sublingual tablet system (Zalviso™) is a handheld, noninvasive patient-controlled analgesia (PCA) device designed to allow hospitalized patients with moderate-to-severe acute pain to self-administer sublingual sufentanil 15 mcg tablets with a pre-programmed 20-minute lockout period. Marketing authorization for the product was received in the European Union in September 2015. During the development of the device, the manufacturer performed system verification testing in order to evaluate the effectiveness of various Zalviso System design changes implemented to reduce the overall device error rate observed in the Phase 3 clinical trials, in particular, those errors that would potentially lead to a disruption in therapy (analgesic gap). While the 7.9% rate of analgesic gaps experienced in the final Phase 3 clinical trial was well below published values for IV-PCA (12%), there was incentive to further reduce this rate from both a regulatory and marketing perspective.1 The objective of this study was to document the execution, results and conclusions of the Zalviso System Verification Test.

MATERIALS/METHODS: 111 Controllers were to be used in the execution of the protocol and were to be a combination of newly manufactured devices and those that had been subjected to a minimum of two uses. A minimum of 700 Systems were to be set-up for dispensing, comprised of at least 175, 455 and 70 1-Cartridge, 2-Cartridge and 3-Cartridge Systems, respectively. This distribution approximated the scope of the entire Phase 3 clinical trial series including a factor of safety. All System errors and any failure of the System to dispense a tablet when requested, was to be recorded as an error by the technicians. The protocol acceptance criterion purported that the System error rate resulting in analgesic gaps would be non-inferior to a target of 3%; this was based on the criterion that the upper limit of a 90% confidence interval of the System error rate would not exceed 5%.

RESULTS: A total of 711 Systems were set up and tested; 176 1-Cartridge Systems, 460 2-Cartridge Systems and 75 3-Cartridge Systems. A total of 51,680 tablets were dispensed from 1292 cartridges. Thirteen (13) System errors were observed in aggregate and of those, 11 were classified as errors that would theoretically have resulted in an analgesic gap. The overall Zalviso System error rate was 1.83%, but calculation of only those errors that theoretically would have led to an analgesic gap, yielded an error rate of 1.55%.

CONCLUSION: The acceptance criterion for the Zalviso System Verification Test Protocol was met without exception, confirming that the modifications to the Zalviso system have significantly reduced the error rate that could theoretically lead to analgesic gaps and the overall device error rate.

S-209.

WITHDRAWN.

S-211.

WITHDRAWN.

S-212.

APPLICATION OF TIME-DRIVEN ACTIVITY-BASED COSTING TO A PROPOSED PERIOPERATIVE PATHWAY FOR CHRONIC PAIN AND OPIOID TOLERANT PATIENTS

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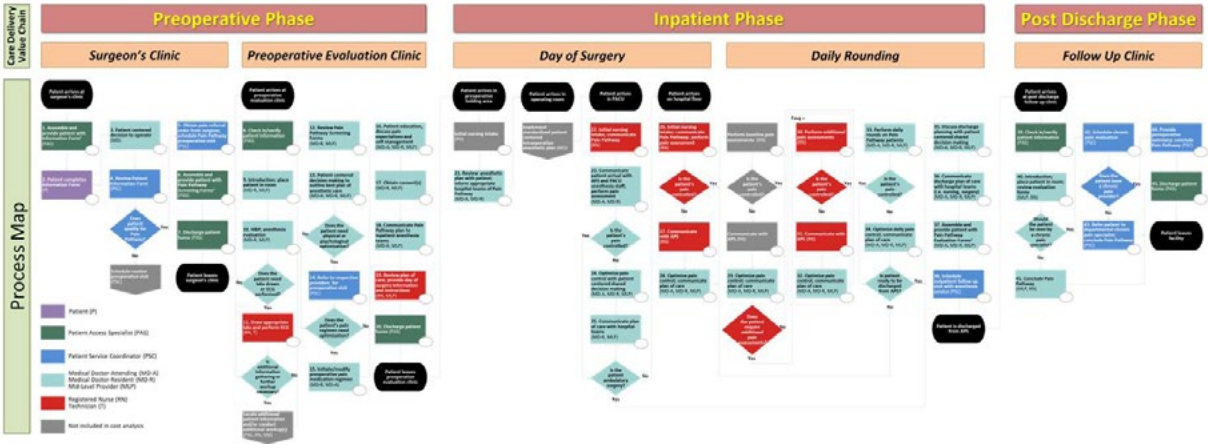
INTRODUCTION: Patients presenting for surgery with preexisting chronic pain and opioid tolerance represent a growing population of challenging perioperative patients. There is no published data reporting the percentage of these patients undergoing surgical intervention; however, a recent chart review at our institution revealed this group to represent approximately 15% of patients that come through our preoperative evaluation clinic. Chronic pain and opioid tolerant patients are at increased risk of inadequate postsurgical pain control;[1-4] consequently, postsurgical complications and negative perioperative outcomes may be increased.[4-6] As a result, the importance of postsurgical pain control was recognized and dedicated acute pain service (APS) teams were employed nationwide. However, over the past decade APSs have been fraught with fiscal and operational barriers,[7,8] and the current data is insufficient to suggest their cost effectiveness or ability to impact outcomes.[8-10] That being said the ethics supporting an APS cannot be understated and the truth of whether an APS is cost effective likely depends on multiple factors.[9-11] We propose that the benefits of identifying chronic pain and opioid tolerant patients preoperatively and placing them into a perioperative pathway, co-managed by an APS, could potentially improve outcomes and produce cost savings. Objectives: The objectives of this concept piece were to (1) design a perioperative pathway for surgical patients presenting with chronic pain and opioid tolerance using the confines of our preexisting institutional infrastructure, (2) predict the purchasing cost of implementing this pathway, and (3) characterize the opportunity to reduce perioperative cost for this group of patients.

METHODS: We used the time-driven activity-based costing (TDABC) method to quantify the overall costs of overlying a perioperative pathway for surgical patients presenting with chronic pain and opioid tolerance onto our preexisting infrastructure. The TDABC method estimates health care cost by combining data about the process of patient care delivery with the cost of each resource used to provide the care.[12]

RESULTS: We defined a care delivery value chain (CDVC) to develop a process map detailing patient care delivery activities (Figure 1). This allowed us to determine the capacity cost rate for each activity (measured as $/min for each resource consumed) and calculate the total cost of implementing our proposed perioperative pathway.

DISCUSSION: The TDABC method is a bottoms-up approach of estimating health care delivery costs based on direct assessment of actual clinical and administrative processes. This method engaged health care providers at our institution in understanding the processes and costing activities of health care delivery, and provided a unique platform to design and integrate a perioperative pathway in an optimized, cost-conscious manner, with the goal of improving perioperative health outcomes for chronic pain and opioid tolerant patients.

REFERENCES: Available on request.



Subspecialty Abstracts

Patient Safety

S-213.

ANESTHESIA CARE FOR AMBULATORY COLONOSCOPIES IS ASSOCIATED WITH 45 % RISK REDUCTION OF 30-DAY EMERGENCY ROOM VISITS AND FLOOR ADMISSIONS

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INTRODUCTION: Ambulatory colonoscopy is a commonly performed procedure that can be completed with different sedation techniques. Recent US trends show that use of anesthesia services is increasing[1]. Improved patient satisfaction and more efficient workflow influence these trends. Still, authors argue that anesthesia care may result in increased complications[2] and unnecessary costs[3]. To assess whether anesthesia care is associated with complications requiring emergency room (ER) visit or floor admission within 30 days from the procedure, we studied the cohort of outpatients who underwent colonoscopy with and without anesthesia care from Nov. 2010 until Oct. 2013 in our academic center.

METHODS: After IRB approval, administrative, billing, and clinical data was extracted from Hospital, Gastroenterology, and Anesthesia electronic databases. This data detailed the number of patients who underwent colonoscopy, along with their demographic and clinical information; type of procedure was also recorded. ICD9-CM and CPT codes were collected on day of exam, and for each ER visit or floor admission occurring within 30 days from the procedure in the facility where the index colonoscopy was performed, and across the whole regional hospital network. Possible colonoscopy-related hospital visits were identified by predetermined acute events ICD9 codes (image 1). After data merging, a propensity score (PS) weighting method was used to adjust for pre-treatment (anesthesia care) patient characteristics. The probability of receiving anesthesia care for each patient (PS) was obtained using generalized boosted methods. With PS, we constructed appropriate weight to estimate the average treatment effect (ATE) and the average treatment effect on the treated (ATT) with anesthesia care. For comparison, we obtained unadjusted, logistic regression model adjusted estimates.

RESULTS: 13,338 patients (43% male, 57% female) underwent 14,560 exams over the study period. Images 2, 3, 4, and 5 describe patients' age, race, Charlson score and colonoscopy type. In 9,545 patients (71.6%) the first study exam was with anesthesia care; in 3,793 (28.4%) under gastroenterologist supervised sedation. 2 patients died on day of exam (1 for each sedation group). 1,003 colonoscopies (6.8% of exams) were followed by at least one related ER visit or floor admission. Without adjustment, the odds ratio (95%CI) of ER visits and hospital admission for those with anesthesia care vs those without is 0.607 (0.530, 0.697); with logistic regression model adjustment, odds ratio (OR) is 0.578 (0.498, 0.670); with cc logistic adjustment OR is 0.34 (0,294, 0.409); with PS weighting, OR for ATT and ATE are similar: 0.55 (0,479, 0.642).

CONCLUSIONS: Anesthesia care for colonoscopy may reduce the risk (odds) of ER visits and floor admission by 45% (95% CI 36%, 52%). Future work will assess the relation of this protective association with specific complications, complexity of procedures, or use of specific sedative drugs.

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Table 1

ICD9-CM CATEGORY	CLINICAL EVENTS
Blood and blood-forming organs	Bleeding Lesion of the spleen
Circulatory system	Cardiac dysrhythmias Heart Failure Hypotension Other venous embolism or thrombosis Acute Myocardial Infarction Cardiovascular disease, unspecified Acute pulmonary heart disease Cerebrovascular Disease Angina Pectoris Other acute and subacute forms of ischemic heart disease Conduction disorders Essential hypertension Acute and subacute endocarditis Hypertensive heart disease Endocarditis
Digestive System	Symptoms involving digestive system Constipation Intestinal obstruction without mention of hernia Diverticula of intestine Peritonitis and retroperitoneal infections Other disorders of peritoneum Noninfectious enteritis and colitis Other symptoms involving abdomen and pelvis Appendicitis Unspecified disorders of peritoneum Gastrointestinal hemorrhage
External causes of injury and poisoning	Accidental falls Sedatives-related adverse effects
Genitourinary System	Acute renal failure
Infectious and parasitic diseases	Septicemia
Injury and Poisoning	Injury to gastrointestinal tract Nervous system complications Other complications of procedures, not elsewhere classified General symptoms (alteration of consciousness, hallucinations, syncope, convulsions, dizziness) Symptoms involving head and neck (headache, speech disturbance) Sprains and strains of joints and adjacent muscles Contusions with intact skin surface Fractures of lower limb Fractures of skull Dislocation Concussion
Nervous system and sense organ	Anxiety states Acute pain
Respiratory System	Asthma Pneumothorax Pneumonitis due to solids and liquids
Symptoms, Signs, and Ill-defined conditions	Symptoms involving cardiovascular system Symptoms involving respiratory and other chest symptoms symptoms involving urinary system General symptoms (fever, malaise and fatigue) Ill-defined and unknown causes od morbidity and mortality (death, respiratory arrest)

Figure 1 - Patients per class of age

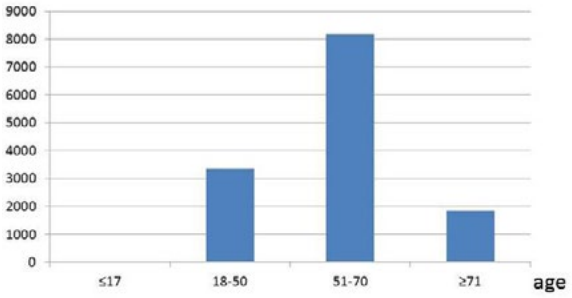

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Figure 2 - Patients' Race

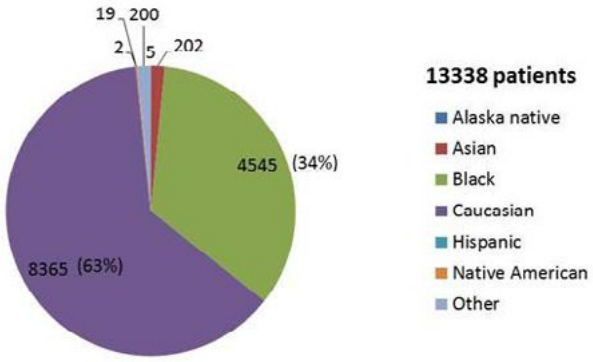

Table 2 – Comorbidities burden (as per Charlson Index) for anesthesia and sedation groups

Charlson 5y score	Number of Patients	Anesthesia	Conscious Sedation
Missing	16	.	.
0-3	8,854	6,327 (71.5%)	2,527 (28.5)
4-6	2,980	2,146 (72%)	834 (28%)
≥7	1,488	1058 (71.1%)	430 (28.9%)

Table 3- Type of procedures

COLONOSCOPY TYPE	NUMBER	PERCENTAGE
Screening	5,188	35.91
Diagnostic	5,578	38.61
Therapeutic/Interventional	3,682	25.48

S-214.

ANESTHETIC SAFETY FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN THE PRONE POSITION BY DIFFERENT ANESTHETIC PROVIDER GROUPS

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP), a diagnostic and sometimes interventional procedure for the biliary system, can be performed with different anesthetic modalities, typically either deep sedation (DS) or general anesthesia (GA) with an endotracheal tube[1]. The choice of modality likely reflects local tradition as well as practitioner's experience and perception of safety[2]. However, the relative safety and outcomes between these two anesthetic modalities have been poorly described, especially for ERCP performed in the prone position. Therefore, we retrospectively endeavored to characterize practice patterns and compared the relative anesthetic safety by three different anesthetic provider groups during the ERCP performed in the prone position.

METHODS: Patient and procedure related data were extracted from electronic anesthesia records for adult prone-positioned ERCP cases performed from 2006 to 2015 at our urban academic medical center. Cases were divided into three anesthetic provider groups [CRNA and attending physician (CRNA/Att), resident and attending physician (Res/Att), and attending physician only (Att)]. Patient demographics, anesthesia modalities, intra-procedure data and perioperative adverse events (conversion from DS to GA, hypoxia, hypotension and unplanned ICU admission) were statistically compared among three groups. Chi-square analysis and one-way ANOVA were used to test for statistical significance of the differences in proportions.

RESULTS: A total of 2571 cases were included in the three groups of CRNA/Att (n=1651), Res/Att (n=670) and Att (n=250). There was no significant difference in the patient demographics among three groups except for more American Society of Anesthesiologists Physical Status (ASA PS) class 4 in the Res/Att group than CRNA/Att group (9.6% vs. 6.1%; $P<0.05$). DS was provided for 1131 cases (68.5%) in CRNA/Att group, 399 (59.6%) in Res/Att group and 172 (68.8%) in Att group, which was significantly more DS in CRNA/Att than Res/Att group ($p<0.01$). No significant difference was observed in perioperative adverse events (e.g.; hypoxia, hypotension and unplanned ICU admission). In the subgroup analysis of DS cases for the three groups, no significant difference was observed in adverse events (e.g.; conversion from DS to GA, hypoxia, hypotension and unplanned ICU admission). Hypoxia, patient movement and unexpected full stomach were the most frequent reasons for the conversion from DS to GA, which occurred in 2.6% of DS cases.

CONCLUSIONS: All three different anesthesia care team compositions safely provided both DS and GA without any significant difference in adverse events for patients who underwent ERCP in the prone position. Attendings with residents performed more GA than DS compared with attendings with CRNAs, possibly due to more ASA 4 patients in that group.

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S-215.

INITIAL ASSESSMENT OF AUTOMATED SSEP FOR DETECTION OF INTRAOPERATIVE POSITIONAL NEUROPRAXIA IN CARDIAC SURGERY

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INTRODUCTION: In anesthetised patients positional neuropraxia may be an accompaniment to inadvertent compression or traction of peripheral nerves, of which upper limb and brachial plexus nerves are particularly vulnerable. The incidence of clinically apparent upper limb neuropraxia in cardiac surgery has been estimated at between 0.5% to 37.5%, depending on the type and duration of retractor usage, patient positioning and is variably influenced by patient comorbidities.[1,2] Intraoperatively, peripheral nerve function can be monitored noninvasively using somatosensory evoked potentials (SSEP) however, conventional SSEP monitoring requires presence of a trained SSEP technician, use of needle electrodes and currently bulky SSEP equipment and is thus not practical for routine clinical usage. In this study we report our initial experiences with a non-invasive, miniaturized and automated SSEP device (EPAD, SafeOpSurgical, Hunt Valley, MD)

METHODS: Following review board approval and written patient consent, 17 patients undergoing cardiac surgery with median sternotomy and cardiopulmonary bypass were enrolled. Adhesive stimulating electrodes were placed on bilateral wrist in median and ulnar nerve distribution with adhesive receiving electrode placed on posterior neck in C5 position and adhesive ground electrode placed on forehead and variably covered with transparent film dressings. Patient's arms were padded and placed neutral (thumbs vertical) at sides. The SSEP monitor screen alternately displayed a 'good' or 'alert' homunculus of relevant nerve signals, or a time-based display of current SSEP data for each nerve, with alert threshold trigger at > 10% increase from baseline latency or 50% decrease in signal amplitude.

RESULTS: Of 17 patients, I died of cardiac failure postoperatively and in a further 3 patients electrode failure resulted in irretrievable data loss. Accordingly electrode adhesive was modified and transparent film dressings applied to all subsequent cases. Of 13 surviving patients with complete SSEP data, intraoperative 'alert' was detected and persisted through end of surgery in 2 patients. No relevant symptoms were reported in 11 patients but of patients with persistent SSEP changes, all complained of numbness and/or tingling in ipsilateral hand on clinical examination. Electromyography studies were performed in these 2 symptomatic patients one of which demonstrated mild left ulnar neuropathy and other showed bilateral ulnar neuropathies worse on symptomatic left side with symptoms suggestive of traction injury to lower brachial plexus.

CONCLUSION: This pilot study shows efficacy and ease of use of a non-invasive automated SSEP device and consistent with other such studies demonstrates an incidence of intraoperative neuropraxia that is associated with a 15% incidence of persistent clinical symptomatology. A randomized blinded clinical trial is underway to determine whether intraoperative interventions can decrease this morbidity.

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S-216.

A PREDICTIVE MODEL TO DETERMINE LANGUAGE RESPONSE IN BILINGUAL PATIENTS EMERGING FROM GENERAL ANESTHESIA

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INTRODUCTION: According to the United States Census, one in five Americans speak a language other than English at home. Of these, about 40% are considered to have limited-English proficiency (LEP). A language gap can pose significant challenges at the time of emergence from general anesthesia. These challenges can occur because the anesthesiologist needs to determine a patient's readiness for extubation based on the patient's response to verbal commands. A non-native English speaker (NNES) may be unable to understand these commands either because of limited English proficiency or because of changes in language facility tied to the disorientation associated with emergence from anesthesia. The purpose of this study is to develop a predictive model to determine which NNES patients would benefit from a translation intervention at the time of emergence from general anesthesia.

METHODS: Sixty-one NNES subjects were enrolled in this IRB-approved study. Demographic data including age at arrival in the US, years of speaking English, age that English was learned, language spoken at home, relative facility with English and the native tongue (self-assessed), country of origin, and language spoken in the subject's dreams. At emergence, three commands were played through headphones in alternation between English and the subject's native tongue. Publicly available iPad translation apps were used to generate the statements ("open your eyes", "squeeze my fingers", and "wiggle your toes"). Whether the subject responded to the command in English, in the native tongue, or both was recorded for each command.

RESULTS: Of the responses, there were significantly more responses to the foreign language compared to the English language commands ($X2= 9.3$, $df=83$, $p=.007$). When comparing subjects that responded in one language more frequently than the other, 41 patients responded more frequently in the language that they spoke at home (OR = 8.3, 95% CI [1.9, 3.6], $p<0.005$). Language spoken at home was the only significant predictor of response. Age, gender, language the patient dreamed in, and years speaking English did not have a significant effect on language response.

DISCUSSION: Our results suggest that when emerging from general anesthesia patients are more likely to respond to the language that they speak at home when they speak more than one language. This finding can be used to identify patients who are at higher risk for miscommunication during the emergence period. Therefore, patients who speak a language other than English in their home might benefit from a translated intervention at the time of emergence from anesthesia.

S-217.

INACCURATE SYRINGE SIZE DETECTION BY THE INFUSION PUMP FROM THE ATTACHED STOPCOCK TO THE SYRINGE

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INTRODUCTION: A wide variety of electronic infusion pumps are commercially available for intravenous administration of anesthetics. Most pumps are configured with softwares and electronic sensors for extremely high precision in infusion settings and sizes of syringes.[1] Despite the manufacturers' safety measures such as electronic sensors and regular institutional inspections, it is possible to result in a medication error from inaccurate detection of syringe sizes by the sensors, resulting in administration of inaccurate doses of medication.

METHODS: A filled 20 ml syringe (BD Luer-Lok Tip REF 302830) was connected to a stopcock (Discofix 4-way Stopcock by B. Braun) before placement to the infusion pump slot (Arias Syringe Module Model 8110 by Carefusion). All the sensors for the syringe size were correctly engaged to the syringe to determine the identity and size from the data base. When the side port of the stopcock is lodged against the pump tightly by a twisting motion, the 20 ml syringe pushed out the holding clamp further. As a result, it is detected as a 30 ml syringe diameter based on the increased extension of the clamp. (Figure 1) After confirming the 30 ml syringe as the correct size, the infusion rate was set at 60 ml/hour to drain the 20 ml in 20 minutes. Before starting the infusion, the detected volume to be infused (VTBI) was recorded against the control (i.e., 20 ml). After 20 minutes when 20 ml of the volume was to be completed, the detected volume infused (VI) was recorded against the control (i.e., the amount remaining in the syringe by visual inspection)

RESULTS: When the filled 20 ml syringe was confirmed as a 30 ml syringe, the pump registered the VTBI as 23.9 ml, overestimating the actual volume by 4 ml. After 20 minutes, the pump registered the VI as 20 ml, the correct amount to be infused during the period. However, there was 3-4 ml still remaining in the syringe.

CONCLUSIONS: Overestimation of the syringe size overestimated the medication amount in the syringe and under-delivered by the amount overestimated during the set infusion period. Overestimation of the syringe size occurred when the stopcock was attached for the purpose of multiple refilling without removing the syringe. When the stopcock was pressed against the wall of the pump, it may have caused a wrong size configuration to be selected based on the altered sensor data. Smart infusion systems are designed to prevent serious medication error and improve patient safety.[2] Nevertheless, the systems can fail from various human and software causes. According to the FDA report there were 80 pump related deaths from 1999 to 2009. The most common faults of infusion pump errors were software causes.[3]

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S-218.

APROTININ IS WITHOUT BENEFIT IN HIGH RISK PATIENTS

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BACKGROUND: Severe bleeding is relatively frequent in cardiac surgery and associated with increased morbidity and mortality. Blood transfusion benefits in the acute phase, but carries potential complications[1]. The anti-fibrinolytic drug Aprotinin (AP) and the lysine analogue tranexamic acid (TA) are used to attenuate blood loss[2]. However, studies documented severe adverse effect after AP3-4 and the use stopped in routine practice. Risk from bleeding may be increased in fragile patients and in high risk procedures. Thus, some continued the use of AP based on individual evaluations of risks and benefits in selected patients. The purpose of the study was to evaluate the beneficial effects and potential adverse outcomes in high risk cardiac surgery patients receiving AP.

METHODS: Consecutive adult on-pump cardiac surgery patients 2007-2014 (N=6,341). Patient characteristics and surgical procedures are primarily described by EuroSCORE. The decision of AP or TA treatment was at the discretion of the surgeon in charge. Propensity score matching was used to reduce the risk of bias due to confounding and non-random assignment of transfusion therapy. Covariates were adequately balanced after propensity score matching (Figure1). Conditional logistic regression was used to estimate crude and adjusted risks.

RESULTS: AP was administered to 598 (9.4%). The remaining patients received TA. 513 of the 598 (85.8%) was matched with a TA patient. Baseline parameters before and after propensity score matching are summarized in Table 1. Patients receiving AP had discrete indications, however not statistical significant, of lower postoperative drainage, less frequent re-do surgery and less treatment with fibrinogen and factor VII A (table 2). Patients receiving AP received significant more often RBC's (50.1% vs. 43.5%; P=0.035; Table 2). The crude regression analysis demonstrated that use of AP was followed by a higher frequency of new postoperative dialysis. However, no independent impact was seen in the adjusted analysis (table 3).

Perioperative vasoconstrictors and transfusions are the primary factors with individual negative impact on postoperative dialysis and 6mth mortality (table 4).

CONCLUSION: In this group of relatively high risk patients Aprotinin had no statistical significant beneficial impact on perioperative bleeding. Although the negative impact was less than previous reported in standardized cardiac cases, there are still indications of negative impact on severe outcome parameters.

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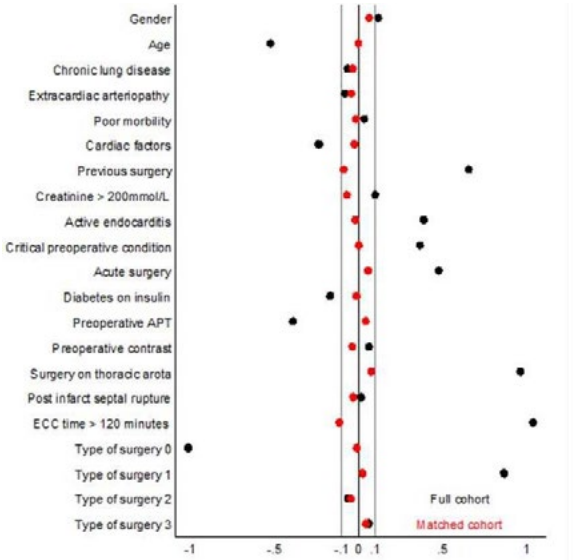

Figure 1 The standardized differences of all matching criterions before and after propensity score matching. The included covariates were; sex, age (longitudinal), chronic obstructive lung disease (COLD), extra cardiac arteriophaty, preoperative central nervous disease/poor mobility, s-creatinine > 200 mmol/L, previous cardiac surgery, active endocarditis, critical preoperative state, cardiac factors (longitudinal sum of scores for unstable angina, left ventricular ejection fraction (3 groups), recent myocardial infarction), acute surgery, operation type (coronary artery bypass grafting only, single-, double-, or triple procedure). All above EuroSCORE I18 and II19 criteria. Extra corporal circulation time (2 groups), preoperative continued antiplatelet therapy and use of contrast plus/minus 7 days before/after surgery.

Factor	Original cohort			After propensity match		
	Trasylol n=598	Control n=5743	*p-value*	Trasylol n=513	Control n=513	*p-value*
Sex, male	397 (66)	4112 (72)	0,007	177 (35)	161 (31)	0.288
Age, mean (sd)	58.8 (17.0)	65.8 (12.7)	0.000*	59.1 (17.1)	59.1 (16.2)	0.706
Cronic lung disease	63 (11)	706 (12)	0.215	52 (10)	57 (11)	0.612
Extracardiac arteriopathy	35 (6)	442 (8)	1.105	29 (6)	34 (7)	0.516
Poor mobility	46 (8)	390 (7)	0.398	42 (8)	44 (9)	0.822
Cardiac factor-score, mean (sd)	0.59 (1.2)	0.90 (1.4)	0.000*	0.60 (1.2)	0.63 (1.2)	0.643
Previous surgery	175 (29)	316 (6)	<0.0001	139 (27)	159 (31)	0.169
Creatinine > 200 mmol/l	30 (5)	176 (3)	0.01	26 (5)	34 (7)	0.287
Active endocarditis	86 (14)	200 (3)	<0.0001	77 (15)	80 (16)	0.795
Critical preoperative condition	108 (18)	358 (6)	<0.0001	81 (16)	80 (16)	0.932
Acute surgery	144 (24)	413 (7)	<0.0001	112 (22)	100 (19)	0.355
Diabetes on insulin	14 (2)	323 (6)	0.001	13 (3)	14 (3)	0.845
Preoperative APT	42 (7)	1143 (20)	0.000	39 (8)	33 (6)	0.463
Preoperative contrast	111 (19)	926 (16)	0.125	95 (19)	102 (20)	0.579
Surgery on thoracic aorta	234 (40)	204 (4)	<0.0001	158 (31)	140 (27)	0.216
Post infarct septal rupture	2 (0.3)	14 (0.2)	0.674	2 (0.4)	3 (0.6)	0.654
ECC time > 120 min	426 (71)	1436 (25)	<0.0001	343 (67)	369 (72)	0.078
Type of surgery						
Single CABG	25 (4)	2423 (42)		25 (5)	26 (5)	
Single non-CABG	448 (75)	2034 (35)	<0.0001	368 (72)	362 (71)	0.820
Two procedures	105 (18)	1153 (20)		101 (20)	110 (21)	
Three procedures	20 (3)	133 (2)		19 (4)	15 (3)	
High Euro-SCORE	223 (37)	841 (15)	<0.0001	185 (36)	181 (35)	0.794
Perioperative Hydroxy-etyl starch	613 (60)	3442 (65)	0.002	300 (58)	313 (61)	0.408

Table 1 Selected factors and parameters before and after propensity match. APT= antiplatelet therapy; ECC=extra corporal circulation, CABG=coronary artery bypass grafting; *) Mann-Whitney test. All other χ2-test

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Group	Drainage	Re-do	Administration of		Red Blood Cells		Plasma		Platelets	
			Fibrinogen	NovoSeven	No	Volume	No	Volume	No	Volume
Aprotinin	489 (280 - 976)	41 (8.0)	50 (9.7)	18 (3.5)	257 (50.1)	1200 (600-2700)	257 (50.1)	1200 (600-2400)	226 (44.0)	600 (300-900)
Tranexamic Acid	513 (310 - 1145)	48 (9.4)	53 (10.3)	25 (4.9)	223 (43.5)	1200 (600-2700)	227 (44.2)	1200 (600-2400)	204 (39.8)	600 (300-1200)
p value	*0.454 #)*	*0.510 !)*	*0.837 !)*	*0.324 !)*	*0.035 !)*	*0.303 *)*	*0.062 !)*	*0.901 *)*	*0.159 !)*	*0.927 *)*

Table 2. Effect drainage and transfusion of Aprotinin compared to tranexamic acid in propensity score matched patients. #) Wilcoxon test; !) McNemar test; *) Mann-Whitney test.

Outcome parameter	Crude OR (95 % CI)	Adjusted OR (95 % CI)
30-day mortality	0.95 (0.50-1.81)	0.96 (0.37-2.47)
New postoperative dialysis	1.78 (1.18-2.67)	1.26 (0.71-2.23)
Postoperative stroke	0.76 (0.40-1.46)	0.93 (0.39-2.19)
Postoperative MI	1.00 (0.46-2.16)	0.98 (0.43-2.22)
6^{mth} Ischaemic event	0.63 (0.38-1.03)	0.59 (0.33-1.05)

Table 3. Conditional regression analysis of propensity score matched data. Parameters in adjusted analysis are together with Aprotinin perioperative use of vasoconstrictors, inotropes, fibrinogen, Novo seven and transfusion of blood or blood products..

Outcome factor	30-day mortality	New dialysis	6^{mth} mortality	6^{mth} ischaemic event
Perioperative Aprotinin	0.96 (0.37-2.47)	1.26 (0.71-2.23)	0.81 (0.46-1.45)	0.59 (0.33-1.05)
Perioperative constrictors	7.02 (0.74-67.0)	6.31 (2.08-19.2)	3.90 (1.24-12.3)	0.94 (0.39-2.29)
Perioperative inotropes	1.96 (0.07-56.9)	0.93 (0.18-4.68)	1.36 (0.28-6.62)	8.79 (1.06-72.6)
Perioperative fibrinogen	1.92 (0.10-35.8)	1.23 (0.38-4.01)	1.67 (0.33-8.59)	0.30 (0.07-1.32)
Perioperative Novo Seven	0.26 (0.01-4.84)	0.73 (0.15-3.63)	0.51 (0.08-3.26)	4.71 (0.41-54.6)
Blood and blood products	4.51 (0.86-23.6)	8.14 (2.33-28.5)	3.37 (1.13-10.0)	2.42 (0.90-6.51)

Table 4. Adjusted conditional regression analysis of propensity score matched data showing individual impact of parameters used in adjustment.

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USING NON-INVASIVE RESPIRATORY VOLUME MONITORING IN THE POST-ANESTHESIA CARE UNIT TO MONITOR POST-OPERATIVE RESPIRATORY DEPRESSION IN PATIENTS IDENTIFIED AS AT-RISK FOR OBSTRUCTIVE SLEEP APNEA UTILIZING THE FLEMON'S CRITERIA

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INTRODUCTION: OSA has traditionally been associated with increased risk for post-operative respiratory complications. Surprisingly, previous research has shown that OSA is not a strong predictor of post-operative apnea (POA) or post-operative respiratory depression (RD). To identify patients in the pre-operative setting that may be at risk for obstructive sleep apnea (OSA), the Flemon's Criteria[1] can be utilized to calculate a Sleep Apnea Clinical Score (SACS), where a value ≥ 15 is a good predictor for OSA[2]. This study used a respiratory volume monitor (RVM) to monitor patient respiratory status in the post-anesthesia care unit (PACU) and assess POA and the incidence of RD3 in patients with High SACS (at-risk for OSA) vs. Low SACS (not-at-risk for OSA).

METHODS: 56 patients were monitored post-operatively with a continuous bio-impedance RVM system (ExSpiron, Respiratory Motion, Waltham, MA). Patients were stratified by SACS: High SACS (> 15) as 'at-risk' and Low SACS (< 15) as 'not-at-risk'. Predicted MV (MVPRED) and Percent Predicted (MVMEASURED/MVPRED x 100%) were calculated for each patient. Low MV (LMV) was defined as MV < 40% MVPRED sustained for > 1 min. Multiple incidents of LMV within a 10-min period following the first LMV incident were considered a single LMV event (LMVe). RD was defined as > 1 LMVe. LMV at Discharge (LMVD) was defined as MV < 40% MVPRED > 1/3 of the 30 minutes prior to PACU discharge. SACS was evaluated as a predictor for RD and LMVD.

RESULTS: Of 56 patients, 43 (77%) had Low SACS (mean: 5, range: 0-14; age: 57 yrs, 18-81; BMI: 30.5 kg/m2, 19.8-66.9). No Low SACS patient had a previous OSA diagnosis. 13 (23%) patients had High SACS (mean 19, range 16-22; age: 57 yrs, 26-71; BMI: 36.2 kg/m2, 21.6-56.9), of which 9 (69%) had a previous OSA diagnosis. OSA patients had BMIs significantly larger than those with Low SACS (40.2 vs. 30.5 kg/m2, $p < 0.05$).

The 43 Low SACS patients experienced more LMVe (3.5 ± 0.4 vs. 2.3 ± 0.5 LMVe/hr) than the 13 High SACS patients. The average duration of LMV for Low SACS patients was 14.5 ± 2.2 min/hr (24% ± 3.7% of the time in the PACU) vs. 6.3 ± 2.2 min/hr (10% ± 3.7%) for High SACS patients. Low SACS patients had a higher likelihood of LMVD than High SACS patients (26% vs. 0%; 11/43 vs. 0/13). Patients with Low SACS and LMVD experienced more LMVe (4.8 ± 0.2 vs 2.3 ± 0.5 LMVe/hr, $p < 0.05$) and had longer duration of time with LMVs (32.6 ± 3.0 vs 6.3 ± 2.2 min/hr, $p < 0.05$) than High SACS patients (all with no LMVD). High SACS patients, despite POA (Fig. 1), tend to have adequate MV, likely because they compensate for apneic pauses with larger rescue breaths (Fig. 2) whereas Low SACS patients do not (Fig. 3).

CONCLUSION: Our data shows that while SACS is a good predictor for OSA, it is a poor predictor of RD during PACU recovery. Since patients with no indication of respiratory risk by OSA or SACS demonstrated significant RD in the post-surgical setting, preoperative stratification may not be sufficient to safely direct care without additional respiratory monitoring postoperatively.

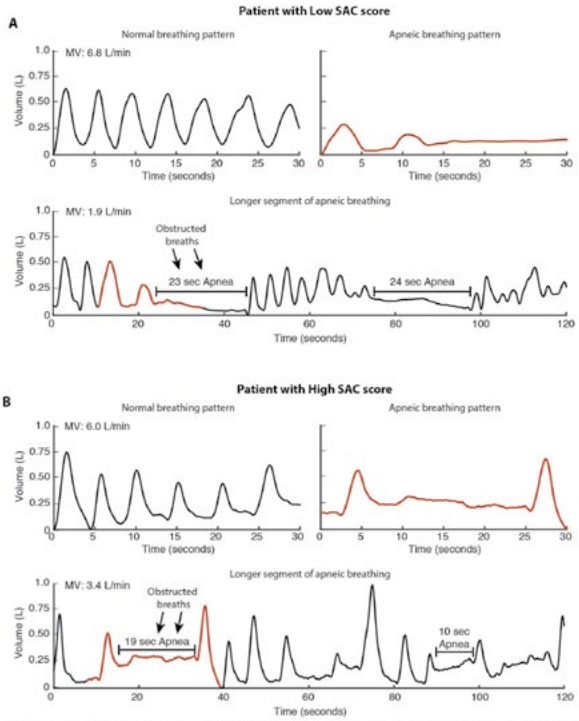

Figure 1: Example respiratory traces from two representative patients who demonstrated apnea and obstructed breaths in the PACU. (A) A patient with Low SAC score and (B) a patient with High SAC score and previously diagnosed OSA by polysomnography. Shown are 30 seconds of normal breathing (top left), 30-sec of apneic breathing (top right) and a longer period of cyclic apneic breathing (bottom). Minute ventilation is reduced in both patients during apneic breathing, but only in the Low SACS patient is apnea associated with respiratory depression as defined by Low MV, whereas the High SACS patient maintains adequate ventilation due to large tidal volume recovery breaths.

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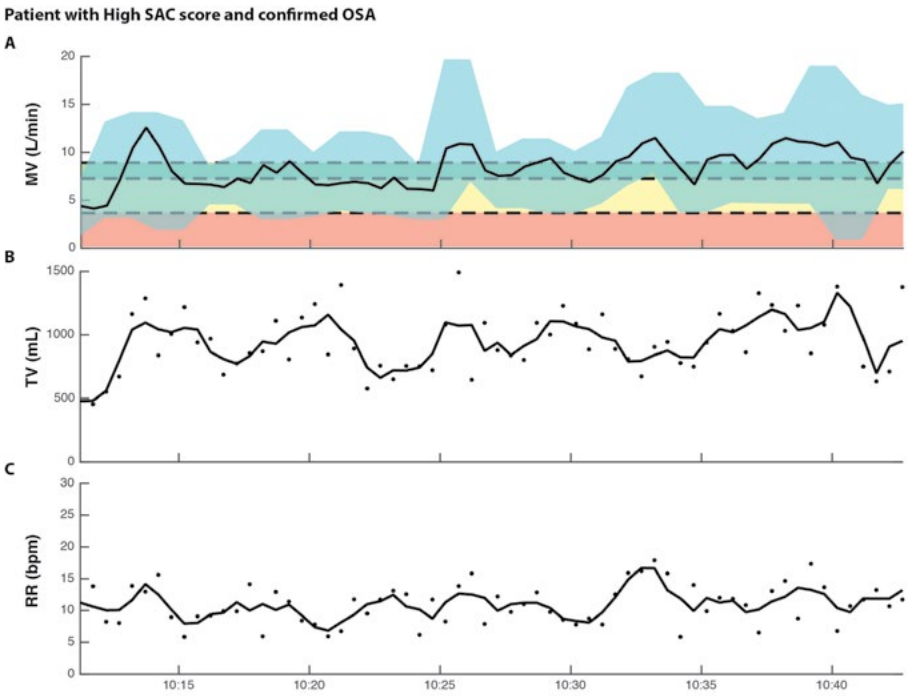

Figure 3: Patient with Low SAC score. Presented are the (A) continuous minute volume (MV), (B) tidal volume (TV), and (C) respiratory rate (RR) trends for a 70-year-old male (186 cm, 99 kg, 28.6 kg/m², 9.0 L/min MV_{PRED}, calculated based on BSA) with a SAC score of 7. The MV plot depicts three zones based on percentage of MV_{PRED}. Example traces showing the amount of time in the three zones: "Not-at-Risk" MV > 80% MV_{PRED} (green), "At-Risk" MV < 80% MV_{PRED} (yellow) and "Un-Safe" MV < 40% MV_{PRED} (red). The combination of the trend line (black) and the envelope (blue) allows for easier identification of areas of adequate ventilation. Here we see low MV (low trend) and POA (large envelope, associated with large variations in MV).

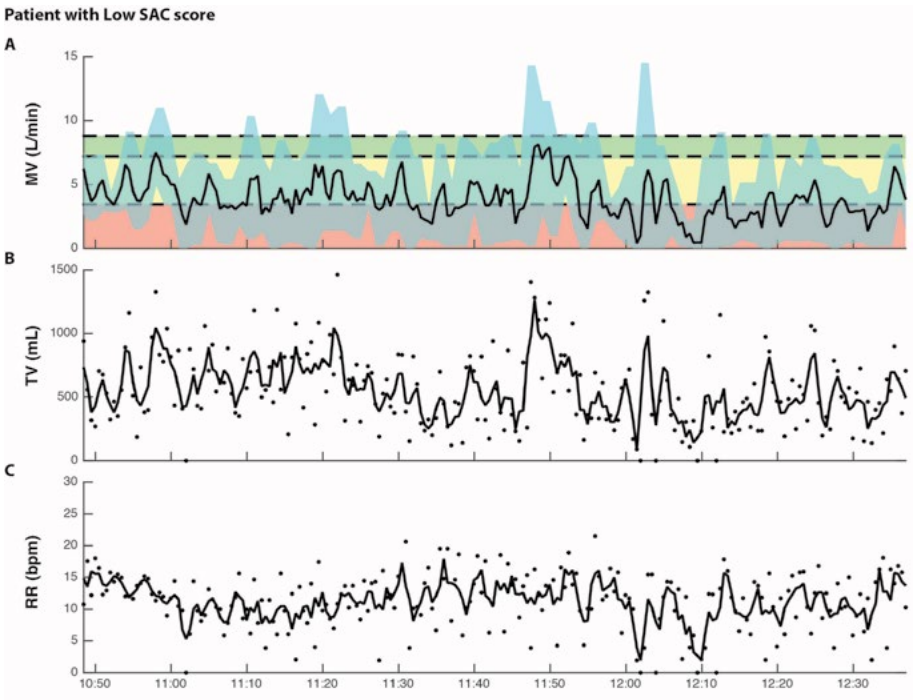

Figure 2: Patient with High SAC score and confirmed OSA. Presented are the (A) continuous minute volume (MV), (B) tidal volume (TV), and (C) respiratory rate (RR) trends for a 45-year-old male (185 cm, 94 kg, 27.6 kg/m², 8.7 L/min MV_{PRED}, calculated based on BSA) with diagnosed OSA. The MV plot depicts three zones based on percentage of MV_{PRED}. Example traces showing the amount of time in the three zones: "Not-At-Risk" MV > 80% MV_{PRED} (green), "At-Risk" MV < 80% MV_{PRED} (yellow) and "Un-Safe" MV < 40% MV_{PRED} (red). The combination of the trend line (black) and the envelope (blue) allows for easier identification of areas of adequate ventilation. Here we see adequate MV (adequate trend) and POA (large envelope, associated with large variations in MV).

S-220.

EFFECT OF NOISE ON ANESTHESIOLOGIST AUDITORY PROCESSING IN THE OPERATING ROOM

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INTRODUCTION: Noise is defined as any sound that is unwanted, causes annoyance or results in deterioration of performance[1]. It is heavily regulated in many fields of work, however no regulations for the operating room are available. Noise can cause hearing loss, decreased staff satisfaction and contributes to miscommunication within the operating room[2]. The purpose of this study was to assess auditory performance by anesthesiologists in a simulated operating room setting. It was hypothesized that there would be poorer auditory performance in the task versus untasked, noise versus quiet, and low versus highly predictable conditions.

METHODS: 14 subjects were recruited from the Department of Anesthesiology. Inclusion criteria specified for anesthesiology residents or attendings with normal hearing and no recent otologic history. Auditory performance was tested through the use of the Speech in Noise Test - Revised (SPIN-R) in 3 separate conditions: quiet, operating room noise and music. This was performed in a tasked (performing an induction sequence on a human simulator) and untasked condition.

RESULTS: Thirteen subjects participated, with 5 being male and 8 female. Six subjects were residents and 7 were attending physicians. A statistically significant effect was seen for auditory performance in noise and predictability but not for task.

CONCLUSIONS: There is an effect of noise on speech understanding by the anesthesiologist in the operating room specifically as it relates to the predictability of sentences.

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S-221.

DIFFICULTY OF REDUCING CATHETER RELATED BLOODSTREAM INFECTION IN THE INTENSIVE CARE UNIT OF A UNIVERSITY HOSPITAL DESPITE STRICT IMPLEMENTATION OF A PREVENTIVE MEASURE BUNDLE

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INTRODUCTION: To prevent catheter-related bloodstream infection (CRBSI) in the intensive care unit (ICU) of our university hospital, we implemented a preventive measure bundle[1]). We joined the national CRBSI surveillance system and implemented several interventions as additional measures for the prevention of CRBSI. To evaluate the effectiveness of our interventions, we compared the rates of CRBSI before and after the additional interventions. Moreover, we investigated the prominent CRBSI factors in our hospital ICU.

METHODS: This prospective observational study was approved by the university ethical committee. The observation period was from July 1, 2013, to December 17, 2015. All central venous catheters inserted in the patients enrolled for surveillance, in the 18-bed medical-surgical ICU of a 1058-bed university hospital, were analyzed. Before surveillance, a bundle of preventive measures was applied in the ICU upon the insertion of central venous catheters, including maximal barrier precautions and skin preparation with 1% chlorhexidine-alcohol, under the observation of nurses. Additional interventions were implemented (Table 1). The following data were collected: patient age, sex, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, duration of ICU stay, duration of catheter inserted, number of catheter lumens, rate of multiple catheter indwelling, insertion sites, number of insertion attempts, and mechanical ventilation status. A surveillance team comprising intensive care and infection control doctors and nurses determined the CRBSI status during weekly conferences. The CRBSI rates were calculated according to the rules of national surveillance, every 3 months. The analyzed factors were compared between CRBSI and non-CRBSI cases. Mann-Whitney U and chi-square tests were used to analyze the differences between CRBSI and non-CRBSI cases, where appropriate.

RESULTS: The rates of CRBSI every 3 months are shown in Table 1. A total of 717 central venous catheters were analyzed. Other data are shown in Table 2. Patients with CRBSI had higher APACHE II scores, longer ICU stay, and longer duration of catheter insertion than those without CRBSI. The rates of femoral insertion were higher in CRBSI cases. The rates of multicatheter indwelling and mechanical ventilation were greater in CRBSI cases.

CONCLUSION: The prominent CRBSI factors were associated with the severity of the initial condition, which might, in turn, be related to the observed longer ICU stay, longer duration of catheter insertion, higher mechanical ventilation rates, and multicatheter requirement. Although we strictly implemented the bundle of preventive measures, the CRBSI rate increased before we started the additional interventions. After several interventions, the CRBSI rates slightly decreased, which might possibly recover the benefits of the additional preventive measures. Further strategies with the medical staff including a surveillance team should be continued with the aim of preventing CRBSI in most severe critical care patients.

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Table 1 Infection rates at every 3 months from July 2013 to September 2015

Duration	2013 Jul–Sep	2013 Oct–Dec	2014 Jan–Mar	2014 Apr–Jun	2014 Jul–Sep	2014 Oct–Dec	2015 Jan–Mar	2015 Apr–Jun	2015 Jul–Sep
Infection rates	3.5	3.44	1.52	5.7	10.75	8.09	8.75	0	3.61
Interventions						(1)		(2)	(3)

Infection rates are expressed as numbers per 1000 catheter days.

Interventions: (1) A skin cover sheet was changed to gauze if an impermeable sheet was soaked with sweat (November 2014–). (2) The side tubes of three-way stopcocks in the central venous infusion tubes were wiped twice with alcohol before and after an injection (Apr 2015–). (3) Infection control nurses started the regular inspections of the condition of the cover sheet fixation, dressing intervals, and the use of protective gloves when changing the infusion tubes (September 2015–).

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Table 2 Comparison of factors between catheter-related bloodstream infection (CRBSI) and non-CRBSI cases

CRBSI	Yes	No	p
Number of catheters	27	690	
Age (years), mean ± SD	68 ± 15	68 ± 15	ns
Male/female	18/9	437/254	ns
APACHE II score, median [quartile range]	24 [8, 26]	18 [1, 23]	<0.01
Duration of ICU stay (days), mean ± SD	57.8 ± 49.1	14.5 ± 26.2	<0.05
Duration of catheter insertion (days), mean ± SD	14.4 ± 9.8	8.2 ± 14.1	<0.01
Number of lumens, n; median (min–max)	3 (2–4)	3 (1–4)	ns
Multiple catheter indwelling, n/total (%)	18/25 (72)	162/567 (28.6)	<0.01
Insertion sites, IJV/subclavian/femoral; n (%)	16 (61.5)/1 (3.8)/9 (34.6)	551 (83.0)/18 (2.7)/95 (14.3)	<0.05
Number of insertion attempts, n; median (min – max)	1 (1–3)	1 (1–5)	ns
Mechanical ventilation, n n/total (%)	17/20 (85)	371/634 (58.5)	<0.05

SD, standard deviation; min, minimum; max, maximum; IJV, internal jugular vein.

Mann-Whitney *U* and chi-square tests were used to analyze the differences between CRBSI and non-CRBSI cases, where appropriate. A p value of <0.05 was considered statistically significant.

S-222.

PRODUCTION PRESSURES AMONG ANAESTHESIOLOGISTS IN SINGAPORE

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INTRODUCTION: Production pressure has been described as the pressure on personnel to place production ahead of safety, as their priority. The authors assessed the prevalence of production pressures among anaesthesiologists in Singapore.

METHODS: A random online survey was conducted among anaesthesiologists in Singapore. Questions were asked about attitudes to production pressures in the work environment, occurrence of situations involving unsafe actions and rating on the intensity of external and internal sources of pressure.

RESULTS: There were seventy respondents. The demographics of the population were largely similar to the population of anaesthesiologists in Singapore, fairly distributed across various tertiary hospitals. Nearly half (45%) have witnessed production pressure with a colleague pressured to conduct anaesthesia in an unsafe manner. Such events include pressure from surgeons to proceed for elective surgery in patients without adequate optimisation, pressure to employ anaesthetic techniques that surgeons wanted, having to source for operating rooms to finish the list, and being misled regarding surgical time. More than half (52%) have made errors in clinical judgement due to excess workload. A heavy elective workload is significantly correlated with proceeding with cases despite lack of appropriate support, making changes to the practice to avoid delaying the start of surgery, sourcing for operating rooms to finish the surgeon's list ($P < 0.05$) and being pressured to proceed with cases that the anaesthesiologist would otherwise have cancelled ($P < 0.01$). The top ranked internal pressure is the need to avoid delaying the start of surgery, and that of external pressure is the need to reduce turnover time between cases.

CONCLUSION: Production pressure is prevalent among anaesthesiologists in Singapore and is correlated with a heavy workload.

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S-223.

ONE PATIENT'S CARDIAC ARREST IN THE OPERATING ROOM: SIX PERSPECTIVES ON EMERGENCY MANUAL USE, READER ROLE, AND TEAMWORK

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INTRODUCTION: Clinician memory degrades under stress, potentially causing inadequate management of perioperative complications and increased hospital mortality rates.[1-2] Research on simulated operating room (OR) critical events shows that using Emergency manuals (EMs), also called crisis checklists or sets of cognitive aids, improves team management actions and a reader role improves EM use.[3-8] Interest in EMs is increasing, with >25,000 downloads in 3 years of free tools linked from Emergency Manuals Implementation Collaborative (EMIC; www.emergencymanuals.org).a Yet, little is known about how clinical teams are using EMs during OR critical events[9-10] and team perceptions about the impact of EM use.

METHODS: Following systematic institutional implementation of perioperative EMs at a large academic medical center, we conducted a qualitative study, informed by an EM implementation framework (Creation, Accessibility, Training, and Culture)[7] to examine one successful EM use as an in-depth case study of a new patient safety tool (EM). The event was post-induction pulseless electrical activity cardiac arrest. In semi-structured interviews, all six OR clinicians (surgical attending, surgical resident, anesthesia attending, certified nurse anesthetist (CRNA), circulating nurse and surgical technician) described how the EM was used, including a reader role, facilitators and barriers to effective use, and perceived impacts of EM use. Questions were open-ended and phrased neutrally.

RESULTS: Thematic analyses of interviews suggest that all team members perceived EM use to have positive impacts, including decreasing stress and enhancing teamwork, with improved event management compared to similar events (Table 1). Each clinician was asked explicitly for any negative impacts or distraction from patient care, all reporting "none." Each clinician planned to use EMs during future critical events (Table 2).

CONCLUSIONS: This study identifies a 'bright spot' of clinical EM use, with a reader and leader during a critical event, in the context of a systematic institutional EM implementation. Clinicians emphasized how EM use enhanced both individual and team ability to function well under stress which may be of interest to ongoing EM implementations and trainings. Larger implementation and effectiveness studies are needed to further assess these themes, and more broadly find positive or negative impacts on patient management and outcomes in clinical settings.[11] EMs are symbiotic with rather than a replacement for good judgment, teamwork, and clinical skills, and may be a useful tool to help OR teams effectively deliver evidence-based care during critical events, given appropriate institutional implementation and training.

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FOOTNOTE:

a. EMIC steering committee communication

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Table 1. Major themes emerging from all six team members on emergency manual use -- with reader and event manager -- during one OR PEA cardiac arrest.[1]

Themes	Representative Quotations
Emergency Manual Use Decreased Stress by Confirming Management Actions	• **"[The EM] really helps you organize your mind and collect your thoughts** and **especially if too many emotional things going on, [EM helps] being in charge of the room**." (Anesthesia Attending, Event Manager) • "Going through [the EM] and making sure they've gone through each step. That they're not missing anything and **you get a sense that everybody kind of knows what to do.**" (Surgery Attending) • "The big thing was ruling out causes, **making sure that nothing was missed....to make sure that we were crossing our T's and dotting our I's**... to be able to look at this [the EM] and know, kind of, the next thing that we were going to do...**it was reassuring**." (Surgery Chief Resident, EM Reader) • **"I felt the anxiety level of the room go down at that point [using EM]** because [the anesthesia attending] did take control of the situation and because we have the book to go by...**[The EM] just brought you through the whole process which is very comforting."** (Surgical Technician) • "You felt like this is exactly what we have to be doing. There's nothing that we're doing that's wrong. **We're doing everything the way we're supposed to."** (Circulator RN) • "[Once the patient is stable], let's try to figure out the diagnosis. **This is what the EM is telling us, 'has anybody thought of this, have we done this yet?'"** (CRNA)
Emergency Manual Use Fostered a Calm, Organized Environment and Enhanced Teamwork, Enabling Improved Event Management	• **"[The EM] brought calm to the crazy."** (RN Circulator) • **"The [team] organization of the room was pretty clear**...rather than have people randomly call out well 'Did you get a blood gas?'" (Anesthesia Attending, Event Manager) • "As stressful as the situation was, I thought **[the anesthesiologist event manager and surgery resident reader] were really amazingly calm and sticking to [the EM]**. Everybody was really focused ..." (Surgery Attending) • **"The emergency manual helped to keep things on track** [and] was **helpful in keeping things under relative control**." (Surgery Resident, EM Reader) • "I thought from a code standpoint **it was very quiet, it was very controlled**... **We had a definitive team leader; you could hear him.** Nobody was speaking unless they had to." (CRNA) • "I think it was very good because nine times out of ten you have people yelling and screaming, I need blood. I need this. I need this. And **when you're following one person who is reading [from the EM], you all have to be quiet to hear. So I think it keeps the room noise down**." (Surgical Technician) • "Sometimes what happens during critical events...is that there isn't a huge amount of talking... among [team members]...**this [with EM] seemed nice because it did spur a [focused] conversation among all the members in the room."** (Surgery Resident, EM Reader) • **"[By using the EM] everyone becomes more focused and more efficient in their efforts.** And things are done in a proper fashion more expediently than they used to be. So that's what I find is different [about having EM]." (Surgical Technician)

1. All interview questions were open-ended and neutrally-phrased e.g. "How, if it all, did EM use impact teamwork or communication negatively or positively?"

Table 2. Clinician perspectives on use of emergency manuals during future critical events (self or colleagues)

OR Team Role	Role During Event	Representative Quotes
Anesthesia Attending	Event Leader	"I think **if we have an event**, I think as I said, **the plan [should be] to get 100% of people on board** to know that there is a manual that can be helpful to improve or at least organize your thoughts when there's an unfortunate event."
Surgery Attending	Chest Compressions	"I think **it was extremely helpful,** just, just to have something...**I was thinking about other people, surgeons who never did much critical care [training]...I'm all for it. I would never assume that a doctor knows everything."**
Surgery Chief Resident	Emergency Manual Reader	"In the future, **certainly if there are enough people involved in the code** able to assist anesthesia at that time, then **undoubtedly the next time we had one of these events I would definitely grab the manual, to make sure everything was moving in the right direction**... I think it's very reasonable to think that this would be something I'll grab immediately next time." **"Now I will use it in every other event that I'm involved with [because] I have experience using it. It was a positive experience and good for the patient. So, now I, moving ahead, will remember to do that and remind people around me to do that**."
CRNA	Clinical Tasks	**"I have used it during further critical events... at least one time [since]**."
Circulator RN	Clinical Tasks	**"It would be very helpful [in future events]. I think it's great.** I mean it's super easy to use especially I mean the front itself but even with the tabs. It's just it's very easy to read and if ...we know what's going on and we know what the issue is then we just kind of like flip through the page and boom, it's done." "For my knowledge, I think it's a great tool not only for the room for code. Also just for my own personal knowledge."
Surgical Technician	Clinical Tasks	"Sure. Yeah. **I wouldn't have a problem with [reading out loud from EM] at all.**"

S-224.

THE INCIDENCE OF INTRAOPERATIVE MAGNETIC RESONANCE IMAGING RELATED ADVERSE EVENTS DURING AWAKE CRANIOTOMY

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INTRODUCTION: Intraoperative magnetic resonance imaging (iMRI) guided neurosurgery with functional mapping under awake craniotomy contributes to maximal surgical resection with minimal risk of postoperative deficits when a pathological lesion is in or adjacent to the eloquent area. However in some cases, psychological and physiological stress caused by the awake craniotomy itself will trigger patient decline. An unsecured airway also becomes critical while the patient is awake. Additionally, the magnetically active environment of iMRI has disadvantages for patient safety management. The aim of this study is to examine the incidence of intraoperative adverse events during iMRI, which were performed while the patient's airway was not secured, as a part of awake craniotomy.

METHODS: Anesthetic charts and surgical records of all awake craniotomy cases conducted at our institution were retrospectively reviewed. The sequences of iMRI scans performed without invasive airways were selected. General convulsive seizure, respiratory arrest, emotional incontinence, and nausea/vomiting were evaluated as critical events. Types of adopted cardiorespiratory monitoring were also examined.

RESULTS: Between November 1999 and December 2015, a total of 371 awake craniotomies were carried out. The iMRI was used for 365 patients with 944 sequences, of which 580 sequences had pure oxygen supplied through a facial mask or nasal cannula. The average number and length of iMRI sequences without airway devices were 1.6 times per patient and 21 minutes, respectively.

Critical events occurred in 21 patients with 24 sequences: general convulsive seizures occurred in 6 sequences; respiratory arrest occurred in 2 sequences; nausea/vomiting occurred in 7 sequences; and emotional incontinence occurred in 9 sequences. The iMRI scan was emergently stopped due to patient decline in 4 cases; antiepileptic drugs were given to two seizure patients and invasive airway management was performed in the other 2 patients. Neither cardiac arrest nor accidental death occurred.

During iMRI, patient blood pressure, heart rate, and peripheral oxygen saturation were continuously monitored in 578, 578, and 555 sequences, respectively. Patient respiratory rate monitoring was poor and only used in 175 sequences. Conscious sedation was provided during 168 sequences with intravenous sedatives.

CONCLUSIONS: Remarkable technological advancement has increased the demand for iMRI-guided neurosurgery. Based on our 16-year experience, we consider that iMRI can be safely performed with careful observation even when a patient's airways were not secured.

S-225.

PNEUMOPERITONEAL AIR ENTRY DURING LAPAROSCOPIC SURGERY WITH VALVE-FREE TROCARS IN PIGS

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INTRODUCTION: In valve-less trocars, an active curtain of forced CO_2 gas insufflation[1] replaces the standard "trap door" physical valve. In order to preserve the pressure differential, a recycling system collects the escaping gas at the proximal end of the trocar and drives it back to the peritoneal cavity[2]. Use of a valve-less trocar might reduce the CO_2 use, absorption, and elimination and reduce the high pressure pneumoperitoneal stress[1,2]. Nevertheless, the absence of valve raises the question of sealing from room air, already questioned with conventional trocars[3,4]. Indeed, 3 to 5 mL/kg of venous air embolism during laparoscopy may be lethal[5]. The purpose of this preliminary, proof of concept animal study was to assess the presence of room air in the CO_2 pneumoperitoneum (PNOP) during laparoscopy with a valve-less insufflation system.

METHODS: The study was approved by the Ministry of Superior Education and Research (number 04297.01). One 35 Kg pig was premedicated with ketamine (20mg/kg) and azaperone (2 mg/kg) and then anesthetized with propofol (2mg/kg). Endotracheal intubation (Portex® 6 mm) was facilitated with rocuronium (0,6 mg/kg). Anesthesia was maintained with isoflurane (2 Vol%; O_2: 40% in air). Minute ventilation was adjusted to keep $P_{ET}CO_2$ between 34 and 40 mmHg. FiO_2, FeO_2, $P_{ET}CO_2$, Pimax and Fi/FET isoflurane were recorded every 5 min. The first 12mm valve-less port, for the optic (Air Seal®, Surgiquest), was inserted in the midline, using an open celioscopy approach and the PNOP was started. Subsequently, two 5mm ports (1 standard and 1 valve-less) were inserted in the abdominal cavity, under visual control. The gas composition of the PNOP was analyzed every 2 min (2 mL samples) for CO_2 and air, with a micro gas chromatograph (SRA, France) equipped with a short Tip Plot column and a nanothermal conductivity detector. After the initial insufflation of the PNOP, the standard trocar was used to successively create active aspiration (AA) or passive leakage (PL) periods of 2 min. These conditions were observed at two different PNOP pressures i.e. 8 and 12 mmHg. All conditions were followed with at least 10 min time intervals in order to allow for return to the baseline PNOP composition.

RESULTS: The initial PNOP insufflation volume of CO_2 was 3L. The insufflation flow rate rose to 10 L/min upon every PL or AA phase. An air fraction superior to 10% was measured after every study phase at both 8 and 12 mmHg PNOP and lasted at least for 6 min [Fig 1, 2]. With the 12 mmHg PNOP, the basal air fraction tended to stay above 4% [Fig 2]. The maximum measured air fraction in the PNOP was 73 % after 2 min PL with a PNOP pressure at 12 mmHg [Fig 2].

CONCLUSIONS: This preliminary experimental observation shows that entrance of air in the PNOP is possible with valve-free trocars during laparoscopy. Further investigations in experimental as well as in clinical conditions are needed in order to assess the relevance of this finding and the way to eventually solve potential related issues.

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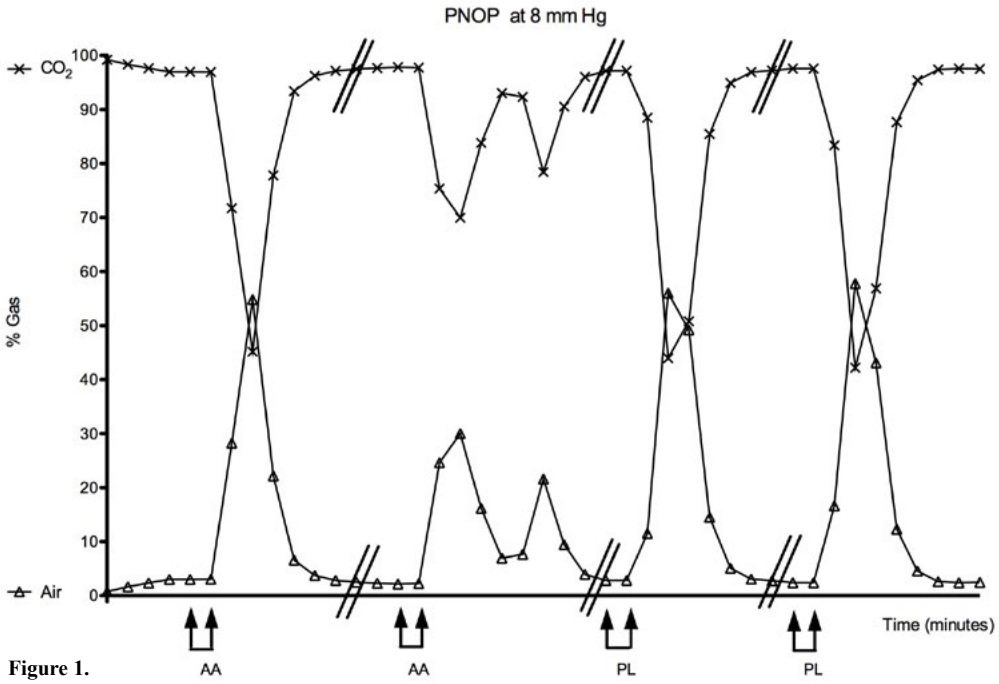

Figure 1.

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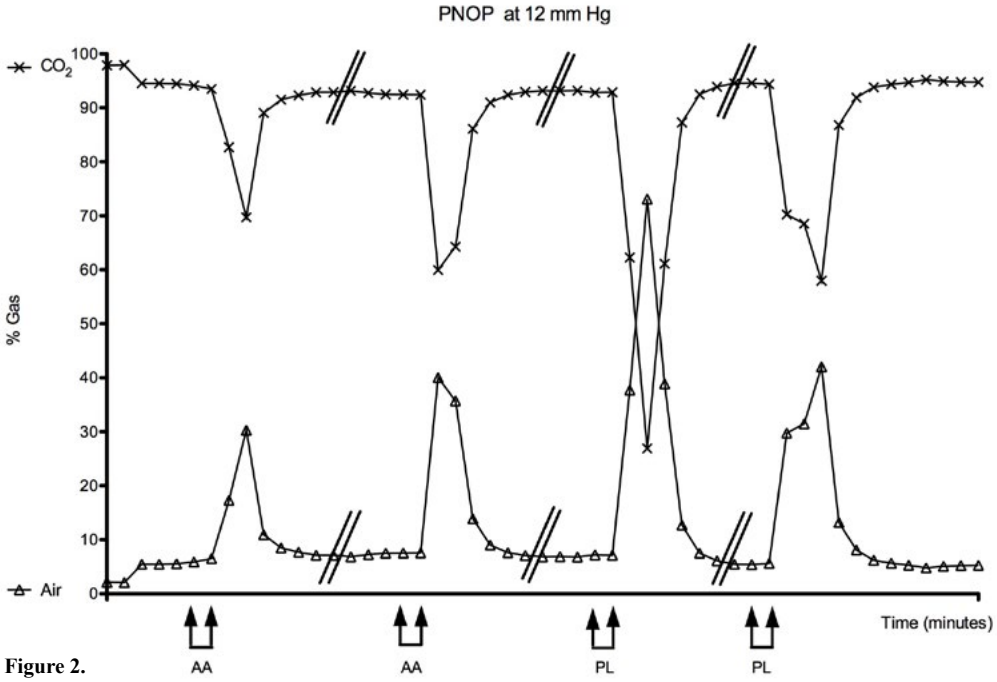

Figure 2.

S-226.

OVERNIGHT NON-INVASIVE RESPIRATORY VOLUME MONITORING FOLLOWING PACU DISCHARGE AFTER GENERAL SURGERY

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INTRODUCTION: Patients with high STOP-Bang (SB) scores have a high probability of obstructive sleep apnea (OSA) & are considered at greater risk for post-operative respiratory complications.[1] The most feasible perioperative monitoring for safe care, however, has yet to be determined. This study used a non-invasive respiratory volume monitor (RVM, ExSpiron, Respiratory Motion, Inc., Waltham, MA) to quantitatively measure tidal volume (TV), respiratory rate (RR) & minute ventilation (MV) in the PACU and through the first post-operative night (PON1) on the general hospital floor (GHF). Here we quantify the incidence of Low MV (LMV) in surgical patients with high (at-risk for OSA) & low (not-at-risk for OSA) SB scores. We also examined whether RR alone could identify periods of LMV.

METHODS: Following IRB approval & written informed consent, RVM data from 32 patients undergoing general surgery were collected in the PACU & during PON1. Patients were stratified into 2 groups by pre-operative SB score: ≥ 5 = 'at-risk' (A, moderate/severe OSA risk), < 5 = 'not-at-risk' (B, low OSA risk). We defined Adequate MV (AMV) as MV ≥ 40% of predicted MV (MV_{PRED}) based on a composite formula combining ideal body weight & body surface area, & LMV as MV < 40 % MV_{PRED}. We tracked AMV & LMV for 30-sec periods, and recorded MV, TV, and RR during each period. We compared differences in TV & RR between AMV & LMV periods using paired t-tests, with $p < 0.05$ considered significant.

RESULTS: 9 (28%) patients (group A; age 60.7 ± 9.2 yr; BMI of 37.0 ± 8.1 kg/m2) met 'at-risk' criteria & 23 (72%) patients (group B; age 58.8 ± 14.1 yr; BMI of 30.0 ± 6.3 kg/m2) were 'not-at-risk' for OSA. Group A was monitored for 17.1 ± 2.6 hr (PACU: 4.7 ± 4.4 hr; GHF: 12.4 ± 4.0 hr) & group B for 19.1 ± 2.4 hr (PACU: 4.3 ± 2.1 hr; GHF:14.7 ± 3.0 hr). The incidence of LMV in both groups was greater in the PACU vs the GHF (3.7 ± 0.5 vs 2.4 ± 0.4 LMV/hr). Group B experienced more LMV events per patient (2.6 ± 0.5 vs. 1.7 ± 0.6 LMV/hr), longer duration LMV episodes (113.2 ± 9.7 vs 93.2 ± 5.9 sec), & a longer duration of time with LMV (6.1 ± 0.5 vs 5.6 ± 0.4 min/hr) than group A (Fig 1, $p>0.05$ for all comparisons). During LMV episodes, MV decreased by ≥ 75%, from 107.2 ± 19.9% to 24.5 ± 4.3% MVPRED, primarily driven by a 65% decrease in TV from 474.2 ± 83.8 mL to 165.9 ± 29.3 mL & to a lesser extent by a 33% decrease in RR from 15.3 ± 2.7 bpm to 10.1 ± 1.8 bpm (Fig 2, $p < 0.05$ for all comparisons).

CONCLUSIONS: The incidence of LMV in this population was relatively low, even in high SB patients. As expected, LMV occurred more often in the PACU during recovery than on the GHF. Interestingly, patients with a low SB score had a trend towards more LMV episodes compared to those with a high SB score. Importantly, during LMV, the decrease in RR was less pronounced than the decrease in TV; RR was maintained > 6 bpm, likely not triggering common clinical RR alarm thresholds. Preliminary data suggest that SB < 5 patients may have a similar risk of LMV compared to SB ≥ 5 patients, & RR monitoring alone may be insufficient to detect LMV. Objective MV monitoring as part of standard postoperative care protocols has the potential to improve patient safety.

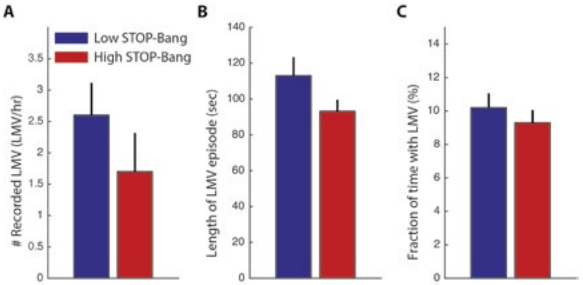

Figure 1: Comparison of LMV episodes in patients with High SB (group A; red) and Low SB (group B; blue). Panels show three metrics defining the incidence of LMV: **(A)** average number of recorded LMV per hour, **(B)** average length of individual LMV episodes and **(C)** fraction of time patients spent with LMV. Results indicate group B has a higher likelihood for LMV and spends a longer duration of time with LMV, but differences were not significant ($p > 0.05$ for all 3 panels).

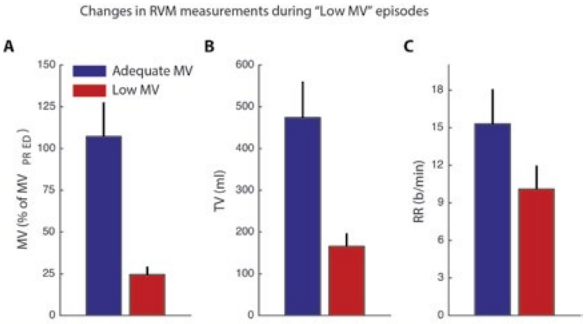

Figure 2: Changes in RVM metrics from periods of Adequate MV (blue) to periods of "Low MV" (red). Panels **(A)** MV, **(B)** TV and **(C)** RR show the observed metrics during the 2 types of periods. Note that in producing these plots we first calculated patient average MV, TV and RR and then averaged these values across patients to get the height of each bar and computed the SEM across patients for the error bars. Reported RVM values during LMV are based on the data from patients having LMV and the SEMs and statistics are computed accordingly ($p < 0.05$ for all 3 comparisons).

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S-227.

BLOOD PRESSURE READINGS: DOES CUFF SIZE MATTER?

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INTRODUCTION: The American Heart Association provides specific recommendations for selecting correct sizes of blood pressure (BP) cuff based on the patient's upper arm circumference. The most common mistake is an inappropriately selected cuff, which results in inaccurate BP measurement.[1,2,3] False high or low BP measurement might lead to misclassification of patients being either hypertensive or hypotensive. If healthcare providers and their support staff continue to select the wrong size BP cuff, such a trend will lead to negative outcomes and potential injury to the patients. In our clinical practice, we continue to see patients presenting to the operating room with inappropriately sized BP cuffs.

METHODS: The sample (n=76) consisted of adult volunteers with or without history of hypertension. Each participant was given 5 minutes of rest time (sitting comfortably in a chair) prior to initial reading of BP. Automatic BP reading machine was used for this study. BP readings were obtained using 3 different size(sz) BP cuffs (small adult sz 10, adult sz 11, and large adult sz 12L) on each participant. Each reading was obtained sequentially with 2 minutes rest periods starting with the smallest cuff. For participants with arm circumference > 32cm, only 2 readings took place (sz 11 and 12L cuff). BP readings were taken exclusively on the left upper arm. Participants with contraindications of a left arm BP cuff placement were excluded from this study.

RESULTS: Seventy-six (22 male, 54 female) adult volunteers provided verbal consent and completed the study. The average age was 42 (ago 23 -71) with a mean of arm circumference 29 cm (22-35.5cm). 16 participants reported a history of hypertension. The results are shown in Table 1.

CONCLUSION: In our pilot study, differences in BP readings were affected by the selected BP cuff sizes. Inappropriate BP cuff size resulted in either higher or lower BP reading supporting the evidence that too small BP cuff results in erroneously higher reading while too large BP cuff results in lower reading. When the cuff is too large for the patient's arm, the average difference in reading may result in hypotensive reading. It is imperative for the staff to select appropriate size BP cuff to obtain accurate reading while providing safe and quality patient care, especially with the rise of obesity.

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Table 1

Subgroup	Difference size 10 vs 11 BP cuff	Difference size 10 vs 12L BP cuff	Difference size 11 vs 12L BP cuff
Small size 10 BP cuff SBP, n (mean*, SD, 95% CI), p-value DBP, n (mean*, SD, 95% CI), p-value	19 (-1.52; 11.3; -7.17-4.12); .03 19 (1.05; 5.9; -1.89-3.99); .07	19 (4.74; 12.5; -1.21-10.6); <.001 19 (3.37; 6.9; .29-6.4); <.001	20 (6.6; 9.5; .65-12.5); <.001 20 (2.8; 6.4; -.27-5.87); .003
Adult size 11 BP cuff SBP, n (mean*, SD, 95% CI), p-value DBP, n (mean*, SD, 95% CI), p-value	31 (5.03; 6.7; 2.56-7.5); <.001 31 (2.84; 5.08; .97-4.7); <.001	31 (9.2; 8.81; 6.7-11.8); <.001 31 (7.8; 6.89; 5.28-10.3); <.001	49 (6.4; 7.4; 4.28-8.52); <.001 49 (4.1; 7.65; 1.84-6.24); <.001
Large size 12L BP cuff SBP, n (mean*, SD, 95% CI), p-value DBP, n (mean*, SD, 95% CI), p-value	 0 0	 0 0	7 (6.14; 7.27; .58-12.86); <.001 7 (4.86; 5.55; -2-20.58); <.001

*Reported in mm Hg

S-228.

IMPROVEMENT IN ADHERENCE WITH LUNG PROTECTIVE VENTILATION STRATEGY IN ONE-LUNG VENTILATION: THE ASSOCIATED BYPRODUCT OF CHANGES MADE TO DEFAULT VENTILATOR SETTINGS AND COGNITIVE AID DEVELOPMENT

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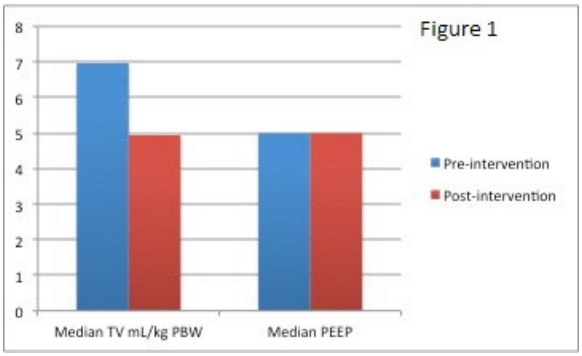
INTRODUCTION: Patients undergoing one-lung ventilation (OLV) for thoracic surgery are at increased risk for post-operative pulmonary complications.[1] Lung protective ventilation (LPV) strategies have been shown to reduce the risk for acute lung injury in two-lung ventilation (TLV)[2], but there are few studies on LPV during OLV. We hypothesized that a change in default ventilator settings and a cognitive aid focused on LPV for TLV would result in an increase in adherence with LPV strategy for thoracic surgical patients with OLV, specifically tidal volume (TV) 4-6mL/kg predicted body weight (PBW) and PEEP 3-10cmH_2O.[3]

METHODS: Pre-intervention default ventilator settings were TV=600 mL and PEEP=0 cmH_2O. These were changed to TV=440 mL and PEEP=5 cmH_20 on all anesthesia ventilators in our department. A cognitive aid displaying PBW for height and gender and the associated TLV TV in mL was attached to each anesthesia machine. There was no specific intervention made for thoracic surgeries with OLV. Patients undergoing thoracoscopy or thoracotomy from 3-month periods both pre- and post-intervention were identified. Ventilator data was queried from the electronic medical record database retrospectively with IRB approval. The lowest set TV was identified as the initiation of OLV in each group. This TV in mL/kg PBW, PEEP, percentage of patients receiving >6mL/kg PBW and percentage of patients receiving PEEP < 3 cmH2O were determined for each group. No patient received PEEP > 10 cmH_2O.

RESULTS: The pre-intervention group (N=36) showed a median TV = 7 mL/kg PBW and 69% of patients receiving > 6mL/kg PBW on OLV. The post intervention group (N = 27) showed a median TV = 4.9 mL/kg PBW and 26% >6mL/kg PBW on OLV (Figure 1). The differences between these two groups were statistically significant. There was a 43% percent reduction in patients receiving > 6mL/kg on OLV after the intervention. There was no statistically significant difference in the use of PEEP 3-10 cmH_2O on OLV between the two groups.



CONCLUSIONS: Our data show that a department-wide change in default ventilator settings and implementation of a cognitive aid aimed at PLV strategies for TLV has the added benefit of increasing adherence with PLV strategies in OLV anesthetics. Though there are few studies focusing on OLV ventilator management, the general consensus is 4-6mL/kg PBW with PEEP 3-10cmH2O resulting in fewer patients with post-operative pulmonary complications.[3,4] Thoracic surgery and lung isolation present several challenges to the anesthesiologist. This study demonstrates that a cognitive aid and systematic departmental approach to improve ventilator management for all surgical patients has the potential added benefit of improvement in safety with this challenging and high-risk subset of patients.

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S-229.

ADJUSTMENT OF DEFAULT VENTILATOR SETTINGS AND COGNITIVE AID IMPLEMENTATION IMPROVES ADHERENCE TO LUNG PROTECTIVE VENTILATION STRATEGY DURING CARDIAC SURGERY

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INTRODUCTION: Intraoperative lung protective ventilation (LPV) employing tidal volume (TV) size reduction and adequate PEEP use has become increasingly accepted.[1] Specifically in cardiac surgery patients, the use of TV = 6mL/kg PBW (Predicted Body Weight) has been shown to increase the proportion of patients free from postoperative ventilation at 6 hours and reduce reintubation rate compared to those receiving TV = 10mL/kg PBW.[2] End-organ dysfunction is also more likely after cardiac surgery in patients receiving TV > 10mL/kg PBW.[3] We hypothesized that a change in default ventilator settings and implementation of TV cognitive aids would lead to greater adherence to LPV recommendations in cardiac surgery patients.

METHODS: IRB approval was obtained for this retrospective observational study. Pre-intervention default ventilator settings were TV = 600mL, PEEP = 0cmH_2O. These were changed to TV = 440mL, PEEP = 5cmH20. Cognitive aids for PBW and decision support programs to alert for TV > 10mL/kg PBW were employed in each OR. Cardiac surgery patients from 3-month periods pre- and post-intervention were identified. Ventilator data was queried retrospectively. Average median TV (mL/kg PBW), average median PEEP (cmH_2O), percentage of patients receiving TV > 10mL/kg PBW, and percentage of patients receiving PEEP < 5cmH2O were determined. Differences in average median TV was assessed by homoscedastic student's t-test. Differences in average median PEEP was assessed using Wilcoxon rank sum test. Differences in percentage of cases with median PEEP < 5cmH_2O and cases with TV > 10ml/kg PBW were analyzed by Fisher's exact test.

RESULTS: Comparing pre-(n=107) and post-(n=143) intervention groups, there was a difference in average median TV (7.4 - 6.9 mL/kg PBW, p<<0.001), average median PEEP (4.7 - 5.3 cmH_2O, p=0.009), and the percentage of patients receiving PEEP < 5cmH_2O (22.4% - 4.9%, p<0.001). There was a trend towards reduction in the percentage of patients receiving TV > 10mL/kg PBW (2.8% - 0.0%, p=0.077). (Figures 1 and 2)

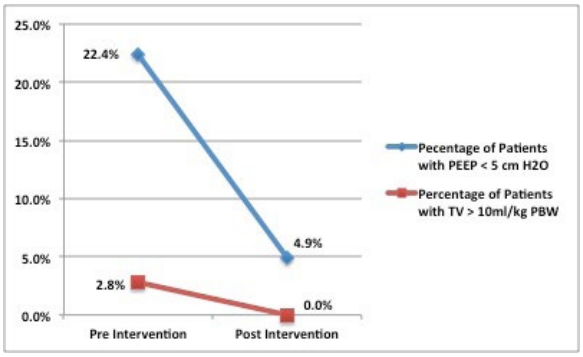

Figure 1.

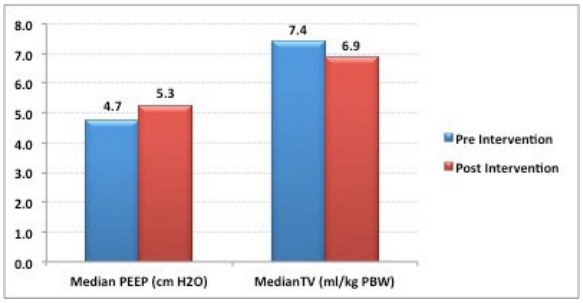

Figure 2.

CONCLUSIONS: Our data show that an increase in adherence to LPV strategy can be attained utilizing the combination of cognitive aid decision support and adjustment of default ventilator settings. There have been numerous recent publications regarding intraoperative LPV strategy in various surgical populations, but the true efficacy of LPV has yet to be fully elucidated in cardiac surgery patients. However, evidence suggests larger tidal volumes and inadequate PEEP could lead to increased complications. This study demonstrates that a thoughtful multi-pronged approach to intraoperative ventilation can lead to change in practice and possibly safer intraoperative ventilation of cardiac surgical patients.

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S-230.

WHAT IS THE MOST EFFECTIVE WAY TO CHANGE NEOSTIGMINE DOSING PRACTICE? INSIGHTS FROM A QI INITIATIVE TO OPTIMIZE THE USE OF NEUROMUSCULAR BLOCKING AGENTS

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INTRODUCTION: Residual neuromuscular blockade (rNMB), defined as a train-of-four (TOF) ratio <0.9, is a persistent issue with a reported incidence between 20 and 50 percent. Optimal reversal requires neostigmine administration guided by TOF-readings. Excessive doses of neostigmine are harmful since a depolarizing neuromuscular block can occur when it is given in the absence of adequate twitches. In an effort to encourage TOF-based dosing of NMBs and neostigmine, a multi-faceted quality improvement initiative (QII) was piloted and its efficacy evaluated.

METHODS: A three-part QII to improve TOF-based dosing of NMB and neostigmine was instituted from April 1 to September 1, 2015 in a large academic anesthesia department. The QII consisted of: 1. Department-wide education to define the incidence and consequences of rNMB and unwarranted use of neostigmine; 2. The creation, tracking, and incentivization of an anesthesia information management system (AIMS)-based QI metric measuring documentation of TOF prior to administration of neostigmine; and 3. A change in the available dose of neostigmine in anesthesia carts from 5mg vials to 3mg pre-filled syringes. For surgical procedures in which non-depolarizing NMBs were administered, we reviewed AIMS data to determine the dose of neostigmine administered. Baseline data prior to the initiative was compared to data from the QII. Mann-Whitney-U test and Chi-Square test were used for significance testing.

RESULTS: During the study period, 14,135 anesthetics included the administration of both NMBA and neostigmine. The percentage of cases receiving both NMBA's and subsequent neostigmine reversal intraoperatively did not differ pre vs. post QII (3,425 [29.8%] vs. 10,710 [29.4%]; p=0.370). Following the QII, there was a significant decrease of the mean total intraoperative neostigmine dose from 2.9mg to 2.5mg (p<0.001). Furthermore, the upper adjacent value of the total neostigmine dose decreased from 7mg to 4.5mg. In addition, there was a significant increase in the documentation rate of the TOF prior to the administration of neostigmine, from 60% to 75% of cases (p<0.001).

CONCLUSIONS: The implementation of a multi-faceted QII substantially reduced the excessive use of neostigmine and improved TOF-guided neostigmine administration.

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S-231.

INTRAVENOUS AIR: THE PARTIALLY INVISIBLE PHENOMENON

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BACKGROUND: Air injection is avoided during intravenous (IV) solution administration; however, dissolved ambient air is in all liquids used for IV therapy. A portion of this air will necessarily come out of solution in the form of bubbles as the solution is warmed/warms to body temperature. We sought to calculate the amount of dissolved air that should theoretically come out of solution upon warming of room temperature crystalloid and 4°C blood products to 37°C, and subsequently compare these calculated values with experimental measurements of outgassed air volumes for these fluids.

METHODS: Equilibrium dissolved air calculations were carried out for sodium chloride (0.9%), packed red blood cells, and fresh frozen plasma at various temperatures according to Henry's Law. Outgassed air volumes were experimentally measured for room temperature sodium chloride (0.9%) and 4°C blood products (packed red blood cells and fresh frozen plasma) warmed to 37°C during infusion into a body temperature water bath. The measured air volumes were quantified as a fraction of the theoretical outgassing volumes required to maintain equilibrium gas saturation.

RESULTS: Theoretical (calculated) outgassed air volumes required to maintain equilibrium saturation at 37°C are 4.7 cc/L for sodium chloride (0.9%), and for the colder starting temperature blood products: 8.3 cc/L for packed red blood cells and 10.9 cc/L for fresh frozen plasma (Table 1). Measured outgassed air volumes in the IV tubing were 1.4 ± 0.3 cc/L (n = 6) for sodium chloride (0.9%), 3.4 ± 0.2 cc/L for packed red blood cells (n = 6), and 4.8 ± 0.8 cc/L (n = 6) for fresh frozen plasma when these fluids were warmed to body temperature from their respective starting temperatures (Table 2). As a fraction of the theoretically available outgassing volumes, the actual outgassed measured air volumes represented 30%, 41%, and 44% for sodium chloride (0.9%), packed red blood cells, and fresh frozen plasma, respectively.

CONCLUSIONS: This in vitro study quantifies the significant and potentially clinically relevant amount of the resident dissolved gas in room temperature crystalloid, and 4°C packed red blood cells and plasma solutions that comes out of solution in the form of collected bubbles upon warming to 37°C body temperature.

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Table 1. Calculated dissolved gas in IV fluids at typical storage and body temperature[a]

Fluid Type	Liquid Temperature (°C)	Dissolved Oxygen[b]	Dissolved Nitrogen[b]	Total Dissolved[b]
Sodium chloride (0.9%)	20	7.3	13.6	20.9
Sodium chloride (0.9%)	37	5.5	10.7	16.2
Packed red blood cells	4	7.2	12.9	20.1
Packed red blood cells	37	4.0	7.8	11.8
Fresh frozen plasma	4	9.5	16.9	26.4
Fresh frozen plasma	37	5.3	10.2	15.5

a Calculated values for the dissolved volumes (normalized to 37°C) of oxygen, nitrogen, and total air per liter of fluid at atmospheric pressure and relevant temperatures for IV fluid administration. Dissolved quantities are reported for sodium chloride (0.9%), packed red blood cells (~70% water), and fresh frozen plasma (~92% water).
b Cubic centimeters of named medium per liter of fluid.

Table 2. Experimental outgassed air collection results[a]

Fluid	Fluid Start Temp (°C)	Fluid Final Temp (°C)[b]	Average Outgassed air volume ± SD[a], n = 6	% of Predicted Outgassing[c]
Sodium chloride (0.9%)	20.5	20.2	0.1 ± 0.0	n/a
Sodium chloride (0.9%)	20.7	37.0	1.4 ± 0.3	30
Packed red blood cells	4.0	37.1	3.4 ± 0.2	41
Fresh frozen plasma	4.0	36.9	4.8 ± 0.8	44

a Total collected air data for each test case reported as cubic centimeters of air/liters of fluid.
b Cubic centimeters of named medium per liter of fluid.
c % of predicted outgassed accommodates calculated expected remaining dissolved gas.

S-232.

TEMPERATURE AND HUMIDITY OF INSPIRED ANESTHETIC GASES INCREASED USING METABOLIC FRESH GAS FLOW (0,35 L/min). AS LOWER THE FRESH GAS FLOW - AS HIGHER THE TEMPERATURE AND HUMIDITY OF INSPIRED ANESTHETIC GASES

AUTHORS: C. W. Hoenemann[1], M. Ruebsam[2]

AFFILIATION: [1]Anesthesia and Critical Care, Marienhosital Vechta, Vechta, Germany, [2]Anesthesia and Critical Care, St. Marienhospital Vechta, Vechta, Germany

INTRODUCTION: The importance of anesthetic gas conditioning for anesthetised patient has been known. Disabling the upper airway and respiratory tract by a laryngeal mask or an endotracheal tube, prevents nose and mouth completely from performing ist physiological functions (humidifying and warming of inspired gases). Inadequate inspired gas conditioning reduces mucociliary chearance. The consequences of inadequate breathing gas conditioning may be morphological damage to the respiratory tract epithelium, resulting, in secretory reflux, obstruction of the bronchioles and the encouragement of microatelectases.

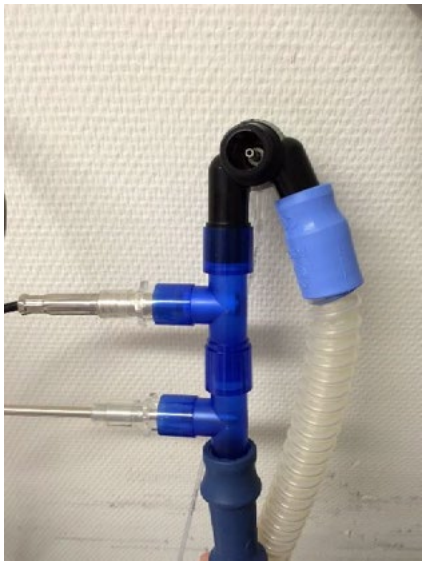
A specific characteristic of an anesthesia circuit systems is a carbon dioxide Absorber. It chemically removes and binds exhaled CO_2 from the exspired breathing gases within the re-breathing circle system. From this chemical reaction, heat (ΔT) and moisture (H_2O) is generated and increases respiratory air conditioning of the breathing gas in the circuit system.

METHOD: To measure these effects, three groups with different fresh gas flows were compared. 6 or 2 L/min and 0,35 L/min. In the 6 L and 2 L group fresh gas flows were retained over the course of anaesthesia. In the 0,35 L/min group, the inhalational anaesthetic (sevoflurane) was washed into the circuit System with a fresh gas flow of 1 L/min (low flow anesthesia). Once 0.9 MAC was reached, the fresh gas flow was reduced to 0.35 L/min (metabolic flow anesthesia). We measured humidity and temperature of the anesthetic gases at the Y-piece in the inspiratory limb of the anaesthesia circuit (Primus/Apollo, Draeger, Germany, Fig. 1).

RESULTS: The humidity and temperatur of inhaled anesthetic gases significantly increased depending on the diales in fresh gas flow ($p < 0,01$, t-test). In short: As lower the fresh gas flow, as higher the humidity and temperature of the inhaled gases (Fig. 2+3) in the circuit system.

DISCUSSION: During prolonged anesthesia, an absolute humidity above 17 mg H_2O/kg with an anaesthetic gas temperature of at least 26°C should be provided. These demands are met by metabolic flow anaesthesia (0,35 L/min): After 15 minutes the desired absolute humidity was established and after one hour the required warming of the breathing gas was achieved. In contrast, high flow anesthesia (2 - 6 L/min fresh gas flow) was not able to increase respiratory air conditioning of inspired breathing gas, in fact thes fresh gas flows decreased humidity and temperature.

CONCLUSION: When ever possible the fresh gas flow should be reduced down 0.5 - 0,35 L/min.



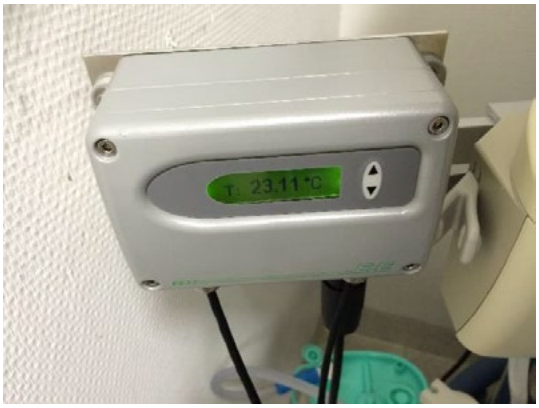


Fig. 1

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Fig. 3

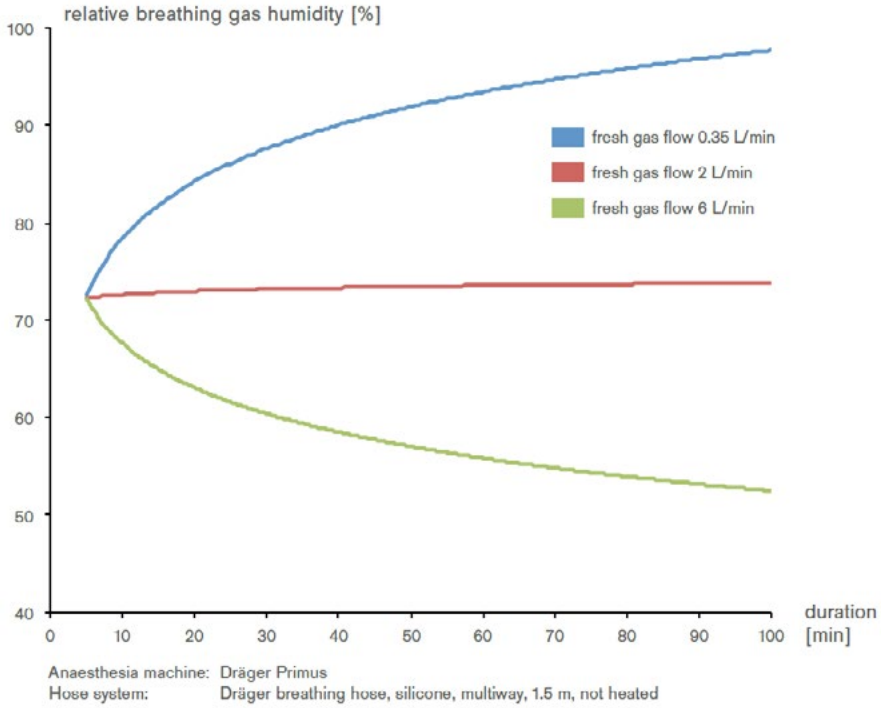
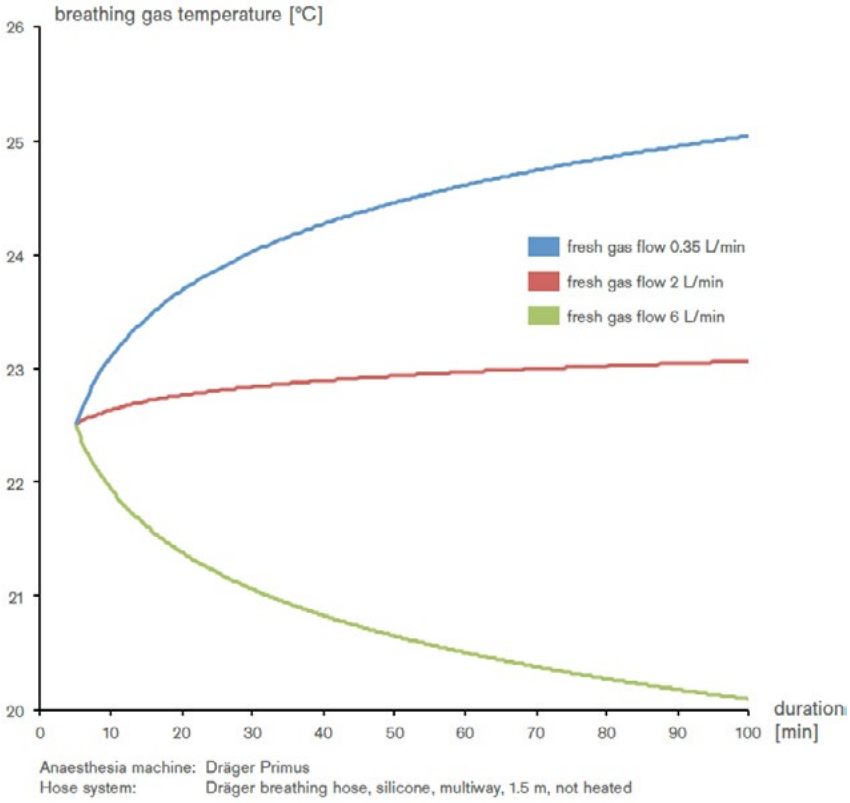


Fig. 2.



S-233.

RAPID ASSESSMENT OF PULMONARY ASPIRATION RISKS USING THE PREOPERATIVE ABDOMINAL CT SCAN

AUTHORS: G. J. Bordelon, J. Diaz, J. Riopelle, A. D. Kaye

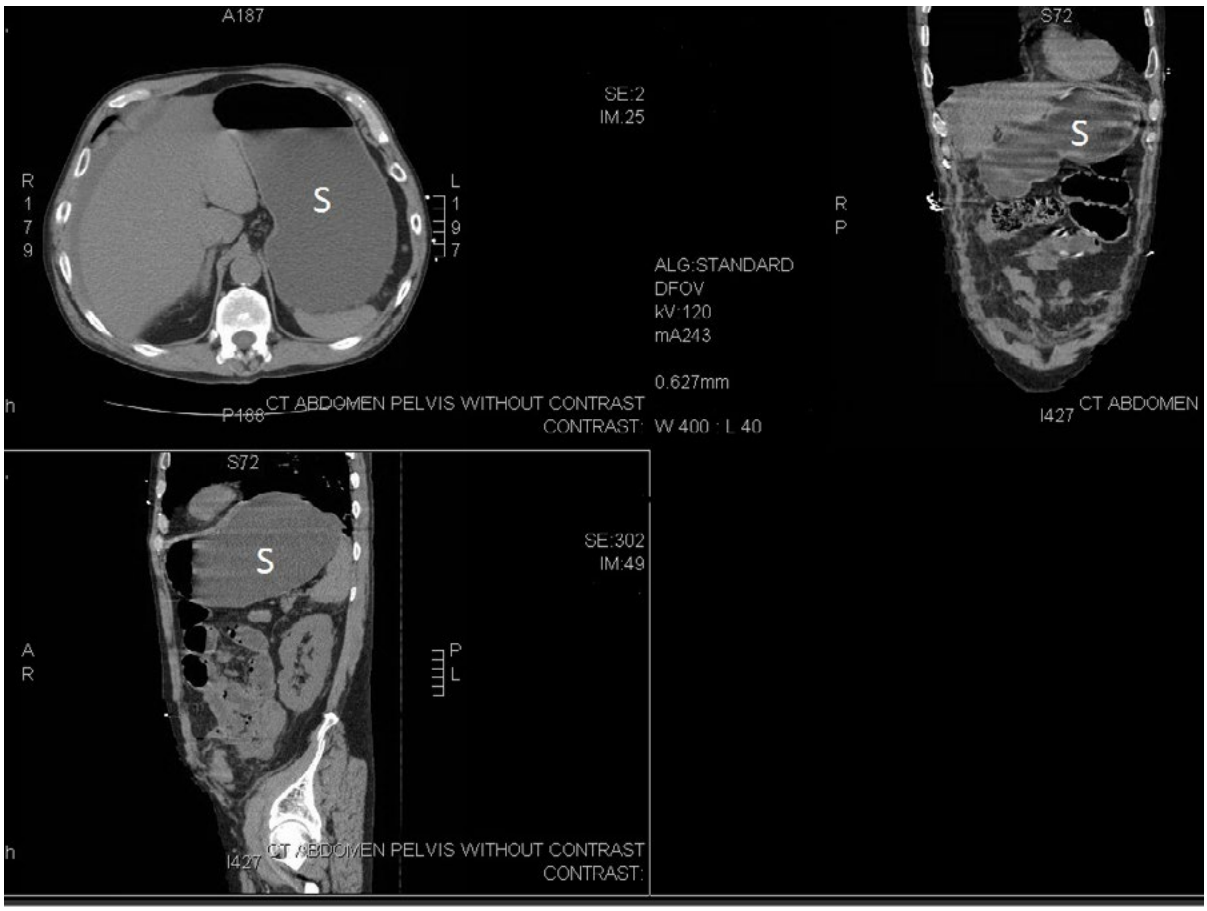
AFFILIATION: Anesthesiology, LSU School of Medicine, New Orleans, LA

INTRODUCTION: Pulmonary aspiration of stomach contents, either particulate or liquid gastric contents, is associated with significant morbidity and mortality and is the most common cause of adult respiratory distress syndrome. The risk factors for pulmonary aspiration, however, are not always evident preoperatively, especially in high-risk patients in emergency situations. These patients are often unconscious and cannot give a reliable medical history, may be taking medications, or have painful surgical conditions that delay gastric emptying.

METHODS: Since the abdominal computerized tomographic (CT) scan has now replaced the abdominal "scout" X-ray in the preoperative radiographic assessment of patients presenting with acute surgical abdomens, we have reviewed the use of abdominal CT scan for a visual assessment of the volume of gastric contents and an objective measure of pulmonary aspiration risks on induction of general anesthesia.

RESULTS: Abdominal 2-D grayscale ultrasound scanning can help identify patients with full stomachs. Sonographic measurement of the cross sectional area of the gastric antrum correlates linearly with gastric volume. However, these measurements were only studied in healthy patients and accurate for volumes up to 300 ml.

CONCLUSION: In the setting of acute abdominal pathology, CT imaging may be better at estimating gastric volume. In many instances, extremely high-quality scanned information regarding gastric contents may already be available from recent abdominal CT scans. Most patients who present with acute surgical abdomens will have CT imaging performed prior to arriving to the operating room. The anesthesiologist should review the imaging specifically focusing on imaging of the stomach for increased gastric contents. We recommend a routine re-interpretation of any recent abdominal CT scans in all patients undergoing general anesthesia for exploratory laparotomies for acute surgical abdomens. Preoperative gastric decompression should be considered after reviewing the CT or ultrasound imaging. If the stomach appears full on the CT, gastric drainage should precede prior to tracheal intubation.



S-234.

IMPACT OF SURGICAL SPECIAL CARE UNITS: A SYSTEMATIC REVIEW

AUTHORS: N. Mendis[1], G. M. Hamilton[1], D. I. McIsaac[2], D. Fergusson[3], H. Wunsch[4], A. Turgeon[5], M. M. Lalu[6]

AFFILIATION: [1]Anesthesiology, University of Ottawa, Ottawa, Ontario, Canada, [2]Anesthesiology, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada, [3]Medicine, Surgery, & Epidemiology and Community Medicine, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, [4]Anesthesia and Critical Care, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada, [5]Anesthesia and Critical Care, Universite Laval, Quebec, Quebec, Canada, [6]Anesthesiology, The Ottawa Hospital, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

INTRODUCTION: Perioperative intermediate care units (termed surgical special care unit, or SSCU) may improve surveillance and identification of at-risk surgical patients. Institution of an SSCU may lead to global improvements across patient outcomes, as well as reduce the workload and financial burden at a systems level. We conducted a systematic review in order to investigate the effects of a 3-level model of care delivery (i.e. ward, SSCU, ICU) compared to a 2-level model of care (i.e. ward, ICU) on post-operative mortality, morbidity, and healthcare resource utilization.

METHODS: Our protocol was registered with PROSPERO (CRD 20154025155). Randomized controlled trials (RCTs) and non-randomized comparator studies (NRCTs) that compared a three vs two level model of care of perioperative non-cardiac surgery patients were included. A systematic search of Medline, CINAHL, Embase, and the Cochrane library was performed (inception-01/2015). Retrieved citations were screened and data extracted independently in duplicate. Data were extracted for mortality (primary outcome) as well as serious adverse events (SAEs), length of stay, and hospital costs (secondary outcomes). We planned pooling data (relative risk) using random effect models with the DerSimonian and Laird method, if applicable.

RESULTS: 1868 citations were retrieved by our search and 21 studies met eligibility criteria (2 RCTs, 19 NRCTs, 44134 patients). SSCUs were characterized by continuous monitoring (11 studies), absence of mechanical ventilation (7 studies), nursing:patient ratios (range 1:2-1:4), and number of beds (5, 3-33; median, range). Thirteen studies reported on mortality, three of which reported overall in-hospital mortality in a 2 vs. 3-level model of care. Significant methodological heterogeneity precluded pooled analysis, however two of the three studies demonstrated no difference in overall hospital mortality, and one demonstrated an increased mortality in a 3-level model of care vs 2-level model. Four studies reported ICU-specific mortality, two of which demonstrated an increased ICU mortality in a 3-level model of care. Four studies compared total in-hospital costs, two of which demonstrated reductions with a 3-level model of care. Nine studies reported on hospital length of stay and demonstrated no significant difference. Four studies reported SAE data, however heterogeneity in reporting precluded analysis.

CONCLUSIONS: In this first systematic review of SSCUs, we observed significant heterogeneity in SSCU design and reporting of outcomes. Available data may suggest a 3-level model of care may increase in-ICU mortality with no difference in overall in-hospital mortality. This may reflect a 'decanting' of lower acuity patients from the ICU to the SSCU in a 3-level model of care. The potential effects of a 3-level model of care on hospitalization costs warrants further investigation.

S-235.

REB CONSENT FORM TEMPLATE DISCLOSURE ELEMENTS: AGREEMENT AND COMPLIANCE WITH BIOETHICS STANDARDS

AUTHORS: T. C. Denisuik, A. J. Villafranca, C. Hamlin, C. Christodoulou, E. Jacobsohn

AFFILIATION: Anesthesia and Perioperative Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

INTRODUCTION: Valid informed consent in research requires that participants are adequately informed[1]. Adequate disclosure is facilitated in steps: 1) Ethicists outline key disclosure elements; 2) REBs create research consent form templates, which disseminate elements to researchers; 3) Researchers use these templates to determine what should be disclosed to participants. Research participants are often under-informed[2,3]. Poor templates could cause this by disrupting the flow of information from ethicists to participants. Therefore, we aimed to determine how well: 1) templates comply with a recommended disclosure standard; and 2) REBs agree amongst themselves regarding which disclosure elements to include in templates.

METHODS: We derived a disclosure standard from ten seminal research ethics documents and evaluated disclosure elements from 94 REB templates across six countries. Overall REB compliance and agreement were calculated using social network methods. We also measured the number of REBs with perfect compliance and the number of elements agreed upon by all REBs. We thematically categorized elements using a process involving standardized theme definitions, multiple classifiers and an evaluation of inter-classifier reliability. Poisson regression models evaluated whether either compliance and/or agreement depended on element theme. Statistical analysis was done using UCINET and SPSS.

RESULTS: From the ten seminal ethics documents we identified 42 unique disclosure elements, 100 additional elements were identified from the 94 templates, resulting in 142 unique elements. Overall REB compliance with the disclosure standard was moderate (63.6%, 95% CI =63.3-63.8)[5,6]. No REB included all recommended elements (0%, 95% CI=0-8.4%). Out of all possible agreements amongst REBs, 22.8% (95% CI=22.7-22.9) were realized, which is no better than chance (p=0.96). Only 1/142 elements, "The name of the principal investigator", was included by all REBs (0.7%, 95 CI=0.7-2.0). Inter-classifier reliability for the thematic categorization of elements was excellent (κ=0.95). The overall compliance and agreement varied significantly depending on theme (both p<0.001). Agreement was especially poor for key themes, such as "risks of participation" (Figure 1).

CONCLUSIONS: REBs did not provide adequate information to participants. On average, templates were missing 33% of the recommended elements. The elements included by REBs were also highly variable. REBs must ensure that their templates contain all the required elements. Elements should also be harmonized across REBs internationally.

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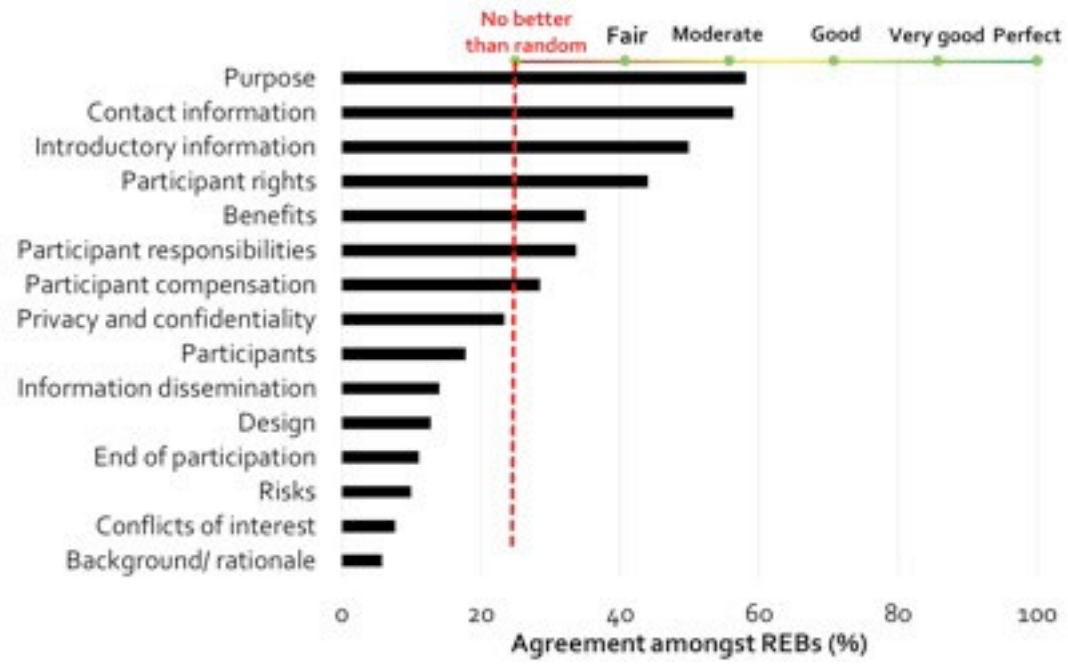

S-236.

DRUGS ERRORS BEFORE AND AFTER IMPLEMENTATION OF A BARCODE BASED ANESTHESIA DRUG SAFETY SYSTEM

AUTHORS: A. Bowdle, S. Jelacic, B. Nair, K. Togashi

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INTRODUCTION: Anesthesia drug errors occur at a rate of 0.5-1% based on studies of self-reported errors[1]. Direct observation studies have reported higher rates of error[2]. Recently we implemented a barcode-based system in which vial barcodes are scanned to produce syringe labels with bar codes and the syringe label barcodes are scanned prior to administration, generating voice feedback of the medication name. In this study we have compared the drug errors reported before and after introduction of the system.

METHODS: Using the computerized anesthesia information system's quality assurance data capture tool, drug error data were recorded from every anesthetic from February 5, 2014 to December 31, 2015, a total of 38,852 cases. Of these cases, 14,576 were performed before and 24,276 were performed following the implementation of the barcode-based system. Errors were classified using the same taxonomy as in a previous landmark study[1]. Actual errors were distinguished from "near errors" that were recognized by the provider and avoided "just in time".

RESULTS: The rate of error prior to introduction of the barcode-based system was 0.47% (59 errors/14,576 cases); there were also 10 near errors (0.069%). Following introduction of the system the rate of error declined significantly to 0.23% (55 errors/24,276 cases) (p=0.002); there were also 6 near errors (0.025%). The number of errors associated with vial or syringe swaps decreased from 10 (10/14576 = 0.069%) prior to introduction of the system to 4 (4/24276 =0.016%) afterwards (p=0.01). Infusions were involved in 10 errors before and 26 errors and 2 near errors after introduction of the system, despite the use of "smart pumps" with built-in drug libraries throughout the study.

CONCLUSIONS: The barcode-based system was designed primarily to prevent vial swap (by reading the barcode on the vial prior to making a label) and syringe swap (by reading the barcode on the syringe prior to drug administration) errors. This is the first study to show an unequivocal reduction in drug errors following implementation of a drug vial and syringe barcode scan system at the anesthesia point of care. The overall rate of errors and the rate of vial and syringe swap errors were substantially reduced. It is possible that some other unknown factors influenced the reduction in errors besides the implementation of the barcode-based system, since the study was not randomized. The incidence of drug errors is likely underestimated since it was determined by self-reporting. Nevertheless, the results suggest that use of a barcode scanning system for prevention of vial swap and syringe swap errors may represent an important advance for anesthesia patient safety. There is a need for additional safety measures focused on preventing drug infusion errors since 29% of the total errors involved infusions. There is also need for improved compliance with use of the barcode-based system since there were 4 vial or syringe swap errors following the implementation of the system that should have been prevented.

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S-237.

COMPARISON OF REACTION TIME AMONG RESIDENT ANESTHESIOLOGISTS BEFORE AND AFTER ON CALL SHIFT

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INTRODUCTION: Sleep deprivation and disturbance of circadian rhythm is a common problem among resident physicians. We evaluated reaction times and motor performance, sleep patterns, and acute changes in the cognition before and after routine shifts and on-call shifts in anesthesiology resident physicians.

METHODS: Two groups of 30 subjects were recruited from among resident anesthesiologists. The routine shift cohort (mean age = 30; 47% female) was recruited and tested before and after a routine shift (RS) , which started at 7 A.M. and ended by 5 P.M. The 'On Call' (OC) cohort (mean age = 30; 43% female) was recruited and tested before and after an on-call shift, which started at 3 P.M. and ended at 7 A.M. The subjects performed two tasks, named ProPoint and AntiPoint which are illustrated and explained in Figure 1, before and after their shift. Initiation Time (IT) and total reaction time (RT) were summarized by mean (Table 1). A mixed effect model with repeated measures was used to compare before and after Routine Shifts and On-Call shifts.

Normal 0 false false false EN-US X-NONE X-NONE MicrosoftInternetExplorer4 Results: Response time Pre shift was no different between the OC and RS cohorts (p-value=0.24 for ProPoint and 0.90 for AntiPoint). When reaction time was compared Pre and Post RS in the AntiPoint task, there was a reduction in the response time reflective of a learning effect (-15.59 ms, p-value=0.031). This learning effect was not present in the OC group, in fact, reaction time was marginally increased (+11.83 ms, p-value=0.057). In the ProPoint group, which reflects reflexive responses to stimulus which do not require substantial executive function, there were no significant difference between Pre RS and Post RS (4.84 ms, p-value=0.32). However, in the OC cohort, there was a significant increase in reaction time between the Pre OC and Post OC assessment (+26.84 ms, p-value<0.001). Reaction time in both AntiPoint and ProPoint tasks were significantly slower in OC group comparing to RS group (p-value=0.003 for both ProPoint and AntiPoint tasks). The magnitude of ProPoint task slowing was 57% for IT and 36% for RT, which is comparable to the defect seen in orthopedic trauma patients.[1]

CONCLUSION: We conclude that the magnitude of change in sensorimotor function (ProPoint) observed following a Post OC shift trended similarly to the changes observed in orthopedic trauma patients. Reaction time for higher executive function (AntiPoint) shows significant slowing between OC and RS. This is of particular importance for the clinical functionality of anesthesiology residents on overnight call.

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S-238.

CAUSES, MANIFESTATIONS, AND FREQUENCY OF SEVERE ALLERGIC REACTIONS DURING THE PERIOPERATIVE PERIOD

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INTRODUCTION: Severe allergic reactions during anesthesia are rare events (1:6000 to 1:20000) that can be challenging to recognize in the operating room because the hypotensive manifestation often overlaps with the effects of anesthetics.[1] Previous studies have shown varying frequencies of agents associated with allergic reactions with neuromuscular blocking drugs most common in European and Australia/New Zealand studies.[2,3] However, recent studies in the U.S. have demonstrated that antibiotics are the most frequent cause.[1,4] The purpose of our study was to examine the causes, manifestations, and frequencies of severe allergic reactions during anesthesia at our medical center.

METHODS: Quality management data from a university medical center from 2013-5 were reviewed for cases of severe allergic reactions during anesthesia. Medical records of these patients were examined for demographics, suspected causative agent, allergic reaction manifestations, and outcome. Causative agents of these reactions were determined by the clinicians caring for the patient and/or those reviewing the cases.

RESULTS: 15 cases of severe allergic reactions during anesthesia were identified from a total of 112,000 (1:7500) cases during the 3-year period (Table 1). Antibiotics were the suspected causative agent in 11 cases (73%). NSAIDs, narcotics, and protamine were responsible for the other allergic reactions. There were no cases of severe allergic reactions to muscle relaxants (Fig. 1). The most frequent manifestations were hypotension and erythema, each presenting in 10 cases (67%) (Fig. 2). Of the reactions that presented intraoperatively, 5 cases were cancelled (33%). In 1 case there was a documented allergy history to medication given. There were no deaths.

CONCLUSIONS: This study demonstrates and reaffirms that severe allergic reactions during anesthesia are rare. At our medical center, these reactions were most commonly caused by antibiotics. This is contrary to some studies which show that muscle relaxants are the most frequent cause of significant allergic reactions. Hypotension was one of the most common clinical manifestations. However, clinicians frequently fail to make the diagnosis of allergic reaction because they attribute hypotension to anesthetic effects. Examination of the skin, which is frequently draped for surgery, and finding erythema in combination with hypotension should direct clinicians to the diagnosis of allergic reaction. Severe allergic reactions during anesthesia can be fatal. There were no deaths or serious adverse consequences in our cases because the allergic reactions were discovered and addressed quickly. Vigilance, diagnosis, and prompt definitive treatment can result in excellent outcomes. Future studies should focus on allergy testing for all cases of suspected intraoperative allergic reactions in order to unquestionably establish the identity of the causative agent.

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Table 1. Summary of patients with allergic reactions during anesthesia

Patient No.	Age (years)	Sex	Scheduled Procedure	Prior Documented Allergies	Suspected Agent	Clinical Features	Time of Event	Procedure Cancelled
1	65	M	Renal transplant	None	Cefazolin	Hypotension	Maintenance	No
2	0.9	M	CT study with contrast	None	Iodine	Hypotension, Bronchospasm Angioedema, Erythema	Maintenance	No
3	59	M	LVAD placement	Iodine	Vancomycin, Cefepime	Hypotension, Erythema	Maintenance	No
4	59	F	Angioplasty	Naproxen	Protamine	Hypotension, PEA, Erythema	Emergence	No
5	25	M	Arthoscopy	Iodine	Cefazolin	Bronchospasm, Erythema, Angioedema	Emergence	No
6	33	F	Hysteroscopy, dilation and curettage, polypectomy	Motrin	Ketorolac	Erythema	Post-op	No
7	70	M	Endovascular aneurysm repair	None	Cefazolin	Hypotension, Bronchospasm	Maintenance	Yes
8	31	F	Sleeve gastrectomy	None	Cefazolin	Hypotension, Bronchospasm, Erythema	Maintenance	Yes
9	64	F	Breast biopsy	Aspirin	Ketorolac	Urticaria	Post-op	No
10	9	M	Alveolar graft	None	Morphine	Urticaria	Post-op	No
11	65	M	Carotid endarectomy	Clams	Cefazolin	Hypotension, Bronchospasm, Erythema	Maintenance	Yes
12	35	M	Gastric banding	None	Cefazolin	Hypotension, Bronchospasm, Erythema	Maintenance	Yes
13	44	F	Laparoscopic cholecystectomy	Codeine, Oxycodone	Cefazolin	Hypotension, Bronchospasm, Erythema	Maintenance	Yes
14	48	M	Shoulder replacement	None	Cefazolin	Urticaria	Maintenance	No
15	72	M	Hernia repair	Oxycodone	Cefazolin	Hypotension, Erythema	Maintenance	No

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S-238 • continued

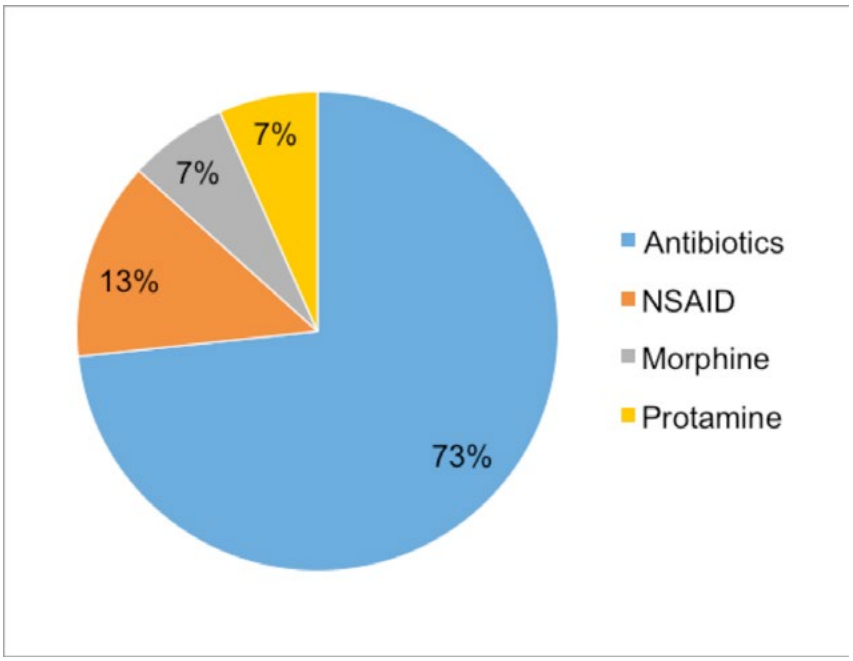

Figure 1. Causes of allergic reactions during anesthesia (N=15)

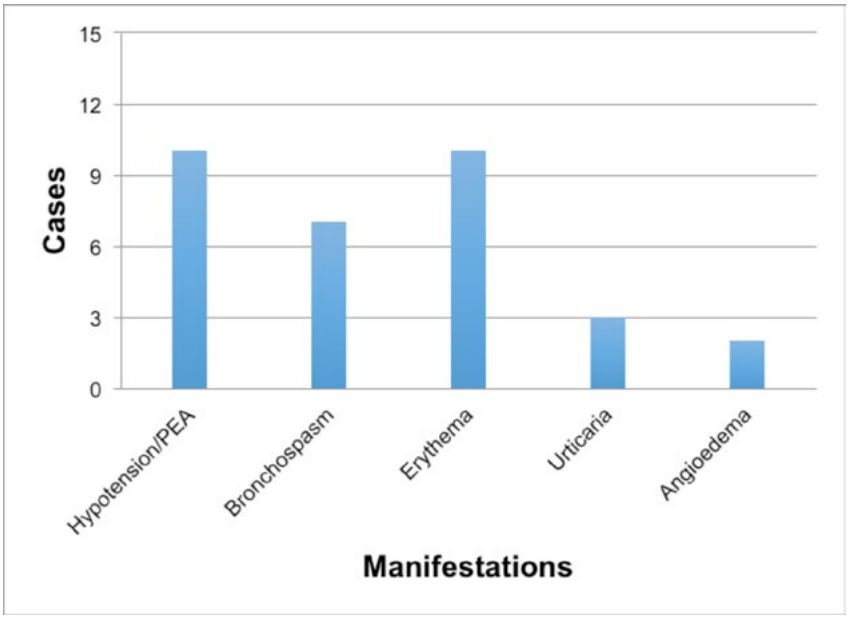

Figure 2. Manifestations of allergic reactions during anesthesia (N=15)

S-239.

THE IMPACT OF DAILY TRACKING AND FEEDBACK ON INTRAOPERATIVE NEUROMUSCULAR BLOCKADE MONITORING AND RESIDUAL PARALYSIS

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INTRODUCTION: In the absence of appropriate monitoring, many patients given neuromuscular blockers (NMB) remain partially paralyzed in the postanesthesia care unit (PACU). We have shown that the incidence of residual paralysis can be dramatically reduced by the introduction and use of intraoperative quantitative blockade monitoring[1,2]. However, we have not reduced the incidence to zero. One factor may be that not all providers were employing the quantitative monitoring system or making appropriate effort to assess neuromuscular blockade. We hypothesized that more intensive efforts to identify and eliminate such "failure to monitor" cases might further reduce the incidence of residual paralysis. We therefore began an oversight and feedback program to achieve this goal - and directly assessed its effect on residual paralysis.

METHODS: All data were collected under Quality Assurance program auspices but analysis and publication was approved by the IRB. Starting 10/26/2014, a daily case-by-case report for all main operating room anesthetics was automatically generated from of our EPIC anesthesia record. The report identifed whether or not a nondepolarizing NMB (rocuronium or cisatracurium) had been given and whether there was any documentation of NMB monitoring (a train-of-4 count and/or ratio). Cases were flagged if a NMB was given and there was no information in the Epic NMB monitoring fields. Flagged cases were manually reviewed to determine whether or not monitoring was, in fact, used. On 12/11/2014, the existence of this monitoring program was announced and direct, daily feedback to "deliquent" providers began. A follow-up announcement was made in mid-January 2015. In July 2015, additional data on the fraction of PACU patients with residual paralysis was obtained.

RESULTS: Between 10/26/2014 and 3/21/2015, there were 4538 adult patients in whom an NMB was given. 272 were flagged and reviewed. 48 were deemed to represent failures to monitor. During the "baseline" period, 2.44% of cases were deemed to be "failures to monitor". With the onset of feedback (in December 2014), this incidence decreased precipitously, to an average of 0.3% of cases in the last monitored month. However, the incidence of residual PACU paralysis did not change: In July 2014, 13% of PACU patients had a TOF ratio below 0.9 and 5% below 0.8. In July 2015, these values were 18 and 3% respectively (NS).

CONCLUSION: Monitoring and feedback effectively eliminated "failure-to-monitor" cases in our Department. It did not, however, further reduce the incidence of residual paralysis. There are several possible explanations. 1). Quantitative monitoring was already so widespread that the additional improvement has an unmeasurable effect in the PACU. 2). Practical factors (e.g. form of monitoring, provider knowledge, use of neostigmine, patient characteristics) have resulted in a de factor lower limit for the incidence of residual paralysis (circa 15%).

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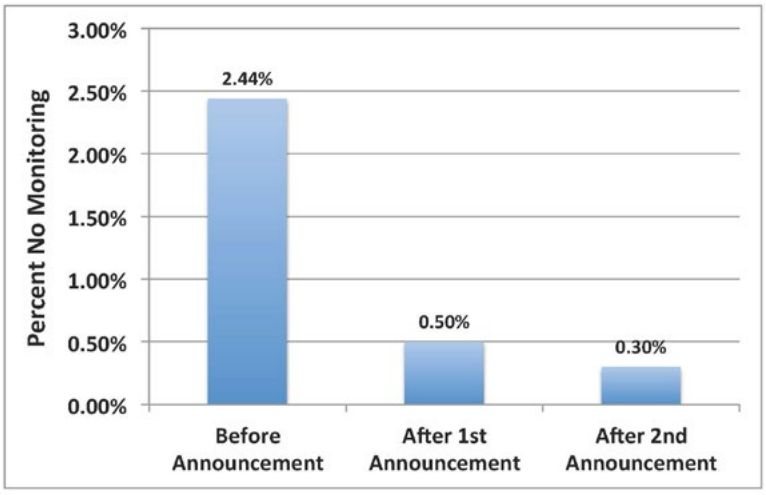

S-240.

INTEGRATED PULMONARY INDEX CAN PREDICT RESPIRATORY COMPROMISE IN HIGH-RISK PATIENTS AT POST-ANESTHESIA CARE UNIT

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INTRODUCTION: Respiratory compromise (RC) can occur in patients undergoing surgery in general anesthesia, but monitoring with oxygen saturation (SpO_2) may be insufficient to detect hypoventilation. Integrated pulmonary index (IPI) is a new parameter monitoring ventilation as well as oxygenation. It is calculated from four parameters including end tidal carbon dioxide ($etCO_2$), respiratory rate (RR), SpO_2 and pulse rate (PR). The aim of this study was to assess the efficacy of measuring IPI in postoperative patients with high risk of hypoventilation at post-anesthesia care unit (PACU).

METHODS: This study is a prospective observational study with high-risk patients who were eldely (more than 75 year-old) or obese (a body-mass index of more than 28). These patients at our PACUs after surgery in general anesthesia were enrolled at 2 centers from October 2014 to February 2015. We monitored IPI with CapnostreamTM20P. The primary end point was the occurrence of RC. We investigated onset of RC defined as following; respiratory events with prolonged stay in PACUs or transfer to intensive care units, because of airway narrowing, hypoxemia, hypercapnia, wheezing, apnea and any other accidents. We evaluated the relationship between several parameters on admission to PACU and the occurrence of RC. In addition, the relationship between IPI variations during stays in PACUs and the occurrences of RC using standard deviations of IPI every five minutes (IPI-SD).

RESULTS: A total of 293 patients were analyzed. Among them, 18 patients (6.1%) suffered RC. Initial IPI at PACU of RC group (mean ± SD, 6.7 ± 2.5) was significantly lower than that of non-RC group (9.0 ± 1.3, $p<0.0001$). Similar results were obtained from onotial SpO_2 (95.9 ± 4.2 % vs. 98.2 ± 1.9 %, $p<0.0001$). However we finally found that sensitivity and specificity of IPI were better than that of SpO2 for onset RC. IPI showed higher area under the curve (AUC) of 0.80, compaired to o.64 for SpO_2. IPI-SD of RC group (mean ± SD, 1.70 ± 0.83) was significantly bigger than non-RAE group (1.03 ± 0.76). This result suggested that IPI in RC group had been more variable.

CONCLUSION: After surgery in general anesthesia, the incidence of RC was 6.1% for postoperative patients with high risk of hypoventilation at PACU. Our results suggested that the initial lower IPI and the variation of IPI at PACU were useful to predict RC. In perioperative period, multidirectional evaluation of parameters including $etCO_2$ might be more useful to evaluate patients with high risk of hypoventilation at PACUs.

Subspecialty Abstracts

Pediatric Anesthesiology

S-241.

OUTCOMES OF HIGH-RISK PEDIATRIC PATIENTS UNDERGOING LOW-RISK SURGERY

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INTRODUCTION: The accurate risk stratification and perioperative assessment of pediatric patients presenting for low risk surgery is limited by a lack of data. In this study, we sought to determine the incidence of postoperative complications in a cohort of pediatric patients who underwent low risk surgeries and we hypothesized that patients with greater illness severity would have an increased incidence of complications.

METHODS: The study included patients who underwent minor procedures of the skin and soft tissue at a continuously enrolled United States ACS NSQIP-P hospital over a two-year period. The primary outcome was a composite of 24 postoperative complications. Univariable analyses were performed to identify associations with preoperative characteristics and post operative complications, readmission and postoperative mechanical ventilation. Multivariable logistic regression models were created to identify independent predictors for postoperative complications and readmission.

RESULTS: The final analysis included 6,851 patients. There were a total of 169 postoperative complications among 152 patients (2.22%) and the majority of complications were wound related. Risk factors for increased postoperative complications included ASA $\geq$ 3, neonate, nutritional deficiency, pulmonary disease, neurologic disease. Significant risk factors for postoperative mechanical ventilation included ASA $\geq$ 3, nutritional deficiency, cardiac disease and pulmonary disease. There were 41 unplanned readmissions (0.6%).

CONCLUSIONS: Patients with an ASA classification $\geq$ 3 had a significantly greater risk of complications and postoperative mechanical ventilation. High-risk patients should be targeted with interventions to optimize pulmonary and nutritional status even before low-risk procedures. Identification of patients at higher risk for wound complications allows the anesthesiologist to insure the patient receives targeted preventative interventions such as glucose control, maintenance of normothermia, optimization of tissue oxygenation and appropriate use of antibiotic prophylaxis.

S-242.

SLEEP DISORDERED BREATHING AS A RISK FACTOR FOR EMERGENCE DELIRIUM IN PEDIATRIC PATIENTS UNDERGOING AMBULATORY SURGERY

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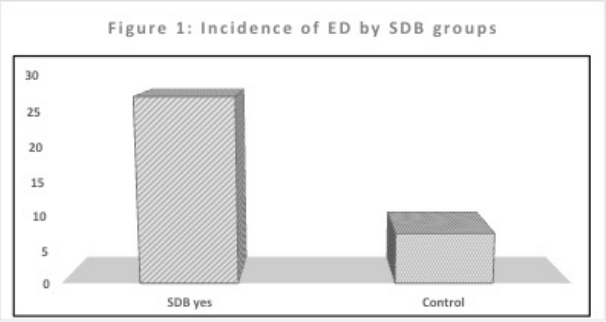
INTRODUCTION: Emergence delirium (ED) covers a spectrum of behavioral disturbances seen in children during emergence from anesthesia. ED in the ambulatory setting is distressing and places a burden on nurses, delays parents being reunited with their child and may prolong PACU stay[1]. Several risk factors for ED have been identified; mainly focused on anesthetic agent[2]. Further identification of patient-level risk factors may help provision of personalized perioperative care. One such risk factor is sleep disordered breathing (SDB) which is increasingly prevalent in the pediatric population. As abnormal sleep behavior (snoring, vocalization and thrashing around) features in SDB, we hypothesize that children with SDB may demonstrate features consistent with ED. This hypothesis has not been tested; therefore, our objectives in this prospective, observational study were to describe the incidence of ED in our subjects and to determine whether history consistent with SDB is significantly associated with ED. The main hypothesis was that the incidence of ED does not differ by SDB category.

METHODS: Using prospective data, 604 children aged 4-17yr undergoing elective ambulatory surgery were grouped into two categories based on history of SDB (exposed). SDB was defined as one or more of the following: history of OSA, habitual snoring (loud snoring on at least 3 consecutive days) or witnessed cessation of breathing during sleep. The primary outcome variable was PACU ED (measured by the Pediatric Anesthesia Emergence Delirium Scale, PAEDS). Perioperative variables were compared between the two groups using Chi-squared test for categorical or t-test for continuous variables. Logistic regression analysis was used to calculate the adjusted odds of ED.

RESULTS: Among 604 children 56 (9.3%) had a history of SDB. The mean age of subjects was 9.6yr. ED was documented in 30 (5%) of subjects. On average subjects with ED were younger ($p=0.04$) than controls. The incidence of ED was significantly higher among the SDB group ($p<0.001$) (Figure 1). In bivariable analysis, severe obesity ($p=0.01$), mask induction ($p=0.01$), intraoperative isoflurane ($p=0.01$), nitrous oxide ($p=0.007$) and intra-operative dexmedetomidine use ($p<0.001$) were significantly associated with ED. IV induction ($p=0.01$) and intraoperative use of Propofol ($p=0.005$) were associated with reduced incidence of ED. Sevoflurane use was not significantly associated with ED ($p=0.39$). Multivariable logistic regression analysis adjusted for age and the preceding variables indicates that SDB ($p=0.04$), severe obesity ($p=0.05$); increasing arousal pain score ($p<0.001$), dexmedetomidine ($p=0.001$) were independent predictors of ED. Conclusion: SDB is an independent predictor of ED in pediatric ambulatory surgery. Contrary to previous reports, we found intraoperative dexmedetomidine use was a strong predictor of ED. Identifying patient factors associated with ED could reduce incidence and severity of ED in children at risk of ED.



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S-243.

INCIDENCE OF ADVERSE EVENTS IN THE OPERATING ROOMS IN A TERTIARY MEDICAL CENTER

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INTRODUCTION: It is widely accepted that collecting and analyzing data of adverse events is helpful in identifying system problems, developing guidelines and improving standards of care.[1,2] In emergencies it is essential to mobilize all available personnel in a timely fashion to prevent adverse events from deteriorating further. In this project we analyzed outcomes from an Anesthesia STAT system implemented at Boston Children's Hospital allowing all anesthesiologists and OR personnel to be notified immediately to assist with the management of an acute event. We hypothesized that children ASA class III and IV as well as infants and toddlers would have a higher incidence of acute events.

METHODS: All members of the perioperative teams underwent training on how to utilize the Anesthesia STAT system. After each STAT episode, a detailed questionnaire was completed by the primary anesthesiologist. The data were stored in a secure RedCap database. We performed univariable and multivariable logistic regression analysis of factors associated with adverse events. An IRB protocol to review the data collection was obtained prior to analysis.

RESULTS: Between August 2011 and September 2015 there were 196 STAT calls in the main operating rooms. Cases that required a change in patients' perioperative status as result of the critical event were marked as "severe events." Univariate analysis was run between age, ASA status, gender, time of day, staff present in the room, and surgical "phase" (intraoperative, postoperative) is presented in Table 1. It confirmed that patients who were ASA 3 or 4 have a significantly higher likelihood of a major change (odds ratio: 3.2, 95% CI: 1.5-6.8, p = 0.003) compared to ASA 1 or 2. STAT calls initiated by a fellow or attending were predictive of a significantly higher likelihood of a major change (odds ratio: 5.1, 95% CI: 1.7-15.5, p < 0.001) compared to CRNAs or residents. Surgical phase was not a significant predictor of a major change by multivariable analysis (p = 0.87) (Table 1). STAT calls were predominantly due to respiratory issues however only 1 in 10 of those calls resulted in severe events (Table 2).

We compared 131 stat calls associated with 84,092 surgical cases at our institution from 6/2012 to 9/2015. Univariate analysis was run between age, ASA status, gender, and prematurity at birth. The analysis indicated that age and prematurity were associated with an increased frequency of STAT calls. Multivariate analysis confirms that both age and prematurity are independently predictive of receiving a stat call (Table 3).

CONCLUSION: Our STAT data collection confirmed that high ASA class, younger age and prematurity are associated with an increased risk of severe perioperative adverse events. Collection of adverse events in the operating room can help identify potential confounders and system problems that point to areas in need of improvement.

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Table 1 - Stat Call Description

Variable	No Major Change of Status	Major Change of Status	P Value
Age			
Infant	78.00%	22.00%	0.962
Toddler	82.00%	18.00%	
School Age	80.80%	19.20%	
Teen	79.30%	20.70%	
Adult	75.00%	25.00%	
ASA			
1 or 2	88.60%	11.40%	0.000
3 or 4	64.80%	35.20%	
Gender			
Male	78.90%	21.10%	0.712
Female	81.70%	18.30%	
Time of Day			
Morning	79.30%	20.70%	0.857
Afternoon	80.80%	19.20%	
Staff Present			
Fellow/Attending	71.30%	28.70%	0.000
Resident/CRNA	94.30%	5.70%	
Surgical Phase			
Induction	69.00%	31.00%	0.052
Intraop	77.20%	22.80%	
Emergence	84.60%	15.40%	
Pacu	93.80%	6.3.%	
Overall	**80.00%**	**20.00%**	-

Table 2 - Stat Calls by Reason

Reason For Call	% of Calls	% of the calls that result in severe events
Cardiac	12%	45%
Respiratory	68%	13%
Other	18%	27%

Table 3 - Stat Call Rates Relative to Hospital Cases

Variable	No Stat Call	Stat Call	P Value
ASA			
1 or 2	99.87%	0.13%	0.008
3 or 4	99.79%	0.21%	
Age			
0 - 1 Year	99.42%	0.58%	0.000
1 - 2 Year	99.79%	0.21%	
2 + Years	99.91%	0.09%	
Prematurity			
Not Premature	99.90%	0.10%	0.000
Premature	99.70%	0.30%	
Gender			
Male	99.83%	0.17%	0.649
Female	99.86%	0.14%	
Overall	**99.80%**	**0.20%**	**-**

S-244.

PHYSICIANS DISPENSE MORE OPIOID THAN NEEDED TO TREAT SAME DAY SURGERY PAIN, A PROSPECTIVE PEDIATRIC COHORT STUDY

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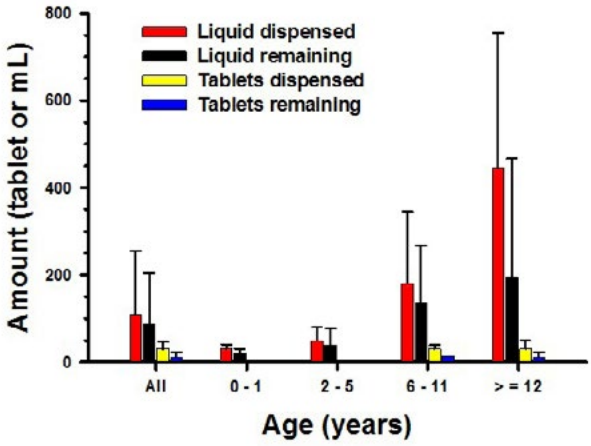
INTRODUCTION: The treatment of pain has become a national priority and has led to increases in both the number of opioid prescriptions written and the amount of drug dispensed. When over-dispensed, unused opioids can be diverted and abused, leading to the epidemic of non-medical use of prescription opioids (NMUPO). The purpose of this study is to determine the amount and formulation of opioids prescribed to pediatric same day surgery patients on discharge, the amount of unused drug at the conclusion of therapy, and its disposition in order to better define the scope of this problem.

METHODS: We recruited 152 English-speaking outpatients who were given opioid prescriptions on discharge from a pediatric same day surgical suite in a university children's hospital. All prescriptions were generated with the hospital's computerized narcotic prescription writer and were analyzed by the investigators following discharge for drug, formulation, and quantity dispensed. Parents were interviewed by phone within 2 days of discharge and again 10-14 days after discharge to determine if prescriptions were filled, if pain was controlled (with a 4-point Likert scale), how long opioids were used, the amount of medication left at completion of therapy, if patients were given instructions regarding disposal of leftover drugs, and if remaining drugs were actually discarded. Additionally, the number and age of all individuals residing in the household were collected. Data are presented as means ± standard deviation.

RESULTS: Parents of 118 (78%) enrolled patients completed the 2 day and/or 10-14 day interviews. The patients (M:F: 101:17) averaged 6.0 ± 5.0 years of age (range, 1-19 years) and 27 ± 19 kg (range, 6.0-96 kg). Oxycodone was prescribed to 85% of the patients while 15% received hydrocodone and acetaminophen (Lortab); 88% received the drugs in a liquid formulation, 12% received tablets. Patients took opioids for 4 ± 3 days (range, 0-11 days). Pain control was rated as excellent (51%), good (31%), fair (7%), poor (1%), and no response (10%). At 14 days, 12 ± 9 tablets (range, 3-25 tablets), 86 ± 118 mL (range, 0-505 mL), and overall 22 ± 14 doses (range, 0-60) of medication remained unused. On average, patients used only 34% of their dispensed drug. Patients averaged 1 ± 1 siblings (range, 0-6), and a quarter (26%) had a sibling aged 12 or older. Most parents (63%) were not told what to do with leftover medicine, and only 7% of parents disposed of leftover medication at the conclusion of therapy.

CONCLUSIONS: In our zeal to provide opioids to patients in moderate to severe pain, providers are dispensing far more medicine than is needed (or used) to treat pain following pediatric same day surgery. These results mirror our previous findings with pediatric inpatients. The enormous amount of "left over" medication may be contributing to the epidemic of NMUPO and is a particular concern because a quarter of our pediatric patients live in homes with adolescent siblings, for whom NMUPO is the gateway to opioid addiction. Finally, our results support the need for an improved method of opioid destruction to help eliminate left over medications from entering the public domain.



S-245.

ASSESSMENT OF NEONATAL PAIN: CORRELATIONS BETWEEN CORTICAL SOMATOSENSORY PROCESSING AND CRY ACOUSTICS

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INTRODUCTION: Providing optimal pain management in neonates requires reliable identification of neonatal pain[1,2]. Infant crying provides potentially valuable information, but published studies suggest that distinguishing cries resulting from painful versus non-painful stimuli is extremely difficult for the human ear[3,4]. To evaluate the potential clinical utility of cry acoustic analysis, we examined the correspondence between pain-related quantitative cry acoustic features and pain-related brain activations reflected in Event-Related Potentials (ERP).

METHODS: We conducted a prospective observational study of 54 healthy full-term newborns. We digitally recorded and analyzed cries elicited in response to standardized stimuli including 50 very brief nonpainful room temperature air puffs and a heel lance clinically required for blood sampling. Acoustical recordings were edited using Audacity to remove any identifying information and background noises. Cry signals which were comprised of a mixture of voiced, unvoiced, and silent intervals were then analyzed in Matlab. Seventy-nine acoustical features were extracted from the cry samples for analysis. These parameters were selected to adequately characterize glottal airflow, resonance of the vocal tract, amplitude and energy distribution of the cry signal, and patterns of phonation, hyperphonation, disphonation, and silence. Cortical somatosensory processing was measured through ERP recordings simultaneously obtained during each stimulus. Previous research indicates that ERP responses (mean amplitude) to pain from heel lances occur in the late time windows (500-700ms) in frontal and centroparietal locations whereas responses to light touch occur in earlier time windows (50-200 ms).

RESULTS: We analyzed the difference in ERP amplitude between the heel lance and light touch stimuli within the 535-635ms window in frontal and centroparietal locations. This derived difference score was computed to represent pain-specific ERP activations. Based on evaluating scatterplots and Pearson correlations between this derived ERP pain index and various acoustical cry features, 7 acoustical features appeared to be potential indicators of pain.

CONCLUSIONS: Results suggest it may be feasible to use cry acoustics to identify neonatal pain. Future work will seek to develop and further validate a cry acoustic algorithm to accurately identify neonatal pain across a range of clinical scenarios.

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S-246.

CLINICAL USE OF BAXTER RETCHING FACES (BARF) AND VISUAL ANALOG (VAS) SCALES TO MEASURE THE SEVERITY OF POSTOPERATIVE NAUSEA IN CHILDREN

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INTRODUCTION: The severity of postoperative nausea (PON) is difficult to evaluate in children and rescue treatment is usually limited to those with vomiting. We determined the clinical usefulness of the recently developed and validated pictorial Baxter Retching Faces (BARF) scale in assessing the incidence and severity of pediatric postoperative and postdischarge nausea with or without emesis[1].

METHODS: In this IRB approved study, 327 children receiving general anesthesia that included clinically indicated prophylactic anti-emetics, rated the severity of nausea at various time points in the preoperative, PACU and post-discharge phases using the BARF and the 10-cm. visual analogue scales (VAS). The degree of changes in nausea at different time points were rated on a 5 point Likert scale. Emetic episodes and rescue therapy were recorded. Test /retest reliability was determined by the correlation in scores in children who rated their nausea as unchanged between two time points. The minimum clinically relevant difference in VAS and BARF nausea scores was calculated from the scores at 2 time points in children who rated their nausea as either a little better or a little worse than before.

RESULTS: Ten of 48 (20.8%) children below 5 years age did not understand how to use the BARF and VAS scales while all aged 5 years or more could. Increased nausea scores from preoperative values were noted in 34.9%, with severe nausea (scores 7 or more) in 4.9 %. The mean (SD) of the highest VAS and BARF scale scores were 1.0 (2.0) and 1.4 (2.2), respectively. PACU emesis occurred in 4.3%; with severe vomiting (3 or more episodes) in 0.3%. Rescue anti-emetics were given to only 2.8% (table 1). In 26 subjects who rated their nausea as unchanged, there was a significant correlation (p=0.016) in the two VAS and BARF scores, indicating test -retest reliability. The minimum clinically relevant difference (95% CI) in nausea scores in 77 children who rated nausea as "a little better or a little worse" was 0.73 (0.36 - 1.1) for the VAS and 1.02 (0.64 - 1.4) for the BARF scales respectively.

Follow-up diaries from 220 subjects documented post-discharge nausea (PDN) in 30.9% with severe nausea in 12.3%, vomiting in 9.1 % and severe emesis in 2.3% (table 2).

DISCUSSION: This study has shown that postoperative and post-discharge nausea is very common in children, occurring more frequently than emesis. Severe PON is at least as common in children as in adults, but the current practice of limiting rescue antiemetics to children with emesis markedly undertreats those with severe nausea, who would have received treatment if they were adults[2]. This study has also shown that the pictorial BARF scale is easy to use in the clinical setting in children who were 5 years or older, has test /retest reliability and determined the minimum clinically relevant difference. The study data can be used in future studies to determine if treatment based on specific nausea scores improves pediatric postoperative outcomes and parental satisfaction.

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Table 1: Postoperative Nausea and Vomiting in the PACU

PACU	This study	Apfel et al (2)
Population n	Children	Adults
N	327	2170
Nausea in PACU	34.9 %	19.9 %
Severe Nausea (Score 7 or higher)	4.6 %	3.6 %
Vomiting in PACU	4.3 %	3.9 %
Severe Emesis in PACU (3 or more episodes)	0.3 %	0.2 %
Rescue Antiemetics in PACU	2.8 %	13.5 %

Post Discharge Nausea and Vomiting (PDNV)

	This study	Apfel et al (2)
Population	Children	Adults
Data available (n)	220	2170
Post-discharge Nausea	30.9 %	36.6 %
Severe Nausea (score 7 or higher)	12.3 %	13.3 %
Vomiting after discharge	9.1 %	11.9 %
Severe emesis (3 or more episodes)	2.3 %	5.0 %

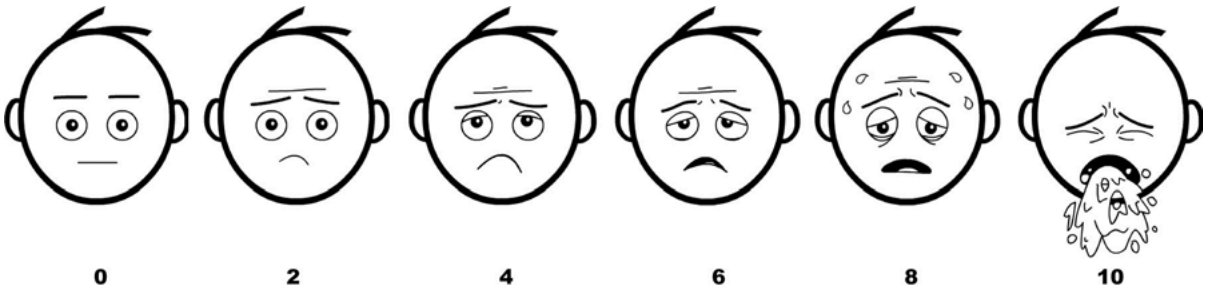

Figure: Baxter Retching Faces Scale

S-247.

DOES EXHALED NITRIC OXIDE PREDICT POSTOPERATIVE COMPLICATIONS?: A PILOT STUDY IN PEDIATRIC ADENOTONSILLECTOMY

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INTRODUCTION: The ability to identify increased perioperative risk in children is of great importance; available tools are few. Airway and respiratory events are among the most significant complications in elective pediatric procedures, Our group therefore investigated whether preoperative measurement of exhaled nitric oxide (eNO), a biomarker of airway inflammation, could predict postoperative outcomes.

METHODS: Following IRB approval, parental consent, and inclusion/exclusion criteria, eNO was measured using a clinical chemiluminescence analyzer (NIOX Mino, Aerocrine, Morrisville, NC) immediately prior to adenotonsillectomy in children aged 4 to 12 years . Using defined variables, complications were recorded by study personnel blinded to the eNO measurement and analyzed by Fisher's Exact test (using a literature-based normal eNO value of 20 ppb). Study was concluded once 103 samples were collected and data was kept blind during the sample collection phase.

RESULTS: One hundred children were studied. There were no intraoperative complications. Postoperative respiratory complications occurred in 52% of the high FeNO patients compared to 35% in the low eNO group. Hospital readmissions occurred in 19% of the high FeNO group compared to 11% of the low FeNO group. These differences did not reach statistical significance (Figure 1).

CONCLUSION: eNO has been used to identify T helper 2 mediated airway inflammation (e.g. asthma) and is feasible to measure in small children. This pilot study, which was underpowered to detect relatively infrequent complications, demonstrated a trend but not significant associations between increased eNO and postoperative complications after pediatric adenotonsillectomy; study of a larger cohort or high-risk subset (e.g. URI) may yield different results.

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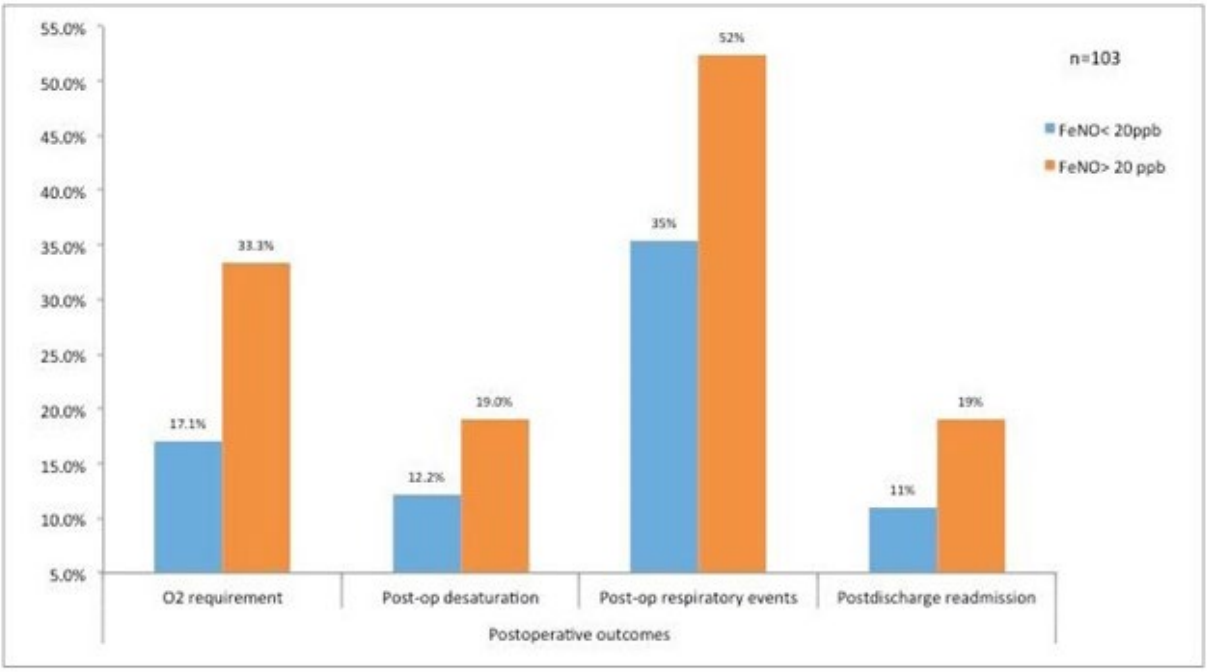

S-248.

FIBRINOLYSIS IN CHILDREN UNDERGOING MAJOR CRANIAL VAULT SURGERY

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INTRODUCTION: Children undergoing major cranial vault reconstruction face significant morbidity such as major blood loss, electrolyte abnormalities and prolonged hospital and intensive care stays. Research has focused on limiting blood loss and exposure to allogenic blood transfusions due to infections, immunomodulation and other morbidities. Recent work has looked at antifibrinolytics to decrease blood loss.[1-3] One of these studies reduced blood transfusion by 40%, despite a lack of detected fibrinolysis by thromboelastography.[2] A previous study questioned whether fibrinolysis could be detected using thromboelastography without the addition of TPA.[4] In the past, D-dimer, a fibrin breakdown product, has been used to quantify fibrinolysis in adult cardiac patients on aprotinin infusions.[5] This study aims to determine how often fibrinolysis occurs at various infusion rates of aminocaproic acid (20, 30, and 40 mg/kg/hr after 100 mg/kg load) in patients undergoing craniosynostosis repair as quantified by D-dimer level assays instead of thromboelastography.

METHODS: After IRB approval, a retrospective chart review was performed in children under the age of 25 months that underwent primary open cranial vault surgery for craniosynostosis. Basic demographic data, type of surgery, perioperative antifibrinolytic administration and lab data especially D-dimer levels were obtained from the charts. Patient were considered to have fibrinolysis if the baseline D-dimer level was less than 0.27 mcg/mL and a subsequent D-dimer level of >0.49 mcg/mL during the intraoperative process. All statistical analyses were performed using the R software package (version 2.15.1). Univariate analyses were performed using Wilcoxon Rank Sum test or Fisher exact test while linear regression was utilized for multivariate analysis. A chi-square test for trend was also employed to assess the effect linearity of the incremental amicar doses.

RESULTS: There were 32 patients that fit the inclusion criteria and 17 of these patients had laboratory data suggestive of fibrinolysis during the operation. Fibrinolysis occurred in 85.7%, 55.6%, and 41.1% of patients on an aminocaproic acid infusion rate of 20 mg/kg, 30 mg/kg and 40 mg/kg, respectively (P-value = 0.038). There was a linear effect trend with increasing amicar dose (P-value = 0.034, Figure 1). Fibrinolysis did not have an effect on estimated blood loss (P-value = 1.0), even when adjusted for weight and synostosis type (P-value = 0.981, Table 1).

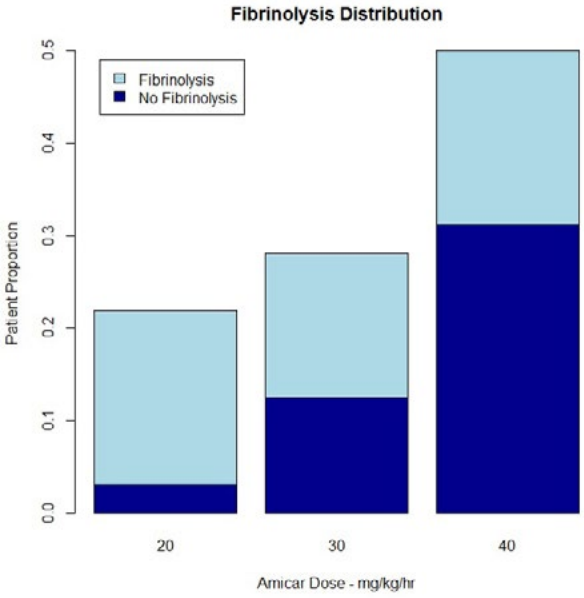
CONCLUSION: Fibrinolysis frequently occurs during major open cranial vault surgery despite infusions of aminocaproic acid. With higher infusion rates, the incidence of fibrinolysis is decreased but still commonly occurs. Further work using D-dimer assays are needed to determine optimal dosing of antifibrinolytics to prevent fibrinolysis in children undergoing primary open cranial vault reconstruction.

Table 1. Estimated Blood Loss (ml per kg) Multiple Linear Regression*

Characteristic	Estimate	95% CI	*P*-value
Fibrinolysis	-0.06	-4.66 to 4.54	0.981
Weight	-1.95	-2.65 to -1.26	<0.001
Synostosis			
Metopic	0.00	(referent)	
Coronal	0.97	-7.02 to 8.96	0.814
Sagittal	-2.97	-8.77 to 2.83	0.326
Lambdoidal	-1.42	-11.08 to 8.24	0.775
Multiple	6.95	1.38 to 12.52	0.022

CI = confidence interval, ASA=American society of Anesthesiology, ml=milliliters, kg=kilogram

*This ANCOVA model was generated using the generalized linear model function (GLM) of the R statistical software package. *P*-value < 0.05 was considered statistically significant.



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S-249.

PERIOPERATIVE OPTIMIZATION IS ASSOCIATED WITH DECREASED POSTOPERATIVE PRBC TRANSFUSION IN THE POSTOPERATIVE PERIOD

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INTRODUCTION: Craniofacial reconstruction is associated with significant blood loss. Many methods have been utilized to decrease allogenic blood transfusion to prevent morbidity.[1] Recently, a publication looked at modifiable intraoperative variables associated with postoperative packed red cell (PRBC) transfusion in children undergoing craniofacial reconstruction, which found that only initial postoperative hematocrit was associated with postoperative packed red cell transfusion.[2] Since this publication, anesthesiologists at our institution have been administering residual PRBC volume at the end of these procedures from a previously given unit to mitigate the incidence of postoperative packed red cell transfusion from another discrete donor. This chart review was performed to determine if transfusing additional PRBC volume in this manner reduced the chances of receiving another postoperative PRBC transfusion from a different donor.

METHODS: After Institutional Review Board approval, a chart review was performed from June 1, 2013, to September 30, 2015, for all patients that underwent craniofacial reconstruction. The implementation date of the residual PRBC administration was May 1, 2014. At the conclusion of the reconstruction, if the HCT $\leq$ 30 and residual PRBC volume was available, the patient was transfused this extra volume. Demographic data including age, weight, ASA status, and type of synostosis were obtained for each patient as well as immediate postoperative HCT and postoperative PRBC transfusions. All statistical analyses were performed using the R software package (version 2.15.1). Population characteristics were examined using the Wilcoxon Rank Sum test or Fisher exact test, as appropriate for the distribution of the data. Logistic regression was performed for multivariate analysis.

RESULTS: Overall, 47 patients underwent major craniofacial reconstruction for craniosynostosis after residual PRBC implementation. In order to determine the impact of this practice, these patients were compared to the 47 patients that had craniofacial reconstruction immediately prior to this implementation date. Demographic data are listed in Table 1. Postoperative PRBC transfusion rate decreased from 44.7% (21/47) to 17.0% (8/47), corresponding to a 27.7% reduction (95% CI 9.8% – 45.5%). Even when controlled for synostosis type, this practice was still associated with a significant decrease in postoperative PRBC transfusion (Table 2).

CONCLUSION: Intraoperative optimization of the hematocrit, by using the residual volume from a previously transfused unit of red cells, is associated with decreased PRBC transfusion from a discrete donor in the postoperative period. These benefits are only applicable if the institution does not allow split units of PRBC in the operative areas or if the institution does not reserve the remaining volume of PRBC from the split unit for the patient. Future studies should look at the possible reduction in morbidity associated with limiting multiple donor exposures.

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Table 1. Demographics and Perioperative Data*

	Preimplementation (N = 47)	Postimplementation (N = 47)	*P*-value
Age (months)	10.60 ± 11.40	10.66 ± 11.34	0.721
Weight (kg)	9.15 ± 4.62	8.62 ± 3.43	0.297
Male/Female Proportion	31/16 (66.0%)	32/15 (68.1%)	1.0
ASA status % (3/2/1)	12.8/78.7/8.5	10.6/85.1/4.3	0.729
Synostosis			0.038
Metopic	20 (42.6%)	15 (31.9%)	
Coronal	2 (4.3%)	6 (12.8%)	
Sagittal	21 (44.7%)	13 (27.8%)	
Lambdoidal	0 (0%)	3 (6.4%)	
Multiple	4 (8.4%)	10 (21.1%)	
Postop HCT	32 ± 6	37 ± 6	<0.001
Postop PRBC Transfusion	21 (44.7%)	8 (17.0%)	0.007

* These characteristics were examined using the Wilcoxon Rank Sum test or Fisher exact test, as appropriate for the distribution of the data. Population statistics for non-proportion data expressed as mean ± standard deviation. *P*-value < 0.05 was considered statistically significant.

Table 2. Synostosis Adjustment*

Characteristic	OR	95% CI	*P*-value
Residual PRBC	0.30	0.11 to 0.80	0.019
Synostosis			
Metopic	1.00	(referent)	
Coronal	0.00	-∞ to +∞	0.990
Saggital	0.87	0.31 to 2.41	0.786
Lambdoidal	0.00	-∞ to +∞	0.994
Multiple	0.95	0.21 to 3.87	0.940

OR = odds ratio, CI = confidence interval.

*This logistic regression model with residual PRBC modeled as a binary variable and synostosis modeled as a categorical variable. *P*-value < 0.05 was considered statistically significant.

S-250.

NEONATAL INTENSIVE CARE UNIT TO OPERATING ROOM HANDOVERS: WHAT WE HAVE LEARNED FROM OBSERVATION

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INTRODUCTION: Failures of communication are a major contributor to perioperative adverse events. Transitions of care may be particularly vulnerable, particularly for complex ICU patients. The demands of system-level support by multiple providers, complex medical regimens and rapidly changing physiologic conditions increase the risk of communication errors and adverse events[1]. Neonatal patients are especially susceptible to medical errors and events due to their limited physiologic reserve, fluctuating body weight, and inability to communicate[2]. While there has been appreciable research on improving the care transition from the OR to the ICU, the ICU-to-OR handover has been understudied.

METHODS: We observed 60 NICU-to-OR handovers to ascertain current handover practices, including the participants involved, handover content, as well as barriers and facilitators of effective handovers. We rated these handovers based on several factors including length of handover, completeness of content, providers present, handover tools utilized and an overall global effectiveness score. We also observed for near misses and non-routine events. A non-routine event is any deviation from a patient's optimal care path, which, if uncorrected, may lead to an adverse event[3].

RESULTS: The observations identified numerous barriers and facilitators to effective NICU-to-OR handovers notably including infrequent prior notification, infrequent structured verbal handovers, unclear roles and responsibilities, lack of a hard stop, frequent interruptions and distractions, lack of necessary transport equipment and absence of attending physicians. On average, handovers lasted 17.25 minutes with many critical items being missed during the handover (weight, consent, allergies, NPO status, past medical history, 24 hour events, medications due, disposition plan, post operative respiratory support plan and whether there were any questions). In only 9/60 observations (15%) were all critical items discussed. The average score of handovers was 2.9 on a 5-category Likert-type scale. Forty-one cases (68.3%) experienced non-routine events or near misses. Memory was used exclusively in 32/60 (53.3%) handovers.

CONCLUSIONS: This study identified issues with NICU-to-OR care transitions that have not been documented previously. These findings highlight the current deficiencies, key areas for future research, and potential interventions to improve the preoperative handovers of neonates.

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S-251.

ANESTHETIC DILEMMA: CHILDHOOD OBSTRUCTIVE SLEEP APNEA IS A RISK FACTOR FOR EARLY POSTOPERATIVE PAIN FOLLOWING AMBULATORY SURGERY

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INTRODUCTION: Obstructive sleep apnea (OSA) presents unique challenges in the ambulatory surgical setting because as many as 80% of patients with OSA are undiagnosed and it is known to be associated with a number of perioperative complications[1]. One of the enduring dilemmas in the care of the OSA patient is the observation that OSA is associated with enhanced nociception as well as increased rates of opioid-induced respiratory depression[2]. To this end, practitioners often withhold or administer lower intraoperative doses of opioids out of concern for delayed recovery from general anesthesia. One unintended consequence of this practice is that patients with OSA are at increased risk of moderate to severe early postoperative pain requiring treatment upon recovery from anesthesia in the post-anesthesia care unit (PACU). Therefore, we sought to determine whether children with preoperative OSA diagnosis (exposure variable) were at increased risk of PACU pain requiring opioid administration (outcome variable).

METHODS: Using prospectively collected data, 515 children aged 4-17yr who underwent elective ambulatory operations were grouped into two categories based on whether they had a positive preoperative history of OSA (exposed) or whether they had no history of OSA (non-exposed). The primary outcome variable was PACU administration of morphine (a proxy for pain requiring intervention). Perioperative variables were compared between the exposed and control groups using Chi-squared test for categorical or t-test for continuous variables. Logistic regression analysis was used to calculate the adjusted odds of requiring PACU opioids.

RESULTS: Among 515 children 38 (7.4%) had a preoperative diagnosis of OSA. All the patients received at least one or more intraoperative opioid (Fentanyl 68.2% and morphine 33.4%). Multimodal analgesia was used in only 24.9% of patients. Children with OSA were more likely to have received perioperative multimodal analgesia (17.3% vs. 3.6%; OR =5.6; p<0.001). Moderately severe pain occurred in 113 (21.9%) of patients. A total of 73 (14.2%) of children were given intravenous morphine in the PACU. Compared with controls, children with history of OSA had significantly higher unadjusted odds of requiring IV morphine in the PACU (19.2% vs. 5.4%; OR = 4.1 (95%CI 2.0-8.4; p<0.001). Logistic regression model (to predict the odds of requiring PACU IV morphine) adjusted for age, gender, race, ASA status (1&2 vs. 3), OSA diagnosis, and perioperative use of multimodal analgesia revealed that factors in Table 1 were independent predictors of PACU morphine requirement.

Table 1. Multivariable logistic regression model to determine the adjusted odds of PACU IV morphine

Parameter	AOR	95%CI	p-value
Age(yr.)	0.99	0.93-1.06	0.94
ASA (1&2vs3)	0.12	0.02-0.94	0.04*
Gender	0.65	0.38-1.11	0.11
Race(black vs. white)	0.41	0.2-0.82	0.01*
Race(other vs. white	0.54	0.17-1.71	0.30
OSA	3.31	1.51-7.26	0.003*
Multimodal analgesia	3.08	1.78-5.33	<0.001*

CONCLUSION: Among children undergoing elective outpatient operations, OSA diagnosis is a significant predictor of clinically important pain in the PACU (indicated by morphine requirement). Given the potential for opioid-induced respiratory depression in children with OSA, these findings represent an important clinical dilemma. Mechanisms underlying this enhanced pain experience deserve further elucidation.

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S-252.

EFFECTS OF CAUDAL BLOCK ON NEPHRO-URETERIC RECOVERY IN INFANTS AFTER URETERONEOCYCTOSTOMY

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INTRODUCTION: Ureteoneocystostomy (ureteral reimplantation) is performed to correct vesicoureteral reflux (VUR) in children. Children with VUR may also have reflux nephropathy, and ureteoneocystostomy can cause edema at the site of ureter implantation, possibly resulting in ureteric obstruction especially in infants.[1] Therefore, adequate function of the kidney and ureter should be confirmed in infants after ureteoneocystostomy. Caudal block is considered the gold standard regional technique in pediatric urologic procedures because it blocks both somatic and visceral pain. However, neuraxial anesthesia such as caudal block may decrease renal blood flow and aggravate the edema of intra-abdominal tissues[2], which may have an effect on nephroureteric function after ureteroneocystostomy. The objective of this study was to evaluate the effects of caudal block on nephroureteric function in infants undergoing ureteroneocystostomy.

METHODS: The medical records of 121 infants (aged less than 1 year) who underwent ureteroneocystostomy due to VUR from January 2010 to October 2014 at our institution were analyzed retrospectively. These patients were divided into Caudal Block group and Control group according to whether the patient received caudal block or not. Urinary output through urethral catheter and ureter catheter for 48 h after the surgery was compared between the two groups. Urethral catheterization and placement of ureteral catheter at one of the two ureters (attached to the suprapubic catheter) is the routine practice of our institution in infants undergoing ureteroneocystostomy. In order to identify the risk factors for postoperative oliguria, logistic regression was used in the analysis. Oliguria was defined as less than 4 ml/kg of urine output for 8 hours (less than 0.5 ml/kg/hr).

RESULTS: Patients' characteristics, VUR severity, preoperative renal function and intraoperative data were comparable between the Control group and Caudal Block group (Table 1). Table 2 demonstrates the data of urine output through each catheter for 48 h after surgery. The incidence of oliguria through urethral catheter by 16 h after surgery was significantly higher in the Caudal Block group than in the Control group (P<0.01). According to multivariate analysis in the logistic regression, caudal block, anesthesia duration, and intraoperative administration of dexamethasone were independently associated with the occurrence of oliguria for 8 h after surgery (Table3). Patients receiving caudal block had a 2.1 odds for the occurrence of oliguria compared with those not receiving caudal block (95% CI: 1.303-7.228, P = 0.010). However, there was no difference in additional recovery profiles between the two groups (Table 4).

CONCLUSIONS: Caudal block may increase the risk of immediate postoperative oliguria in infants undergoing ureteroneocystostomy. However, it may not be associated with prolonged duration of hospitalization or additional deterioration of renal function.

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Table 1. Patients' characteristics and intraoperative data

	Control (n=58)	Caudal block (n=63)	P-value
Age (months)	6.8 (2.2)	7.0 (2.3)	0.671
Weight (kg)	8.6 (1.2)	8.6 (1.2)	0.938
Height (cm)	69.7 (6.4)	69.9 (4.8)	0.876
BMI (kg/m²)	17.9 (2.1)	17.6 (2.0)	0.550
Sex (M/F)	46/12	55/8	0.328
Serum creatinine (mg/dl)	0.31 (0.10)	0.33 (0.13)	0.308
VUR grade			
UC side	4 (3-4)	4 (4-5)	0.181
non-UC side	4 (3-4)	4 (3-4)	0.782
Split renal function on DMSA scan (%)			
UC side	47.5 (15.0)	46.8 (14.9)	0.814
non-UC side, %	52.5 (15.0)	53.3 (14.9)	0.788
Duration of surgery (min)	130.4 (36.2)	130.7 (32.6)	0.966
Duration of anesthesia (min)	153.3 (38.9)	160.2 (34.6)	0.304
Administered fluid (mL)	149.8 (69.4)	161.6 (67.2)	0.344
Blood loss (mL)	5.9 (12.4)	5.9 (18.1)	0.997
Dexamethasone administration	27 (46.6%)	32 (50.8%)	0.717

Data are shown as mean (SD), median (IQR), or number of patients. VUR, vesicoureteral reflux; UC, ureter catheter; DMSA, dimercaptosuccinic acid.

Table 2. Urinary output for 48 hours after the surgery

	Control (n=58)	Caudal block (n=63)	P-value
Administered fluid (mL)			
0-8 h	230.3 (92.3)	251.4 (109.8)	0.256
8-16 h	244.3 (89.0)	258.6 (92.8)	0.390
16-24 h	224.1 (79.6)	250.9 (92.5)	0.090
24-32 h	240.2 (85.3)	244.8 (79.5)	0.759
32-40 h	230.2 (93.1)	234.8 (85.6)	0.779
40-48 h	213.7 (72.9)	227.9 (86.7)	0.354
Oliguria from urethral catheter			
0-8 h	32 (55.2%)	50 (79.4%)	0.006
8-16 h	18 (31.0%)	34 (54.0%)	0.009
16-24 h	15 (25.9%)	25 (39.7%)	0.077
24-32 h	15 (25.9%)	15 (23.8%)	0.479
32-40 h	15 (25.9%)	20 (31.7%)	0.549
40-48 h	17 (29.3%)	16 (25.4%)	0.686
Oliguria from ureter catheter			
0-8 h	25 (43.1%)	22 (34.9%)	0.455
8-16 h	5 (8.6%)	2 (3.2%)	0.258
16-24 h	1 (1.7%)	1 (1.6%)	1.000
24-32 h	1 (1.7%)	0 (0%)	0.479
32-40 h	0 (0%)	1 (1.6%)	1.000
40-48 h	0 (0%)	1 (1.6%)	1.000

Data are shown as mean (SD) or number of patients (proportion, %).

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Table 3. Analysis of risk factors for 8h-oliguria after ureteroneocystostomy

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (months)	0.961 (0.810-1.141)	0.651	-	-
Sex (Female vs. Male)	1.132 (0.399-3.213)	0.815	-	-
BMI (kg/m²)	1.108 (0.914-1.343)	0.296	-	-
Preoperative Cr (mg/dl)	0.431 (0.017-11.225)	0.613	-	-
Split renal function of non-UC side (%)	1.015 (0.989-1.042)	0.260	-	-
VUR grade of non-UC side				
I	ref	ref	-	-
II	1.857 (0.293-11.756)	0.511	-	-
III	3.000 (0.489-18.415)	0.235	-	-
IV	2.077 (0.368-11.735)	0.408	-	-
V	1.667 (0.275-10.094)	0.578	-	-
Caudal block	3.125 (1.404-6.955)	0.005	3.069 (1.303-7.228)	0.010
Duration of surgery (min)	1.000 (0.997-1.021)	0.129	-	-
Duration of anesthesia (min)	1.012 (1.000-1.024)	0.043	1.017 (1.004-1.032)	0.014
Administered fluid in OR (ml)	0.998 (0.993-1.004)	0.574	-	-
Estimated blood loss and urine output (ml)[a]	0.991 (0.968-1.014)	0.449	-	-
Dexamethasone administration in OR	0.444 (0.210-0.980)	0.044	0.339 (0.141-0.815)	0.016
Administered fluid in ward (ml)	0.998 (0.994-1.002)	0.269	-	-

[a]Estimated blood loss and urine output were included in the total. CI, confidence interval; OR, odds ratio; BMI, body mass index; Cr, creatinine; UC, ureter catheter; OR, operating room

Table 4. Additional recovery profiles after the surgery

	Control (n=58)	Caudal block (n=63)	P-value
Postoperative dexamethasone administration	5 (8.6%)	10 (15.9%)	0.277
Duration of urethral catheter (h)	97.9 (48.5)	92.3 (48.2)	0.524
Duration of ureter catheter (h)	69.9 (47.6)	63.4 (42.8)	0.431
Postoperative serum creatinine (mg/dl)	0.40 (0.25)	0.42 (0.27)	0.649
Hospitalization duration (days)	4 (3-6)	4 (3-6)	0.578

Data are shown as mean (SD) or median (IQR).

S-253.

DEXMEDETOMIDINE AND REMIFENTANIL AS TOTAL INTRAVENOUS ANESTHESIA IN INFANTS: A CASE SERIES

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INTRODUCTION: On October 13, 2015, SmartTots released an updated consensus statement urging caution but not alarm in regards to infants and children younger than age 4 receiving anesthetics and sedatives. There is growing evidence in animals that exposure to such agents at a very young age can negatively impact learning ability, behavior, and memory. As a result of media exposure, we encountered a number of parents who specifically requested an alternative "safe" anesthetic for their child when they presented for surgery under general anesthesia. The only anesthetic agents known not to cause apoptosis are dexmedetomidine and opiate analgesics. We present 8 cases where dexmedetomidine and remifentanil were used for total intravenous anesthesia.

METHODS: With IRB approval, the anesthetic records of 8 patients, whose parents specifically asked for an alternative anesthetic, were reviewed. They were scheduled for general, orthopedic, urology, and ophthalmology surgeries. Following pre-oxygenation and application of standard ASA monitors, a mixture of 70/30 nitrous oxide/oxygen was used for intravenous catheter insertion. Anesthesia was induced with boluses of Dexmedetomidine and Remifentanil, followed by continuous infusions. All of the patients were intubated and mechanically ventilated. All surgical patients, except for those undergoing eye surgery, also received 0.5-1 mL/kg of local anesthetic infiltration during the procedure. Results: The demographic and anesthetic data are presented in Table 1. All patients remained hemodynamically stable for the duration of the surgery. There were no noted episodes of significant bradycardia or hypertension requiring rescue agents. Additionally, no episodes of gross movements were appreciated and the level of anesthesia was deemed adequate for the type of surgery. The time from the last dose of dexmedetomidine and remifentanil infusions until extubation was 9.3 ± 5.8 minutes and 10.6 ±5.29 minutes, respectively. All of the patients were extubated in the operating room with a mean time of 3 ± 2.83 minutes from the end of surgery to removal of the endotracheal tube. No complications were noted during the recovery period.

CONCLUSIONS: Since most anesthetic agents cause neuroapoptosis in young animals and human epidemiological studies have raised concerns, finding a "not-toxic" anesthetic regimen is gaining interest. An open label prospective pilot study to determine the feasibility of an alternative anesthetic (dexmedetomidine-remifentanil-caudal anesthetic) in infants undergoing lower abdominal surgery (T REX study) is currently enrolling patients. (https://clinicaltrials.gov/ct2/show/NCT02353182) We used a similar anesthetic regimen in infants and young children where regional anesthesia was not an option due to the type of surgery. The dexmedetomidine-remifentanil combination provided anesthesia without clinical or physiological signs of light anesthesia or complications in this wide range of surgical procedures.

Table 1
Demographic and anesthetic data

	Mean (±SD)	Range
Weight (kg)	8.63 (±3.58)	3.75-11.54
Age (months)	8.44 (±7.22)	0.9-24.0
Gender	100% male	
ASA		1-2
Duration of Anesthetic (mins)	113.25 (±69.45)	45-221
Dexmedetomidine Induction Bolus (mcg/kg)	1.01 (±0.61)	0.38-2.13
Dexmedetomidine Total Dose (mcg/kg)	2.17 (±0.92)	1.06-3.76
Dexmedetomidine Total Dose (mcg/kg/hr)	1.30 (±0.36)	0.95-1.71
Remifentanil Induction Bolus (mcg/kg)	4.34 (±1.62)	2.17-7.00
Remifentanil Total Dose (mcg/kg)	128.19 (±128.70)	26.08-376.94
Remifentanil Total Dose (mcg/kg/hr)	56.10 (±28.75)	29.65-102.34
Rocuronium (mg/kg)	0.96 (±0.40)	0.51-1.49
Time from last dose of Dexmedetomidine to Extubation (mins)	9.33 (±5.82)	0-17
Time from last dose of Remifentanil to Extubation (mins)	10.63 (±5.29)	5-22
Time from Surgery End to Extubation (mins)	3.00 (±2.83)	0-8

S-254.

LOW VS MODERATE DOSE NALOXONE INFUSION COMBINED WITH PATIENT CONTROLLED ANALGESIA FOR PEDIATRIC PATIENTS AFTER POSTERIOR SPINE FUSION: A RANDOMIZED CLINICAL TRIAL

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INTRODUCTION: Posterior spinal fusion (PSF) and instrumentation for adolescent idiopathic scoliosis is typically performed when curves progress beyond 50 degrees. Pain is managed postoperatively with intravenous opioids administered by patient controlled analgesia (PCA), which is commonly associated with opioid induced side effects including nausea and pruritus. The use of low dose naloxone, a mu-opioid receptor antagonist, as an infusion in pediatric patients with PCA has been shown to reduce the incidence of opioid-induced pruritus and nausea while preserving analgesia[1-3], although ideal dose is not known. We implemented a prospective randomized clinical trial comparing low (0.5 mcg/kg/hr) and moderate dose (2.5 mcg/kg/hr) naloxone infusion on the time to tolerate liquids after surgery as well as PCA opioid requirements, nausea and pruritus ratings, and hospital length of stay.

METHODS: Patients age 10-21 years old were eligible to participate. Standard anesthetic during PSF surgery consisted of propofol and opioid infusion. Intrathecal morphine (10 mcg/kg) was given at the conclusion of surgery. Naloxone was started in a blinded fashion after surgery along with hydromorphone PCA (demand dose 4 mcg/kg, 8 minute lock out). A visual analog scale (VAS) was used daily during PCA use to rate nausea and pruritus. Pain scores were recorded by the bedside nurse every four hours while awake.

RESULTS: A total of 37 patients were allocated to the low dose naloxone group and 42 to the moderate dose naloxone group. Demographics were similar for the two groups with the exception of length of surgery, which was significantly longer in the moderate group, although the number of spine levels for fusion was similar for the two groups (Table 1).The groups had similar time to oral liquid intake after surgery and transition from PCA to oral pain medication (Table 2). The VAS scores for pruritus and nausea were also similar, as was need for diphenhydramine and ondansetron to treat these side effects. PCA use was similar on post-operative day (POD) zero and POD1. The moderate infusion group had significantly higher PCA use on POD2 (Table 3), although pain scores did not differ significantly. Hospital length of stay was similar for the two groups. There was a trend toward a higher incidence of respiratory depression patients in the low dose group compared to those in the high dose group (14% vs 2.4%; P =0.09).

CONCLUSION: Moderate dose naloxone infusion does not offer additional advantage over low dose in terms of side effect profile from PCA opioids in this setting. Interestingly, PCA use was higher POD2 in the moderate infusion group, this may represent partial reversal of opioid analgesia as the patient recovers and surgical pain improves. Further study is warranted regarding a possible beneficial effect on respiratory depression at the moderate naloxone infusion rate.

Table 1 Demographics low and moderate naloxone infusion groups. Data are mean ± SD.

	Low dose (N= 37)	Moderate dose (N=42)
Age (years)	14.6 ± 1.6	14.43 ± 1.9
Weight (Kg)	56.8 ± 12.4	58.09 ± 13.8
Length surgery (hours)	5.6 ± 1.0	6.2*± 1.0
Spine levels surgery (mean)	10.7 ± 1.9	11.2 ± 2.4

*P < 0.05

Table 2 Outcome Measures

	Low dose (N=37)	Moderate dose (N=42)	P value
Hospital length of stay (days)	5.6 ± 1.9	5.5 ± 1.0	0.79
VAS Pruritus POD[1] 0	3.11 ± 2.6	2.66 ± 2.1	0.43
VAS Pruritus POD 1	2.28 ± 1.9	2.62 ± 2.5	0.50
VAS Pruritus POD 2	2.5 ± 1.9	2.44 ± 2.5	0.63
VAS Nausea POD 0	2.65 ± 2.62	2.22 ± 2.6	0.47
VAS Nausea POD 1	2.27± 2.1	1.81 ± 1.8	0.30
VAS Nausea POD 2	2.5 ± 2.4	2.99 ± 2.7	0.5
Hours to oral intake	26.5 ± 11	25.4 ± 9.1	0.63
Days to transition po pain meds	2.49 ± 0.5	2.53 ± 0.55	0.73
Respiratory depression N (%)	5 (14)	1 (2.4)	0.09
Doses diphenhydramine	1.22 ± 1.4	1.21 ± 1.4	1
Doses ondansetron	4 ± 1.9	2.36 ± 2	0.94

[1]Post-operative day

Table 3. PCA use, morphine equivalents, post-operative day (POD) 0-2. Data are mean ± SD.

	Low dose N=37	Moderate dose N=42	P value
POD 0 (mg/kg)	0.69 ± 0.5	0.64 ± 0.4	0.61
POD 1 (mg/kg)	1.54 ± 0.57	1.57 ± 0.7	0.85
POD 2 (mg/kg)	1.04 ± 0.6	1.4 ± 0.9	0.04

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S-255.

ISOFLURANE EXPOSURE IN NEONATAL C57BL/6 MICE CREATES A CONCENTRATION DEPENDENT DEFICIT IN CONTEXT PRE-EXPOSURE FACILITATION EFFECT AS JUVENILES BUT NOT ADULTS

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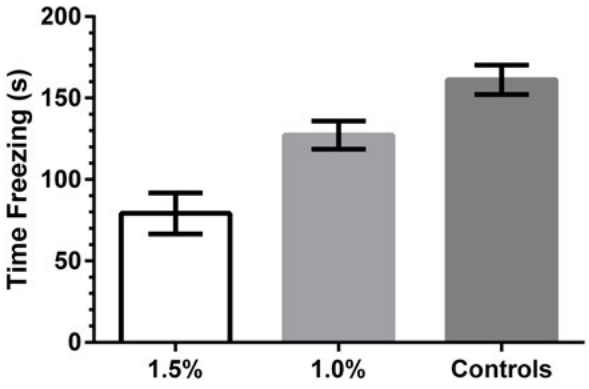
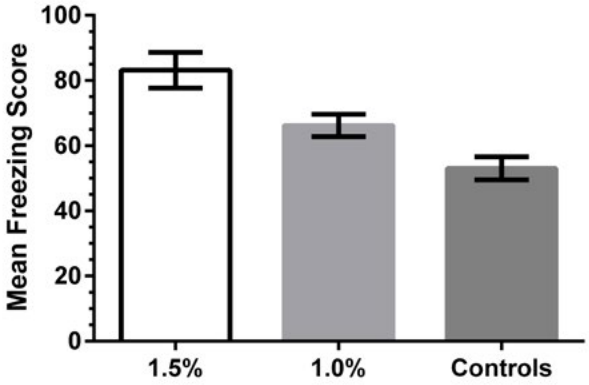
INTRODUCTION: Anesthesia is used to facilitate surgical and radiological procedures in millions of children every year, but has repeatedly been shown to cause extensive apoptotic cell death in developing animals.[1] Despite overwhelming histological evidence that exposure to anesthesia can cause neuronal cell death, the clinical consequences of this phenomenon remain unknown. Our previous work has shown anesthetic exposure to postnatal day (PND) 7 mice caused extensive apoptotic damage and transient deficits in Context Pre-exposure Facilitation Effect (CPFE) as juvenile mice. Few studies have correlated the amount of apoptosis with a concurrent stepwise worsening in a learning/behavioral effect.

METHODS: PND 7 day old C57BL/6 mice (n=74) were either fasted in 30% Oxygen or exposed to either 1% or 1.5% isoflurane anesthesia in 30% oxygen for 6 hours. Groups of mice from control and PND 7 exposures at 1% and 1.5% isoflurane were then subjected to a 3 day CPFE paradigm at either PND 28 or PND 49. Day 1 the animal was placed in the context environment for 5 minutes. Day 2 the animal was placed in the context, given a shock at 0.5mA for 2 seconds and removed from the context 30 secs later. On Day 3 the animal was returned to the context and freezing behavior was recorded for 5 minutes.

RESULTS: Using t-test analyses, statistical difference for mean freezing scores and total time freezing, but not latency to start of the first freezing episode was observed between the PND 7 1% and 1.5% exposed animals as well as the controls, when CPFE was done at PND 28. No statistical difference was observed for either the 1% or 1.5% exposure and the controls, when tested at PND 49.





CONCLUSION: In this study we evaluated the concentration effect of isoflurane on a learned behavior paradigm (CPFE) in an attempt to link the effect of increasing apoptosis with an increasing learning/behavioral effect. These results suggest a transient deficit that did not persist into adulthood in which the magnitude of the deficit correlates with the amount of anesthesia the animal was exposed. This mirrors clinical retrospective studies that demonstrated links with multiple general anesthetic exposures or total duration of the exposure to neurocognitive deficits later in life.[2] Given the rodents' ability to recover later in life, the clinical consequences of this neuronal destruction may be transient in nature and the human brain potentially can overcome anesthetic insult incurred during any window of vulnerability. The results of this study also suggest that the total amount of anesthesia and time under anesthesia should be limited to the best of our clinical abilities to keep our patients safe while under our care and beyond.

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S-256.

A COMPARISON OF MIDAZOLAM AND ZOLPIDEM AS ORAL PREMEDICATION IN CHILDREN

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INTRODUCTION: The anxiety associated with pediatric surgical procedures can be stressful for patients and parents/guardians. Oral midazolam is the most investigated, commonly used, and well-accepted premedication in the pediatric patient. However, oral midazolam was found to be of benefit only 57% of the time at parental separation and 71% at the time of induction,[1] and paradoxical reactions to midazolam premedication can be association with agitation rather than sedation.[2] Zolpidem is a short-acting nonbenzodiazepine hypnotic drug of the imidazopyridine class that potentiates GABA by binding to the same receptors as benzodiazepines. Zolpidem has oral availability, quick onset of action (~15 minutes) and 2-3 hours duration.[3] We sought to compare zolpidem to midazolam for pediatric premedication.

METHODS: This is a departmentally funded, prospective randomized double-blinded clinical trial (NCT02096900), designed to compare the effectiveness of oral midazolam and zolpidem for premedication. ASA class I-II pediatric patients between 2 and 9 years old scheduled for surgery of at least 2 hours duration and at least 23 hours postoperative admission were included in the study. Randomization was done on a 1:1 basis, with 0.5mg/kg midazolam (based on prior investigations in children for premedication[4]) or 0.25mg/kg zolpidem (based on prior investigations in children for sleep[2]) administered orally to the child. Sample size was calculated to require 80 participants total, with a planned interim analysis at 40 participants. The primary outcome measured was the between group difference in patient anxiety at the time of separation using the Modified Yale Preoperative Anxiety Scale (mYPAS).[5] Evaluators were trained and inter observer agreement verified prior to study initiation. Our secondary outcomes included mYPAS change and mask acceptance at induction.

RESULTS: One procedure was canceled in each group, so interim analysis was performed using the remaining 19 participants in each group. There were no significant demographic differences between the groups (Table 1). All patients were awake at the time of separation. There was no significance between group difference in anxiety at separation, evaluated using mYPAS, or change in mYPAS (Figure 1). 11 (57.9%) zolpidem patients had increased mYPAS at separation compared to 7 (36.8%) midazolam patients, but this did not reach significance (difference -21.1%; -48.7 to 10.6%; p=0.19).

CONCLUSIONS: At interim analysis, the current data supports our null hypothesis in that there is no significant difference in anxiety at separation between midazolam and zolpidem. Enrollment will be continued to ascertain if the larger number of zolpidem patients who had increased mYPAS reaches significance.

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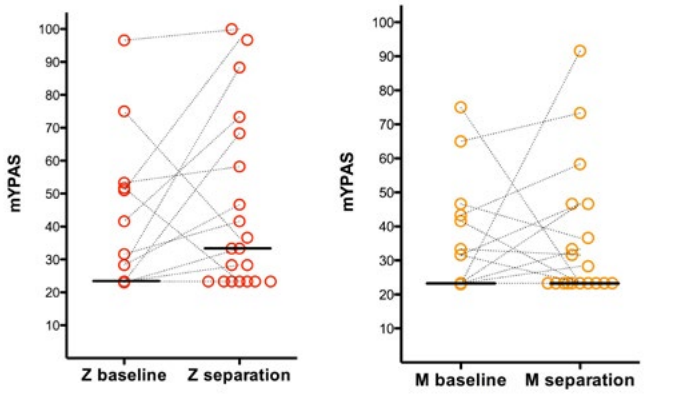
	Midazolam n = 19	Zolpidem n = 19	p-value
Sex # F; M	11; 8	8; 11	0.33
Age median 95% CI	6.9 5.5 to 8.0	6.7 4.8 to 7.5	0.50
Weight mean 95% CI	23.0 20.2 to 25.7	23.5 20.2 to 26.8	0.81
%ile weight for age median; 95% CI	41.8 29.9 to 59.1	49.6 32.6 to 72.3	0.47
ASA status #1; 2	6; 13	3; 15	0.29
Time from administration to separation minutes mean 95% CI	31.3 24.2 to 38.3	35.2 27.1 to 43.2	0.45
mYPAS baseline median; 95% CI	27.6 25.0 to 35.9	30.1 26.2 to 44.4	0.54
mYPAS at separation median; 95% CI	29.0 25.7 to 38.5	37.1 29.9 to 57.1	0.24
mYPAS change median; 95% CI	1.2 -2.5 to 7.8	4.9 1.0 to 13.0	0.23
Mask acceptance score #1; 2; 3; 4	14; 2; 2; 1	8; 5; 1; 5	0.12

Table 1



Comparison of modified Yale Preoperative Anxiety Scale (mYPAS) in patients given midazolam (M; n=19) compared to zolpidem (Z; n=19) premedication. Dotted lines connect scores from individual patients; heavy horizontal lines indicate median score. At the planned interim analysis, there were no significant between group differences in mYPAS at baseline or separation.

S-257.

WITHDRAWN.

S-258.

REDUCING PAIN ASSOCIATED WITH PROPOFOL INJECTION IN THE PEDIATRIC POPULATION: A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Propofol is a widely used anesthetic with many advantages. However, pain experienced during injection of propofol is very common with 70% of adults and 85% of children reporting this association. The largest meta-analysis conducted to review pain-reducing methods supported pretreatment with lidocaine in conjunction with venous occlusion as well as using an IV in the antecubital vein rather than hand vein produces the greatest reduction in pain. The topic has been extensively studied including non-pharmacological interventions as well as differing propofol formulations and mixtures. A definitive gold standard has never become apparent through these multiple studies and there still remains to be limited studies conducted within the pediatric population. The objective of this study is to determine if common techniques used to reduce pain with both venipuncture and/or propofol injection are superior to a control group of patients receiving no pre-treatment.

METHODS: 200 patients, aged 7-17 years were enrolled at University of MN Masonic Children's Hospital. Three interventions were studied with one control group. Interventions included 1) ice pack placed at the site of injection prior to propofol injection, 2) lidocaine injection with tourniquet placed ~10cm proximal to IV catheter, and 3) Buzzy (vibratory device shown to stimulate A-beta and C fibers) placed above injection site before and throughout propofol infusion. The control group received no pre-treatment intervention. The primary outcome was change in pain scores using the visual analog scale (VAS) reported by the study participant's nurse prior to injection and during injection. VAS scales were also completed by the parent/guardian. Secondary outcomes measured were self-reported facial images scales (FIS) for anxiety completed by the study participant. Further characteristics were recorded including age, vein location and side, IV gauge, ASA status, and premedication with fentanyl and/or midazolam.

RESULTS: Characteristics of patients enrolled in each of the 4 groups were very similar (Table 1). No significant differences were found among change in nurse and guardian VAS scores as well as FIS scores among the 4 interventions. Interestingly, change in scores of the control group was very similar to the groups receiving pre-treatment (figure 1, 2, 3). Using regression analysis, factors which were significant predictors of a decrease in scores were vein site and IV gauge. Scores decreased as IV gauge size decreased and the vein utilized became more proximal. Overall, findings illustrated need for further research on this topic in the pediatric field. IV site and gauge were major predictors in pain reduction and should be taken into consideration during placements of IVs for propofol injection.

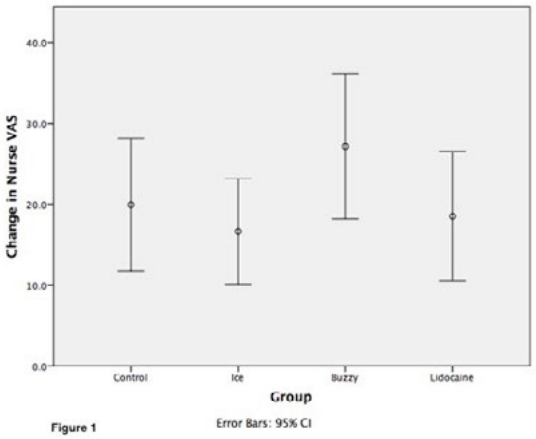

Figure 1

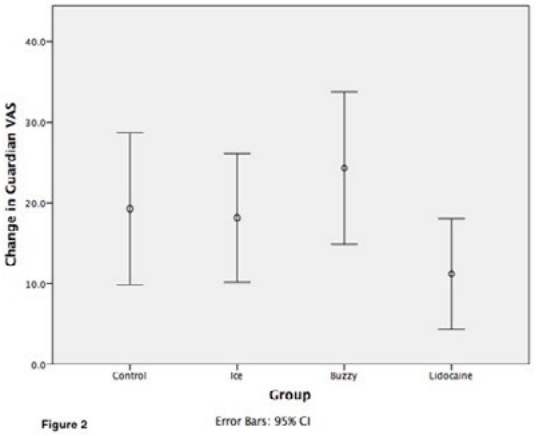

Figure 2

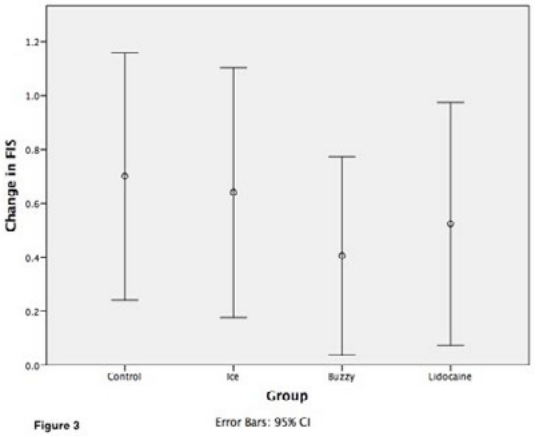

Figure 3

Table 1. Characteristics of patients.

Characteristic	Group				Total
	Control	Ice	Buzzy	Lidocaine	
n (no. patients)	52	50	50	51	203
Mean Age (yrs)	12.52	11.62	12.94	11.39	12.12
ASA Status					
1	11	18	11	11	51
2	29	26	29	26	110
3	10	6	10	14	40
IV Side					
Right	25	29	32	22	108
Left	26	21	18	29	94
IV Site (vein)					
Hand	27	37	30	32	116
Forearm	12	5	7	7	31
Antecubital	11	16	13	11	51
Upper Arm	1	2	0	1	4
Gauge					
20	5	3	6	9	23
22	30	30	32	25	117
24	16	17	12	16	61

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S-259.

DELAYED EMERGENCE IN PEDIATRIC PATIENTS WITH NEUROLOGIC DISEASE PRESENTING FOR AMBULATORY SURGERY

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INTRODUCTION: Management of children with pre-existing neurologic disease can be challenging for anesthesiologists. In clinical practice, it has been anecdotally reported that delayed emergence is more common in patients with neurologic disease, however, there is limited published data to support this observation. We sought to identify whether the mere presence of neurological disease in children can serve as a risk factor for prolonged emergence.

METHODS: Following approval by the Institutional Review Board, we conducted a search of our database from November 2012 to July 2014. Patients were included if they were under 18 years of age, carried a chronic neurological diagnosis profoundly affecting development, underwent ambulatory surgery requiring general endotracheal anesthesia, and were extubated awake. A healthy case-control group, otherwise meeting inclusion criteria, was also abstracted. The primary outcome was emergence time, defined as time from anesthetic gas off to extubation. A secondary outcome of time from extubation to actual discharge was also calculated. Statistical analysis was performed using JMP version 9 (SAS, Cary, NC). Descriptive statistics were employed for demographic data, and the student's T test was used to determine differences in outcomes. Confidence intervals were calculated. Regression analysis was performed on the study group to delineate fit of independent inputs to outcome variables.

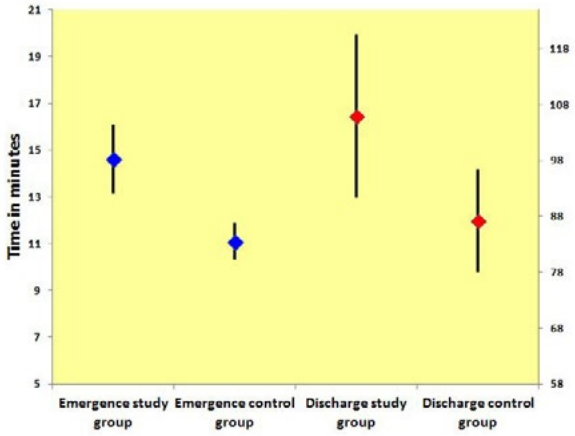
RESULTS: Data from 89 patients and 177 controls met criteria. Co-existing diseases and procedures performed are listed in table 1. There were no significant differences between groups for age, lowest intra-operative temperature, amount of pre/intraoperative medications, or intraoperative temperatures. The study group was significantly sicker (ASA 2.4 vs. 1.4), weighed less (16.5 kg vs. 22.1 kg), and had longer procedural times (50.0 vs. 32.1 minutes). No major morbidity or mortality was observed. Use of chronic neurologic medications did differ between study and control cohorts ($p < 0.0001$). Emergence time differed between the study and control groups (14.6 ± 1.51 vs. 11.1 ± 0.79 min), as did time to actual discharge (106 ± 14.7 vs. 87.2 ± 9.2 min) (figure 1). Multivariate regression analysis performed on the presence/absence of a neurological disorder, did correlate to both longer emergence and discharge times. Surgical length and presence or absence of chronic, outpatient neurological medications did not yield statistical correlations to either emergence or discharge times.

CONCLUSIONS: In this retrospective case-control study, pediatric patients with neurological disease undergoing ambulatory surgery, demonstrated an increased emergence time and postoperative time to discharge as compared to a control group. These findings imply that certain medical conditions may cause delayed emergence independent of pharmacologic, metabolic or perioperative variables. Knowledge of this association encourages the anesthesiologist to adjust intra- and post-operative expectations, possibly preventing a burdensome work-up for the culprit etiology.

Table 1. Common Diagnoses and Procedures Performed

Diagnosis	patients	Procedure	patients	controls
Syndrome NOS	26	Myringotomy/Adenoids	24	73
Down's syndrome	19	Tonsillectomy/Adenoids	22	50
Cerebral palsy	16	Tendon release/lengthen	9	0
Prematurity	7	Strabismus repair	7	0
Cyanotic heart disease	6	EGD	6	16
Mitochondrial disorder	4	Hernia repair	0	5
Epilepsy/seizure disorder	3	Genitourinary surgery	0	5
Spina bifida	3	Other	21	28
Jacobsen syndrome	1			
Schizencephaly	1			
Craniosynostosis	1			
Arythrogryposis	1			
Myotonic dystrophy	1			

Figure 1. Study outcomes and 95% confidence intervals



S-260.

EFFECT OF TRANEXAMIC ACID BASED ON PHARMACOKINETICS IN PEDIATRIC PATIENTS UNDERGOING CRANIOSYNOSTOSIS SURGERY: RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Craniosynostosis surgery possesses significant bleeding risk and needs for massive blood transfusion in young children. Various efforts had been made to resolve such difficulties, one of which is the use of antifibrinolytic agent.[1] Antifibrinolytic effect of tranexamic acid (TXA) had been shown to reduce hemorrhage and the amount of transfusion by many studies, although none had presented its usage according to pharmacokinetic model. Therefore, the aim of the study was to investigate the role of TXA on intraoperative blood loss, RBC transfusion, and the changes in coagulopathy in terms of rotational thromboelastometry (ROTEM).

METHODS: A total 50 children undergoing surgery for craniosynostosis were enrolled, of which 25 patients received TXA according to pharmacokinetic model (TXA group) and 25 patients received the same amount of normal saline (non-TXA group) intraoperatively. Population pharmacokinetics of TXA had been adopted from related study, where loading dose of 10 mg/kg over 15 minutes followed by a 5 mg/kg/h maintenance infusion to produce steady-state TXA plasma concentration above the 16 μg/mL threshold.[2] ROTEM analysis was done at preop, postop, and at postoperative day 1. The amounts of blood loss, transfusion, complete blood count were investigated throughout the surgery and until postoperative day 2. The amount of blood loss was evaluated using calculated blood loss (CBL) from pre- and postoperative hematocrit and the volume of the RBC transfusion. Results The amount of CBL was significantly lower for patients receiving TXA compared with the non-TXA group during surgery and postoperative day 0 (811 ± 369 ml vs. 1120 ± 389 ml, P = 0.009; and 87 ± 31 ml vs. 161 ± 90 ml, P = 0.001, respectively). In addition, the weight-adjusted amount of RBC transfusion during surgery, postoperative day 0 and 1 were significantly lower for patients receiving TXA than non-TXA [57 ± 17 ml vs. 62 ± 31 ml, P = 0.047; 0 (0-0) ml vs 0 (0-5) ml, P = 0.018; and 0 (0-0) ml vs. 0 (0-4) ml, P = 0.008, respectively]. The weight-adjusted amount of FFP transfusion was significantly lower for TXA group during surgery (14 ± 9 ml vs. 21 ± 13 ml, P = 0.043). The ROTEM data showed no difference between the two groups during perioperative period.

CONCLUSIONS: The use of TXA based on pharmacokinetic model in children undergoing craniosynostosis surgery reduces the amount of blood transfusion and CBL, but no changes in ROTEM parameters were noted.

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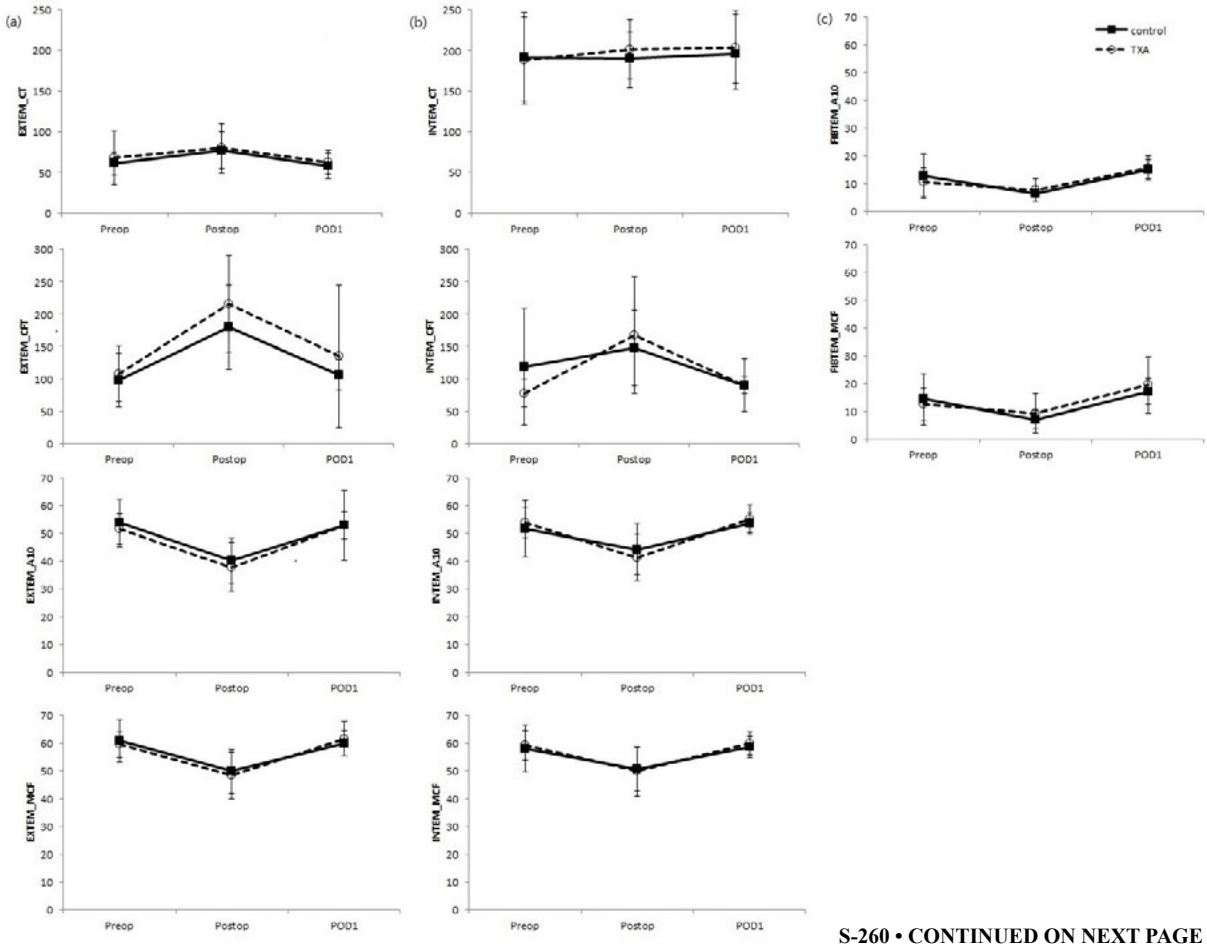

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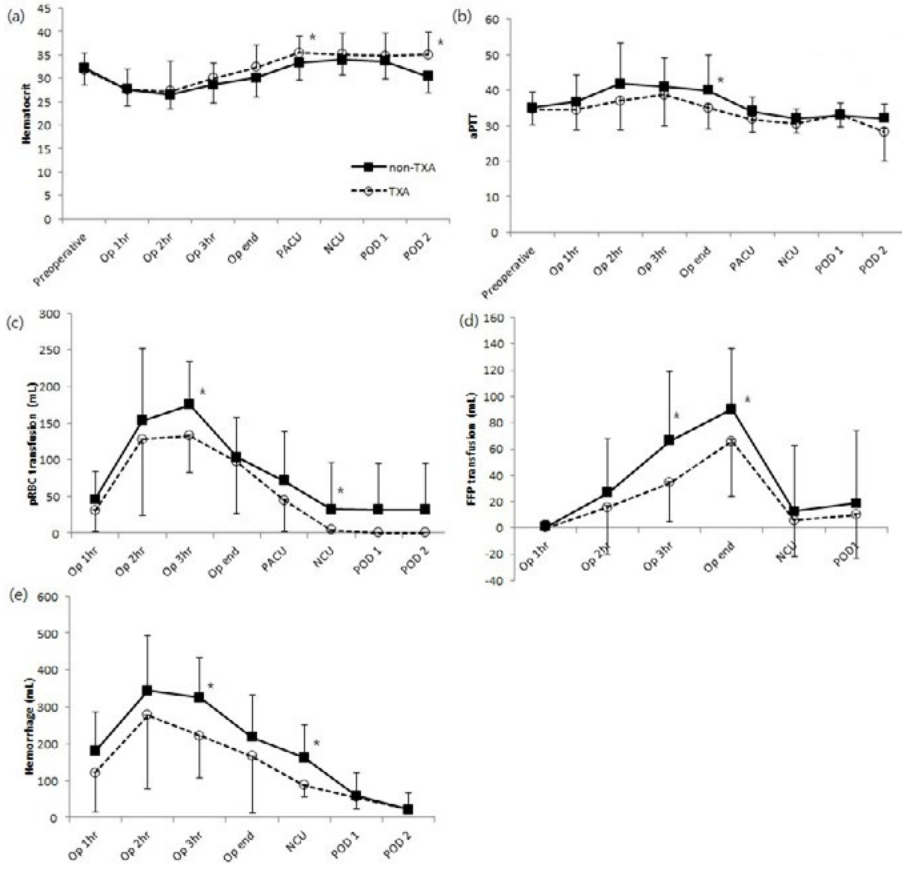

S-261.

EFFECTIVENESS OF ANTIEMETICS IN POST DISCHARGE NAUSEA AND VOMITING IN CHILDREN

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AFFILIATION: Anesthesiology, Stony Brook Medicine, Stony Brook, NY

INTRODUCTION: The adult literature demonstrates a stratified approach to PONV in which an increasing number of risk factors can be attenuated with a multimodal technique[1]. In adults, PONV and PDNV appear to be related entities, with some overlapping factors[2]. The objective of this study is to determine whether the same holds true for the pediatric population.

METHODS: To date, we have enrolled 77 patients ranging from the ages of 5-10 years old to an ongoing IRB-approved study of post-operative/post-discharge nausea and vomiting and pain in children. Patients were either ASA class 1 or 2 and were receiving anesthesia for elective surgical procedures. Antiemetic administration was provided at the discretion of the attending physician. The BARF scale[3] was given to patients preoperatively, before going into surgery, and postoperatively, right before they were discharged. Nausea was defined as present if the child self-rated above or equal to a two while circling the face that described how they were feeling on the scale (Fig 1). Nausea and emesis were both tracked for 3 days after discharge by using a question packet that was sent home with the parent. Children continued to self-rate each night using the BARF scale. Data was compared between groups by using nonparametric tests: Mann-Whitney U Test and Kruskal-Wallis Test.

RESULTS: Intraoperative administration of an antiemetic had no effect on the chance of the patient having nausea postoperatively. In the PACU, whether a patient was given or not given an antiemetic did not have an effect on lowering their score on the BARF scale (Fig 2a). Nausea was also present post-operatively and on POD1 regardless of how many antiemetics a patient was given (Fig 2b & 2c). Of the patients that received antiemetics, 3 of them had emesis and 4 patients who did not receive antiemetics also had emesis on POD0.

CONCLUSION: This data is significant in indicating that the presence or absence of antiemetics did not have a profound effect on postoperative nausea/emesis in children. Apfel's studies have shown that increasing the number of antiemetics in adults is effective in decreasing PONV[4]. The opposite was seen in our data: increasing the number of antiemetics administered did not decrease the incidence of nausea.

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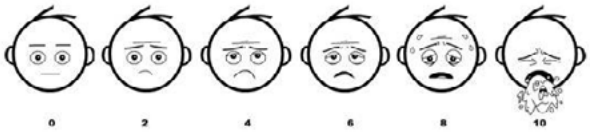

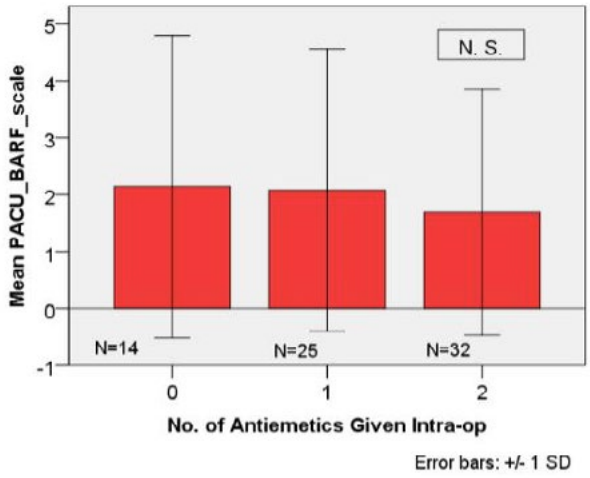

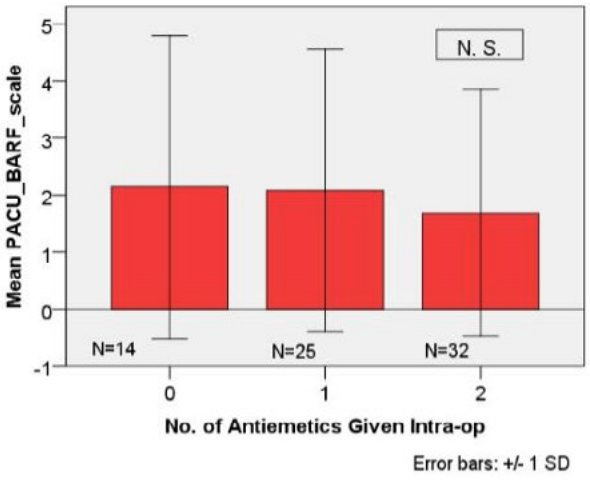

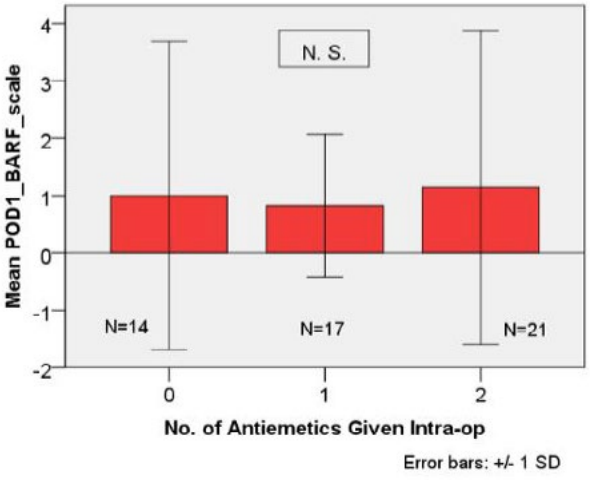

S-262.

RACIAL DISPARITIES IN THE PAIN MANAGEMENT OF CHILDREN IN THE POST ANESTHESIA CARE UNIT

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INTRODUCTION: Racial disparities in health care have been well-documented. In the ED, differences in wait time, medications for abdominal pain and admission rates have been reported[1]. Furthermore, black and Hispanic children are less likely to receive opioid drugs for acute pain treatment[1].

Pediatric ambulatory surgery is increasingly popular in the United States and 20-60% of these children experience significant postoperative pain[2]. In many hospitals, pain in PACU is managed "as needed" or based on a predetermined pain score. Pain in PACU in pediatric ambulatory surgical patients provides an appropriate paradigm for investigating racial differences in analgesic administration. Since PACU pain and culture are different from those in the ED, we tested the hypothesis that minority children would be equally likely to receive analgesia for pain in the PACU as their white peers.

METHODS: Following IRB approval, clinical, demographic and anthropometric data were prospectively collected on 775 children aged 4-17yr who underwent ambulatory surgery. Primary outcome measure was reception of PACU analgesia (overall, opioid and non-opioid). Primary exposure variable was racial identity defined as white or minority (black, Hispanic and others). Univariate factors associated with PACU pain treatment were assessed with Chi-squared or t-test. Probability of receipt of PACU analgesia was modeled using multivariable logistic regression analysis with age, gender, race, pain category (mild vs. moderately severe), surgical specialty, intraoperative morphine dose, use of intraoperative multimodal analgesia and duration of surgery included as predictors.

RESULTS: Of 775 children, 55.1% were boys. Mean age of subjects was 9.6 (3.2) yr. 38.2% of patients received some form of analgesia; 27.9% received at least one opioid. There was no statistically significant difference by race in the frequency of moderately severe PACU pain (white 19.4%; minority 21.7%; P=0.46). There were no statistically significant differences in the rates of administration of any analgesia (white 23.0%; minority 18.2%; P=0.10) or any opioid (white 23.7%; minority 18.5%; P=0.09). Stratified by type of opioid, white children were significantly more likely to receive IV morphine (white 29.9%; minority 18.4%; P=0.006). Stratified by pain categories, white children were more likely to receive IV morphine for severe pain (white 60.0% vs. minority 40.0%; P=0.002). On multivariable analysis adjusted for race, age, gender, surgical specialty, duration of surgery and PACU pain scores, race remained a strong predictor of IV morphine use (adjusted OR=1.8, 95%CI =1.17-3.09; p=0.02).

CONCLUSION: We found racial differences in PACU analgesic administration especially in rates of IV morphine use. Documenting and understanding such disparities is an important first to improve the equity of care in the ambulatory setting.

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S-263.

WITHDRAWN.

S-264.

SURGERY FOR LIVING DONOR PEDIATRIC LIVER TRANSPLANTATION- INDIA VS. USA: A SNAPSHOT PERIOPERATIVE CARE COMPARISON AT TWO CENTERS

AUTHORS: S. Johng[1], A. D'Cruz[2], R. Foreman[1], S. Chinnakotla[3], S. Rao[2], C. Murugesan[4], K. G. Belani[5]

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INTRODUCTION: Living donor liver transplantation (LDLT) is an optimal option for treatment of End-stage liver disease (ESLD), a worldwide problem in infants and children. Site 1 and Site 2 are appropriate health-care destination for these high-tech procedures at suitable institutions. In this report, we compared the demographics and outcome of LDLT in infants and children at Site 1 versus Site 2.

METHODS: After IRB approval, a cohort review of perioperative care was conducted in 44 children at Site 1 versus 18 at Site 2 during the following time frames: 1997-2014 for Site 2 and 2006-2014 for Site 1. The demographic data is listed in Table 1.

RESULTS: Isoflurane was the predominant anesthetic in both centers. The surgical time was longer in Site 1 (12±2.4 vs 8.4±2.6 hrs, $p<0.05$). The duration of intubation between the two centers was not significantly different (7.7±14 vs 12.6±32 days, $p=0.44$). Intraoperative blood loss was similar at the sites (1413±1023 vs 1143±702 ml, $p=0.32$). The duration of ICU stay at Site 1 and Site 2 was also not different (23±15 vs 14.3± 32 days, $p=0.21$). The return rate to the operating room (O.R.) within a few days of surgery was 61% at each site. The long-term survival was similar (Figure 1). The average total hospital cost was significantly different (Site 1 $20,000 vs Site 2 $290,0001). Figure 2 lists the causes of mortality in the first year in each country - sepsis and multiple organ failure (MOF) occur more commonly in Site 1.

CONCLUSIONS: Infants and children at Site 1 and Site 2 receive similar perioperative and anesthetic care. Surgical time was significantly longer at Site 1, while perioperative costs are approximately 14 times higher at Site 2. Intraoperative blood loss, duration of intubation, duration of ICU stay, return rate to the operating room, and long-term survival were not found to be significantly different between the two centers.

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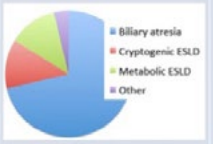
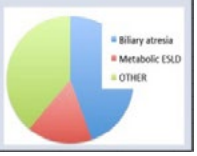
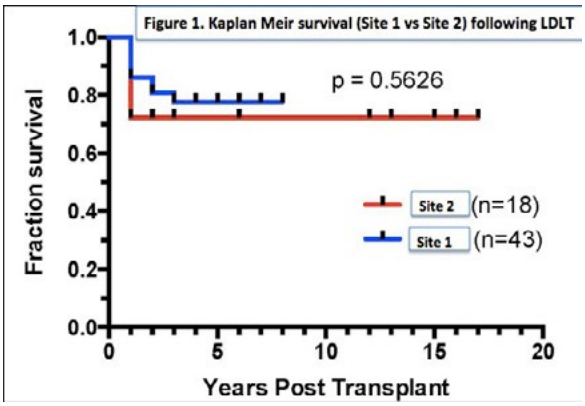
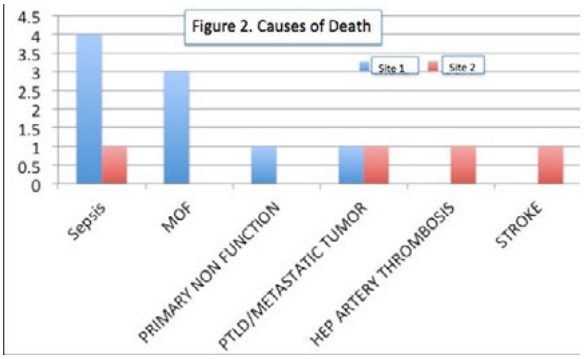
Table 1. Demographic information and primary disease

Criterion	Site 1	Site 2
Age (months)	39±37	30.5±39
Gender	M=29; F=15	M=10; F=8
Primary Disease		





S-265.

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S-266.

THE TIMING AND CHARACTERIZATION OF POST-ANESTHETIC COMPLICATIONS IN PEDIATRIC PATIENTS WITH PULMONARY HYPERTENSION UNDERGOING GENERAL ANESTHESIA- A RETROSPECTIVE STUDY

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INTRODUCTION: Children with pulmonary hypertension are more likely to experience adverse events when undergoing anesthesia.[1] Little data exists to guide post-anesthetic disposition and care.[2] This study aims to describe the incidence of post-anesthetic minor and major complications in children with PH at a single center. Associated factors including timing of post-anesthetic complications and setting of care are explored.

METHOD: After IRB approval, electronic medical records of patients with PH undergoing general anesthesia from 2010-2015 were reviewed, excluding cardiopulmonary bypass cases. For inpatients, clinical data from 48 hours prior (baseline) and 48 hours after the anesthetic event were collected when available. For those discharged before 48 hours, records were searched for postoperative call and readmission information if present. Minor and major complications and related information were analyzed. See Table 1 for definitions.

RESULTS: There were 109 anesthetics for 32 patients, 0-18 years old. See table 2. Postoperative complications were 4 (3.6%) major and 23 (21%) minor involving 16 patients. Major complications (table 3) were associated with long procedure and anesthesia durations ($p=0.02$ each) and major surgery ($p=0.005$). Young age had borderline significance ($p=0.05$). No deaths occurred. All minor complications involved desaturations, significantly associated with airway procedures ($p<0.01$). Five minor complications occurred in outpatients planned as same-day-discharge to home. One was admitted for repetitive desaturations. Four went home as planned but two were readmitted with respiratory issues responding to minor therapy. Major complications occurred at 0.5-48 hrs post-anesthesia (mean 27.4h, SD 17.7h) and minor complications at 0.1-42 hrs (mean 17.2 h, SD 15 h). The 2 readmitted outpatients presented to the emergency department 32 hrs and 5 hrs respectively after the anesthetics. The following were not significantly associated with any type of complications: age at diagnosis, pre-operative oxygen use, therapy naiveness, ASA status and inpatient status.

CONCLUSIONS: Postoperative complications occurred frequently in children with PH. Minor complications occurred in 21% of cases, with airway procedure being a significant risk factor. Major complications (3.6%) were significantly related to major surgeries and long procedural/anesthetic durations. Complications can first occur many hours after the anesthetic with important clinical implications for postoperative care. The retrospective nature, small sample size and insufficient post-discharge data place significant limitations on the results obtained.

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Table 1: Definitions

Pulmonary hypertension	*Biventricular circulation:* mean pulmonary artery pressure > 25 mmHG at rest. *Univentricular circulation after cavopulmonary anastomosis:* pulmonary vascular resistance index > 3 Wood units m^2 or transpulmonary gradient > 6 mmHG even if mean pulmonary artery pressure < 25 mmHg
SPAP/ SABP grading Ratio: pulmonary artery systolic blood pressure or as estimated by right ventricular pressure over systolic systemic artery pressure	• Subsystemic level (SPAP/SABP <0.7) • Systemic level (SPAP/SABP 0.7-1) • Suprasystemic level (SPAP/SABP > 1)
A major complication is defined as a potentially life-threatening event requiring immediate treatment:	• arrhythmias requiring electrical or chemical cardioversion • unexpected hypotension requiring continuous inotropic support (milrinone, dopamine, epinephrine) and rapid boluses of IVF > 20 mL/kg or blood products • unexpected initiation of iNO • unplanned tracheal intubation • unexpected failure to extubate within reasonable clinical time frame • cardiac massage or cardiopulmonary resuscitation • institution of extracorporeal life support (ECMO) • death • Pulmonary hypertensive crisis: defined as an increase in PAP to exceed systemic BP, a decrease in systemic BP, and a decrease in SpO2
A minor complication is defined as a TRANSIENT disturbance resolved after a minor intervention :	• SpO2 decrease > 10% during stable oxygen therapy prompting an increase in FiO2. No significant change in BP nor rhythm. • Isolated BP decrease prompting a fluid bolus • Arrythmia- self- limiting with no BP perturbation
Procedure Types	*Surgical major* - Extensive procedure on the abdominal, pelvic and/or thoracic cavities, cranium or spine associated with large fluid shifts and systemic inflammatory effects. Surgical minor- Minor invasive procedures with minimal fluid shifts and systemic inflammatory effects. i.e central line placement, laryngoscopy, bronchoscopy, GI endoscopy, tonsillectomy, ear tubes. *Non surgical* - noninvasive procedures i.e. MRI, echo, CT *Diagnostic Catheterizations* *Interventional Catheterizations*

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Table 2. Patient Characteristiscs

Age	15 days - 18 years old
Gender	56 (51%) males, 53 (49%) females
Weight	1.5 - 64 kg
ASA	3 77 (71%) 4 32 (29%)
Etiologies	*NICE group 3, due to lung disease 52 (47%)* NICE 1.4.4 --congenital heart disease 16 (15%) Combined 3.7 and 1.4.4 11 (10%) NICE 2.4 --due to L heart disease 4 (4%) NICE 1.1-- idiopathic 2 (2%) Other NICE classes 24 (22%)
Circulation type	9% - univentricular circulation, all as Glenn physiology 91%- biventricular circulation
SPAP/ SABP Ratio: Pulmonary Artery Systolic Blood Pressure or estimated by right ventricular pressure over Systolic Systemic Artery Pressure	*Subsystemic level (SPAP/SABP <0.7) 74 (68%)* Systemic level (SPAP/SABP 0.7-1.0) 35 (32%) Suprasystemic level (SPAP/SABP > 1) 0 (0%)
Number of Preoperative Pulmonary Antihypertensive Agents	0 (Therapy naïve) 34 (31%) 1 51 (47%) 2 20 (18%) 3 3 (3%) 4 1 (1%)
Pre-operative Oxygen use	Yes 75 (69%) No 34 (31%)
Preoperative status	Outpatient 47 (43%) Inpatient 62 (57%)
Post-procedural disposition	Discharged on the procedure day 23 (21%) Admitted overnight 22 (20%) Admitted for 48 hrs or longer 64 (59%)
Procedure types (Some procedures are combined)	Surgical Major 12 (9%) Surgical Minor 49 (45%) Airway 15(14%) Nonsurgical 9 (8%) Diagnostic catheterization 32 (29%) Interventional catheterization 7 (6%)

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Table 3. Summary of Major Complications

Case 1	Infant < 1 yo for abdominal procedure. Chromosomal abnormality present. NICE classification 3.7 (developmental lung disease). Systemic level pulmonary hypertension, on 2 pulmonary antihypertensive agents and oxygen. Inpatient status. Extubated and transported to PACU. Apnea and desaturation occurred shortly after arrival to PACU which was unresponsive to additional doses of neuromuscular reversal and naloxone. Required continued PPV with increased FiO2 and eventual re-intubation. Patient was extubated in the PICU 4 hrs later but continued with episodes of apnea and desaturations that were not reflective of the preoperative baseline.
Case 2	Infant < 1 yo with repaired AV canal, heterotaxy syndrome and biliary atresia for abdominal procedure. NICE classification 1.4.3 (portal hypertension). Subsystemic level pulmonary hypertension, on 1 pulmonary antihypertensive agent and oxygen. Inpatient status. Required dopamine intraoperatively. Transported to ICU intubated. At 27 hr post- anesthetic event, multiple episodes of desaturation, bradycardia and arrhythmia occurred requiring increased inotropic support, oxygen and boluses of albumin 5%. Also, sedation and paralysis were increased.
Case 3	Infant < 1 yo with bronchopulmonary dysplasia for abdominal procedure. Fetal alcohol syndrome present. NICE classification 3.7 (developmental lung disease). Systemic level pulmonary hypertension, on 1 pulmonary antihypertensive agent. Inpatient status. Transported to ICU intubated. At 6 hr post- anesthetic event, multiple episodes of desaturation and arrhythmia prompted use of iNO and increased FiO2.
Case 4	Infant < 1 yo with bronchopulmonary dysplasia for interventional catheterization. NICE classification 3.7 (developmental lung disease). Subsystemic level pulmonary hypertension. Therapy naïve. On O2 by NC. Planned intervention unsuccessful. Transported intubated to ICU. At 48 hrs post-anesthetic event, profound desaturations with bradycardia noted prompting initiation of iNO, milrinone and sildenafil. This was deemed consistent with pulmonary hypertensive crisis. Stimulation was thought to be triggering the events.

S-267.

WITHDRAWN.

S-268.

REDUCTION IN CRYOPRECIPITATE WASTE IN THE PEDIATRIC CARDIOVASCULAR OPERATING ROOM: A GOAL-DIRECTED TRANSFUSION ALGORITHM BASED ON ROTATIONAL THROMBOELASTOMETRY

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INTRODUCTION: Patient blood management (PBM) is a multidisciplinary concept designed to manage anemia, optimize hemostasis, and establish decision thresholds for administration of blood products[1]. The Joint Commission has partnered with the American Association of Blood Banks to develop a hospital certification for PBM[2]. As part of a Quality Improvement (QI) initiative, we implemented a goal-directed transfusion pathway based on rotational thromboelastometry (ROTEM®, TEM Systems, Inc., Durham, NC) in the pediatric cardiovascular operating room to improve blood product utilization. Cryoprecipitate was targeted as the blood product to track due to its consistently high rate of waste.

METHODS: This study targeted the use and waste of cryoprecipitate in the cardiovascular operating rooms at our institution. A ROTEM-guided goal-directed transfusion pathway was developed after review of published evidence, and in collaboration with the Transfusion Medicine Service[3,4]. This pathway (see figure 1) recommends human fibrinogen concentrate (RiaSTAP®, CSL Behring, King of Prussia, PA) as a substitute for cryoprecipitate for bleeding secondary to hypofibrinogenemia in patients weighing more than 5 kg. The transfusion pathway, ROTEM® ordering and interpretation instructions, and fibrinogen concentrate administration were presented in anesthesiology and multidisciplinary conferences, and the study started in April, 2015. Data on cryoprecipitate waste, ROTEM® use and fibrinogen concentrate use were collected for 7 months before and after introduction of the transfusion pathway. Results: The run chart (Figure 2) demonstrates a sustained decrease in cryoprecipitate wastage after education and implementation of the transfusion pathway. The increase in use of ROTEM® and fibrinogen concentrate is shown graphically in Figure 3. The numbers of cases per month for the periods before and after the initiation of the project were 78.7 ± 5.4 and 86.4 ± 8.5 (Mean ± SD).

CONCLUSION: Patient Blood Management is a concept formulated to optimize patient safety and blood utilization. Implementation of PBM in adult cardiac surgery has been associated with reduced transfusion and improved outcomes[5-7]. We introduced a goal-directed transfusion pathway, improved the efficiency of ROTEM® measurement, and provided education about human fibrinogen concentrate, an alternative to cryoprecipitate. The future of transfusion medicine will involve PBM, point of care testing, pharmacologic coagulation factors, and goal-directed guidelines. Our study involves these strategies in a high volume, high acuity pediatric cardiac surgery program. We plan to study the effect of our pathway on transfusion of all blood products and other outcome measures.

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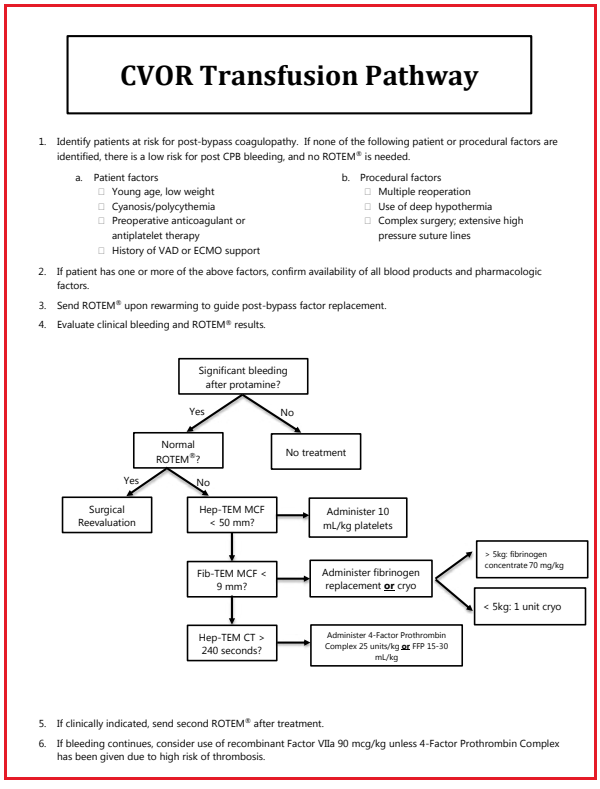

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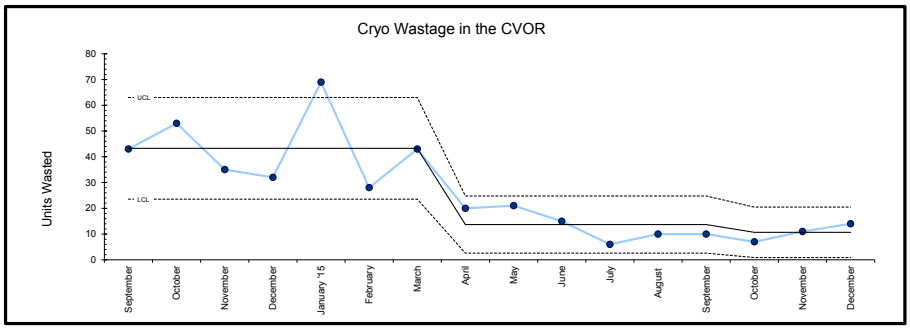

Figure 2

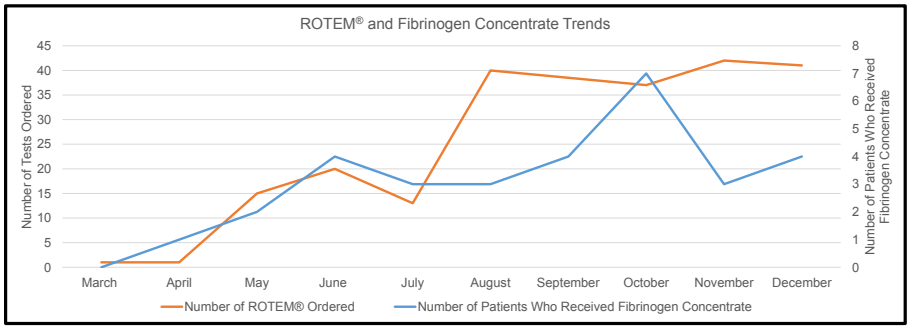

Figure 3

Subspecialty Abstracts

Perioperative Anesthesia

S-269.

ROLE OF PULMONARY OXYGEN UPTAKE AS A PREDICTOR OF INCREASED RISK FOR ADVERSE OUTCOME FOLLOWING ADULT NON-CARDIAC ANESTHESIA

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INTRODUCTION: Several intraoperative parameters have been found to be associated with adverse outcome following general anesthesia including intraoperative hypotension (low MAP) and low end-tidal anesthetic gas concentrations (low MAC)[1-2], thus raising the possibility of insufficiently met intraoperative oxygen requirements. Since intraoperative oxygen requirements are not readily available based on routinely captured data the present study was designed to estimate patients' average intraoperative minute-to-minute oxygen uptake and examine its association, along with those of average MAC and MAP, with 30-day all-cause mortality following adult non-cardiac surgical procedures performed under general inhalational anesthesia.

METHODS: Electronic anesthesia and hospital records were reviewed for adult, non-cardiac general anesthetics performed under inhalational anesthesia. Average pulmonary oxygen uptake rates (ViO_2) were estimated from the minute-to-minute values of the synchronized recordings of FiO_2, FeO_2, tidal volume (TV) and respiratory rates (RR) (captured at 15 second intervals) and indexed according to body surface area ($ViO_2 \approx (FiO_2 - FeO_2) * RR * TV / BSA$). Similarly, age-adjusted MAC-equivalents3 and MAP were averaged over the course of these anesthetics. Each of these parameters were examined for their association with 30-day postoperative mortality derived from the Social Security Death Index, using logistic regression, with $p < 0.05$ considered significant.

RESULTS: In 18,373 patients tested, ViO_2, MAC and MAP each exhibited independent associations with adverse outcome. While low MAP was associated with overall greater mortality (Fig. B compared to Fig. A), both low MAC and high ViO_2 were independently associated with greater 30-day mortality, regardless of MAP (Figs A & B). The worst outcome tended to associated with low MAP, low MAC and high ViO_2 whereas low ViO_2 portended better outcomes, regardless of MAP and MAC.

CONCLUSIONS: The association of low MAP and low MAC with adverse outcome (also known as "double low") was predicated on higher estimated pulmonary oxygen uptake suggesting the possibility of higher (i.e., potentially insufficiently suppressed) oxygen consumption contributing to the adverse postoperative outcome associated with low MAC anesthesia.

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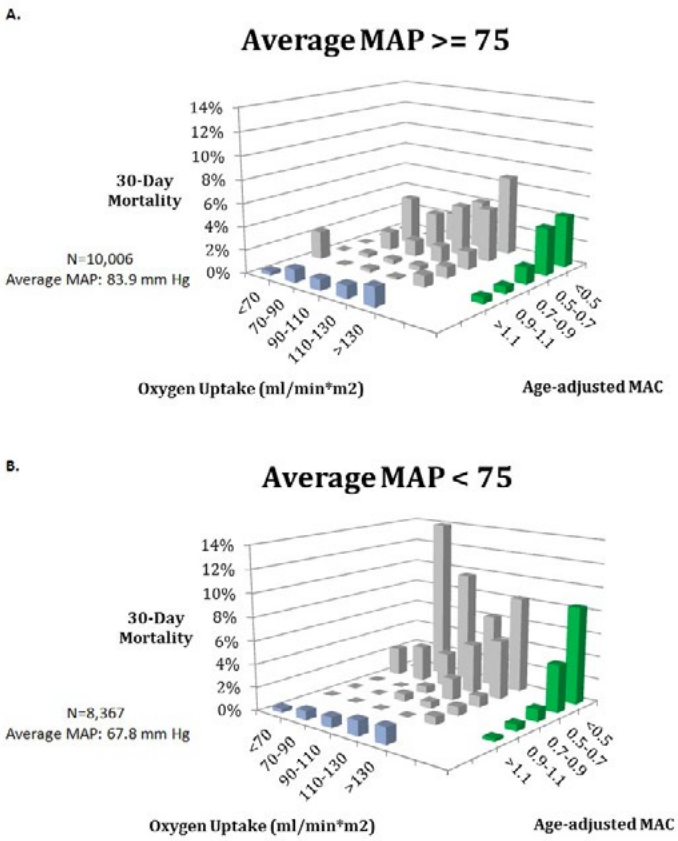

S-270.

THE EFFECTIVENESS OF DEXMEDETOMIDINE AS A PROPHYLACTIC TREATMENT FOR EMERGENCE DELIRIUM AMONG COMBAT VETERANS WITH HIGH ANXIETY: A RANDOMIZED, CONTROLLED TRAIL

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INTRODUCTION: Emergence Delirium is characterized by agitation, confusion, and violent physical and verbal behavior associated with awakening from general anesthesia. The 20% incidence of emergence delirium (ED) among combat veterans is much higher than the general surgical population.[1] Preoperative baseline anxiety was shown to be the best predictor of ED and combat veterans are known to be at high risk for anxiety as well as depression and PTSD.[2-3] Perioperative use of dexmedetomidine has demonstrated promising benefits in the pediatric setting of ED but has not been evaluated in combat veterans.[4]

METHODS: This study is a multi-site, prospective, randomized controlled investigation of 380 patients with a history of military combat exposure who are scheduled for elective surgery with a general anesthetic as the primary means of anesthesia. All subjects are administered the State Trait Anxiety Inventory (STAI) to evaluate baseline anxiety. Those enrolled subjects with a low anxiety level (STAI < 39) (N=228) are placed in the observational arm of the study. Those with a high anxiety level (STAI ≥39) are placed in the experimental arm (N=152) and are further randomized to treatment with intraoperative dexmedetomidine infusion (1 μg/kg bolus at induction, followed by a 0.6 μg/kg/hr infusion continued until emergence) or a placebo intraoperative infusion. Following the delivery of the prescribed anesthetic, all subjects are observed for signs of emergence delirium using the Pediatric Anesthesia Emergence Delirium (PAED) Scale. The patient and data recorder are blind to the randomization results.

RESULTS: To date 185 subjects have been enrolled; 123 subjects in the observational group, and 62 subjects in the randomized group. The incidence of ED in the observational and randomized groups is 30% and 36%, respectively. The attrition rate is 5%. No adverse events or complications have occurred in those subjects assigned to the treatment group. The treatment arm remains blinded to infusion until full interim analysis at 200 subjects.

CONCLUSIONS: The rate of ED among participants in this study is higher than previously described. Psychological indicators of combat and deployment stress (anxiety, depression, PTSD) may serve as a predictor for emergence delirium in the post-surgical patient. The overall safety of a dexmedetomidine infusion in this population mirrors that observed in other populations at high risk for ED.4 Results shall inform anesthesia practitioners in use of prophylactic treatment with dexmedetomidine for combat veterans at high risk for ED.

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S-271.

A PERIOPERATIVE SMOKING CESSATION INTERVENTION WITH VARENICLINE VS. BRIEF ADVICE

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INTRODUCTION: Interventions for perioperative smoking cessation can be an important part of the Perioperative Surgical Home. The effectiveness of perioperative interventions to quit smoking with varenicline has not been compared to brief interventions. The objective of this study was to determine the efficacy of a smoking cessation program with varenicline compare to brief advice on abstinence in patients undergoing elective surgery.

METHODS: REB approval was obtained from the 2 participating institutions and informed consent was obtained from all participants for this multi-centered, randomized controlled trial. A total of 296 patients were randomized to receive either: 1) a smoking cessation program consisting of a standardized 10-15 min counseling session by anesthesiologists trained to provide smoking cessation interventions, varenicline for 3 months, and a fax referral to Smokers' Helpline; or 2) standardized brief advice (<5 min) by anesthesiologists or pharmacists trained to provide smoking cessation interventions and provision of the Smokers' Helpline number for self-referral. The primary outcome was biochemically (urine cotinine) confirmed 7-day point prevalence abstinence at 12 months. Secondary outcomes included: 7-day point prevalence abstinence at 1, 3, 6 months. An intention-to-treat analysis was performed. Chi-square test or Fisher's exact test (for categorical variables) and unpaired Student t tests (for continuous variables) were used. Multivariable logistic regression was performed to identify independent variables related to abstinence. $P<0.05$ was considered statistically significant.

RESULTS: The demographic variables were similar between the two groups, except the nicotine dependence was higher in the smoking cessation program group vs. the brief advice group (Fagerstrom test-score 5.0 ± 2 vs. 4.4 ± 2, $p<0.01$). The 7-day point prevalence abstinence at 12 months for the smoking cessation program vs. brief advice was 46.6% vs. 29.2% ($p<0.01$). At 1, 3, and 6 months, the 7-day point prevalence abstinence for the smoking cessation program group vs. brief advice group was 51.1% vs. 24.8% ($p<0.01$), 53.3% vs. 28.2% ($p<0.01$), 50.8% vs. 29% ($p<0.01$), respectively (Figure). The rate of quitline contact was higher in the smoking cessation program group vs. the brief advice group 78.8% vs. 8.3% ($p<0.01$). The smoking cessation program was associated with higher abstinence at 1, 6, 12 months (OR 2.0; 95% CI 1.02-3.92, $p<0.05$, OR 1.9; 95% CI 1.12-3.20, $p=0.02$, OR 2.1; 95% CI 1.22-3.54, $p<0.01$), respectively. Smokers' Helpline utilization was associated with abstinence in both groups at 1, 3, 6 months (OR 2.1; 95% CI 1.06-4.26, $p=0.03$, OR 4.8; 95% CI 2.23-10.22, $p<0.01$, OR 7.7; 95% CI 1.66-35.31, $p<0.01$), respectively.

CONCLUSION: Perioperative smoking cessation interventions with counseling, pharmacotherapy with varenicline, and a fax referral to Smokers' Helpline more effectively increase both long-term and short-term abstinence compared to brief advice and self-referral to Smokers' Helpline.

S-272.

DIFFERENT METHODS OF MODELING HYPOTENSION AND THEIR ASSOCIATION WITH POSTOPERATIVE TROPONIN ELEVATION IN PATIENTS UNDERGOING NONCARDIAC SURGERY

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INTRODUCTION: Postoperative myocardial injury (POMI), defined as elevated cardiac troponin, occurs in 5 to 19% of noncardiac surgical patients, with a 30 day mortality rate of 8 to 24%[1-3]. Intraoperative hypotension (IOH) appears to be a risk factor for development of POMI[4,5]. However, no consensus currently exists regarding the optimal threshold to define IOH[6] nor for the method to include IOH in statistical models. We aim to examine whether different methods to model IOH are associated with postoperative elevation of troponin.

METHODS: The study included 4283 patients aged ≥ 60 years underwent intermediate or high risk noncardiac surgery under general or spinal anesthesia with a postoperative hospital stay of ≥ 24 hr. POMI was defined as cardiac troponin I ≥ 0.06 µg/L within three days after surgery. To summarize different methods to model IOH, we performed a systematic review (figure 1). For the current analysis, we chose four predefined thresholds to define IOH (mean arterial pressure (MAP) < 55 mm Hg, MAP < 50 mm Hg, a decrease of 40% and a decrease of 50% from baseline BP) on which the methods presented in figure 1 were applied. Baseline BP was calculated as done previously 6. The local ethics committee approved the study protocol and waived the need for informed consent (REB, number 12-245).

RESULTS: Eligible patients were on average 72 yr old, 47% were female and 53% were hypertensive (table 1). Postoperative troponin elevation was observed in 28% of the patients. Patients with troponin elevation more often were males (60%), had comorbidities more frequent and patients more often underwent emergency and/or high risk surgery. Table 2 presents descriptive statistics of the IOH exposures based on the different methods being modeled, while table 3 presents odds ratio estimates for each IOH method. As can be seen (table 2), IOH exposures increase as IOH thresholds increase (i.e., are less stringent). Conversely, as IOH thresholds increase, the odds ratios showing the association between IOH and elevated troponin decrease (table 3). For both absolute thresholds, all methods of measuring IOH were significantly associated with elevated troponin, but for the relative threshold methods, not all methods showed significant associations with elevated troponins.

CONCLUSION: The threshold used to define IOH has previously been shown to affect incidence of IOH[6]. We additionally showed that both statistical method and applied threshold appear to affect the association of IOH with outcome, in this case postoperative troponin elevation. Further analyses are required to determine which method(s) are most useful in modeling troponin elevation when adjusting for other covariates, and for modeling other outcomes.

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S-273.

METHODS TO EXPRESS THE AMOUNT OF INTRAOPERATIVE HYPOTENSION IN CLINICAL STUDIES: A SYSTEMATIC REVIEW

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INTRODUCTION: In recent years, intraoperative hypotension (IOH) has been investigated in various studies. However, there is no consensus on, and hence considerable variation in, the threshold used to define IOH[1]. Additionally, it is also unclear which method best summarizes the amount of IOH the patient experienced throughout a surgical procedure and how to include this in statistical analyses. We conducted a systematic review to investigate which methods have been used to express and analyze IOH in the past decade in leading scientific journals in anesthesia.

METHODS: A systematic search (PubMed) was performed in seven selected anesthesia journals (*Anesthesia & Analgesia, Anesthesiology, British Journal of Anaesthesia, Anaesthesia, Canadian Journal of Anaesthesia, European Journal of Anaesthesiology* and *Journal of Clinical Monitoring and Computing*) between 2005 and 2015. Inclusion criteria were original research papers reporting intraoperative blood pressure measurements during noncardiac surgery for at least 30 consecutive minutes with a measuring interval of at most 5 minutes contained at least one threshold to define IOH and describing at least one method to model hypotension. Articles were excluded in case only the incidence of hypotension was reported. From the selected articles we extracted the following information: method to model IOH, surgical specialty, anesthetic method, year of publication and whether it concerned patient care as provided in daily clinical practice or rather investigation of a closed-loop algorithm of an anesthetic information management system (AIMS) (example in [2]).

RESULTS: Screening of 1267 titles and abstracts resulted in eventual inclusion of 81 articles (figure 1), showing an increasing number of publications on IOH over the past five years (figure 2). Most frequently studied specialties were gynaecology (n = 29), noncardiac surgery (n = 14), and neurology (n = 10) (table 1). Spinal and general anesthesia was studied 31 and 37 times respectively. In 13 out of 81 articles, results of an algorithm of a closed loop automated anesthesia system (AIMS) were reported, whereas the other 68 articles investigated actual patient management in daily clinical practice. Figure 3 depicts various methods to express IOH. In the 81 selected articles, duration of hypotension was most frequently used (n = 47), followed by lowest value below threshold (n = 33) and number of hypotensive episodes (n = 29). Most articles used 1 (n = 35) or 2 (n = 32) methods to include the amount of IOH in their analyses.

CONCLUSIONS: The number of studies on IOH has increased over the past decade. Our investigation in seven leading anesthesia journals shows that, next to variation in thresholds, there is also considerable variation in methods used to express the amount of IOH. We are currently investigating to which extent the choice of method is associated with the clinical outcome, and which method is to be preferred for different type of research questions.

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Figure 1 Flow diagram of selected

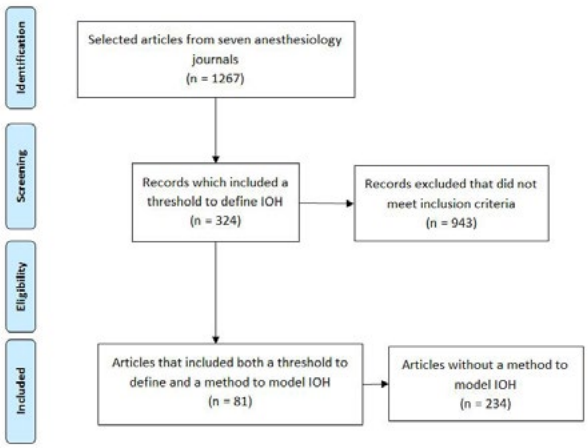

Figure 2 Number of publications with methods to model intraoperative hypotension per year

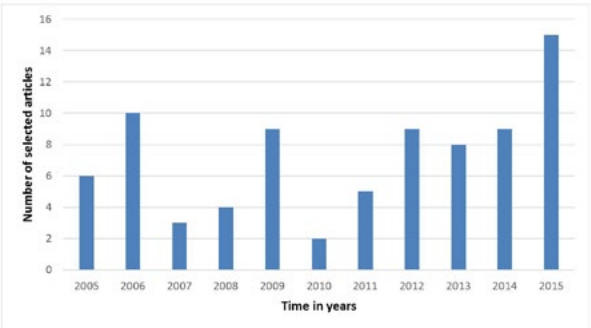

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Figure 3 Categories of methods to model intraoperative hypotension

Method	# (%)	Description in figure
Presence	81 (100)	At least two measurements are below the threshold; in this case yes.
Number of episodes	29 (36)	Number of hypotensive episodes; 1+2+3+4+5; in this case 5 episodes occurred
Duration/time	47 (58)	Total duration of hypotension in minutes: A+B+C+D+E Mean duration of a hypotensive episode in minutes: (A+B+C+D+E) / 5 Maximal duration of a hypotensive episode in minutes: episode with longest duration, in this case A Mean time between different episodes in minutes: (I + II + III + IV) / 4
AUC	6 (7)	Total Area under Threshold (AUT) : sum of pink colored areas in mm Hg/min Mean AUT per episode : sum of pink colored areas / 5 Maximum AUT per episodes: largest pink colored area; in this case 1
Lowest value (under threshold)	33 (41)	Maximum fall in mm Hg: lowest absolute value in ↓ Maximum fall in %: largest proportional difference to lowest values in ↓ and the predefined threshold Mean blood pressure under threshold: (sum of ↓) / 5
Change/variability	10 (12)	Not shown in figure; variance (example in [3])
Performance	11 (14)	Not shown in figure; applied in articles studying an algorithm of a closed loop automated anesthesia system
Other	8 (10)	Not shown; example is number of hypotensive readings during an anesthetic period

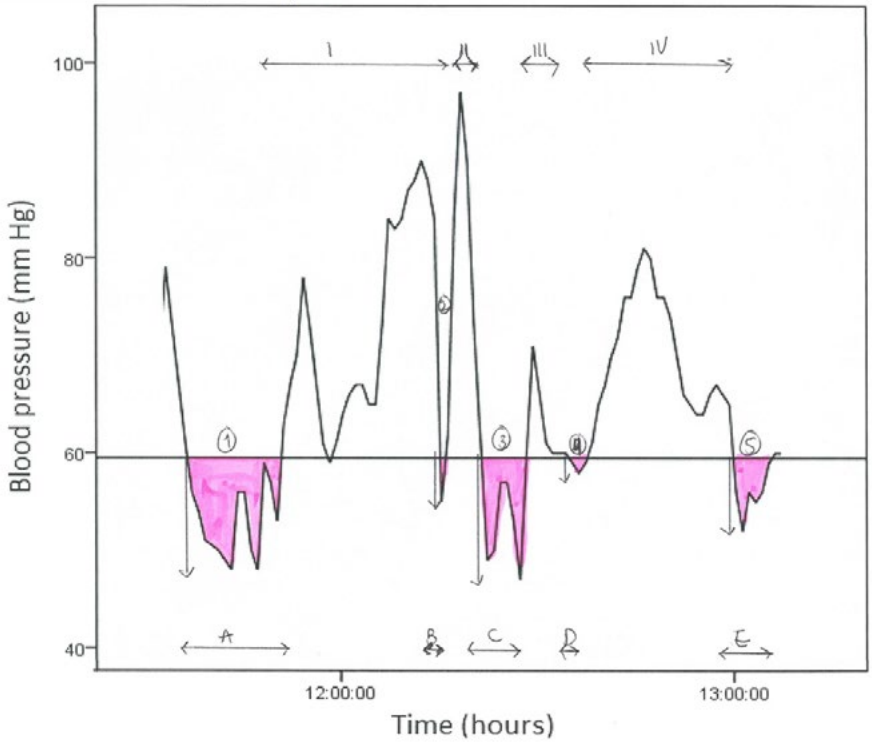

Table 1 Descriptive characteristics of the study related features

Specialty	#	Anesthetic method	#
Gynecology	29	General	37
Noncardiac surgery	14	Spinal	31
Orthopedic	13	Both	7
Neurology	10	Not mentioned	6
General	7		
Vascular	4	AIMS / patient treatment	#
ENT	3	Patient treatment	68
Not mentioned	3	AIMS*	13
Urology	2		
All	1		

* Anesthesia Information Management System; these articles reported results of an algorithm of a closed loop automated anesthesia system[2].

S-274.

CHARACTERIZING FADE UPON TRAIN-OF-FOUR STIMULATION DURING ONSET AND OFFSET OF NEUROMUSCULAR BLOCK PRODUCED BY SUCCINYLCHOLINE

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INTRODUCTION: Although previous studies[1,2] have demonstrated that even small doses of succinylcholine can produce fade on train-of-four (TOF) stimulation, the classic teaching in anesthesia remains that small doses of succinylcholine cause a phase I block. The phase I block is thought not to be associated with fade on TOF stimulation. We have conducted the following study to reinvestigate whether small doses of succinylcholine result in fade on TOF stimulation and to further characterize the fade if it was found to occur.

METHODS: Following approval by the local IRB, twenty ASA I or II adults (18-60 years of age with BMI <25 kg/m2), who were scheduled to undergo a surgical procedure under general anesthesia were enrolled. Anesthesia was induced with fentanyl (5-6 mcg/kg) and propofol (2-3 mg/kg). Anesthesia was maintained with 70% N_2O in O_2 and propofol infusion at 120-150 mcg/kg/min. The ulnar nerve was then stimulated at the wrist (single twitch 1 Hz) and after obtaining a stable baseline, the stimulation sequence was changed to a TOF pattern (2 Hz every 12 seconds). Resultant force of contraction of the thumb was recorded using a mechanomyograph (Gould FT03 force transducer). Subjects were randomly assigned to one of four succinylcholine dose groups, 0.15mg/kg, 0.20 mg/kg, 0.25mg/kg, and 0.30mg/kg. Muscle contractions were recorded until return to baseline twitch strength. For each individual patient, the force of the first twitch (T1) was plotted against the ratio of the fourth to the first twitch (T4/T1 ratio).

RESULTS: In all the individuals studied, a fade in TOF developed following the administration of succinylcholine (Figure 1). Analyzing the pooled data from all subjects, fade (T4/T1) appeared to correlate with the corresponding twitch depression (T1) obtained in any one individual subject during the onset of the NMB (r2=0.74, p<0.0001) (Figure 2). Similarly during the offset or recovery of the NMB twitch depression (T1) appeared to correlate with the corresponding T4/T1 ratio (Figure 3) (r2=0.54, p<0.0001). The degree of fade (T4/T1 ratio) for any given degree of twitch depression was similar during onset and during offset. The slopes of the regression lines of T1 versus T4/T1 ratios during onset and offset were similar (0.30 during onset and 0.26 during offset)

DISCUSSION: Administration of succinylcholine consistently produces fade upon TOF stimulation. However, the peak fade caused by succinylcholine is modest when compared with previous reports of fade caused by non-depolarizing muscle relaxants[3]. Also, unlike the fade caused by non-depolarizing muscle relaxants[3] fade caused by succinylcholine is similar during onset and offset of the neuromuscular block.

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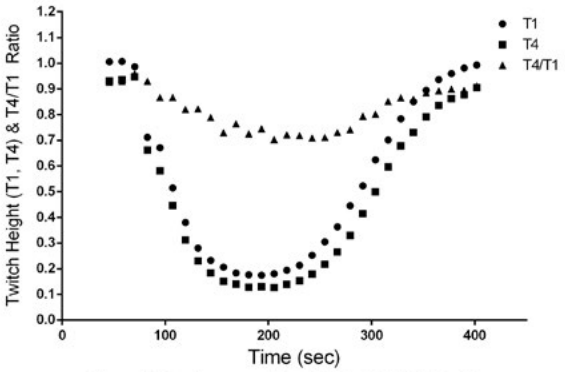

Figure 1. Data from one subject twitch height (T1, T4) and T4/T1 ratio plotted against time following the administration of succinylcholine 0.30 mg/kg.

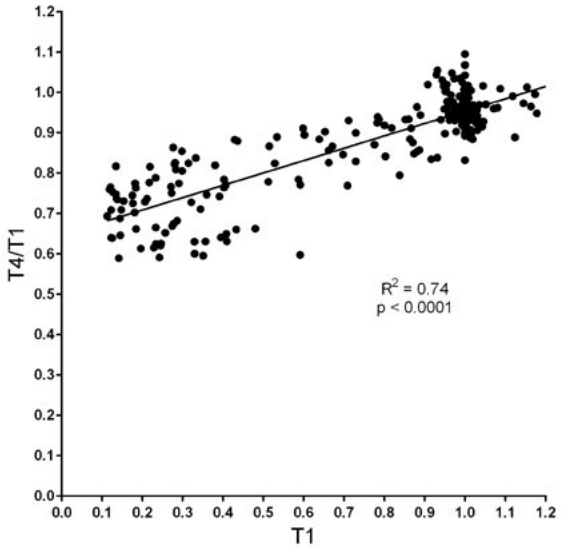

Figure 2. Pooled data from all 20 patients during onset of NMB. Each T1 point for an individual patient is plotted against the corresponding T4/T1 ratio.

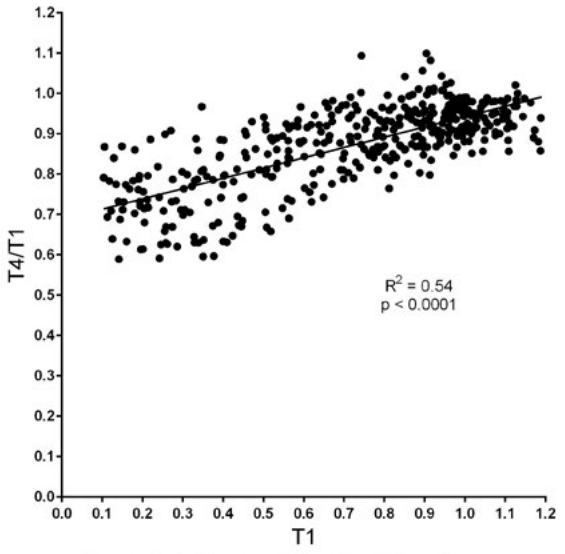

Figure 3. Pooled data from all 20 patients during offset of NMB. Each T1 point for an individual patient is plotted against the corresponding T4/T1 ratio.

S-275.

PERIOPERATIVE SURGICAL HOME DECREASES HOSPITAL LENGTH OF STAY, WITH CONTINUED IMPROVEMENT WITH FURTHER IMPLEMENTATION

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INTRODUCTION: The anesthesiologist led Perioperative Surgical Home (PSH) has been examined as a way to improve patient care and realize cost savings. PSH has recently been implemented at our institution for Urology patients. We desired to compare length of stay in these patients before, during, and after PSH implementation.

METHODS: A before and after comparison of length of stay in all patients scheduled for cystectomies, partial nephrectomies, radical nephrectomies, and prostatectomies was examined. Pre-PSH (1/2014 to 10/2014): Patients were evaluated in the Pre-Anesthesia Consultation and Education (PACE) clinic prior to surgery, with perioperative care managed by individual practitioners. Postoperative care was managed by the surgical team.

PSH patients (1/2015 to 10/2015): Patients were also evaluated in the PACE clinic prior to surgery, with optimization prior to surgery directed by the PSH Anesthesiologist. Postoperative care plans were discussed and patients were educated regarding expected recovery milestones, pain control, and discharge plans. Intraoperative care was provided by anesthesia teams of Anesthesiologists supervising residents or CRNAs. Patient specific care plans were communicated emphasizing desired intraoperative management goals.

Post-operative care was provided by the PSH team: PSH Anesthesiologist, Urology Chief Residents, a nurse practitioner, and an anesthesia resident. This team addressed co-morbidities, pain management, nutrition, ileus, and discharge planning.

The patients were divided into pre-PSH (baseline) and PSH groups. The primary outcome measure was postoperative length of stay (LOS). The PSH group was further divided into Transition (1/2015 through 5/2015) and PSH (6/2015 through 10/2015) patients to compare transitional LOS.

RESULTS: There were no significant differences in patient characteristics (Fig 1). LOS was overall significantly shorter in PSH (Fig 2). Evaluation of LOS in each type of surgery showed a significant difference in LOS for cystectomies but not in other surgeries (Fig 3). Incremental improvements made to PSH were associated with greater decreases in LOS in PSH compared to pre-PSH and transitional patients (Fig 4).

CONCLUSION: PSH is an opportunity to improve healthcare and better serve patients. We found an overall LOS decrease, with differences between types of surgeries. While LOS was shorter in PSH cystectomy patients, LOS following partial and radical nephrectomies was shorter in PSH but did not reach significance; a larger sample size may show significance. It may be difficult to show decreased LOS after prostatectomy surgery, as LOS is short with minimal room for improvement.

However, implementing change can be challenging. Our findings support ongoing process improvement results in additional decrease in LOS. While early outcomes support PSH as a quality-based implementation to decrease LOS, this study demonstrates that the resulting decrease in LOS may take time to achieve. With an anesthesiologist led PSH, decreased LOS can lead to reduced costs while simultaneously increasing healthcare value.

	Pre PSH N = 118	PSH N = 122	Difference	p-value
Age years	64.0 61.0 to 66.8	64.6 62.6 to 67.0	1.0 -2.0 to 4.0	0.532
Sex # (%) Female	27 (11.3%)	24 (10.0%)	-3.2% -13.5 to 7.2%	0.544
Body mass index kg/m2	27.9 26.9 to 29.2	27.8 27.0 to 29.0	-0.11 -1.52 to 1.12	0.863
ASA PS #2; 3; 4	41; 72; 5	40; 74; 8		0.717
Postop LOS days	3.6 3.2 to 4.2	2.7 2.2 to 3.0	-1.0 -2.0 to 0.0	0.0002

Figure 1: there were no significant differences in age, sex, body mass index or ASA Physical Status in 118 Pre PSH compared to 122 PSH patients. Postoperative length of stay (LOS) was significantly shorter in PSH overall.

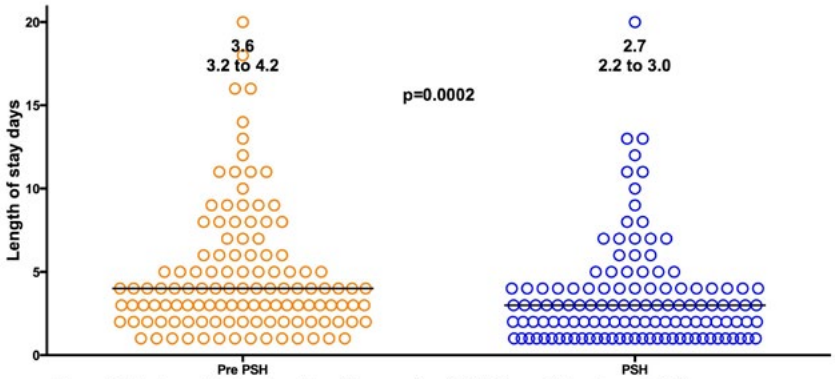

Figure 2: Postoperative length of stay (days median; 95% CI) was 1 day longer in 118 Pre PSH patients (1/2014 to 10/2014) compared to 122 PSH patients (1/2015 to 10/2015); p=0.0002 (Wilcoxon with Hodges Lehman comparison of differences).

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S-275 • continued

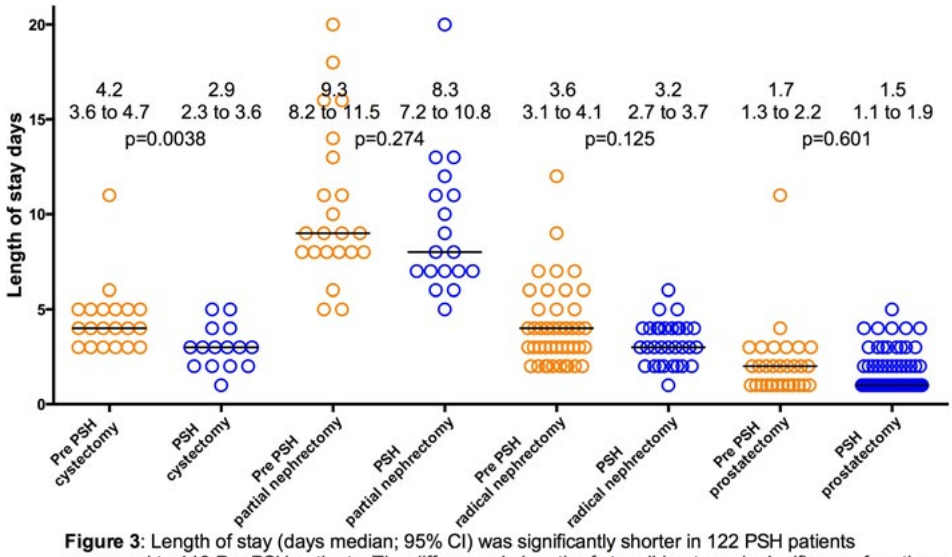

Figure 3: Length of stay (days median; 95% CI) was significantly shorter in 122 PSH patients compared to 118 Pre PSH patients. The difference in length of stay did not reach significance for other surgery types studied.

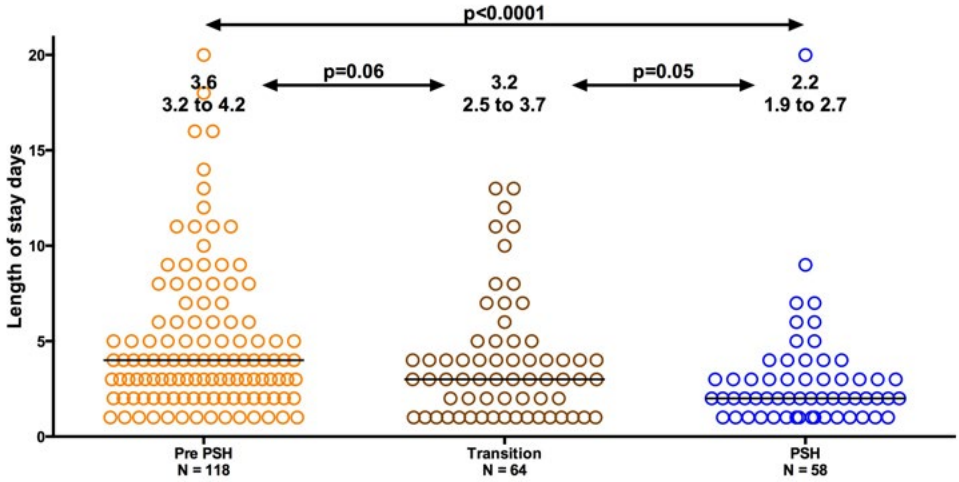

Figure 4: Length of stay (days median; 95% CI) decreased from Pre PSH (1/2014 to 10/2014) in increments as processes were improved during PSH implementation. The difference from Pre PSh compared to 64 patients in the transition period (1/2015 to 5/2015) did not reach significance. However LOS was significantly shorter in 58 PSH (6/2015 to 10/2015) patients compared to Pre PSH.

S-276.

COMPLEX MODULATION OF THE IMMUNE RESPONSE TO SURGERY BY IMMUNE ENHANCING NUTRIENTS

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INTRODUCTION: The recent emphasis on enhanced recovery after surgery (ERAS) protocols in perioperative care highlights the significance of efforts towards improving surgical recovery. However the elements of these protocols that may improve recovery are uncertain. A better understanding of the biological mechanisms of ERAS protocols is critically needed.

Arginine-rich nutritional supplementation (Arginine Immuno-Nutrition, AIN) is a component of ERAS protocols integral to the perioperative management of patients undergoing colorectal surgery. AIN has been the center of much debate, as AIN consistently decreased post-operative infectious complications after elective surgery, but increased morbidity and mortality in critically ill patients. Thus, a mechanistic understanding of the immune modulatory properties of AIN is essential to unify these apparent discrepancies. In this study, we applied high-dimensional mass cytometry[1] to comprehensively characterize the effects of perioperative AIN on major immune cell subsets and associated intracellular signaling pathways of patients undergoing elective colorectal surgery.

METHODS: 22 patients scheduled for elective colorectal surgery were randomized to AIN treatment (IMPACT, 950mL/day for 5 days prior to surgery) vs. no treatment. Whole blood samples were collected before surgery (Baseline) then 4h, 24h, 72h and 7 days after surgery and submitted to mass cytometry analysis of immune cell subset frequencies and intracellular signaling responses. Plasma cytokine levels were quantified on a Luminex 63-plex platform. An Elastic Net analysis[2] that integrated immune cell frequencies, intracellular immune responses and plasma cytokine levels was applied to identify groups of correlated immune features that best predicted the effect of AIN on patients immune response to surgery.

RESULTS: Consistent with speculations that AIN restores adaptive cell function after surgery, a robust but transient increase in STAT1 signaling in memory $CD8^+$ cytotoxic T cells was a prominent feature of the immune network associated with AIN. However, AIN also induced a prolonged increase in $CD11b^+CD14^+HLA\text{-}DR^{low}$ myeloid derived suppressor cell (MDSCs) frequencies, a cell type intimately involved in Arginine-dependent suppression of adaptive immune cells in the context of malignancy, sepsis and traumatic injury.

CONCLUSION: The high dimensional mass cytometry analysis of peri-operative AIN immune modulation revealed systems-wide alterations in immune cell subsets of patients undergoing colorectal surgery. While functional aspects of adaptive cell subsets were transiently restored, AIN also induced a prolonged increase in MDSC frequencies, a cell type associated with immune suppression in sepsis and cancer. These findings have important implications for the selection of patients that may benefit from peri-operative AIN. Future studies will examine the utility of peri-operative immune profiling to tailor pre-habilitation interventions to patient-specific immune states.

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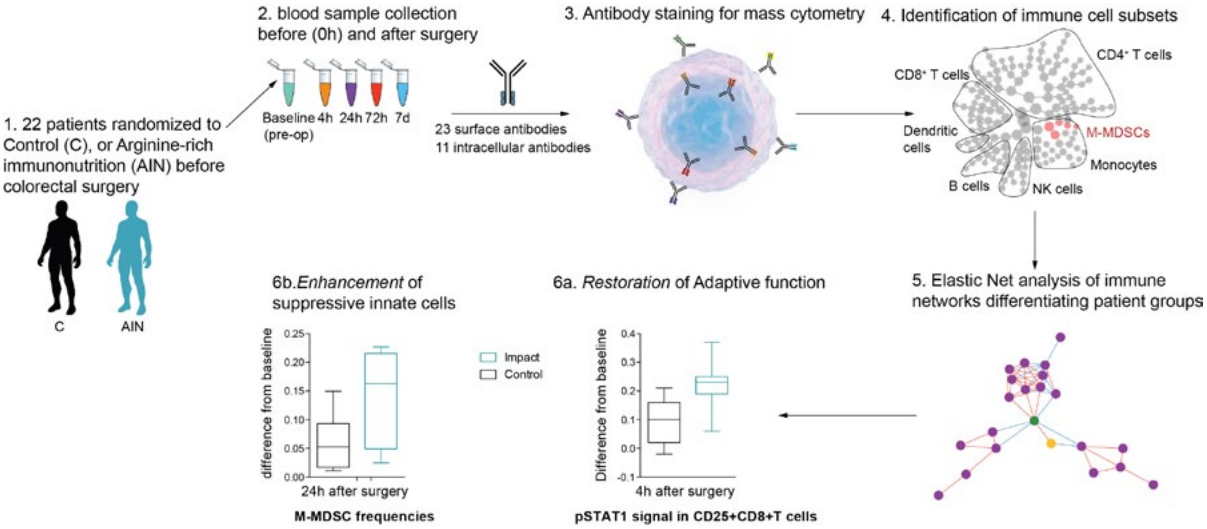

S-277.

SMOKING CESSATION: THE ROLE OF THE ANESTHESIOLOGIST

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INTRODUCTION: Perioperative interventions for smoking cessation reduce the risk of surgical complications, and provide smokers an opportunity to engage in long-term abstinence.[1] The main objective of this narrative review is to highlight the evidence for smoking cessation interventions and provide a practical strategy for implementation of such interventions as part of the Perioperative Surgical Home.

METHODS: We searched MEDLINE, EMBASE, and Cochrane for cohort studies and randomized controlled trials on perioperative smoking cessation. The search strategy yielded a total of 1,717 articles. After evaluating title, abstract, and full-text of studies, 95 articles were included in this review.

RESULTS: Smoking increases the risk of postoperative complications. (Table 1)[2] Brief simple advice given by physicians promotes smoking cessation, and increased intensity of such advice is associated with an additional benefit-[3] A combination of behavioural support and pharmacotherapy, initiated as late as four weeks before surgery may reduce postoperative complications and increase the likelihood of long-term abstinence.[1] A lack of time and training are the main barriers to implementation of intensive interventions by anesthesiologists.[4] One strategy is that anesthesiologists ask their patients about their smoking status, advise smokers to quit, and refer them {Ask, Advise, Refer (AAR)} to resources such as tobacco telephone quit-lines for counseling and follow-up. However, many smokers who are given the telephone number of quit lines fail to call for assistance.[4] Proactive telephone counseling in which calls to smokers are initiated by a counselor is more effective than reactive counseling, in which the first call is made by smokers.[5] A new approach Ask, Advise, and Connect (AAC) has demonstrated that directly connecting smokers to counseling resources such as quit lines using an electronic connection system, results in a 13-fold rise in the treatment enrollment, compared to the AAR approach. AAC greatly increases the reach and impact of the intervention, and shifts the burden of intensive counseling away from anesthesiologists.6 (Table 2)

CONCLUSIONS: The "Ask, Advise, Connect" is a practical strategy anesthesiologists can incorporate in the perioperative period. All anesthesiologists should ask their patients about smoking, and strongly advise smokers to quit. Directly connecting patients to existing counseling resources such as telephone quit lines, using fax or electronic referrals, increases the reach and the impact of the intervention.

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Table 1 - Odds ratios of postoperative outcomes among current and former Smokers compared with patients who never smoked

Postoperative outcomes	Never smokers OR (95%CI)	Former smokers OR (95%CI)	Current smokers OR (95%CI)
Wound healing delay and dehiscence	1	_	2.07 (1.53-2.81)
Hernia	1	_	2.07 (1.23-3.47)
Necrosis of wound and tissue	1	_	3.60 (2.62-4.93)
Sepsis	1	_	1.38 (1.11-1.72)
Septic shock	1	_	1.40 (1.33-1.47)
Surgical site infection	1	1.11 (1.05- 1.17)	1.18 (1.13-1.24)
Long bone fracture non-union	1	_	2.32 (1.76-3.06)
Cerebrovascular accident/stroke	1	1.10 (0.96-1.26)	1.55 (1.36-1.76)
Myocardial infarction	1	1.28 (1.14-1.44)	1.77 (1.57-1.99)
Ventilation for longer than 48h	1	1.26 (1.16-1.38)	1.55 (1.43-1.68)
Unplanned reintubation for respiratory/cardiac failure	1	1.36 (1.26-1.47)	1.67 (1.55-1.79)
Pneumonia	1	1.22 (1.13-1.31)	1.77 (1.66-1.90)
30-day postoperative mortality	1	1.17 (1.09-1.27)	1.29 (1.20-1.39)
One-year postoperative mortality(3)	1	1.14 (1.10-1.19)	1.55 (1.50-1.61)

Former smoker = noncurrent smoker with more than 0 recorded pack years of smoking.

Table 2 - Current strategies for preoperative smoking cessation

Five A's	AAR	AAC
Ask to identify all tobacco users at every visit. **Advise** tobacco users in a clear and personalized manner to quit at every visit. **Assess** their willingness to make a quit attempt. **Assist** them through offering medications and providing counseling. **Arrange** for follow-up meetings beginning the first week after the quit date.	**Ask** to identify all tobacco users at every visit. **Advise** tobacco users briefly to quit and offer cessation assistance via the quit-line. **Refer** tobacco users to quit line delivered counseling and provide them with quit line numbers.	**Ask** to identify all tobacco users at every visit. **Advise** them briefly to quit and offer cessation assistance via the quit-line. **Connect** tobacco users directly with quit line delivered counseling through an automated connection system.

S-278.

WITHDRAWN.

S-279.

DOES MANAGEMENT OF ADVANCED DIRECTIVES IN THE PERIOPERATIVE PERIOD MIRROR CLINICAL GUIDELINES?

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INTRODUCTION: While updated guidelines on the perioperative management of advance directives were published nearly twenty years ago, these recommendations still may not be realized in everyday practice[1-3]. In this study, clinicians were surveyed regarding management decisions for a patient with an advance directive preparing to undergo surgery.

METHODS: After IRB approval, informed consent was obtained and an electronic survey was distributed using REDCap software[4] to clinicians at an academic medical center who routinely provide perioperative care. Respondents were asked about their familiarity with perioperative advance directive guidelines and asked four management questions about a hypothetical operative patient with an advance directive. These questions have best practice answers as defined by multiple guidelines[1-3]. Chi-squared tests were used to evaluate whether correct response rates were related to clinician category or self-reported guideline familiarity. Respondents also identified motives that were important to their intraoperative resuscitation decisions.

RESULTS: One hundred-fifty surveys were completed (Table 1). At least one of the four management questions was answered incorrectly by 49% of clinicians. Clinician category was associated with correct responses on the 2nd question (p=0.02), but not the other three management questions (all p-values >0.25). Thirty-five percent of clinicians reported that they were somewhat or very familiar with their professional organization's guidelines regarding the management of advance directives in the perioperative period. There was no association between guideline familiarity and correct management decisions (all p-values > 0.33).

Motives identified as important to intraoperative resuscitation decisions are shown in Table 2.

CONCLUSIONS: While most clinicians indicate that they would carry out preoperative management of advance directives in line with current guidelines, 38.7% of clinicians indicated that they would support initiating CPR and/or defibrillation intraoperatively in a patient who had refused them. There was no association between reported familiarity with guidelines and correct management. This indicates a critical need for further investigation and education regarding management of advance directives in the perioperative setting.

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Table 1: Correct Responses To Four Management Decisions For A Patient With A DNR In Place. [No.(%)]

	Attending physician (N=38)	Physician trainee (N=23)	NP/RN/CRNA (N=89)	Total (N=150)
1. The specific resuscitation measures the patient is willing to accept should be revisited and clarified.	35 (92.1%)	23(100%)	84(94.4%)	142(94.7%)
2. If he undergoes surgery, his advance directive should be modified as necessary to be compatible with both his goals of care and his operative management.	30(78.9%)	23(100%)	65(73%)	118(78.7%)
3. Would you support initiating chest compressions[in a patient who refused it]?	24(63.2%)	18(78.3%)	53(59.6%)	95(63.3%)
4. Would you support initiating electric defibrillation [in a patient who refused it]?	24(63.2%)	16(69.6%)	55(61.8%)	95 (63.3%)

Table 2: Reasons Reported As Very Important To Decision Whether To Initiate Resuscitative Therapies In a Patient Who Refused Them. [No.(%)]

	Clinicians responding that they would not apply refused resuscitation therapies intraoperatively(N=92)	Clinicians responding that they would apply one or more refused resuscitation therapies intraoperatively (N=58)	Total (N=150)
Prioritization of patient survival as an outcome	21(22.8%)	28(48.3%)	49(32.7%)
Fear of legal liability regarding intra-operative complications	14(15.2%)	10(17.2%)	24 (16.0%)
Legally obligated to comply with patient's decision	65(70.7%)	28(48.3%)	93(62.0%)
Respect for patient's decision to refuse care	89(96.7%)	41(70.7%)	130(86.7%)
Successful resuscitation is relatively likely with this event	12(13.0%)	26(44.8%)	38(25.3%)
The possibility that there was an iatrogenic cause of his ventricular tachycardia	21(22.8%)	28(48.3%)	49(32.7%)
My interpretation of the applicability of his DNR directive to this particular event	54(58.7%)	30(51.7%)	84(56.0%)
Concern that patient's surrogate(s) would disagree with decision	16(17.4%)	13(22.4%)	29(19.3%)

S-280.

WITHDRAWN.

S-281.

IMPACT OF POSTSURGICAL ANALGESIA INTERVENTION ON HOSPITAL LENGTH OF STAY (LOS), DISCHARGE STATUS, AND HOSPITAL COSTS FOLLOWING TOTAL KNEE ARTHROPLASTY (TKA)

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INTRODUCTION: Total knee arthroplasty (TKA) is a common surgical procedure for which different interventions are available to manage postsurgical pain. The purpose of this study was to examine the impact of three postsurgical analgesia interventions on clinical and economic perioperative outcomes, including hospital LOS, discharge status, and costs.

METHODS: This study examined data from the Premier Database, which includes >600 hospitals across the United States. The analysis focused on patients undergoing TKA (ICD-9 code 81.54) between 7/1/2013 and 9/30/2014 who received one of three interventions to manage postsurgical pain: single-injection peripheral nerve block (sPNB), continuous peripheral nerve block (cPNB), or continuous wound infiltration (CWI). Groups were compared using t-tests and Chi-square as appropriate for baseline patient characteristics (e.g. age, gender) and hospital characteristics (e.g. teaching status, number of beds). Poisson and logistic regression models were used to compare hospital LOS and home discharge for each intervention while controlling for patient and hospital characteristics. Hospital charges for each intervention were categorized as related to anesthetic medication, opioids administered through patient-controlled analgesia (PCA), other opioids, equipment and supplies, pump, or professional services. Hospital costs for these charges were estimated by Premier using hospital-specific charge to cost ratios and aggregated to determine total hospital costs during the inpatient stay for each intervention.

RESULTS: The study population consisted of 136,300 patients undergoing TKA at Premier hospitals, of whom 11,927 were identified using our methodology as having received one of the three interventions of interest, including 5,820 (48.8%) who received sPNB, 2,108 (17.7%) who received cPNB, and 3,999 (33.5%) who received CWI for postsurgical analgesia. The three groups were similar in age, gender, and payer type, though more patients receiving sPNB had elective surgeries at rural teaching hospitals, those receiving cPNB were more likely at urban academic hospitals, and patients who received CWI were at smaller hospitals. Unadjusted results are shown in the Table. After controlling for patient and hospital characteristics, the mean hospital LOS was 2.93 days for sPNB, 2.97 days for cPNB, and 3.15 days for CWI; these differences were statistically significant ($p<0.001$) but did not appear meaningful. Overall, more patients who received sPNB (OR=1.34; 95% CI 1.20-1.51) and cPNB (OR=1.23; 95% CI 1.07-1.43) were discharged home or to home health than those who received CWI. The estimated hospital costs (using Premier charge to cost ratios) for these interventions were $697 for sPNB, $1,376 for cPNB, and $350 for CWI.

CONCLUSIONS: This analysis of hospital chargemaster data identified small but statistically significant differences between sPNB, cPNB, and CWI in hospital LOS and discharge status after TKA. Additional analyses are needed to determine the full economic impact of these and other interventions used to manage postsurgical pain under different payment models.

Length of Stay and Discharge Location among Patients Undergoing TKA

Outcome	sPNB	cPNB	CWI	P-value
N	5,280	2,108	3,999	
Hospital length of stay (days), mean (SD)	2.97 (1.37)	3.01 (1.44)	3.06 (1.47)	0.0101
Discharge location, n (%)				<0.001
Home	1,020 (17.53)	207 (9.82)	1,017 (25.43)	
Home health	3,215 (55.24)	1,355 (64.28)	1,772 (44.31)	
Skilled nursing/intermediate care facility	1,189 (20.43)	360 (17.08)	907 (22.68)	
Other rehab facility	324 (5.57)	178 (8.4)	272 (6.80)	
Other	72 (1.24)	7 (0.33)	20 (0.50)	
Unknown	0 (0)	1 (0.05)	11 (0.28)	

S-282.

RETROGRADE AMNESTIC EFFECT OF MIDAZOLAM

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INTRODUCTION: While an anterograde amnestic effect of midazolam is well described, midazolam's retrograde effects on memory formation and consolidation are unclear. Some studies point to a retrograde facilitation of memory consolidation in humans[1], while others suggest a retrograde amnestic effect of midazolam in rats[2] and also in humans[3]. Our study seeks to provide further insight into the retrograde effects of midazolam on memory formation and consolidation in patients undergoing general anesthesia with routine, pre-operative administration of midazolam.

METHODS: Over five years, 296 subjects undergoing general anesthesia were enrolled in this IRB-approved study. Six words were sequentially voiced to each subject over eight minutes with word four given at the time of midazolam administration and words three and five given one minute before and one minute after midazolam, respectively (Table 1). Subjects were contacted twenty-four hours after surgery and then asked to recall the six words. Differences in subject ability to recall sequential words were assessed using McNemar's test.

RESULTS: Recall of words one and two were each 74%, but there was a significant decrease in number of subjects recalling word three (50%) compared to that of words one or two with $p < 0.001$ (Figure 1). This downward trend continued with words four through six with recall of 36%, 27%, and 10% respectively. Each of these stepwise declines in proportion of subjects able to recall was statistically significant ($p < 0.03$).

CONCLUSION: Our data suggest a retrograde amnesia effect one minute before administration of midazolam and also support the drug's well-documented anterograde amnestic effect. These findings suggest that midazolam may impair both memory acquisition and memory consolidation through an unclear mechanism. When considering timing of conversations and consent, it is important for patients and providers to be aware that midazolam may cause retrograde amnesia in some patients.

REFERENCES:

1.Psychon Bull Rev. 2007 Apr; 14(2): 261-269.

2.Behav Brain Res. 2013 Mar 15;241:198-205.

3.Clin Neuropharmacol. 2015 Mar-Apr;38(2):47-51.

Table 1.

Timeline of Word Administration						
Time (mins):	-5	-3	-1	0 (Midaz)	+1	+3
Pre-op Word:	Word 1	Word 2	Word 3	Word 4	Word 5	Word 6

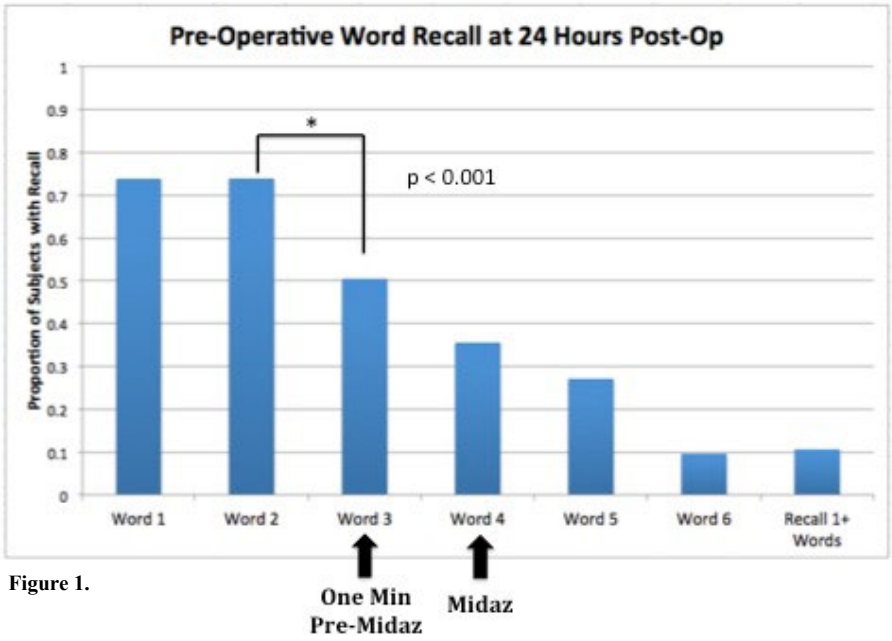


Figure 1.

S-283.

HARNESSING THE ELECTRONIC ANESTHESIA RECORD TO MEASURE NON-OPERATIVE OR UTILIZATION

AUTHORS: C. Simmons[1], B. Scott[1], J. Melendez[2]

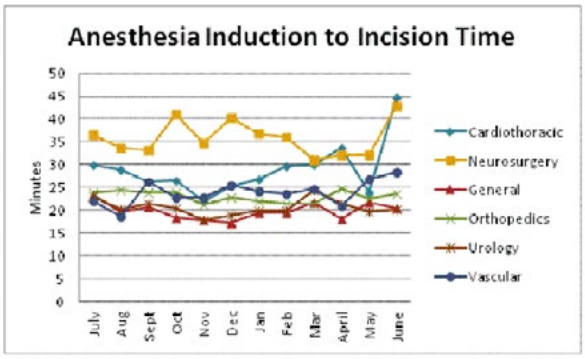
AFFILIATION: [1]Anesthesiology, University of Colorado, Aurora, CO, [2]Anes, University of Colorado, Aurora, CO

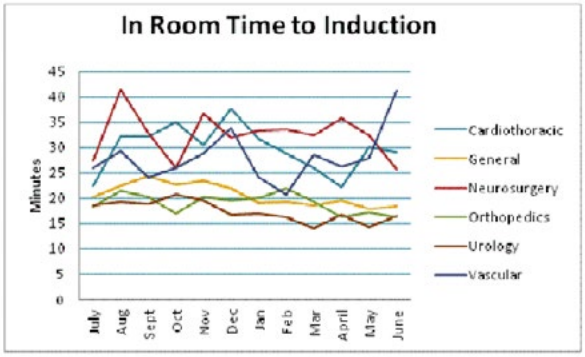
INTRODUCTION: Operating rooms (OR) account for approximately 40% of hospital costs and generate roughly 70% of revenue. Efficient use of OR time is essential for any successful hospital. Likewise, growing economic pressures to reduce cost, the spectra of decreasing reimbursement and greater competition all lead to the necessity for enhanced operative efficiency. The objective of this study was to identify areas in which non-operative time, specifically, in-room to induction, in-room to incision, and induction to incision, could be optimized.

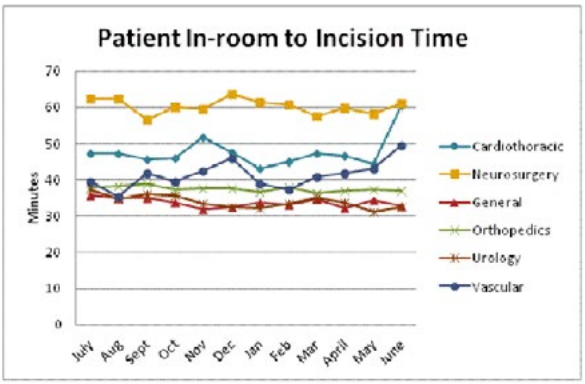
METHODS: The University of Colorado Hospital (UCH) Epic Clarity database was queried for all inpatient surgeries between June 30, 2014 and July 1, 2015. Built in to the Electronic Anesthesia Record (EAR) are standardized markers that each anesthesia provider must input for every case: patient in room, induction, and surgical incision. For each record, these time-stamps were extracted and compared to provide a number of minutes for each time-period of interest (see figures 1-3). All times were then sorted by surgical subspecialty and tracked by month to create monthly averages. Cases performed in outpatient or off-site were not included.

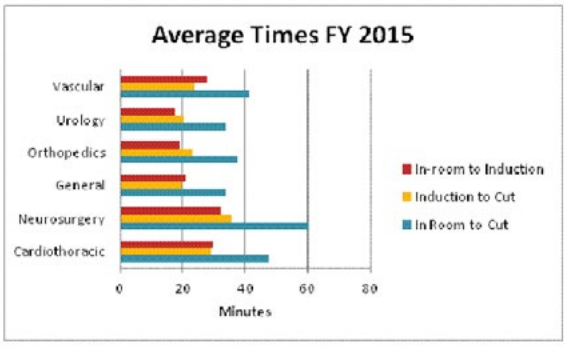
RESULTS: A total of 13,901 cases were included. For all services average in-room to induction time, 20.7min, induction to incision, 21.2 min, and in-room to incision, 34.3min. Data analyzed by service revealed longer perioperative times for Neurosurgery and Cardiothoracic surgery (see figures 1-4)Minimal variation in times was noted within specialties, indicating relative consistency in processing (see figures 1-3). Average monthly variation in time was highest in Neurosurgery at 12% and 29% in CT surgery. Average total times for above specialties were 60.2 min and 47.6 minutes respectively (see figure 4). There was variability by service with ranges from 17.7min to 60.2min. Specialties often regarded as highly efficient, ex. Orthopedics, however displayed higher than expected average times. (see figure 2).

CONCLUSIONS: Little data exist regarding how long it takes a perioperative team to prepare a patient for incision, yet non-operative time represents a significant percentage of OR utilization. As expected, surgical specialties requiring significant perioperative preparation time, invasive monitoring, and unique positioning had the longest observed times. Given the amount of time required for set-up and case preparation it is likely that inefficiencies exist, and may be important targets for process improvement. Minimal month-to-month variation indicates consistent performance, but does not necessarily reflect adequacy. Further analysis of outlier months should be undertaken to identify case/month specific variation, including surgeon specific differences, case type and frequency, or ASA classification. Financial impact of reduction in non-operative time is potentially considerable. At 13000 cases per year and average non-operative time of 35 minutes per case, a reduction of 50% would equate to significant savings. Further study utilizing EAR is indicated to locate these inefficiencies and develop strategies to minimize them.









S-284.

FREQUENCY, SEVERITY AND LOCATION OF POSTOPERATIVE HYPOXEMIA IN PATIENTS WITH NO RESPIRATORY DISEASE

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INTRODUCTION: The frequency of postoperative hypoxemia after PACU, when respiratory monitoring is reduced, is not well known. A recent study (Sun *et al.,* Anesth&Analg 2015:121(3):709-715) suggests that postoperative hypoxemia is common and persistent. This study found that 21% of adult patients presented ≥10min/h of SpO2<90% during the first 48h after non-cardiac surgery, but included patients with a variety of respiratory comorbidities and type of anesthesia (general, regional). The frequency, severity and location of postoperative hypoxemia in surgical patients with no respiratory disease in our hospital system (at ~1,600m above sea level) are unknown. We hypothesized that hypoxemic events occurring in surgical patients without any respiratory disease would be more frequent on the postoperative floor after general anesthesia, compared to those not receiving general anesthesia.

METHODS: The Epic Clarity database was queried for all procedure encounters performed in adults under anesthesia care at the University of Colorado Health System (2 community and 1 academic hospital) from 1/1/2012 to 12/31/2014. Emergencies, ICU transfers and subsequent encounters for each patient were excluded. Patients with asthma, COPD, any respiratory disease or at risk for OSA were excluded. General anesthesia was identified by the presence of any airway intervention. We analyzed the presence of ≥1 episode of hypoxemia, defined as a SpO_2<90% reading by continuous pulse oxymetry for a minimum of 3 contiguous measurements and/or ≥3 minutes (OR/PACU) or of any duration if validated and/or manually entered in the medical chart by the patient's nurse (floor). Hypoxemic events were classified as mild (lowest SpO2 85-89%) or moderate/severe (SpO_2≤85%). Demographics, comorbidities, postoperative respiratory therapies, and hospital length of stay were collected. Chi Square tests were used to compare the frequency of hypoxemic events in patients with and without general anesthesia at different perioperative locations. Statistical significance was accepted at p<0.010 to adjust for the large sample size.

RESULTS: A total of 16,473 patients met study criteria: 9,548 (58.0%) with and 6,925 (42.0%) without general anesthesia. At least one episode of hypoxemia was observed in 17.5% of all patients in the OR, 8.0% in the PACU and 32.8% on the floor. Table 1 shows the distribution by severity per location. Patients after general anesthesia, compared to those without, had a lower frequency of any degree of hypoxemia in the OR (p<0.001 for both mild and moderate/severe), higher in the PACU (p=0.007 for both mild and moderate/severe), and higher frequency of moderate/severe (p<0.001) but not mild (p=0.692) hypoxemia on the floor.

CONCLUSIONS: Postoperative hypoxemia in patients with no respiratory disease is common. The highest frequency observed was for moderate/severe hypoxemia on the postoperative floor after general anesthesia. Further analysis of our findings is needed to identify those patients at risk. Increased awareness, monitoring and interventions may be beneficial for these patients at low risk for postoperative hypoxemia.

Table 1.

Variables	Total(n=16,473)	General Anesthesia(n=9,548)	No General / Unknown(n=6,925)	P-value
OR				
SpO_2 86-89%	1,916 (11.6)	982 (10.3)	934 (13.5)	<0.001
SpO_2 85%	967 (5.9)	507 (5.3)	460 (6.6)	<0.001
PACU				
SpO_2 86-89%	912 (5.5)	570 (6.0)	342 (4.9)	0.007
SpO_2 85%	411 (2.5)	266 (2.8)	145 (2.1)	0.007
FLOOR				
SpO_2 86-89%	1,881 (11.4)	1,086 (11.4)	795 (11.5)	0.692
SpO_2 85%	3,517 (21.4)	2,225 (23.3)	1,292 (18.7)	<0.001
Post-extub. Hypoglycemia, n (%)	3 (0.4)	4 (0.5)	0.57	

S-285.

PATIENT FACTORS PROTECTIVE OF FAILURE TO RESCUE AFTER OPEN ABDOMINAL AORTIC SURGERY

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INTRODUCTION: Failure to Rescue (FTR), defined as mortality rate among patients having one or more postoperative complications, is an important indicator of preoperative mortality and increased healthcare costs. Factors influencing FTR are not completely understood. The aim of the study was to explore patient characteristics associated with decreased likelihood of FTR. We elected to use elective open abdominal surgery (EOAS) as an example because it is associated with high rates of complications and FTR.

METHODS: The Nationwide Inpatient Sample was analyzed to identify patients undergoing EOAS between 2000 and 2010 in the U.S. The main outcome was FTR after any major postoperative complication. The following major postoperative complications were defined using specific ICD-9-CM codes: pulmonary failure, pneumonia, myocardial infarction, deep venous thrombosis/ pulmonary embolism, acute renal failure, hemorrhage, surgical site infection, and gastrointestinal bleeding. Multivariate regression models were used to assess predictors of FTR. Independent variables included year of procedure, patient sex, age, and comorbidities (hypertension, diabetes, obesity, renal failure, liver disease, alcoholism, drug abuse, malignancy). All the models were adjusted for annual hospital volume of open aortic surgery, primary insurance payer, income for ZIP code, and hospital characteristics (teaching status, rural/urban location, and geographic region). Odds ratios with 95% confidence intervals were calculated. Significance level was set at a P value of 0.05. SAS 9.4 software (Cary, NC) was used for all the analyses.

RESULTS: A total of 45,682 elective open abdominal aortic procedures were performed during the study period. In general, the incidences of postoperative complication, in-hospital mortality, and FTR in the whole cohort were 32.1%, 3.2%, and 8.8%, respectively. Adjusting for hospital volume of aortic surgery, demographics, and hospital characteristics, the logistic regression models identified the following patient characteristics as independent protective factors for FTR: male sex (odds ratio [OR], 0.73, 95% CI, 0.63 to 0.84; P<0.0001), hypertension (OR, 0.42, 95% CI, 0.37 to 0.49; P<0.0001), diabetes mellitus (OR, 0.67, 95% CI, 0.53 to 0.85; P=0.0012), and obesity (OR, 0.62, 95% CI, 0.40 to 0.98; P=0.040). In contrast, chronic renal failure (OR, 2.01, 95% CI, 1.65 to 2.46; P<0.0001), and liver disease (OR, 2.31, 95% CI, 1.40 to 3.82; P=0.0011) were associated with increased odds of FTR.

CONCLUSIONS: The overall rate of FTR after complications related to EOAS is about 9% in the U.S. Our data suggest that male sex, obesity, history of hypertension, and diabetes are independently associated with decreased likelihood of FTR. Although the lower risk of complications in men after vascular surgery and paradoxically protective effects of obesity on postoperative adverse outcomes[1,2] are well known, the protective effects of the comorbidities investigated needs further confirmation.

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1. Clin Cardiol. 2015 Feb;38(2):76-81

2. Obesity (Silver Spring). 2012 Feb;20(2):460-2

S-286.

WITHDRAWN.

S-287.

THE REDUCTION OF PREOPRATIVE TESTING FOR PATIENTS UNDERGOING SURGERY WITH A BIER BLOCK ANESTHETIC

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INTRODUCTION: Despite an abundance of evidence that supports a de-emphasis on preoperative evaluation for low-risk surgery, systems for reducing unnecessary preoperative testing have rarely been implemented.[1-3] Any reduction in unnecessary perioperative testing can reduce healthcare costs in two ways: not testing or reducing false-positives.[4] We examined retrospectively and prospectively the preoperative testing patterns in patients who underwent upper extremity orthopedic surgery under Bier block anesthesia after we implemented a multi-disciplinary workflow change.

METHODS: The Institutional Review Board approved the study protocol and design. From our patient electronic medical record (EPIC®, Verona, WI), we performed a retrospective (2013) and prospective analysis of all laboratory data ordered for patients undergoing upper extremity procedures with a Bier block anesthetic during the 30 days prior to their procedure. We chose the 30-day limit before surgery because all history and physicals must be current within 30 days prior to the day of the procedure. Concurrently, we redesigned the preoperative process. First, we drafted a letter from the Department of Anesthesiology and Pain Medicine which asked the primary care physician to refrain from ordering any labs unless they were clinically indicated. Then, we asked the orthopedic surgeons and schedulers to hand out this letter (Figure 1) to the study patients and asked to bring the document to their primary care physician.

We included any patient undergoing outpatient surgery with a Bier block anesthetic and any laboratory tests within 30 days. We excluded any patients undergoing surgery with a general or regional anesthetic. We extracted all the cases from WiseOR® (Palo Alto, CA) and respective patient identification numbers from Optum® (Eden Prairie, MN). We developed an index [total # of lab tests ordered]/[total # of patients] in order to compare the effect of the intervention. We used Microsoft Excel for index calculations (Redmond, WA) and Stata 13.1 (StataCorp LP, College Station, TX) to conduct the statistical analysis ($p < 0.05$ to test for significance).

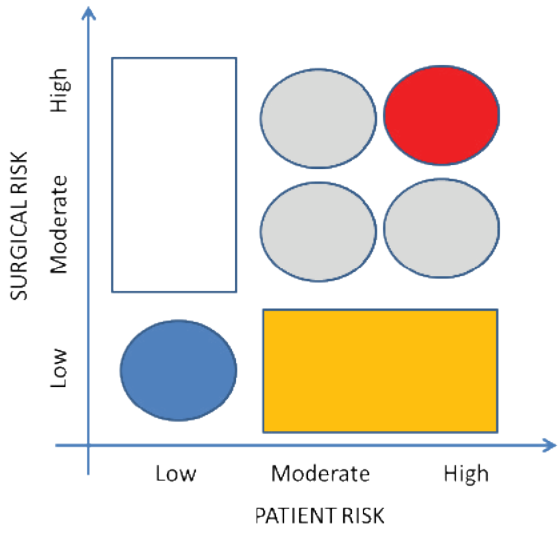
RESULTS: In Table 1, the retrospective sample index ([total # of lab tests ordered]/[total # of patients]) for the year 2013 (Jan-Dec) was 13.31 From March to October 2015, the index was reduced to 4.53. The change in tests ordered per patient was highly significant ($p=<0.001$) by a Chi-square test.

DISCUSSION: We have shown that a simple intervention in the preoperative process reduces preoperative testing in patients undergoing surgery with a Bier block. In fact, we will expand this intervention to patients scheduled for an inguinal hernia repairs in 2016. We believe that this model can serve as the infrastructure necessary to expand reduction of perioperative tests in a step-wise manner across different cohorts of patients (Figure 2).

REFERENCES:

1. Anesthesiology 2011; 116(1): 25-34.
2. Arch Intern Med 2009; 169(6): 595-602.
3. Anesthesiology 2013; 118(5): 1028-37.
4. AHRQ Publication No. 14-EHC009-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2014.

Figure 2. The ACC/AHA cardiac risk stratification redrawn as a three by three matrix.



By framing the discussion of the preoperative evaluation for surgical patients with this matrix, we show that there are several opportunities to fundamentally change the way we deliver perioperative services. Patients in the BLUE CIRCLE (low risk patient, low risk surgery) and YELLOW RECTANGLE (moderate-high risk patient, low risk surgery) should not need any further cardiac risk stratification or a history and physical by a primary care physician, regardless of the risk of the patient.

Table 1. Number of retrospective and prospective preoperative tests and patients ordered.

Period	Total Number of Lab Tests	Total Number of Patients	Index (Labs/Patients)
Jan-Dec 2013	8,642	654	13.31
Mar-Oct 2015	1,928	426	4.53

S-288.

PALONOSETRON-DEXAMETHASONE COMBINATION FOR PROPHYLAXIS OF POST-OPERATIVE NAUSEA AND VOMITING AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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AFFILIATION: Anaesthesiology, Sanjay Gandhi Post Graduate Institute of Medical S, Lucknow, India

BACKGROUND AND AIMS: Pain is the single most fearsome cause for anxiety in patients undergoing surgery. In fact, the raison d'être of anaesthesia is to to anticipate and prevent or eliminate this very pain. Opioid based anaesthesia is very widely practised which, when expertly given obviates post-surgical pain but at the cost of a higher incidence of post-operative nausea and vomiting (PONV).

Next to pain, PONV is the single most distressing symptom after surgery. PONV is a very unpleasant symptom complex which affects a smooth emergence from anaesthesia. PONV greatly reduces patient satisfaction in the post-operative period. PONV incidence after laparascopic cholecystectomy is as high as 50%[1].

OBJECTIVES: The presented study compares the efficacy of palonosetron-dexamethasone combination compared with each drug alone for prophylaxis of PONV after laparoscopic cholecystectomy performed under general anaesthesia (GA).

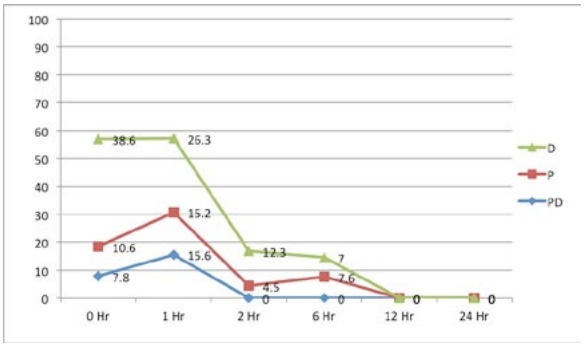
METHODS: After institutional ethical clearance and written informed consent from patient 180 ASA Grade I and II patients aged between 18-75 yr of either sex were enrolled in this prospective, randomized, double-blind trial to receive one of the three treatments: palonosetron 75 mcg (Group P); dexamethasone 8 mg (Group D); or palonosetron 75 mcg + deamethasone 8 mg (Group PD). Standardized balanced anaesthesia technique utilizing lignocaine, propofol and vecuronium and fentanyl was used in all patients. Perioperative pain management was by fentanyl as per the institutional protocol. Primary outcome was incidence of PONV in the three study groups whereas postoperative shivering, sedation and pain were the other outcomes.

RESULTS: Mean Incidence of PONV after laparoscopic cholecystectomy in the 1st 24 hr post surgery was 23.4%, 27.2% & 56.14% in groups PD, P and D respectively. Incidence of PONV in groups PD and P were lower than in group D (Statistical significance $P < 0.05$). However, difference in PONV incidence between groups PD and P were not statistically significant ($P > 0.05$).

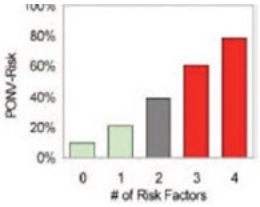
CONCLUSION: Palonosetron and palonosetron-dexamethasone combination were better than dexamethasone alone for preventing PONV in patients of laparoscopic cholecystectomy.

REFERENCES:

1. Apfel et al. 2012; Br J Anaesth;(109); 742-53



Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV	1
Postoperative Opioids	1
Sum =	0 ... 4



S-289.

FAILURE TO CHILL: AN EXPRESS TICKET TO WASTED BLOOD PRODUCTS!

AUTHORS: A. L. Screws[1], J. R. Pelletier[2], J. D. White[3]

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INTRODUCTION: According to the American Red Cross, someone in the U.S. needs a blood transfusion every two seconds[1]. A significant percentage of blood transfusions are given during surgery, requiring their delivery from and return to the hospital Blood Bank. Of the blood products that are wasted in the hospital setting, <70% of the loss can be attributed to the operating room[2]. We undertook this study to decrease operating room blood product waste.

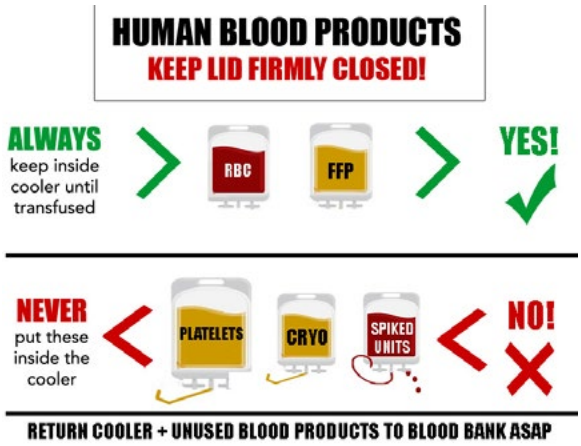
METHODS: A multidisciplinary committee consisting of blood bank staff, anesthesiology staff and operating room managers met to identify the factors affecting blood product waste in our hospital's operating rooms. Data on blood product waste was reviewed. It was determined that a significant reason for blood product loss was units being stored and/or returned outside the required temperature range established by the American Association of Blood Banks (AABB).[3] It was proposed that new transport cooler labels might better illustrate the proper handling of blood products.

RESULTS: New transport cooler labels were implemented hospital wide at the end of September 2015 (Figs. 1a, 1b). We compared data for blood product waste collected from October/November 2014 with October/November 2015. During October/November 2014, 235 product units were marked for waste, with 25.5% of these being returned to the blood bank outside of regulation temperature range. The total calculated cost of this waste was over $9,000 (Table 1). For October/November 2015, only 149 blood product units were wasted, with only 10.7% returned outside of temperature range (Table 2). Focusing on the $6000 saved for October/November 2015, platelet units are the most expensive product; 6 units were lost in the data period of 2014 vs. only 2 units in 2015.

CONCLUSIONS: Blood product waste is a multifactorial problem. Following the example set by Brown et al.2 and seeking the goal of zero waste of blood products in our hospital, we started with one intervention: replacing text-heavy instruction labels for blood transport coolers with new ones rich in clear iconography. We chose to compare 2 similar calendar months of data to minimize seasonal variations in surgical volume, especially trauma. Our one simple intervention has shown benefit. We have identified several further changes that may favorably impact future results. Massive transfusion protocol blood products are dispensed in large transport coolers that did not yet have our new labels. We also plan new labeled bags for platelet transport to prevent them from being improperly placed inside coolers. Last, we wish to create an electronic medical record reminder to encourage proper and timely blood product return.

REFERENCES:

1. Blood Facts and Statistics | American Red Cross http://goo.gl/FxwIZj
2. Implementation of an intraoperative blood transport and storage initiative and its effect on reducing red blood cell and plasma waste. Transfusion. 2014 Mar; 54(3):701-7 Jun 30.
3. Standards for Blood Banks and Transfusion Services 29th edition Section 5.1.8A. American Association of Blood Banks



Oct to Nov 2014 products wasted due to improprer storage				
Total wasted		235		
# out of temp		60		
% out of temp		25.5		
Full RBC		$ 4,392.00	24	40%
Divided RBC		$ 222.00	6	10%
Full Plasma		$ 1,173.00	23	38%
Pooled Cryo		$ 260.00	1	2%
Full Apheresis Platelet		$ 3,120.00	6	10%
Divided Apheresis Platelet				
Pooled Platelets				
	$$$	$ 9,167.00	60	

October to November 2015 products wasted due to improprer storage				
Total wasted		149		
# out of temp		16		
% out of temp		10.7		
Full RBC		$2,013.00	11	68.8%
Divided RBC		$ 74.00	2	12.5%
Full Plasma		$ 51.00	1	6.2%
Divided Plasma				
Full Apheresis Platelet		$1,040.00	2	12.5%
Divided Apheresis Platelet				
Pooled Platelets				
	$$$	$3,178.00		

S-290.

COMPARISON OF VARIOUS PREOPERATIVE ECHOCARDIOGRAM MEASUREMENTS FOR PREDICTING 30 DAY MORTALITY AFTER NON-CARDIAC SURGERY

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INTRODUCTION: Heart failure is a well accepted preoperative risk factor for patients undergoing noncardiac surgery[1-6]. Attempts to extrapolate this relationship to abnormal echocardiographic findings have produced mixed results[7-10], and further study is needed to understand the perioperative implications of these findings. Left ventricular ejection fraction (LVEF) on the preoperative echocardiogram report is often used to summarize systolic function. However, LVEF is independent of heart size, and other echocardiographic measurements may be more prognostic due to their different relationship to stroke volume (SV). We hypothesized that other common echocardiographic measurements have a stronger association with 30-day mortality than the reported LVEF in the setting of noncardiac surgery.

METHODS: The Institutional Review Board approved this study and waived the requirement for informed consent due to minimal risk. All adults undergoing noncardiac surgery at a single institution who had a preoperative echocardiogram report in the medical record were included unless the reports contained missing data. Exams were performed by certified sonographers and interpreted by level III trained, board certified cardiologists. The reported LVEF, left ventricular internal diameter during systole (LVIDS), left ventricular internal diameter during diastole (LVIDD), fractional shortening (FS), left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), SV, and calculated LVEF were analyzed. Bivariate logistic regression was performed to determine the association between each measurement and 30-day mortality. The areas under the receiver operating characteristic curves were used to compare each measurement to the reported LVEF using DeLong's method. A p-value <0.05 was used to denote statistical significance.

RESULTS: Reported LVEF (odds ratio [OR] 0.986, $p<0.001$), LVIDS (OR 1.014, $p=0.004$), FS (OR 0.984, $p<0.001$, LVESV (OR 1.004, $p=0.001$), SV (OR 0.994, $p=0.002$), and calculated LVEF (OR 0.989, $p<0.001$) were associated with 30-day mortality while LVIDD ($p=0.676$) and LVEDV ($p=0.339$) were not. When compared to the reported LVEF (AUC 0.519), LVIDS (AUC 0.526, $p=0.048$), FS (AUC 0.545, $p=0.042$), LVESV (AUC 0.526, $p=0.048$), SV (AUC 0.539, $p=0.002$), and calculated LVEF (AUC 0.544, $p=0.005$) had a stronger association with 30-day mortality.

CONCLUSIONS: Several commonly reported echocardiographic measurements may be more useful than the reported LVEF for predicting mortality after noncardiac surgery. Additional studies are needed to maximize the information obtained from these reports for use in preoperative risk stratification.

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S-291.

ANESTHESIA MAINTENANCE WITH DESFLURANE AND TARGET-CONTROLLED REMIFENTANIL: COMPARISON OF BISPECTRAL INDEX-GUIDED AND FIXED-GAS CONCENTRATION TECHNIQUES

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INTRODUCTION: Desflurane anesthesia balanced with remifentanil can be maintained with either fixed or titrated desflurane concentration. We compared the fixed-gas concentration (FG) method with the bispectral index (BIS)-guided (BG) method from the perspectives of convenience of practice, economy and anesthetic stability.

METHODS: Forty-two patients were randomly allocated to the BG (n = 21) or the FG (n = 21) groups. In the BG group, desflurane was titrated to maintain BIS at 50 during anesthesia maintenance. In the FG group, inspiratory desflurane was set at 1 MAC. Remifentanil was titrated to maintain systolic arterial pressure (SAP) at 120 mmHg in both groups. SAP and BIS, dose and adjustment frequency of anesthetics and recovery time were measured. Stability of anesthesia was evaluated with performance analysis.

RESULTS: SAP was maintained stable in both groups with less frequent adjustment of remifentanil in the FG group compared to the BG group (9 [2-16] vs 19 [10-28] times, P = 0.027). Anesthesia cost was less in the FG group by 25%. BIS was stable but significantly lower (32 ± 5 vs 47 ± 2, P < 0.001) in the FG group than the BG group. Recovery time and adverse events were not different between two groups.

CONCLUSIONS: Both balanced anesthesia techniques showed stable anesthesia and fast recovery time. However, reduced workload of anesthetists and lower cost with the FG method is more preferable from the practical viewpoint. Future study is needed for the deep hypnosis measured with BIS monitoring during anesthesia maintenance.

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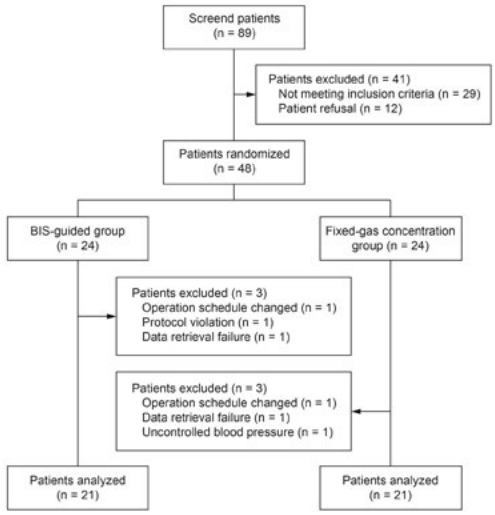

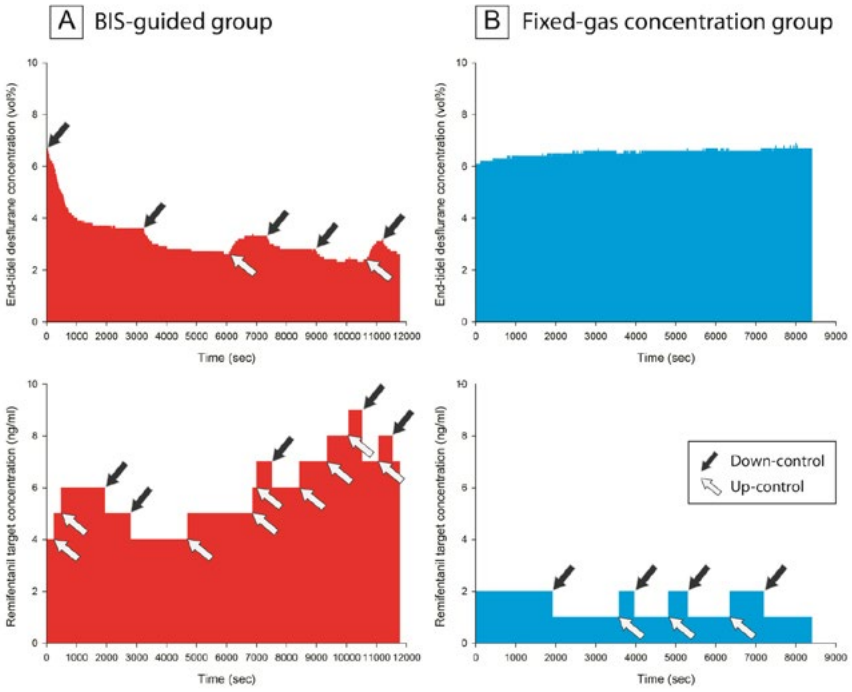

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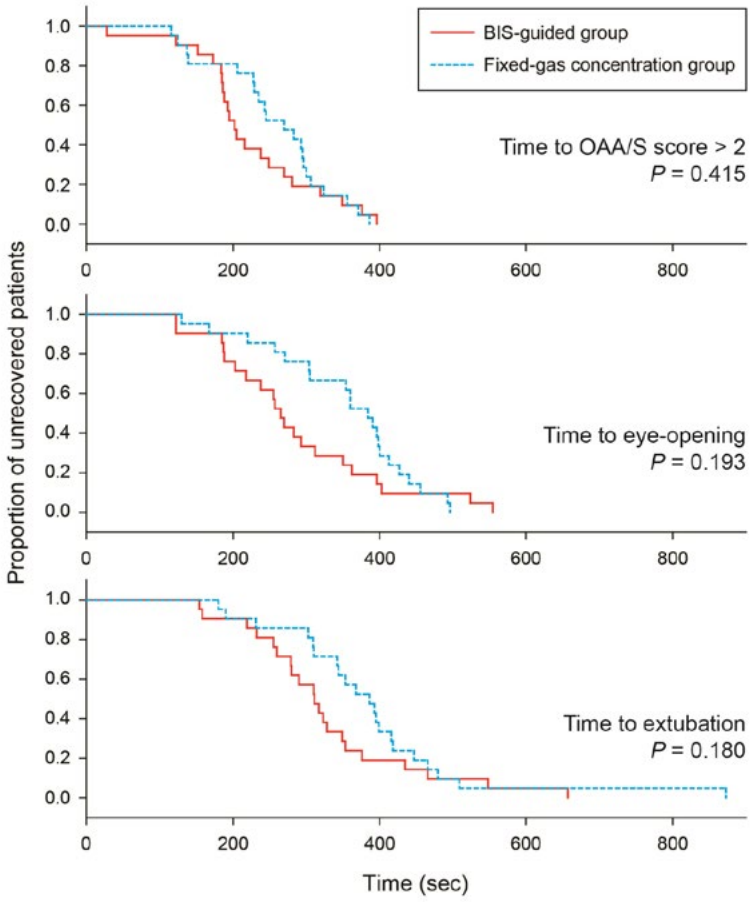

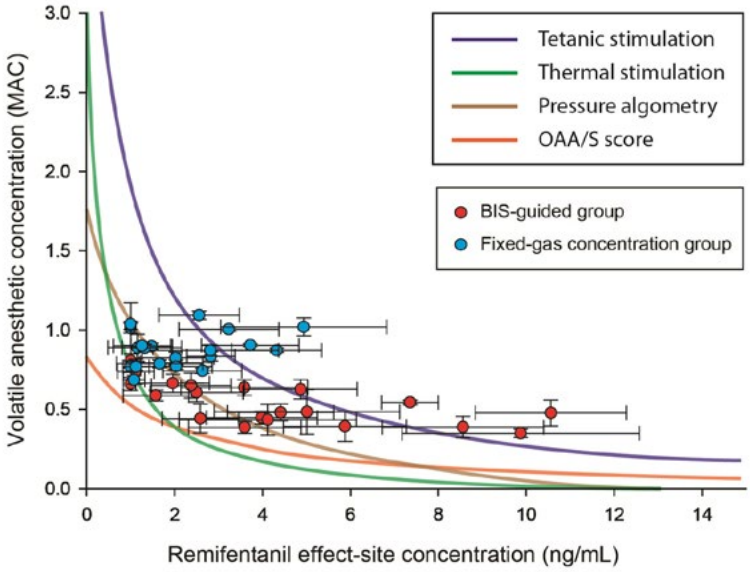

S-292.

ASA PHYSICAL STATUS ASSIGNMENT BY NON-ANESTHESIA PROVIDERS

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INTRODUCTION: The American Society of Anesthesiologists physical status (ASA-PS) scoring system remains a valuable method of communicating a patient's current physical health with other providers[1]. It is increasingly used to determine the level of perioperative testing and risk stratification. Often, this status is assigned preoperatively by non-anesthesia providers who do not have formal training in ASA-PS. Errors in the accuracy of the ASA-PS prior to surgery lead to unnecessary, costly preoperative testing, delay in operative procedures, and potentially case cancellations on the day of surgery.[2,3] Our study aimed to determine whether there is significant variation between anesthesia and non-anesthesia provider assignment of ASA-PS.

METHODS: We administered an IRB-approved survey asking the ASA-PS of 20 hypothetical case vignettes to 229 clinicians in various departments. Classifications were then compared to a consensus of expert anesthesiologists who specialize in the preoperative anesthesia clinic. A p-value of <0.01 was used to determine statistical significance because of multiple comparisons.

RESULTS: The department of anesthesiology showed 90% agreement in median score responses (18/20 vignettes). Median score agreement between residents and faculty also showed good agreement (95% or 19/20). Median scores by other departments were significantly different in a majority of case vignettes (55% or 11/20, $p<0.011$). Furthermore, all other departments were statistically different when compared to the department of anesthesiology ($p<0.01$, figure below).

CONCLUSIONS: The department of anesthesiology showed good intradepartmental agreement, regardless of level of experience. All other departments, however, were significantly different ($p<0.01$) in their assignment of ASA-PS. This is very important since errors in accurate assignment may lead to unnecessary and costly preoperative testing, delays in operative procedures, and case cancellations. Our study shows a clear opportunity for interventions to improve the accurate assignment of ASA-PS by non-anesthesia providers in the perioperative period, and should be the subject of future studies.

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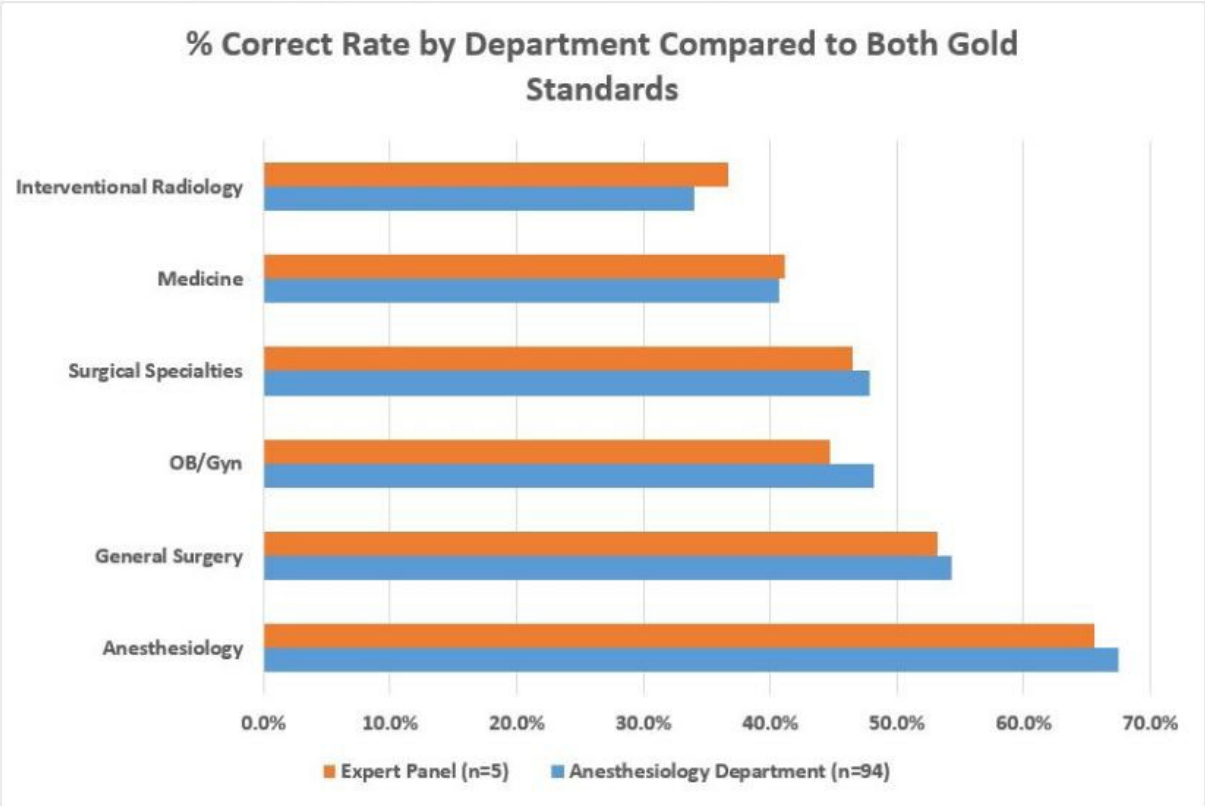

S-293.

IN PRIMARY TOTAL HIP ARTHROPLASTY, DOES THE USE OF A STANDARDISED, SPINAL-BASED ANAESTHETIC TECHNIQUE AND STANDARD SURGICAL LOCAL ANAESTHETIC INFILTRATION AFFECT POSTOPERATIVE OXYCODONE CONSUMPTION

AUTHORS: N. Campbell[1], J. J. Dickens[2], B. Ayres[1], M. P. Margarson[3], M. J. Husband[4], C. M. Eitel[5]

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INTRODUCTION: Enhanced recovery programmes for joint arthroplasty improve patient experience and facilitate early discharge[1]. Our Trust introduced the Chichester and Worthing Enhanced Recovery Programme (CWERP) for primary hip arthroplasty. This includes attendance at a preoperative joint school. Standardised oral premedication 2 hrs prior to surgery include paracetamol 1g, gabapentin 600mg (reduced to 300mg if > 80 years) and dexamethasone 10mg. Standard protocol anaesthetic technique is a spinal block (without opiate) and propofol sedation. If spinal block is unsuitable, the patients enter the non protocol group and receive a general anaesthetic; regional analgesia is discouraged but is occasionally used. All patients have surgical local infiltration with 150-200ml 0.2% ropivacaine. A standardised multimodal postoperative analgesic regime is prescribed (± NSAID) with oxycodone for breakthrough pain. We hypothesise that patients receiving the standard anaesthetic protocol combined with intraoperative local infiltration, require lower postoperative oxycodone consumption in the first 48hrs postop than the non protocol group.

METHODS: All patients having primary hip arthroplasty were entered into the programme. A single data analyst collated results. The anaesthetic was recorded and all drugs administered pre, intra and post operatively documented. The results were presented and analysed in Excel 2010. Statistical analysis using PRISIM observed if there was a significant difference in oxycodone consumption comparing the standard anaesthetic protocol and non protocol groups.

RESULTS: From December 2012-April 2015, 1324 primary hip arthroplasties were performed, 62% of these were female, mean age was 71 years (SD±10), median length of stay was 4 days.

There was no statistical difference in oxycodone consumption in patients who followed the standard protocol compared to non protocol group p=0.499 (Table 1).

Average oxycodone consumption was calculated by anaesthetic technique, with the lowest consumption seen in patents who received a GA & Regional Block 14.50mg (± 19.92), although this was only 10 patients. The next lowest amount was in patients who received a GA & Spinal (21.39mg (± 20.25)) (Table 2).

Average oxycodone consumption is significantly lower in patents who received NSAIDs mean 20.5mg vs 27.9mg (P<0.0001) and the highest in patients who received gabapentin only 38.54mg (± 44.85) (Table 3).

CONCLUSIONS: We found that patients who adhered to a standard anaesthetic and surgical protocol compared to non protocol anaesthetic showed no difference in consumption of oxycodone post operatively. Postoperative NSAIDs did have a significant effect on oxycodone consumption.

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1. Ng Man Sun, SM, Bailey, MEA, Pearce, OJ, The enhanced Recovery Programme in Hip and Knee Arthoplasty: A Review Article, Ambulatory Anaesthesia 20:2 July 2014: 22-24.

Table 1. Average oxycodone consumption in Standard Protocol and Non Protocol Groups.

	Average mg (±SD)	No. Patients	% Patients
Full Protocol	22.52 (± 24.19)	1128	85.3%
Non Protocol	22.62 (± 22.55)	195	14.7%
	22.53	**1323**	

Table 2. Average Oxycodone consumption with Anaesthetic Technique

Anesthetic	Average mg (±SD)	No. Patients	% patients
Spinal & Sedation	22.50 (± 24.17)	1147	86.8%
GA	24.19 (± 23.39)	86	6.5%
GA & Spinal	21.39 (± 20.25)	79	6.0%
GA & Regional Block	14.50 (± 19.92)	10	0.8%
Overall	**22.53**	**1322**	

S-294.

IN PRIMARY TOTAL KNEE ARTHROPLASTY, DOES THE USE OF A STANDARDISED SPINAL BASED ANAESTHETIC TECHNIQUE, TOGETHER WITH POSTOPERATIVE LOCAL ANAESTHETIC INFILTRATION, AFFECT POSTOPERATIVE OXYCODONE CONSUMPTION

AUTHORS: N. Campbell, J. Dickens, B. Ayres, M. Margarson, M. Husband, C. M. Eitel

AFFILIATION: Anaesthesia, St Richards Hospital, Chichester, United Kingdom.

INTRODUCTION: Enhanced recovery programmes for joint arthroplasty improve patient experience and facilitate early discharge[1]. Our Trust introduced the Chichester and Worthing Enhanced Recovery Programme (CWERP) for primary knee arthroplasty. This involves preoperative education. Standardised oral premedication 2 hrs prior to surgery of Paracetamol 1g, Gabapentin 600mg (reduced to 300mg if > 80 years) and Dexamethasone 10mg. Standard anaesthetic is spinal (without opiate) and propofol sedation. If spinal is unsuitable, the patients become non protocol and receive a general anaesthetic. All patients have surgical local infiltration with 150-200ml 0.2% ropivacaine, with an intra-articular catheter for infusion of 0.2% ropivacaine at 10ml/hr for 20 hrs. A standardised multimodal postoperative analgesic regime is prescribed (± NSAID) with oxycodone for breakthrough pain. We hypothesise that patients who receive the standard anaesthetic protocol combined with postoperative intra-articular infusion, require less postoperative opioid in the first 48hrs postop than the non protocol group.

METHODS: All patients scheduled for primary knee arthroplasty were entered into the programme. A single data analyst collated results prospectively. Anaesthetic technique was noted plus all drugs administered pre, intra and post operatively. The results were presented and analysed in Excel 2010. Statistical analysis using PRISIM tested for significant difference in oxycodone consumption comparing the standard protocol and non protocol groups.Results

From December 2012-April 2015, 1407 primary knee arthroplasties were performed, 58% of these were female, mean age was 70 years (SD±9), median length of stay was 3 days.

Patients who followed the standard protocol required less oxycodone than the non protocol group (Table 1).

Patients that received the standard anaesthetic protocol but did not receive post operative intra-articular ropivicaine infusion required a greater amount of oxycodone post operatively (40mg ± 0). This was not significant (p = 0.716) (Table 2).

Of the non protocol group the lowest consumption of oxycodone was in two patients that received GA & Spinal & Regional anaesthesia (RA) (Table 3).

Average oxycodone consumption was calculated by post-operative analgesia, with the lowest consumption seen in patents who received gabapentin, NSAIDs & paracetamol 27.81mg (± 26.91) and the highest in patients who received gabapentin only 57.08mg (± 39.34)

CONCLUSIONS: We found no statistical difference in oxycodone use post operatively in protocol versus non protocol groups. The addition of NSAID was significantly significant in reducing oxycodone consumption (p<0.001).

REFERENCE:

1. Ng Man Sun, SM, Bailey, MEA, Pearce, OJ, The enhanced Recovery Programme in Hip and Knee Arthoplasty: A Review Article, Ambulatory Anaesthesia 20:2 July 2014: 22-24.

Table 1. Average oxycodone consumption in Standard Protocol and Non Protocol Groups.

	Average mg (±SD)	No. Patients	% Patients
Full Protocol	30.54 (± 27.57)	1025	72.9%
Non Protocol	31.69 (± 29.27)	382	27.1%
	30.85	**1407**	

Table 2. Average oxycodone consumption accounting for the use of intra-articular infusion pump post operatively

	Average mg (±SD)	**No. Patients**	**% patients**
Protocol minus Pump	40.00 (± 0.00)	132	9.4 %
Non Protocol + Pump	35.90 (±28.66)	139	9.9%
Non Protocol minus Pump	30.50 (±30.60)	75	5.3%
	30.85	1407	

Table 3. Non Protocol Anaesthesia and Average oxycodone consumption.

Anaesthetic	**Average mg (±SD)**	**No. Patients**	**% patients**
GA	38.39 (±31.63)	87	6.2 %
GA + Spinal	36.44 (±31.63)	45	3.2 %
GA + RA	33.10 (±19.83)	25	1.8 %
Spinal + RA	26.16 (±25.95)	56	4.0 %
GA + Spinal + RA	17.50 (±3.54)	2	0.1 %

Post-op Analgesia	**Average mg (±SD)**	**No. Patients**	**% patients**
Gabapentin, NSAIDs & Paracetamol	27.81 (± 26.91)	881	62.8%
Gabapentin & NSAIDs	32.86 (± 24.98)	21	1.5%
Gabapentin & Paracetamol	35.53 (± 29.18)	375	26.7%
Gabapentin only	57.08 (± 39.34)	12	0.9%
NSAIDs & Paracetamol	34.07 (± 29.64)	75	5.3%
Paracetamol only	38.95 (± 26.10)	38	2.7%
Overall	**30.85**	**1402**	

S-295.

STOPBANG CRITERIA ADJUSTED TO ACCOMMODATE GENDER DIFFERENCES MAY CREATE A MORE INCLUSIVE OSA SCREENING TOOL

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Obstructive Sleep Apnea (OSA) is associated with debilitating systemic diseases and treatment mitigates their severity. Thus, reliable OSA diagnosis (dx) is important to a patient's health. The Snoring, Tiredness, Observed apnea, high blood Pressure (STOP)-Body mass index (BMI), Age, Neck circumference, and gender (BANG) is a validated OSA screening tool. Females (F) may be underdiagnosed for OSA, and recent publications suggest that F may be more resistant to therapy, which could reflect the timing of the dx and subsequent intervention. Here, we hypothesized that when gender is dropped as a characteristic of the screening tool (STOP-BAN), prevalence of OSA characteristics would be similar in male and female surgical patients.

METHODS: The Epic Clarity database was queried for all surgeries performed at the University of Colorado Health System (2 community and 1 academic hospitals) from 1/1/2012 to 12/31/2014. The evaluation on the standardized pre-operative anesthesia medical evaluation and a preexisting diagnosis (DX) was used to identify patients (pt) with (OSA) and without (NoOSA) OSA. Database extraction variables included: pre-admission DX, STOP-BANG elements, BMI, age, gender. Only the initial encounter for each pt was used; pts with critical missing data were excluded. The number of comorbid DX and the number of STOP-BANG criteria were reported and compared in M-OSA and F-OSA pts by t-test (T) or Pearson's Chi-Square test (P) as appropriate. To adjust for the large sample size, significance level was set at $p<0.01$.

RESULTS: 124,856 pt encounters were extracted; there were 36,248 inpatient surgeries with complete data elements: 30,580 NoOSA, 5,668 OSA pts. F pts constituted 41.1% (2,444) of OSA group and 55.1% (16,849) of NoOSA group. The mean number of comorbidities was greater in F-OSA than M-OSA pts ($p<0.0004$) The distribution of the number of comorbidities between the F-OSA and M-OSA) was not significantly different ($p<0.0117$) (Table 1). The objective STOP-BANG criteria (Table 2) showed that F-OSA pts were younger, less likely to be >50 years, more obese, more likely to have a BMI >35 kg/m2, and less likely to have hypertension than M-OSA pts. ($p<0.0001$). The number of STOPBANG criteria present in each patient had a different distribution in F-OSA than in M-OSA pts ($p<0.0001$). When M gender criteria was excluded (STOP-BAN) the distribution between genders was the same ($P<0.885$) (Figure 1, Figure 2).

CONCLUSIONS: When traditional STOP-BANG criteria were applied to a cohort of 36,248 inpatient surgeries, the incidence of OSA in F was 14% lower than the percent of F in the NoOSA group. When gender is removed from the checklist (STOP-BAN), the pattern OSA criteria did not differ between M and F suggesting very similar characteristics. Variations in other criteria like age, degree of obesity1 (difference between ideal BMI and actual BMI) suggests more research is needed. The current STOP-BANG checklist may need adjustments to better identify both F and M-OSA pts.

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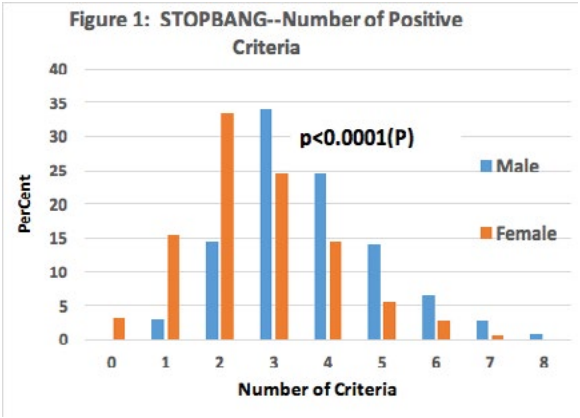

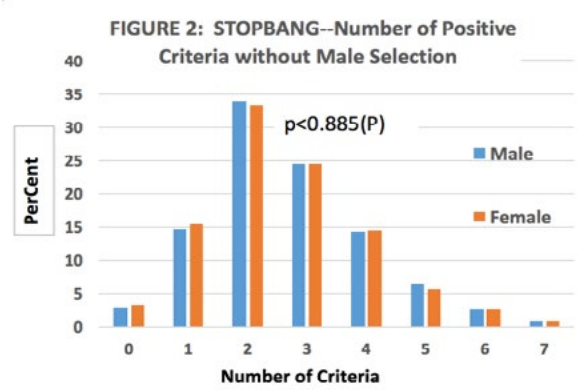

Table 1: Number of Co-morbid conditions in OSA patients MEAN p<0.0004, COUNT p<0.0117

Number of Co-morbid Conditions	M-OSA, n=3244 (%)	F-OSA n 2444 (%)
MEAN (std)	2.27 (1.6)	2.42 (1.6)
COUNT 0	375 (11.6)	215 (8.8)
1	757 (23.5)	585 (23.9)
2	810 (25.1)	608 (24.9)
3	607 (18.8)	463 (18.9)
4	400 (12.4)	306 (12.5)
5	171 (5.3)	155 (6.3)
6	74 (2.3)	73 (3.0)
7-9	30 (1.0)	39 (1.6)

Table 2: Tally of the number of patients with each STOPBANG criteria.

"STOPBAN" criteria	M-OSA n (%)	F-OSA N (%)	P value, p<
Snoring	918 (28.5)	645 (26.4)	0.082(P)
Tired	317 (9.8)	252 (10.3)	0.553(P)
Observed Apnea	450 (14.0)	246 (10.1)	<.0001(P)
Thick Neck	993 (30.8)	688 (28.2)	0.0305(P)
Hypertension dx	2,302 (71.4)	1,608 (65.8)	<.0001(P)
BMI>35kg/m2	1,003 (31.1)	1,155 (47.3)	<.0001(P)
BMI MEAN (std)	32.6 (7.3)	35.5 (9.1)	<.0001 (T)
Age>50 years	2,601 (80.1)	1,817 (74.3)	.0001 (P)
AGE MEAN (std)	61.19 (12.7)	58.66 (13.7)	<.0001 (T)

S-296.

TISSUE DAMAGE INDUCED PERIOPERATIVE INFLAMMATION IS ASSOCIATED WITH A GREATER RISK OF POSTOPERATIVE DELIRIUM IN ELDERLY PATIENTS UNDERGOING SPINE SURGERY: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION AND GENERAL PURPOSE: Postoperative delirium (POD) is a common and severe complication in elderly surgical patients. Although perioperative inflammation appears to play a significant role[1], there is an urgent need to further clarify the pathophysiology of POD. We hypothesized that greater surgical tissue damage is associated with a greater incidence of POD within 3 days after spine surgery in elderly patients. We also hypothesized that perioperative inflammation mediates this association.

METHODS: This is a prospective observational study conducted at Columbia University Medical Center between December 12, 2014, and November 6, 2015. All subjects aged 65 and older scheduled for elective spine surgery during that period were approached. We used the Confusion Assessment Method (CAM) to identify patients with POD within 3 postoperative days[2]. The degree of tissue damage was approximated based on the number of intervertebral levels requiring surgical correction. In addition to demographic and medical data, we collected blood samples serially at baseline, one hour after incision, and one day after surgery to measure plasma levels of 12 cytokines (table 1). All samples were sent to an independent laboratory for blinded analyses using multiplex quantitative methods. We summarized the data using standard descriptive statistics. To test our hypothesis, we built explanatory multivariable logistic regression models sequentially introducing potential inflammatory mediators.

RESULTS: 26 out of 81 (32%) patients met CAM criteria for postoperative delirium (table 2). Greater surgical tissue damage was significantly associated with POD (Q50: 2.0 vs. 2.5 levels, IQR: 1.0-3.0 vs. 2.0-6.0, p=0.019). This effect remained significant after adjustment for age and baseline cognitive performance (adjusted OR for delirium per additional intervertebral level: 1.51, p=0.007). Defining major spine surgery as any procedure of at least 3 intervertebral levels, greater tissue damage was associated with greater postoperative median concentrations of TNFα (2.29 vs. 1.24 pg/mL, p=0.010), IL-6 (30.84 vs. 13.65 pg/mL, p=0.005), and IL-8 (8.49 vs. 4.25 pg/mL, p=0.003). Comparing patients with and without POD, greater postoperative median concentrations of IL-6 (39.68 vs. 13.53 pg/mL, p=0.001) and IL-8 (8.99 vs. 4.66 pg/mL, p=0.002) were associated with a worse outcome. On the other hand, greater median concentrations of IL-12 at baseline (1.49 vs. 2.18 pg/mL, p=0.015) were also associated with a better outcome. Such effects remained significant after adjustment for age and baseline cognitive performance. Both IL-6 and IL-8, but not IL-12, appeared to at least partially contribute to the observed relationship between the degree of tissue damage and POD.

CONCLUSIONS: Greater tissue damage during spine surgery is associated with both a greater increase in pro-inflammatory cytokines and a higher incidence of POD in elderly patients.

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Cytokine	Threshold [pg/mL]	Baseline [pg/mL] Q50(IQR)		Intraoperative [pg/mL] Q50(IQR)		Postoperative [pg/mL] Q50(IQR)	
IL-1β	0.98	1.66 (1.22-1.91)	1.17 (1.11-1.74)	1.27 (1.21-1.72)	1.42 (1.18-2.04)	1.38 (1.17-2.38)	1.46 (1.11-2.05)
IL-2	0.98	2.35 (1.24-2.81)	1.99 (1.50-3.72)	2.12 (1.51-3.38)	1.85 (1.33-2.92)	1.82 (1.203.14)	2.22 (1.52-4.38)
IL-5	0.98	1.62 (1.07-2.23)	1.70 (1.25-2.71)	1.37 (1.17-2.32)	2.17 (1.52-3.10)	1.70 (1.26-2.43)	2.13 (1.31-2.92)
IL-6	0.36	0.90 (0.71-2.10)	0.97 (0.65-1.95)	1.33 (0.59-1.69)	0.96 (0.71-1.69)	39.68 (23.71-112.63)	13.53 (2.50-27.10)
IL-8	0.98	2.98 (1.99-5.08)	3.35 (2.28-4.87)	4.25 (2.44-8.03)	2.97 (2.13-4.76)	8.99 (5.17-18.72)	4.66 (3.06-6.18)
IL-10	2.93	6.51 (4.24-7.85)	4.59 (3.76-7.01)	6.00 (4.38-18.43)	12.56 (4.59-17.64)	7.50 (4.27-12.16)	7.19 (4.01-11.27)
IL-12	0.98	1.49 (1.25-1.82)	2.18 (1.52-3.32)	1.85 (1.15-2.68)	1.88 (1.41-3.16)	1.17 (1.05-2.04)	2.24 (1.59-3.97)
IL-13	0.49	1.90 (1.31-4.54)	2.6 (1.40-6.09)	1.98 (0.79-5.91)	2.68 (1.29-6.32)	1.25 (0.78-6.02)	2.92 (1.52-5.79)
IL-17	1.46	2.12 (1.87-6.57)	3.75 (2.95-6.90)	9.09 (1.78-22.83)	2.91 (2.21-5.72)	7.33 (2.95-50.16)	2.92 (2.17-4.67)
IL-23	15.07	46.28 (19.55-156.44)	40.43 (26.82-56.31)	40.73 (28.13-86.52)	47.05 (34.33-82.30)	47.41 (24.54-138.89)	45.10 (28.36-96.72)
TNFα	0.85	2.21 (1.15-3.82)	1.56 (1.15-2.94)	1.50 (1.06-2.48)	2.03 (1.30-3.0)	2.09 (1.43-2.72)	1.56 (1.08-2.75)
IFNγ	1.22	4.08 (3.36-7.16)	3.85 (2.51-7.85)	4.52 (3.18-8.29)	4.96 (2.84-8.43)	5.67 (1.87-8.19)	3.93 (2.12-6.32)
		POD	No POD	POD	No POD	POD	No POD

Table 1
Cytokine plasma concentrations in pg/mL at baseline, intraoperatively (1 hour after incision), and postoperatively (1 day after surgery)

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Variable	Patients with POD (N=26)	Patients without POD (N=55)
Age [yr], Q50(IQR)	72.5 (69-77)	71.0 (68-74)
Male gender, N (%)	13 (50.0)	36 (65.5)
BMI [kg/m^2], Q50(IQR)	27.2 (26.3-31.7)	27.3 (25.4-30.9)
Hypertension, N (%)	21 (80.8)	41 (74.5)
Diabetes mellitus, N (%)	6 (23.1)	14 (25.5)
Obstructive sleep apnea, N (%)	4 (15.4)	9 (16.4)
Cancer, N (%)	3 (11.5)	15 (27.3)
Coronary disease, N (%)	5 (19.2)	10 (18.2)
Stroke or TIA, N (%)	5 (19.2)	3 (5.5)
Taking aspirin, N (%)	12 (46.1)	23 (41.8)
Taking steroids, N (%)	1 (3.9)	7 (12.7)
Taking statin, N (%)	18 (69.2)	36 (65.5)
Taking fish oil, N (%)	12 (46.1)	18 (29.1)
Taking vitamin D, N (%)	16 (61.5)	33 (61.1)

Table 2

Demographic and medical characteristics of the cohort

S-297.

PERIOPERATIVE ANESTHETIC AND SURGICAL RISK FACTORS ASSOCIATED WITH POSTOPERATIVE DELIRIUM IN ELDERLY PATIENTS UNDERGOING ELECTIVE SPINE SURGERY: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION AND GENERAL PURPOSE: Postoperative delirium (POD) is a common and severe complication in elderly patients following various surgical procedures[1]. Although several demographic and medical risk factors have been associated with delirium following spine surgery[2], we aimed to assess whether anesthetic and surgical management also affect the risk of POD in this population.

METHODS: This is a prospective observational study conducted at Columbia University Medical Center between December 12, 2014, and November 6, 2015. All subjects aged 65 and older scheduled for elective spine surgery during that period were approached. We screened for postoperative delirium using the Confusion Assessment Method (CAM)[3]. We used the CAM and CAM-ICU instruments to assess patients daily while in hospital, and the FAM-CAM instrument for those discharged within three days after surgery. All study subjects were assessed by a trained investigator, who reviewed all results with the principal investigator. Before surgery, in addition to acquiring demographic and medical data, we also assessed cognitive performance using the Telephone Interview Cognitive Status (TICS) instrument. We collected intraoperative and postoperative data from electronic medical records (EMRs) and Sedline electroencephalographic (EEG) monitors.

RESULTS: 26 out of 81 (32%) patients met CAM criteria for postoperative delirium. As summarized in table 1, patients with POD had worse cognitive performance and needed more help at home at baseline. Overall, although they underwent more extensive spine surgery lasting longer and causing greater estimated blood losses, they were not more likely to receive blood products during surgery. In patients with POD, both intraoperatively and during follow up, several variables associated with oxygen carrying capacity such as blood pressure or hematocrit/hemoglobin measurements appeared not only to decline more sharply, but also to remain low longer. Interestingly, intraoperative EEG burst suppression was more commonly observed in patients with POD. Finally, despite reporting greater postoperative pain scores, patients with POD did not receive more analgesics except when admitted intubated and sedated in the ICU.

CONCLUSIONS: We identified 10 risk factors associated with POD in elderly patients undergoing elective spine surgery (table 2). In the future, such clinical markers may be combined with biological markers. These markers may be used to design a predictive scale identifying subjects at risk for developing POD, who may benefit from prophylactic measures.

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Variable	Patients with POD (N=26)	Patients without POD (N=55)
Age [years], Q50(IQR)	72.5 (69-77)	71.0 (68-74)
Male gender, N (%)	13 (50.0)	36 (65.5)
BMI [kg/m^2], Q50(IQR)	27.2 (26.3-31.7)	27.3 (25.4-30.9)
Graduate level of education, N (%)	7 (26.9)	24 (43.6)
Subjective memory loss, N (%)	9 (34.6)	15 (27.3)
TICS score [points/40], Q50(IQR)	23.5 (20.0-29.0)	28.0 (25.0-32.0)
Independent for ADLs, N (%)	15 (57.7)	16 (29.1)
Preoperative NRS [level/10], Q50 (IQR)	6.0 (3.3-7.8)	4.0 (1.0-6.0)
Pain for more than 3 months, N (%)	23 (88.5)	38 (69.1)
Hypertension, N (%)	21 (80.8)	41 (74.5)
Diabetes mellitus, N (%)	6 (23.1)	14 (25.5)
Obstructive sleep apnea, N (%)	4 (15.4)	9 (16.4)
History of cancer, N (%)	3 (11.5)	15 (27.3)
History of coronary disease, N (%)	5 (19.2)	10 (18.2)
History of stroke or TIA, N (%)	5 (19.2)	3 (5.5)
Taking aspirin, N (%)	12 (46.1)	23 (41.8)
Taking steroids, N (%)	1 (3.9)	7 (12.7)
Taking statin, N (%)	18 (69.2)	36 (65.5)
Taking fish oil, N (%)	12 (46.1)	16 (29.1)
Taking vitamin D, N (%)	16 (61.5)	33 (61.1)
Major surgery, N (%)	16 (61.5)	18 (32.7)
Min. SBP [% baseline], Q50 (IQR)	63.7 (56.5-70.2)	67.8 (60.9-75.2)
Min. DBP [% baseline], Q50 (IQR)	62.13 (53.6-72.6)	69.5 (62.5-77.6)
Min. MAP [mmHg], Q50 (IQR)	62 (58-67)	65 (61-70)
Min. Hemoglobin [g/dL], Q50 (IQR)	10.4 (8.9-11.0)	11.4 (9.5-12.4)
Min. Hematocrit [%], Q50 (IQR)	31.7 (26.8-33.0)	34.7 (27.8-38.2)
Estimated blood loss [mL], Q50 (IQR)	725 (450-1275)	250 (100-600)
Intraoperative transfusion, N (%)	5 (19.2)	5 (9.1)
Admitted to the ICU, N (%)	8 (30.8)	3 (5.5)
Min. SBP on POD1 [% baseline], Q50 (IQR)	73.7 (63.5-82.2)	81.1 (73.5-91.7)
Min. DBP on POD1 [% baseline], Q50 (IQR)	67.2 (57.6-83.6)	79.9 (69.3-88.4)
Min. Hemoglobin [g/dL], Q50 (IQR)	10.4 (8.9-11.0)	11.7 (9.9-12.7)
Min. Hematocrit [%], Q50 (IQR)	30.9 (26.9-33.2)	34.5 (29.4-38.6)
Max. NRS on POD1 [level/10], Q50 (IQR)	5 (4-8)	3 (1-5)
Hydromorphone on POD1 [mg], Q50 (IQR)	4.7 (3.2-6.5)	4.6 (2.2-6.4)

Table 2

Preoperative, intraoperative, and postoperative characteristics of the cohort

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Perioperative Period	Risk Factor For Delirium After Spine Surgery In Elderly Patients
Preoperative	Cognitive dysfunction
Preoperative	Loss of autonomy for activities of daily living
Preoperative	Non-resolving chronic pain
Intraoperative	Major surgery
Intraoperative	Maximal intraoperative blood pressure drop relative to baseline
Intraoperative	Minimal intraoperative hemoglobin level
Intraoperative	Significant and persistent intraoperative burst suppression on EEG
Postoperative	Admission to the ICU intubated and sedated
Postoperative	Severe pain one postoperative day 1
Postoperative	Persistent low blood pressure relative to baseline on postoperative day 1

Table 2

Preoperative, Intraoperative, and Postoperative risk factors associated with delirium following spine surgery in elderly patients

S-298.

USE OF PROPOFOL VS MIDAZOLAM FOR PREMEDICATION A PLACEBO CONTROLLED, RANDOMIZED, DOUBLE BLINDED STUDY

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INTRODUCTION: Midazolam is a commonly administered IV premedication prior to entering the operating room (OR) in the ambulatory setting.[1,2] It has been previously suggested that subhypnotic doses of propofol could offer advantages over midazolam for premedication because of its rapid onset and recovery profile.[3,4] The present study was designed to test the hypothesis that a 20 mg IV dose of propofol would be more effective than a standard 2 mg IV dose of midazolam for reducing acute anxiety prior to induction of anesthesia. The secondary objectives were to compare the effects of propofol and midazolam on the level of sedation and recall at induction of anesthesia.

METHODS: After obtaining IRB approval and written informed consent, 120 outpatients scheduled to undergo minor orthopedic procedures were randomly assigned to one of three study groups (n=40/group): Control (Saline); Propofol (20mg); or Midazolam (2mg). Immediately before administering the study medication, each patient evaluated their level of acute anxiety and sleepiness (sedation) on 11-point verbal rating scales (0=none to 10=extremely high), and they were also shown a picture. Upon arrival in the OR 4-5 min after administering the study medication), anxiety and sedation levels were reassessed and a second picture was shown to the patients. Upon discharge from the recovery area, anxiety and sedation levels were again assessed using the VRSs and their ability to recall the two pictures were recorded. Perioperative assessments included: demographic data, level of anxiety and sedation dosages of all anesthetic drugs, duration of surgery, anesthesia and PACU stay, and postoperative side effects.

RESULTS: The three groups were comparable with respect to demographic characteristics, dosages of anesthetic drugs, recovery times and side effects (Table 1). Compared to the saline group, both propofol and midazolam produced significant increases in the patient's level of sedation (or sleepiness) upon entering the OR (+2.5±2.4 vs. +4.6±2.5 and +5.2±2.3, respectively [$p<0.001$]). However, propofol was more effective than midazolam and saline in reducing the patient's level of preinduction anxiety (from 3.2±2.2 to1.8±1.8 vs. 3.1±2.2 to 2.3±2.1 and 2.7±1.8 to 2.8±2.1), respectively). Propofol produced more pain on injection than midazolam and saline (40% vs 23% and 10%, respectively $p\leq 0.007$) and midazolam significantly reduced recall of the second picture compared to propofol and saline (30% vs 75% and 95%, respectively, $p\leq 0.001$). (Table 2)

CONCLUSION: When administered 4-5 min prior to entering the OR, propofol, 20mg IV, appears to be a more effective anxiolytic than midazolam, 2mg IV. Compared to midazolam, propofol produced a similar level of sedation but had less effect on patient recall.

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Table 1: Demographic characteristics, anesthetic drugs, duration of anesthesia, surgery and recovery stay, Incidence of Side Effects surgery type, hemodynamic values, OAAS and Ramsay sedation scale for the three premedication treatment groups

		Saline (n=40)	Propofol (n=40)	Midazolam (n=40)	p-value
Age (yr)		49±14	52±13	51 ±15	0.7
BMI (kg/m^2)		28±5	28 ± 5	28 ± 6	0.9
Gender (n) F/M		15/25	24/16	17/23	0.1
ASA (n) I/II/III		16/19/5	6/28/6	12/24/4	0.2
Race (n) Asian/Black/Caucasian /Hispanic		1/4/35/0	3/5/31/1	3/6/31/0	0.8
Taking sleeping or anti-anxiety drugs (n)		12	13	11	0.9
Anesthesia time (min)		107±45	116±48	130±61	0.2
Surgery time (min)		79±41	84±44	102±54	0.1
Recovery stay (min)		145±86	163±100	152±86	0.6
Time from baseline assessment to study drug (min)		28±28	32±42	24±26	0.5
Time from administration of study drug until the intraoperative assessments were performed (min)		4±2	4±2	5±2	0.1
Anesthetic drugs					
	Lidocaine 50-100 mg (n)	6	10	3	0.1
	Fentanyl ug (mcg)	88±40	113±65	125±82	0.4
	Propofol (mg)	500±357	577±360	681±505	0.2
	Succinylcholine (mg)	110±11	90±50	96±38	0.74
	Cisatracurium 6-20 mg(n)	3	3	3	NA
	Bupivacaine (mg)	31±23	31±15	40±19	0.30
	Ondansetron 4 mg (n)	20	13	18	0.3
	Hydromorphone (n)	0	3	3	0.2
	Morphine mg (n)	0	3	0	NA
	Total Fluids (mL)	1471±818	1646±708	1595±651	0.5
Side Effects	Nausea (n)	5	6	4	0.8
	Itching (n)	0	1	0	NA
Type of orthopedic surgery:					
	Minor procedures (biopsy, tendon repair)	12	8	11	0.6
	Major procedures (arthroplasty, arthroscopy)	28	32	29	0.6
Mean arterial blood pressure (mmHg)					
	Baseline level	90±13	88.9±11	88±8	0.6
Heart Rate (bpm)	Before induction level	92±13†	92±10†	90±12†	0.6
	Baseline level	71±12	71±14	70±11	0.8
	Before induction level	73±12†	74±12†	75±12†	0.8
SPO2%	Baseline level	98.7±1.2	98.6±1.8	99±1.6	0.7
	Before induction level	99.6±0.7†	99.5±0.9†	99.2±1.8†	0.8
OAAS (n) (4 /5)	Baseline level	0/40	0/40	0/40	NA
(4/5)	Before induction level	2/37	6/34	7/33	0.2
Ramsey (n)	Baseline level	40	40	40	NA
	Before induction level	40	40	40	NA

Values are mean ± SD or numbers (n). No significant differences between the three treatment groups. † Significantly different from the Baseline value, $p< 0.05$.
OAAS: Observer Assessment of Alertness and Sedation Scale

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Table 2. Anxiety level, sedation level, picture recall and pain on administration of the study drug in the three premedication treatment groups.

Anxiety and sedation level §	Saline (n=40)	Propofol (n=40)	Midazolam (n=40)	P-value
Anxiety level:				
Baseline level	2.7±1.8	3.2±2.2	3.1±2.2	0.5
Before induction level	2.8±2.1	1.8±1.8†	2.3±2.1†	0.1
Postoperative level	1.8±2.4	0.8±1.1†	1.2±1.8†	0.1
P-value	0.1	0.0001	0.0002	
Sedation level:				
Baseline level	2.5±2.4	2.8±2.8	2.9±2.6	0.9
Before induction level	2.5±2.4	4.6±2.5*†	5.2±2.3*†	<0.001
Postoperative level	4.7±2.9†	3.7±2.2	4.4±2.7	0.3
P-value	0.0001	0.005	0.0002	
Memory [picture] recall:				
Pre-picture # 1 (n) yes/no	40/0	39/1	40/0	NA
Post-picture # 2 (n) yes/no	38/2	30/10*†	12/28*†‡	<0.001
Pain on administration (n)	4	16*	9	0.007

Values are mean ± SD or numbers (n).
* Significantly difference from Saline group, $p< 0.05$.
† Significantly different from the Baseline value, $p< 0.05$.
‡ Significantly different from the Propofol group, $p< 0.05$.
§ Anxiety level (0=none to 10= extremely nervous) and Sedation level (0=none to 10= extremely sedated/sleepy)

S-299.

EFFECTS OF AN ENHANCED RECOVERY AFTER SURGERY PROTOCOL IN PEDIATRIC PATIENTS UNDERGOING MAJOR HIP SURGERY

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INTRODUCTION: Perioperative surgical home models that include enhanced recovery after surgery (ERAS) protocols have been shown to enhance patient satisfaction and reduce perioperative complications and costs in adult orthopedic surgery patients.[1-3] The evidence supporting the efficacy of ERAS protocols in the pediatric population is limited.[4] Perioperative goals in this population include optimal analgesia, early mobility, and rapid return to physical function, but the orthopedic procedures encompass multiple diagnoses and procedures, increasing the difficulty of protocol implementation. We created a perioperative surgical home model with ERAS protocol for pediatric orthopedic hip surgery and hypothesized that it would decrease perioperative opioid consumption, postoperative nausea and vomiting (PONV), and length of stay.

METHODS: We created and implemented a perioperative surgical home model incorporating an ERAS protocol performed in ASA 1 and 2 patients undergoing major hip surgery at our children's hospital. The ERAS protocol included preoperative gabapentin, celecoxib, and acetaminophen. Intraoperative management included spinal anesthesia and total intravenous anesthesia with propofol, ketamine, and lidocaine infusions. Postoperative management included a multimodal opioid-sparing analgesia regimen. We then performed chart review of pediatric patients undergoing a defined set of surgical hip procedures by two orthopedic surgeons both before and after implementation of the ERAS hip surgery protocol. This study was determined by the Vanderbilt IRB to be a quality improvement project and IRB exempt.

RESULTS: We evaluated 132 patients from 2010-present prior to the ERAS protocol and 19 patients following implementation. The median age of the patients was 13.8 years. Prior to protocol implementation, 7% of patients received preoperative acetaminophen, 2% received gabapentin, and 4% received intraoperative ketamine, compared to 100% after implementation. There was a statistically significant reduction in intraoperative morphine equivalents per kg administered (0.26931 vs. 0.0107, $p<0.0001$), as well as a significant reduction in PACU morphine equivalents per kg administered (0.07489 vs. 0.0178, $p<0.0001$), following institution of the ERAS protocol. The incidence of PONV decreased after implementation of the ERAS protocol (14% vs. 0%, $p=0.077$). Median length of stay was no different after ERAS implementation (3.25 vs. 3.12, $p=0.49$).

CONCLUSION: Implementation of the perioperative surgical home model with ERAS protocol in pediatric patients undergoing major hip surgery can reduce perioperative opioid administration and postoperative nausea and vomiting. Future confirmatory studies are required to investigate if this model improves patient satisfaction scores, reduces time to meeting discharge criteria and decreases adverse events.

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S-300.

HUMAN FACTORS STUDY OF A PROTOTYPE PERIOPERATIVE HEMODYNAMIC DECISION SUPPORT SYSTEM

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INTRODUCTION: Decision support systems (DSS) are tools to assist clinicians with diagnostic and care decisions by recommending interventions based on clinical rules and algorithms. We tested a perioperative hemodynamic DDS in development which provides real-time fluid, vasopressor, and anesthetic recommendations based on advanced hemodynamics and bispectral index data. We conducted a human factors (HF) study stratified by user group on an early prototype to assess technology usability and potentially misleading interface processes that could lead to patient harm.

METHODS: The HF study was conducted with 5 faculty anesthesiologists, 4 anesthesiology residents and 4 nurse anesthetists. Users participated in a training session, followed 1-14 days later with a patient scenario simulation. Objective data was collected on 27 specific user-device interactions during the simulation. Subjective data was collected through user interviews after the simulation. The HF aspect was graded as correctly and quickly completing a task (pass), correctly completing task after some time (pass with difficulty), requiring assistance (assistance failure), or failing task (fail). Each interaction not scored as pass was reviewed by video to determine if the error or difficulty was due to software design, device training, clinical education or a genuine user error.

RESULTS: Objective data: out of 348 user-device interactions, 326 (94%) passed successfully, 5 (1%) passed with difficulty, 0 (0%) required assistance, and 17 (5%) were failures. Of the failures, 5 were genuine user errors, 6 were due to clinical education and 6 were due to software design. Specific software changes were suggested to correct software design issues and to avoid clinical education errors. Subjective data: Users suggested adding an audio alert and flashing with recommendations, displaying cumulative fluids by type, and changing how recommendations were displayed. 92% of users said they would be willing to use the device in clinical practice.

CONCLUSIONS: This HF study revealed frequency and cause of user-device interaction errors for a novel perioperative hemodynamic DSS. Consented video recording enabled researchers to determine cause of errors and make specific suggestions for design changes, in addition to user interview responses.

S-301.

A PROSPECTIVE STUDY ON THE IMPLEMENTATION OF A PRE-OPERATIVE TEAM BRIEF AND ITS IMPACT ON PERIOPERATIVE CARE

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INTRODUCTION: According to the National Patient Safety Agency in 2009, a pre-induction team brief has been shown to improve communication, patient safety and teamwork and efficiency in workflow within the operating room (OR)[1]. Through better coordination and prediction of surgery timings, the team brief also prevents over-fasting of patients which is associated with increased morbidity in the perioperative period[2]. However there has been no established mandatory team brief implemented in the local setting, or studies examining the impact a team brief could have on patient's peri-operative care. The primary objective of this study was to implement a preoperative team brief, to investigate its effects on perceived team work and communication, as well as the impact the team brief had on preoperative fasting times in patients listed for elective surgery.

METHODS: Between March and October 2015, implementation of a team brief which consisted of anaesthesiologists, surgeons, nurses and attendants was conducted prospectively over two separate 2-week periods. Questionnaires and feedback forms pertaining to team work and communication post team briefs were evaluated. The patient's fluid and food fasting times were recorded as a secondary measure of the impact of team brief.

RESULTS: A total of 164 subjects were studied. Eighty percent of the respondents felt that there was an overall improvement in the 9 main domains evaluated (anaesthesia, surgical, nursing, attendant issues, communication, team work, empowerment, smooth running of the list and patient's safety). There was significant improvement in each domain ($p<0.05$) with communication as the leading category with 90.9% respondents feeling that team brief has made it better. The pre-operative team brief also led to significant interventions that impacted on patient care. Average fluid fasting time pre implementation was 10.4 hours compared to 7.0 hours (p-value <0.001) and 5.1 hours (p-value <0.001) post implementation of the team brief in the March (n=99) and October (n=43) runs, respectively. This translates to a 50.0% reduction in fasting fluids duration pre and post team brief implementation over the 8 months period. There was also a 19.7% reduction in starvation time.

CONCLUSION: Our study highlights the potential of a team brief in reducing perioperative surgical complications. It is also an inexpensive intervention that may contribute to a safer healthcare environment for patients. The implementation of a team brief on a routine basis remains promising and should be considered as a compulsory routine in all healthcare institutions.

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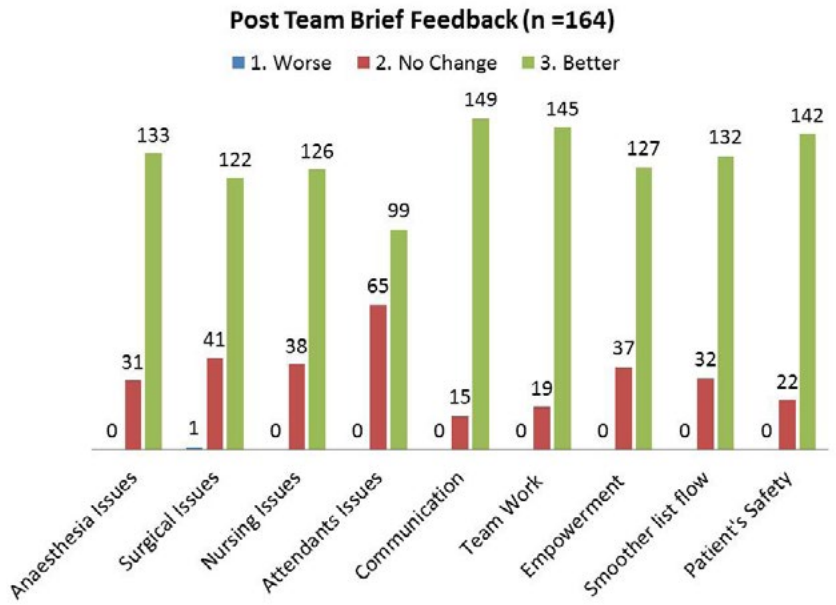

S-302.

EFFECT OF GOAL-DIRECTED FLUID THERAPY USING STROKE VOLUME VARIATION IN FREE FLAP RECONSTRUCTION

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INTRODUCTION: Adequate fluid administration improves organ perfusion and tissue oxygen supply by increasing circulating blood volume, while excessive fluid increases perioperative complications by fluid accumula tion in interstitial space. Ideal fluid management had been emphasized in various surgery. In free flap reconstructive surgery, excessive fluid administration had shown to affect patient morbidity and exacerbate flap outcomes. The aim of this study was to investigate the role of goal-directed fluid therapy using stroke volume variation (SVV) toward patient morbidity and flap outcomes.

METHODS: Forty-seven patients scheduled for free flap reconstructive surgery after head and neck cancer resection were randomly assigned into two groups: goal-directed fluid therapy group using SVV (SVV, n=24) and traditional fluid therapy group (control, n=23). Additional fluid was given when mean blood pressure (MBP)<65 mmHg and CVP<14 mmHg in control group, and when SVV>12% in SVV group. Supplemental dobutamine or norepinephrine were given according to the changes in cardiac index in SVV group. Flap outcomes were assessed and classified as total survival, partial survival, and flap failure. Reoperation, hospital stay, intensive care unit stay, postoperative complications, and postoperative chest X-ray findings were also assessed.

RESULTS: Flap outcomes were not significantly different between the two groups. However, significantly more patients had reoperation due to flap dysfunction in control group compared to the SVV group [7 (30%) vs. 1 (4%), P = 0.046]. Hospital stay, postoperative complications, and postoperative chest X-ray findings were not significantly different although the intensive care unit stay tended to be longer in control group than SVV group.

CONCLUSIONS: Goal-directed fluid therapy using stroke volume variation in patients undergoing free flap reconstruction after head and neck cancer resection reduces the reoperation events compared to the traditional fluid therapy.

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S-303.

GABAPENTIN: DOES A SINGLE PREOPERATIVE DOSE PROLONG EXTUBATION OR PHASE 1 RECOVERY TIME?

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INTRODUCTION: One critical element of Enhanced Recovery After Surgery (ERAS) pathways is multimodal analgesia. Preoperative administration of gabapentin has been shown to help with postoperative pain management, anxiolysis, prevent chronic post-surgical pain and reduce postoperative nausea and vomiting.[1] One of the potential adverse effects of gabapentinoids is the risk of augmented postoperative sedation and respiratory depression.[1,2] We recently instituted a Thoracic ERAS pathway for patients undergoing a pulmonary wedge resection or lobectomy, which includes use of multimodal analgesia with a preoperative dose of gabapentin. We investigated potential differences in extubation times and time spent in phase 1 recovery for patients in our ERAS pathway who received gabapentin, and in a similar cohort prior to implementation of ERAS where gabapentin was not given.

METHODS: With IRB approval, medical records of patients who underwent pulmonary wedge resection or lobectomy via thorascopy or thoracotomy with the ERAS pathway were reviewed (ERAS). A case matched control group of similar patients was selected in the pre-ERAS pathway (CON). All ERAS patients received a single preoperative dose of 300mg of gabapetin orally before induction. All patients received paravertebral catheters for postoperative analgesia. The patient's records were reviewed and the times from procedure end to extubation and the time from patient arrival in phase 1 recovery until discharge criteria met were recorded.

RESULTS: We included 47 CON patients and 24 ERAS patients. Wake up data was available for 37/47 CON patient and 21/24 ERAS patients. Discharge data was available for all patients. Mean extubation time was 8.9±5.5 minutes for CON (range 1-25) and 9.9±6.2 for ERAS patients (range 1, 23) (p=.558) Mean discharge time was 105.6±36.1 for CON (range 54-233) and 109.5±38.2 minutes for ERAS (range 55-185) (p=.65).

CONCLUSION: We found no significant difference in extubation times and time spent in phase 1 recovery in patients receiving gabapentin as a single preoperative dose, indicating that it can be included in multimodal analgesia as part of ERAS programs.

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S-304.

PREVALENCE OF ANEMIA IN PRESURGICAL PATIENTS IN SINGAPORE

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INTRODUCTION: Anemia is associated with increased perioperative blood transfusion, postoperative morbidity and mortality. The prevalence of preoperative anemia in many population has been well described, however, to date, no prevalence study of anemia has been conducted in our country. Such data would be helpful in developing guidelines for preoperative screening for anemia in the local context. The objectives of this study are to determine the prevalence, severity, and type of preoperative anemia (whether normocytic, macrocytic or microcytic) in pre-surgical patients, and to stratify the risk of preoperative anemia based on ASA status, age, gender and racial group.

METHODS: The electronic pre-operative anesthesia assessment record of all patients aged 16 and above who underwent surgery in our institution between 1 June 2012 and 30 June 2014 were reviewed. Only the preoperative results of the index surgery was assessed. 42310 patients were analyzed.

RESULTS: Based on the WHO definition of anemia severity, the incidence of mild, moderate and severe anemia in our population was 14.9%, 10.3% and 1.4% respectively. A higher incidence of mild anemia compared to moderate and severe anemia was present in all races, although Malays (OR=1.49, 95% CI: 1.37 to 1.63, P < 0.01) and Indians (OR=1.12, 95% CI: 1.01 to 1.25, P < 0.029) are more likely to have moderate/severe anemia compared to Chinese. The higher the ASA score, the higher the odds ratio of having moderate/severe anemia compared to ASA I (P< 0.01). Males (OR=0.51, 95% CI: 0.48 to 0.54) are less likely to have moderate/severe anemia compared to females (P < 0.01).

In females, the incidence of anemia in various age groups was between 24.5% - 40.6%, and was highest in females older than 70 years old (40.6%). Anemia was also more common in women of reproductive age (16-49 years) compared to women in their 5th and 6th decade. In males, the incidence of anemia in various age groups was between 5.9% - 47.0%, increased with increasing age, and was highest in males older than 70 years old (47.0%). In both genders, the higher the age, the higher the odds ratio of moderate/severe anemia (P < 0.01). See figure 1.

Normocytic anemia was most common (87.3%), followed by microcytic (10.8%) and macrocytic (2.0%). Compared to males of the same age group between 16-49 years, the incidence of microcytic anemia in women was higher (18.5% vs 10.3%) (P<0.01).

CONCLUSION: Age, ASA status, race and gender significantly affect the severity of preoperative anemia, and future screening guidelines should take these factors into consideration.

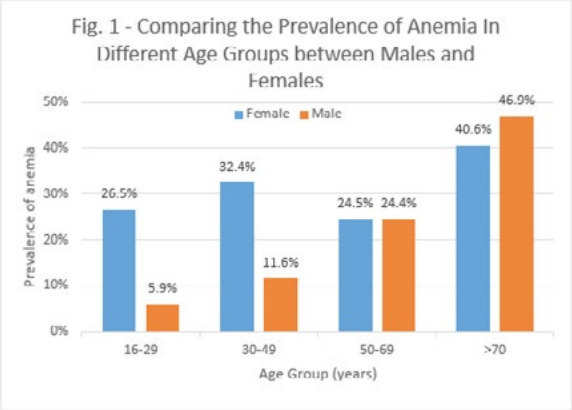

Table 1. Odds of moderate/severe anemia

	Unadjusted Odds Ratio (95% CI)	P-value
Race (ref: Chinese)		
Malay	1.49 (1.37 to 1.63)	<.001
Indian	1.12 (1.01 to 1.25)	0.029
Others	0.97 (0.87 to 1.09)	0.628
Gender (ref: female)		
Male	0.51 (0.48 to 0.54)	<.001
ASA score (ref: ASA I)		
II	2.03 (1.83 to 2.26)	<.001
III	6.44 (5.79 to 7.17)	<.001
IV	10.06 (8.56 to 11.82)	<.001
V & VI	7.92 (3.29 to 19.06)	<.001
Age group (ref:16 to 29)		
30 to 49	1.86 (1.63 to 2.12)	<.001
50 to 69	1.66 (1.46 to 1.89)	<.001
>70	3.56 (3.11 to 4.06)	<.001

S-305.

PATIENT BLOOD MANAGEMENT REDUCES CONSUMPTION OF PACKED RED BLOOD CELLS IN AN ACADEMIC TEACHING HOSPITAL

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INTRODUCTION: Patient blood management (PBM) is an evidence-based, multidisciplinary approach to optimizing the care of patients who might need transfusion[1,2,3]. PBM encompasses management of transfusion decision-making process, minimization of blood loss and optimization of patient red cell mass. PBM is known to reduce the need for allogeneic blood and consecutively, to prevent associated side effects such as TRALI and immunomodulation as well as to decrease health-care costs[4].

METHODS: We compared the consumption of packed red blood cells in 2008 (before pbm) and over the following 7 years. Statistical analysis (chi2 -test) of the yearly transfused prbc, a comparison of the transfused units with the total number of hospitalized patients.

RESULTS: In 2008 we treated 14,641 hospitalized patients and transfused 2,414 units of prbc, in 2015 19,968 patients (+ 36.38%) and used 1,688 units prbc (- 30,07 %, chi2 < 0.001) (see figure 1 and 2). The mean units transfused per hospitalized patient decreased from 0.165 down to 0.084 (- 51.27 %) (see figure 3).

CONCLUSION: In this study, we were able to show that a consequent implementation of PBM even in an non-university hospital leads to a reduction of > 50% of the consumption of packed red blood cells. This management includes the evaluation of adequacy of iron stores, the optimization of hemoglobin, awareness and assessment of medications and complementary medicines that might increase bleeding risk as well as the treatment of iron deficiency using a targeted administration of iron carboxy maltose in order to prevent transfusion undergoing planned procedures in which substantial blood loss can be anticipated5.

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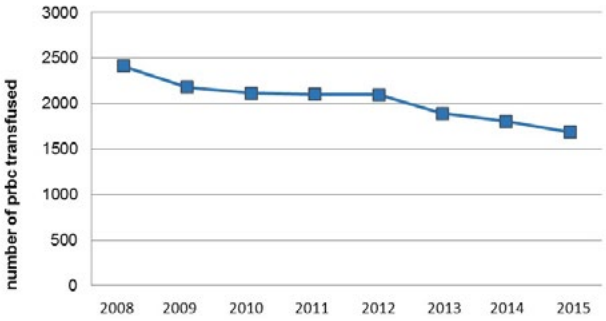

Figure 1. consumption of prbc from 2008 to 2015

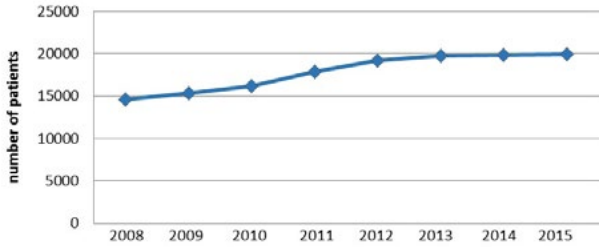

Figure 2. number of hospitalized patients from 2008 to 2015

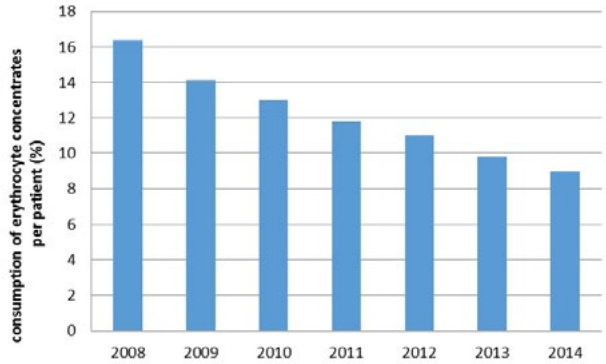

Figure 3. Proportion of transfused patients in the St. Marienhospital Vechta from 2008 until 2014

S-306.

BLEEDING COMPLICATIONS IN POST-PCI PATIENTS UNDERGOING NON CARDIAC SURGERY. A PROSPECTIVE COHORT STUDY

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INTRODUCTION: Patients who underwent percutaneous coronary intervention (PCI) and require non-cardiac surgery (NCS) pose significant challenge to anesthesi ologists and perioperative physicians[1]. Guidelines call for continuation of anti-platelet therapy in these post PCI patients. Bleeding complications due to peri-operative anticoagulation management (DVT prophylaxis or a bridging strategy) in patients with a requirement for antiplatelet therapy is poorly understood. Therefore, the aim of this prospective cohort study on post-PCI patients undergoing NCS is to: (1) analyze the role of peri-operative risk factors in prediction of bleeding complications and (2) analyze the impact of anti-platelet management and anti-coagulation management on postoperative bleeding complications.

METHODS: After receiving IRB approval and obtaining written informed consent 201 post-PCI patients having NCS were included in this study. Their anti-platelet therapy was continued till preoperative period and resumed after surgery. If anti-platelet therapy could not be continued bridging therapy was introduced as per American College of Cardiology/American Heart Association Guidelines on peri-operative management of post-PCI patients undergoing NCS. Platelet inhibition caused by aspirin and/or clopidogrel was measured with use of Platelet Mapping Assay modification of thromboelastography. We analyzed following outcomes: (1) The incidence of major bleeding defined as need for transfusion of more than 2 units of red blood cells (RBC) or blood loss exceeding 1000 cc during perioperative period. (2) The association between anticoagulation management and postoperative bleeding (3) The association between perioperative bleeding and major adverse cardiac events (MACE) defined as perioperative MI, exacerbation of congestive heart failure of death.

RESULTS: Excessive blood loss (> 1000 cc) was seen in 25 (12. 4%) patients. Major Transfusion (>2 units of RBC) occurred in 34 (17%) patients. Clinically important bleeding was seen in 66 patients; 29 of these patients experienced MACE. Adequate platelet inhibition or lack of it did not have association with clinically important bleeding. We found that there was significant post-operative bleeding in patients who received low molecular weight heparin (LMWH). In post hoc analysis we found that LMWH therapy resulted in 3-fold risk of clinically important bleeding. Patients who had significant bleeding were more likely to experience MACE.

CONCLUSIONS: The incidence of clinically important bleeding is common complication (15%) in post-PCI patients undergoing NCS. This complication is associated with the incidence of MACE. Post-operative therapy with LMWH in post-PCI patients undergoing NCS is associated with significant risk of clinically important bleeding.

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S-307.

THE RELATIONSHIP BETWEEN THE PREOPERATIVE ALBUMIN LEVEL AND ACUTE KIDNEY INJURY IN PATIENTS UNDERGONE BRAIN TUMOR SURGERY

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INTRODUCTION: Postoperative acute kidney injury (AKI) is one of the most common postoperative complication and associated with increased morbidities and mortalities.[1] Previous reports have shown that hypoalbuminemia is associated with an increased risk of AKI.[2] However, there are limited information of the relationship between the preoperative albumin level and AKI after brain tumor surgery. The aim of this study is to identify the relationship between the preoperative albumin level and postoperative AKI in patients undergoing brain tumor surgery.

METHODS: We retrospectively reviewed the electronic medical records and laboratory results of 2363 patients who underwent resection of brain tumor. Postoperative AKI was defined according to Kidney Disease: Improving Global Outcomes Definition and Staging (KDIGO) criteria using the maximal change in serum creatinine during the first 7 postoperative days compared with the preoperative baseline values.[3] We assessed the association of preoperative serum albumin stratified into two groups on the basis of preoperative serum albumin (Group 1; serum albumin ≥ 3.8 g/dL and Group 2; serum albumin < 3.8 g/dL) with postoperative AKI and mortality.

RESULTS: In total, 43 patients (1.8%) had postoperative AKI. The incidence of AKI was high in group 2 (4.5%) compared to group 1 (1.3%) ($p < 0.001$). Moreover, mortality was higher in group 2 than to group 1 (4.8% vs 2.3%, $p = 0.007$). Multivariate logistic regression analysis revealed that preoperative serum albumin < 3.8 g/dL (OR 2.465, 95% CI 1.310-4.640; $p = 0.005$) and diabetes (OR 4.223, 95% CI 1.871-9.575; $p = 0.001$) increased the risk of AKI after brain tumor surgery. In multivariate Cox proportional hazards model, preoperative low serum albumin(< 3.8 g/dL) was associated with an increased the mortality after resection of brain tumor (HR 3.223, 95% CI 1.959-5.305; $p < 0.001$).

CONCLUSIONS: Our study demonstrated that preoperative low serum albumin (< 3.8 g/dL) increases the risk of AKI and mortality after brain tumor surgery.

TABLE 1. Baseline and postoperative characteristics of the study patients stratified by preoperative serum albumin

	Preoperative Albumin		*p*
	Group 1 (*n* = 1709)	Group 2 (*n* = 654)	
Age (year)	48.58 ± 12.81	54.45 ± 12.78	<0.001
Male	700 (41.0%)	245 (37.5%)	0.120
Body mass index (kg/m^2)	24.10 ± 3.29	23.93 ± 3.40	0.273
Hypertension	157 (9.2%)	100 (15.3%)	<0.001
Diabetes mellitus	72 (4.2%)	49 (7.5%)	0.001
Ischemic heart disease	12 (0.7%)	10 (1.5%)	0.061
Preoperative medication			
ACEi or ARB	157 (9.2%)	84 (12.8%)	0.009
Beta-blocker	195 (11.4%)	136 (20.8%)	<0.001
Calcium channel blocker	302 (17.7%)	186 (28.4%)	<0.001
Insulin	123 (7.2%)	83 (12.7%)	<0.001
Oral hypoglycemic agents	95 (5.6%)	57 (8.7%)	0.005
Statin	150 (8.8%)	70 (10.7%)	0.149
Aspirin	39 (2.3%)	24 (3.7%)	0.061
Plavix	14 (0.8%)	6 (0.9%)	0.816
Preoperative laboratory values			
Hemoglobin(g/dL)	13.80 ± 1.48	12.93 ± 1.53	<0.001
Creatinine(mg/dL)	0.76 ± 0.17	0.71 ± 0.20	<0.001
eGFR (mg/dL)	74.29 ± 13.47	75.41 ± 14.25	0.017
AST(IU/L)	21.20 ± 8.22	22.59 ± 13.98	0.720
ALT(IU/L)	22.97 ± 16.04	25.71 ± 24.45	0.137
Total bilirubin(mg/dL)	0.72 ± 0.32	0.61 ± 0.29	<0.001
Uric acid(mg/dL)	4.53 ± 1.38	4.17 ± 1.44	<0.001
Postoperative AKI	23 (1.3%)	20 (4.5%)	<0.001

Data are expressed as the mean ± standard deviation (median) or number (percentage).

Group 1, preoperative albumin ≥3.8 g/dL; Group 2, preoperative albumin <3.8 g/dL; *eGFR*, estimated glomerular filtration rate, *ACEi*, angiotensin-converting enzyme inhibitor, *ARB*, angiotensin receptor blocker; *AST*, aspartate aminotransferase; *ALT*, alanine aminotransferase; *AKI*, acute kidney injury,

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S-307 • CONTINUED ON NEXT PAGE

S-307 • continued

TABLE 2. Univariate and multivariate logistic analysis for acute kidney injury in patients who underwent brain tumor surgery

	Univariate		Multivariate	
	Odds ratio (95% CI)	***p***	**Odds ratio (95% CI)**	***p***
Preoperative albumin (<3.8 g/dL)	3.078 (1.679–5.644)	<0.001	2.465 (1.310-4.640)	0.005
Diabetes mellitus	4.464 (2.024–9.846)	<0.001	4.223 (1.871–9.575)	0.001
Hemoglobin	0.783 (0.649–0.944)	0.010		
eGFR	0.968 (0.946–0.991)	0.007	0.969 (0.946-0.992)	0.010
Uric acid	0.759 (0.594-0.969)	0.027		
ACEi or ARB	2.047 (0.939-4.466)	0.072		
Calcium channel blocker	2.092 (1.108–3.948)	0.023		
Aspirin	2.825 (0.850–9.388	0.090		

eGFR, estimated glomerular filtration rate; *ACEi*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker;

TABLE 3. Univariate and multivariate Cox proportional hazards models in patients who underwent brain tumor surgery.

	Univariate		Multivariate	
	Hazard ratio (95% CI)	***p***	**Hazard ratio (95% CI)**	***p***
Preoperative albumin (<3.8 g/dL)	2.955 (1.802–4.845)	<0.001	3.223 (1.959-5.305)	<0.001
Female	0.600(0.366-0.984)	0.043	0.607(0.369-0.997)	0.049
Diabetes mellitus	1,894 (0.964–3.723)	0.064		
Calcium channel blocker	1.680 (0.981–2.878)	0.059		
Mannitol	1.004 (1.002–1.007)	0.001	1.142 (1.000-1.304)	0.050
Lasix	2.937 (0.921-9.365)	0.069	1.004 (1.002-1.007)	0.001

S-308.

A NEW ANESTHETIC AND SAMPLING PROTOCOL FOR TRANSBRONCHIAL LUNG CRYOBIOPSY

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AFFILIATION: [1]TeamHealth Anesthesia, TeamHealth Anesthesia, Tampa, FL, [2]Internal Medicine, Tampa General Hospital, Tampa, FL

INTRODUCTION: Fibrotic interstitial lung disease is challenging to diagnose since radiological imaging is often inconclusive. Surgical lung biopsy is the standard; however, because of its invasive nature, it is associated with complications[1]. Transbronchial lung cryobiopsies (TBLC) allow for the collection of large pieces of tissue by cryoadhesion and, thus, are a better diagnostic tool for this group of fibrotic diffuse parenchymal lung diseases[2-4]. This method has been shown to be superior to transbronchial lung biopsy in several studies but results vary because of different techniques.

METHODS: After IRB approval, we conducted a retrospective chart review of patients who had undergone TBLC to diagnose interstitial lung disease at our institution (2012-2014). Our protocol entails general anesthesia with tracheal intubation, ultimately providing serval improvements over published techniques[5]. We avoid the mediastinal areas of the lung for biopsy. We use a small diameter bronchoscope (6.5mm) with a thin cryoprobe (1.9mm diameter), and utilize a shorter freezing cycle (3-4 sec) as compared to Casoni[5]. To minimize risk of pneumothorax, we verify by radiological assessment that the tip of the cryoprobe was retracted at least 1.5 cm from the pleura immediately before freezing the sample. In this abstract, we collected data on the incidence of complications associated with our technique.

RESULTS: Four out of our 76 patients (5.3%) experienced a pneumothorax in our study population, as compared to 19 out of 69 (27.5%) of Casoni's study population. This represents a decrease in the incidence of pneumothorax ($p = 0.002$) according to chi-squared test. Of the 4 patients who experienced pneumothorax, only 3 patients required chest tubes. Additionally, our methodology was associated with only minor bleeding, managed with topical application of thrombin and epinephrine. No Fogarty catheters were inserted in the vicinity of the bronchoscope. In the Casoni paper, 1 patient experienced prolonged bleeding. The median length of stay in the hospital after our procedure was 0 days with only one patient needing to stay for 11 days. Two patients in our study population died but the cryobiopsy was likely not contributory.

Table 1. Comparison of Safety Outcomes with Casoni et al. (2014)

	Casoni et al. (2014) [5]	Current Study
Study Population	69	76
Incidence of pneumothorax	19	4*
Chest tube insertion required	14	3
Prolonged bleeding	1	0
Median Length of Stay (LOS)	3 days	0 days
Death	1	2

* = p 0.05

CONCLUSIONS: Overall, our modified protocol for transbronchial cryobiopsies presents a refined approach to diagnosing fibrotic interstitial lung disease while significantly reducing the risk of pneumothorax.

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S-309.

WITHDRAWN.

S-310.

EFFECT OF DURATION OF ANESTHESIA ON POST-OPERATIVE MEMORY FORMATION

AUTHORS: K. G. Palmer[1], M. Alaka[1], A. Feldner[2], A. Rubinstein[2], N. Kliestik[2], M. O'Connor[2], D. Glick[2]

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INTRODUCTION: Traditionally, efforts to prevent and study unintended intraoperative awareness with recall have focused on the operating room. However, since anesthesia awareness requires memory formation and consolidation before recall is possible[1], our interest lies in characterizing memory formation and consolidation in the perioperative period in which patients are awake, though perhaps still influenced by the effects of anesthesia. Specifically, we examine the relationship between duration of anesthesia (DOA) and post-operative memory formation. The relationship between DOA and post-operative memory formation has not previously been explored. We sought to determine if DOA impacted patient ability to recall words given in the PACU.

METHODS: Two hundred and ninety-six subjects undergoing general anesthesia were enrolled in this IRB-approved study. Each subject was presented with six words over the course of two hours in the PACU. Each word was repeated seven times over two minutes. Twenty-four hours after completion of post-operative word delivery, patients were contacted and asked to recall each of the words.

RESULTS: Overall, twenty-four hour recall of words given in the PACU was low with recall of individual words at 20-30% per word and only 57% of patients recalling even one of the words (Figure 1). After controlling for age and gender, DOA was inversely correlated with ability to recall words (OR = 0.68 per additional hour of anesthesia ± 0.15, $p < 0.001$). Figure 2.

CONCLUSION: Our data show DOA impacts ability to form memories of words spoken to patients during their time in the PACU with a dose-dependent response noted. Additionally, recall of any words spoken to patients during the first two hours in the PACU was low with nearly half of patients failing to recall even one of the words and only about one-third of patients recalling any specific word. Providers and patients should be aware that memory formation of conversations or instructions during the post-operative period may be impaired for some patients and that longer periods of anesthesia make remembering words and perhaps events more challenging. As most outpatients are discharged home from the PACU in two hours or less, our findings highlight the importance of clear, written information and the role of family and friends to help the patient recall consequential information and instructions. Further research is needed to determine the mechanism underlying this effect.

REFERENCES:

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Figure 1.

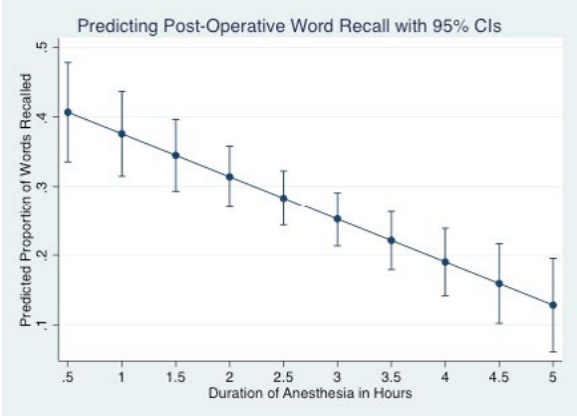

Figure 2.

S-311.

DURATION OF ANESTHESIA AND PRE-OPERATIVE MEMORY FORMATION

AUTHORS: K. G. Palmer[1], M. Alaka[1], A. Feldner[2], N. Kliestik[2], A. Rubinstein[2], M. O'Connor[2], D. Glick[2]

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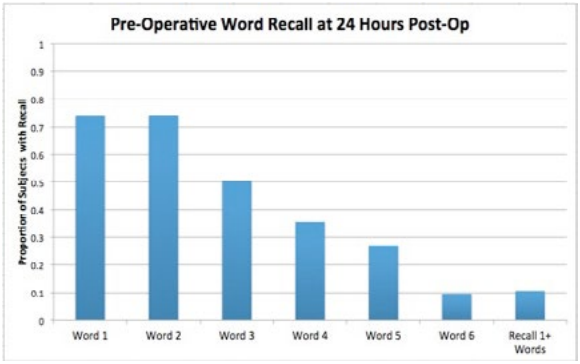
INTRODUCTION: Unintended intraoperative awareness with recall (AWR) is a highly traumatic event[1] effecting approximately 1-2 patients per 1000 undergoing surgery with general anesthesia, yet it remains poorly understood[2]. Given that memory formation under anesthesia is required for recall of the event to occur, our interest lies in characterizing memory formation in the pre-operative period in which patients are awake, though perhaps still influenced by the effects of anesthesia. Specifically, we explore the relationship between duration of anesthesia (DOA) and pre-operative memory formation, a relationship that has not yet been studied.

METHODS: Over five years, 296 subjects undergoing general anesthesia were enrolled in this IRB-approved study. Six words were delivered sequentially to each subject over eight minutes with word four given at the time of premedication with midazolam. Subjects were contacted twenty-four hours after surgery and asked to recall the six words.

RESULTS: Irrespective of DOA, at twenty-four hour follow-up 89% of subjects recalled at least one word given pre-operatively, and recall of individual words varied according to the timing of word administration. The first two words, given five and three minutes before midazolam administration, were recalled by approximately 75% of subjects, whereas words three through six were recalled by 50%, 35%, 27%, and 10% respectively (Figure 1). After controlling for age and gender, DOA was not correlated with ability to recall any specific word, ability to recall at least one word, nor proportion of words recalled ($p > 0.05$).



CONCLUSION: Our data indicate that DOA is unrelated to the ability to form memories of words and, inferentially, spoken dialogue and events in the pre-operative period. Recall of pre-operative words before anesthetic agents was relatively high with ¾ of subjects recalling each of the first two words. However, the proportion of subjects recalling words progressively drops surrounding midazolam administration, with only one in 10 recalling the word given three minutes after midazolam (Figure 1). Though this decline in memory formation surrounding midazolam administration is not surprising, it is informative. With future policy changes likely to include patient satisfaction with their anesthesiologist as a factor affecting reimbursement[3], it is important to note that patients may not remember the anesthesiologist if introductions occur in the pre-operative period. In addition, patients may not remember discussions in the pre-operative time that may include important information regarding consent, type of anesthesia used, changes to original anesthetic plan, and care instructions. Therefore, it is important for patients and providers to be aware that recall of discussions and perhaps events in the pre-operative period may be impaired.

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S-312.

MASIMO® PLETHYSMOGRAPH VARIABILITY INDEX AS A TOOL FOR ASSESSMENT OF FLUID RESPONSIVENESS IN ELECTIVE MAJOR ABDOMINAL SURGERIES

AUTHORS: A. M. Essam[1], M. Z. Ali[1], M. A. Maher[1], A. M. Mokhtar[2], H. H. El-Sabae[1], S. H. Omar[1], M. H. Hafiz[2]

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INTRODUCTION: Adequate assessment of the intravascular volume is important to maintain cardiac output to avoid hypovolemia and tissue hypoxemia.[1] Maximizing the stroke volume (SV) as measured by esophageal Doppler (ED) optimizes preload, & is a goal-directed fluid therapy technique that has been used in a variety of clinical settings.[2]

Masimo Plethysmograph variability Index (PVI) was recently introduced as a reliable, safe & noninvasive tool to guide fluid management. PVI is an automated measure of the dynamic change in the perfusion index (PI) that occurs during a respiratory cycle.(3)

We designed this study to determine whether PVI, measured using finger co-oximetry is an efficient predictor of fluid responsiveness in low-risk patients undergoing elective major abdominal surgery during preoperative steady state and dynamic intraoperative conditions.

SUBJECTS AND METHODS: After research ethics committee approval and patients' written informed consents, 60 ASA I-II patients of either sex, 25-60 years old, undergoing major abdominal or pelvic surgery (duration>120 minutes & blood loss>1000 ml) were enrolled in this study.

A Masimo Radical-7 Pulse CO-Oximeter probe & a Cardio Q Esophageal Doppler (ED) probe were applied to each patient after induction of anesthesia.

In all patients, a fluid bolus of 500 ml of 130/0.4 tetrastarch colloid solution was administered rapidly via pressurized IV infusion. Maintenance & deficits were calculated routinely. If the SV decreased by 10%, a 250-mL bolus of colloid solution was given via fast infusion.

Patients' demography, Doppler derived measurements: (SV & Flow Time corrected (FTc)), Masimo derived measurements: (PVI & PI), HR and MAP were all collected and statistically analyzed. Measurements were done at five minutes post-induction T1, Ten minutes after volume expansion (500 ml colloid) T2, If the SV decreased by 10%, (guided by ED) T3, Then 250 ml colloid is given. Ten minutes after a 250-ml colloid bolus T4.

RESULTS: Demographic data of the patients is shown in table-1. Hemodynamic data (HR, MAP), esophageal Doppler data (FTc, SV) & Masimo data (PVI, PI) were compared during the procedure before (T1) & after (T2) (table 3).

There was no significant difference in the baseline (T1) FTc, SV, HR, MAP between responders & non-responders (P>0.05) while there was a significant difference in PI & PVI (P<0.05) (table 4).

There was high significant difference between T3 & T4 in FTc, SV, PVI, PI, MAP (P<0.01) (table 5).

There was a high significant difference between responders & non-responders in SV and PVI (P<0.01) while FTc, PI, HR, MAP show no significant difference (P>0.05) (table 6).

There was no significant difference between percent changes of SV and PVI at T3 & T4 (figure 1). ROC analysis is shown in figure 2.

CONCLUSIONS: From this adaptive study we can conclude that Plethysmograph Variability Index (PVI) measured by Masimo oximeter probe is an efficient predictor of fluid responsiveness as stroke volume measured by esophageal Doppler in low risk patients undergoing elective major surgery.

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1. Crit Care 2005;9:R771-9

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Table 1: Demographic data of the studied patients

Characteristics	Patients (n= 60)
Age (yrs)	53.17± 7.21
Gender (F-M)	4 (6.7%) - 56 (93.3%)
Weight (kg)	82.67 ± 4.39
BMI (kg/m2)	23.45 ± 1.14
ASA (I-II)	50 (83.3%) - 10 (16.7%)

Data are expressed as mean ± SD or number (%).

Table 2: Type of surgery of the studied patients.

Type of surgery	Number
• Radical cystectomy	24
• Whipple	14
• Total Colectomy	10
• Gastrectomy	10
• Retroperitoneal cyst	2

Table 3: Hemodynamics before & after a 500-ml colloid solution bolus before the start of surgery

Characteristics	T1 (n= 60)	T2 (n= 60)	P-value
FTc (mSec.)	362.83 ± 23.71	391.07 ± 23.27	0.001**
Stroke volume (ml/beat)	69.37 ± 19.96	81.33 ± 25.70	0.001**
PI (%)	1.84 ± 1.06	2.43 ± 1.14	0.001**
PVI (%)	16.97 ± 3.47	10.20 ± 1.72	0.001**
HR (beat/min.)	80.30 ± 12.40	79.80 ± 11.38	0.779
MAP (mmHg)	93.83 ± 13.70	97.97 ± 14.02	0.028*

Data are expressed as mean ± SD.
NS= p> 0.05= not significant; *p< 0.05= significant; **p< 0.01= highly significant

Table 4: Comparison between hemodynamic variables in responder and non-responders for 1st bolus.

Characteristics	Non-responders (n= 20)33.3%	Responders (n= 40)66.7%	P-value
FTc (mSec.)	364.2 ± 29.11	362.15 ± 20.89	0.755
Stroke volume (ml/beat)	67.6 ± 21.69	70.25 ± 19.27	0.632
PI (%)	2.29 ± 1.16	1.62 ± 0.94	0.019*
PVI (%)	15.8 ± 1.77	17.55 ± 3.96	0.021*
HR (beat/min.)	77.8 ± 16.03	81.55 ± 10.14	0.273
MAP (mmHg)	96.1 ± 10.88	92.7 ± 14.92	0.369

Data are expressed as mean ± SD.
NS= p> 0.05= not significant; *p< 0.05= significant

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S-312 • continued

Table 5: Hemodynamic variables T3 vs. T4 in the studied patients.

Characteristics	T3 (n= 66)	T4 (n= 66)	P-value
FTc (mSec.)	325.64 ± 31.36	386.67 ± 23.18	0.001**
Stroke volume (ml/beat)	58.94 ± 19.56	79.76 ± 20.33	0.001**
PVI (%)	17.12 ± 2.42	11.91 ± 4.79	0.001**
PI (%)	1.29 ± 0.88	1.69 ± 0.80	0.001**
HR (beat/min.)	84.91 ± 15.94	83.33 ± 11.37	0.213
MAP (mmHg)	78.88 ± 13.54	93.36 ± 12.84	0.001**

Data are expressed as mean ± SD.
NS= p> 0.05= not significant; **p< 0.01= highly significant

Table 6: Comparison between responders and non-responders hemodynamics for subsequent boluses.

Characteristics	Non-responders (n= 10)15%	Responders (n= 56)85%	P-value
FTc (mSec.)	310.80 ± 24.09	328.29 ± 31.94	0.079
Stroke volume (ml/beat)	78.40 ± 19.63	55.46 ± 17.55	0.002**
PI (%)	1.75 ± 1.25	1.20 ± 0.78	0.197
PVI (%)	15.2 ± 1.55	17.18 ± 2.52	0.004**
HR (beat/min.)	85.00 ± 14.89	84.89 ± 16.24	0.802
MAP(mmHg)	81.00 ± 9.71	78.50 ± 14.15	0.351

Data are expressed as mean ± SD.
NS= p> 0.05= not significant; **p< 0.01= highly significant

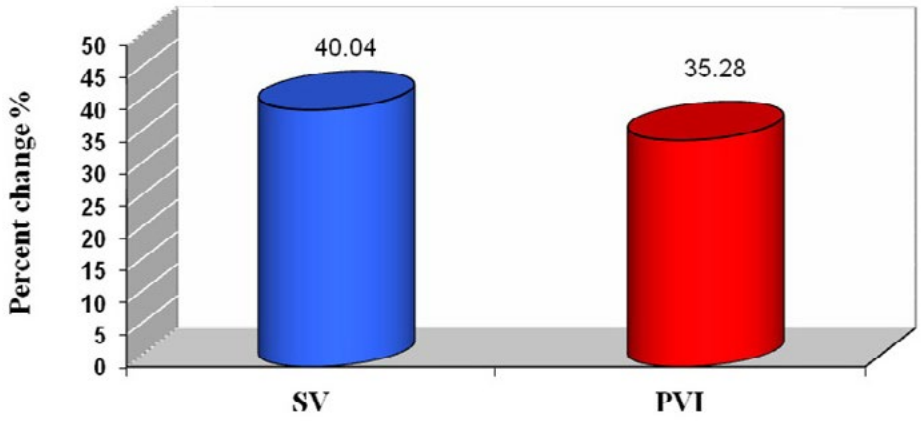

Fig. 1: Percent change in the two techniques

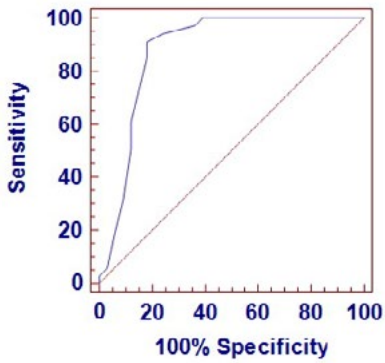

Fig.2: ROC curve of PVI

ROC analysis demonstrated significant predictive ability of an increase in SV for PVI at the intraoperative state. Area under the curve was 0.877 (95% confidence interval [CI], 0.809 –0.928; P value 0.0001). A baseline PVI cutoff value of 11 had 91.04% sensitivity and 81.82% specificity for predicting > 10% SV increase; PPV was 83.6% while NPV was 90.3%.

S-313.

VISUAL FACIAL ANXIETY SCALE FOR ASSESSING PREOPERATIVE ACUTE (STATE) ANXIETY

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INTRODUCTION: Preoperative anxiety is common prior to elective surgery with a reported prevalence of up to 80%.[1] A rapid and objective assessment of preoperative anxiety is helpful might be useful for patient care. The current "gold standard" for anxiety evaluation is the State-Trait Anxiety Inventory (STAI) which consists of two separate 20-item questionnaires.[2] this measure is time consuming which limits it utility in the preoperative setting. The numeric Verbal Rating Scale (VRS) has been utilized for assessing preoperative anxiety; however this 11 point scale has never been validated. The purpose of the study was to create a reliable, concise, and user-friendly facial anxiety scale which could be used to evaluate patients' preoperative anxiety.

METHODS: The Visual Facial Anxiety Scale (VFAS) was comprised of 11 new, similarly styled faces named A0-A10 to correspond to the 11-point verbal rating scale, with 1= no anxiety and 10= highest level of anxiety (Table 1). After obtaining IRB approval (Pro00041348), a total of 265 participant-healthcare providers-anesthesiologists (n=98), anesthesia residents (n=27) and nurses (n=140) who worked in the preoperative holding area were recruited to participate in this study. The study consisted of ranking the 11 facial expressions to the numeric VRS from 0 to 10 and matching one facial expression with the level of anxiety when using a categorical scale. The participants were asked to: 1) match each face to numeric VRS corresponding number, 0 through 10 based on their own opinion (0 = no anxiety, while 10 = highest anxiety), and 2) assign one face to each of six anxiety categories: none, mild, mild-moderate, moderate, moderate-high and highest anxiety.

RESULTS: The highest frequency of a face assigned to a level of the numerical anxiety scale resulted in a finalized order of faces from lowest to highest anxiety: A0, A1, A2, A3, A4, A5, A7, A6, A8, A9 and A10 (Table 2). Spearman analysis showed a significant correlation between the faces A10 and A9 (r=0.70), but A10 was chosen due to its higher frequency (Figure 1). The correlation of the faces A7 and A6 was significant (r=0.87), but A7 remained because of its higher frequency (Figure 1). Similarly, significant correlations were found among the faces A2, A3, A4 and A5 and the face A5 was ultimately chosen due to having the highest frequency. Ultimately, using frequency and Spearman correlations, the final order of the faces, A0, A1, A5, A7, A8 and A10, was determined and assigned to the following categories, respectively: none, mild, mild-moderate, moderate, moderate-high and high anxiety levels (Table 3).

CONCLUSIONS: The six face VFAS which best correlated to the six categorical anxiety variables represents a simple tool for assessing acute preoperative (state) anxiety (Table 3). Further research will be performed to determine if this new scale can provide a strong correlation to the STAI and/or the numeric VRS for preoperative assessment of acute [state] anxiety.

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2. Arthritis Care Res 2011; 63: 467-472

Table 1: The Visual Facial Anxiety Scale (VFAS) was initially comprised of 11 new, similarly styled faces named A0-A10

Serial Number	A0	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10
											

Table 2: The participants ranked the 11 facial expressions to the numeric VRS from 0 to 10 and the highest frequencies of the 11 smiley faces were listed

NVRS	0	1	2	3	4	5	6	7	8	9	10
	 A0	 A1	 A2	 A3	 A4	 A5	 A7	 A6	 A8	 A9	 A10
Frequent(n)	261	250	139	122	106	109	162	159	256	262	260
Percent (%)	98.49	94.34	52.45	46.04	40.00	41.13	61.36	60.23	96.97	99.24	98.48

Table 3: The six-face Visual Facial Anxiety Scale (VFAS) was finally determined.

Anxiety Level	None	Mild	Mild-Moderate	Moderate	Moderate-High	High
Faces						

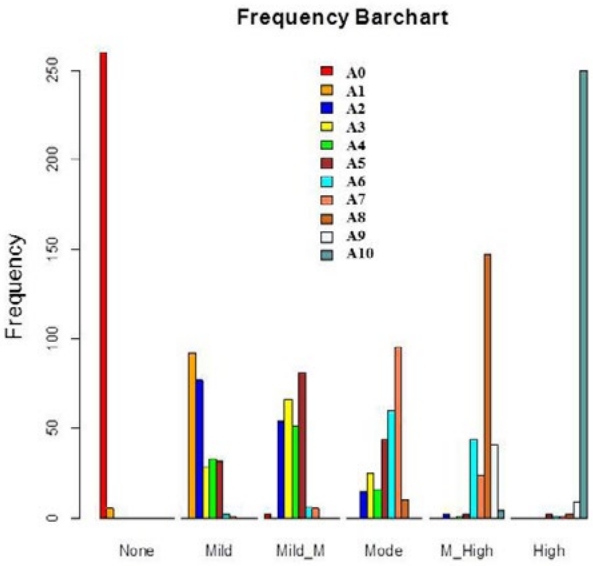

Figure 1: The frequency of 11 smiley faces in six anxiety categories

S-464.

INCLUSION BODY MYOSITIS AND ANESTHESIA

AUTHORS: A. Mortenson[1], J. Sprung[1], J. Watson[2], T. Weingarten[1]

AFFILIATION: [1]Anesthesiology, Mayo Clinic, Rochester, MN, [2]Neurology, Mayo Clinic, Rochester, MN

INTRODUCTION: Inclusion body myositis (IBM) is a painless inflammatory myopathy affecting older adults. IBM manifests as progressive muscle atrophy and weakness, typically affecting proximal lower extremity muscles initially, but insidiously progressing to impact other muscles, including bulbar muscles (mouth and throat) and diaphragm, leading to dysphagia and respiratory insufficiency. Little has been published about anesthetic management for patients with IBM, and our systematic literature review identified only six individual case reports. This study reviews the perioperative outcomes of patients with IBM who received general anesthesia. Specifically, we were interested in determining perioperative aspiration complications, postoperative respiratory complications, and unexpected reactions to muscle relaxants in patients with IBM who underwent general anesthesia.

METHODS: The medical records of surgical patients with IBM from October 1, 2009 to September 30, 2015 were retrospectively reviewed for perioperative outcomes with emphasis on respiratory complications and unexpected reactions to muscle relaxants.

RESULTS: Sixteen patients with IBM underwent 18 procedures requiring general anesthesia. Succinylcholine was used during induction in 6 cases (33.3%) and nondepolarizing muscle relaxants in 11 cases (61.1%), 10 of which were reversed with neostigmine. In 13 (72.2%) patients, the trachea was extubated at the end of surgery, and none experienced perioperative aspiration events or postoperative respiratory complications. The 5 patients who remained postoperatively tracheally intubated were expected to require continuous mechanical ventilatory support. No patients experienced notable unexpected reactions to muscle relaxants. Three patients died within 30 days of surgery, one who underwent a tracheostomy for planned long-term mechanical ventilation, however decision was made to transition to comfort cares after 22 days, and two following endoscopic retrograde cholangiopancreatography after 11 and 15 days following general anesthesia from unknown causes.

CONCLUSION: Our patients with IBM had uneventful perioperative outcomes following general anesthesia using depolarizing and nondepolarizing muscle relaxants. Perioperative mortality did not appear to be related to the effects of general anesthesia. The small number of patients in our series precludes a definitive conclusion regarding the safety of anesthetic agents.

Subspecialty Abstracts

Regional Anesthesia

S-314.

EFFECT OF LOCAL ANESTHETIC VOLUME WITHIN THE ADDUCTOR CANAL ON QUADRICEPS FEMORIS FUNCTION EVALUATED BY ELECTROMYOGRAPHY: A RANDOMIZED, OBSERVER- AND SUBJECT-BLINDED, PLACEBO-CONTROLLED STUDY IN VOLUNTEERS

AUTHORS: U. Grevstad[1], P. Jaeger[1], J. Sorensen[1], B. Gottschau[1], B. M. Ilfeld[2], M. Ballegaard[3], J. B. Dahl[1]

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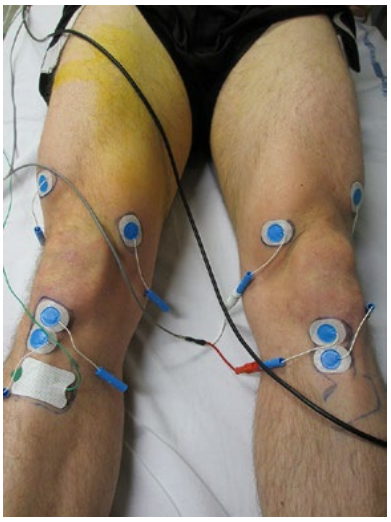
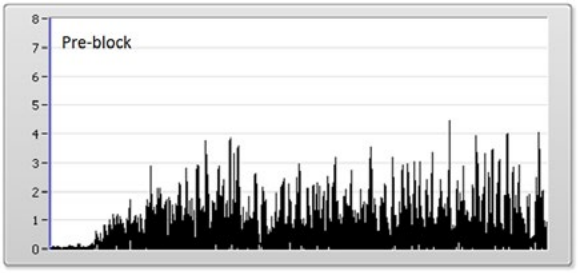
BACKGROUND: The adductor canal is an aponeurotic tunnel within the thigh containing both vascular structures and various peripheral sensory and motor nerves. Single injection adductor canal block (ACB) provides analgesia following knee surgery. The specific nerves blocked by an ACB and what influence—if any—local anesthetic volume has on the effects remain undetermined. We hypothesized that effects on the nerve to the vastus medialis muscle (which besides being a motor nerve innervates portions of the knee) are volume-dependent.

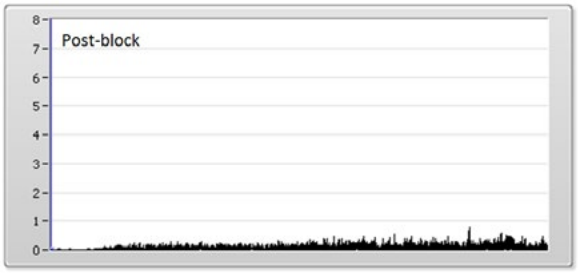
METHODS: In this assessor- and subject-blinded randomized trial, 20 volunteers were included. On three separate days (1-2 day interval between days), they received an ultrasound-guided ACB with three different volumes (10, 20 and 30 mL) of lidocaine 1%. In addition, they received an ultrasound-guided femoral nerve block and a placebo ACB. The effect on the vastus medialis (primary endpoint) and the vastus lateralis was evaluated using non-invasive electromyography (EMG; Figures 1 and 2). Quadriceps femoris muscle strength (MVIC) was evaluated using a dynamometer.

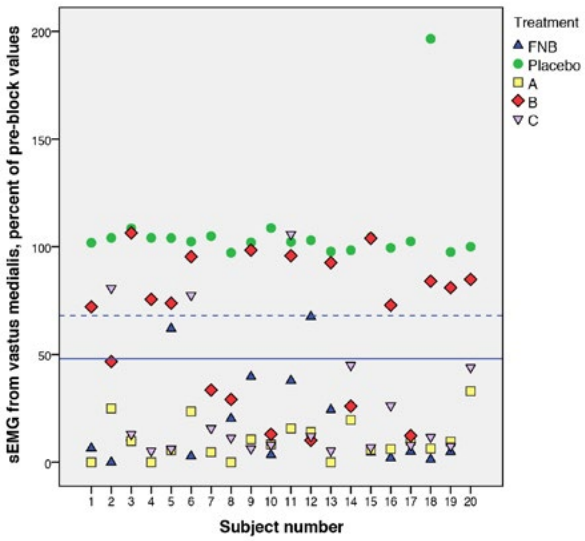
RESULTS: There was a statistically significant difference in EMG response from the vastus medialis, dependent on volume (Figure 3). Thirty-five percent (95% CI: 18 - 57) of the subjects had an affected vastus medialis following and ACB with 10 mL compared to 84% (95% CI: 62 - 94) following 20 mL (P=0.03) and 100% (95% CI: 84 - 100) when 30 mL were used (P=0.0001). No statistically significant differences were found between volume and effect on the vastus lateralis or in muscle strength (Figure 4). In spite of the rather large differences in EMG recordings, only a trend toward a decline in quadriceps femoris muscle strength was noted (Figure 5). Subjects preserved median MVIC values of 95% (10 mL), 99% (20 mL) and 92% (30 mL) of their pre-block values compared to 18% after the FNB (P < 0.001). No blocks (except placebo) resulted in a completely preserved sensation, so by our a priori definition there were no "failed blocks". However, some subjects had only a partial loss of sensation: 3/20 after the FNB (the excluded subjects), 4/20 after the ACB 10, 1/20 after the ACB 20 and 1/20 following the ACB 30, P=0.22. The remainder had complete loss of sensation.

CONCLUSION: For ACB, there is a positive correlation between local anesthetic volume and effect on the vastus medialis muscle. This finding suggests that a volume of less than 30 ml does not consistently block the vastus medialis muscle. Since no association between volume and adverse effects (effect on vastus lateralis or MVIC) was demonstrated, our findings may indicate that higher volumes improves the analgesic effect of an ACB after knee surgery, without increasing adverse motor effects from the block.









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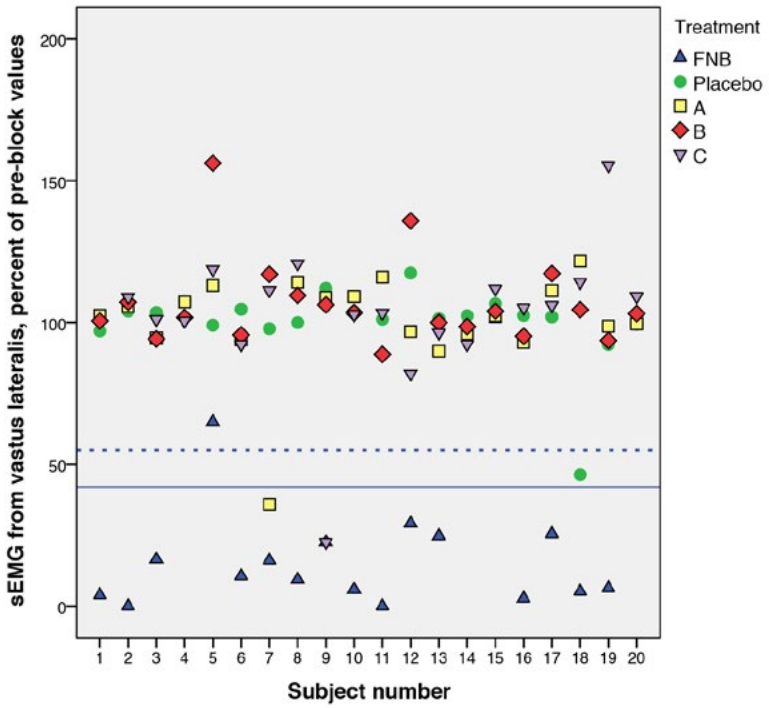

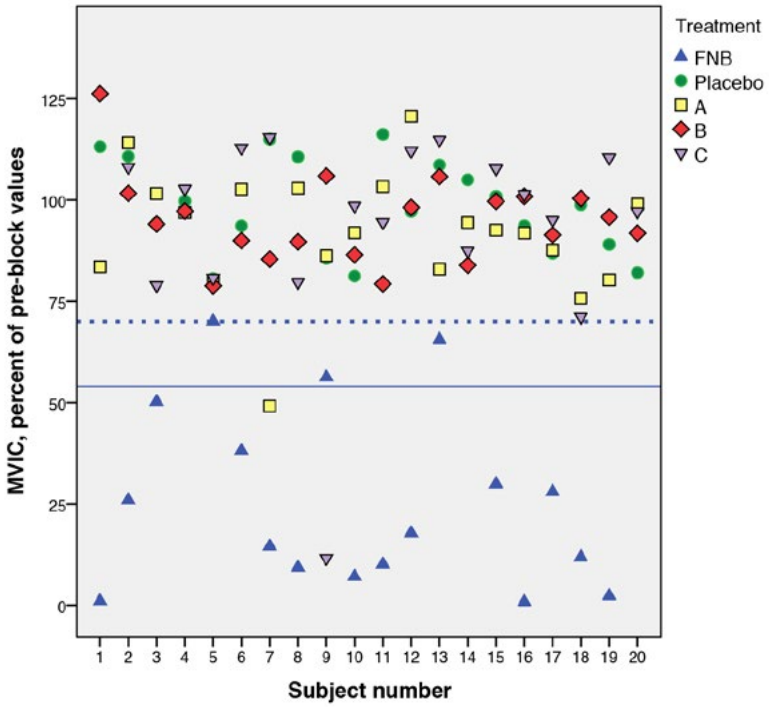

S-315.

NEUROSTIMULATION FOR POST-SURGICAL ANALGESIA: A NOVEL ELECTRICAL LEAD ENABLING ULTRASOUND-GUIDED PERCUTANEOUS PERIPHERAL NERVE STIMULATION

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INTRODUCTION: While neurostimulation—the activation of neural tissue via electrical current—has been used to treat chronic pain[1], its use as a treatment for post-surgical pain has been limited. Here we report a proof-of-concept study on the clinical application of a novel lead to provide analgesia following total knee arthroplasty inserted through a Tuohy-type needle using ultrasound guidance.

METHODS: IRB and US FDA (i.e., investigational device exemption) approvals were obtained prior to enrollment. All subjects provided written, informed consent. Adults following primary, unilateral, total knee arthroplasty with surgery-related knee pain uncontrolled (self determined) with oral analgesics were enrolled. The tip of a monopolar test needle electrode was positioned 0.5-1.0 cm remote from the femoral nerve using ultrasound guidance (in-plane technique). Test stimulation (100 Hz, 15-200 μsec, 0.2-20 mA) verified the optimal position of the electrode by producing comfortable sensations within the region(s) of pain without evoking muscle contractions. The needle electrode was subsequently withdrawn and replaced with a 12.5 cm, 20 g needle and in-plane ultrasound approach (Fig. 1). The final needle tip location was placed in the same location as the optimal position of the monopolar electrical needle tip. A pre-loaded, monopolar, helically-coiled, small diameter insulated electric lead was deployed by withdrawing the introducer needle over the lead (Fig. 1). If the participant also reported posterior knee pain, a second percutaneous lead was placed 1.0-3.0 cm posterior to the sciatic nerve using the same technique. The lead(s) was subsequently attached to a small stimulator(s) (Figs. 2 & 3). All participants underwent pain assessment at rest and during passive and active range of motion (ROM), with and without the stimulation using a 0-10 pain rating scale. Leads were removed the same day.

RESULTS: Pain (n=5) decreased an average of 63%, 43%, and 50% during rest, passive and active knee flexion, respectively (Table 1). Neither maximum passive nor active knee flexion was consistently affected (Table 2). Leads were removed the same day without difficulty.

CONCLUSIONS: This proof-of-concept case series provides evidence that peripheral nerve stimulation delivered via a helically-coiled percutaneous lead permits ultrasound-guided percutaneous insertion without a surgical incision and provides analgesia following knee arthroplasty and, may therefore be a practical modality for the treatment of post-surgical pain. Unlike continuous peripheral nerve blocks, this technique theoretically does not induce sensory, motor, or proprioception deficits, and therefore should not similarly increase the risk of falling[2]. If future research confirms delivery of adequate analgesia with an acceptably low adverse event profile, the technique has the potential to become a viable post-surgical analgesia option.

REFERENCES:

1. Rauck. Neuromodulation 2014; 17: 188 2. Ilfeld. A&A 2010; 11: 1552

Figure 1.

Figure 2.

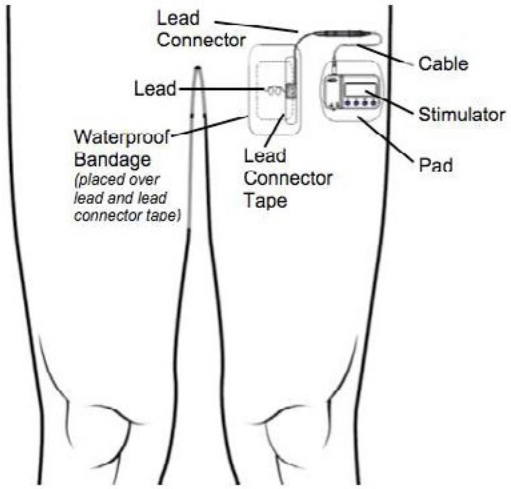

Figure 3.

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S-315 • continued

Table 1. Pain at baseline and during percutaneous peripheral nerve stimulation with electric current

Subject	Days Since Surgery	At Rest			During Passive Flexion			During Active Flexion		
		At Baseline	With Current	% Change	At Baseline	With Current	% Change	At Baseline	With Current	% Change
A	8	9	3	67%	7	4	43%	NC	NC	NC
B	9	7	6	14%	9	NC	NC	NC	NC	NC
C	6	2	0.5	75%	4	5	-25%	3	1	67%
D	92	7	3	57%	8	6	25%	6	4	33%
E	97	4	0	100%	6	NC	NC	6	NC	NC
Mean	42	5.8	2.5	**63%**	6.8	5.0	**43%**	5.0	2.5	**50%**

Pain evaluated using a Numeric Rating Scale (0-10)
NC: not collected

Table 2. Subject **knee flexion** at baseline and during percutaneous peripheral nerve stimulation with electric current

Subject	Passive Flexion			Active Flexion		
	At Baseline	With Current	Change	At Baseline	With Current	Change
A	75	90	15	NC	NC	NA
B	75	NC	NA	NC	NC	NA
C	48	58	10	44	45	1
D	115	114	-1	112	113	1
E	58	NC	NA	87	NC	NA
Mean	74	87	**8**	81	79	**1**

Data presented in degrees of flexion

S-316.

WITHDRAWN.

S-317.

WITHDRAWN.

S-318.

TO COMPARE THE EFFICACY OF INTERCOSTAL NERVE BLOCK AND PERITUBAL INFILTRATION OF ROPIVACAINE FOR POSTOPERATIVE ANALGESIA FOLLOWING PERCUTANEOUS NEPHROLITHOTOMY- A PROSPECTIVE RANDOMIZED DOUBLE BLIND STUDY

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BACKGROUND: Percutaneous nephrolithotomy (PCNL) is the most common and less invasive endourological procedure for management of renal calculi. Although it is minimally invasive it still causes significant postoperative pain demanding analgesia. Intercostal nerve block1 (ICNB) and peritubal infiltration2 of the nephrostomy tract are well established forms of regional anesthetic techniques in alleviating the pain after PCNL. In our present study we investigated the efficacy of ICNB to peritubal local anesthetic infiltration in providing superior analgesia following percutaneous nephrolithotomy.

METHODS: A prospective study was designed in 60 ASA-1 and II patients scheduled for PCNL were randomized in to two groups. A standard general anesthesia was administered and PCNL with nephrostomy tube was performed in all patients. At completion of the procedure, patients in group P received peritubal infiltration with15 ml of 0.5% ropivacaine using 23G spinal needle along the nephrostomy tract at "6 and 12" O clock position under fluoroscopic guidance. Group I receive intercostal nerve block at 10, 11, 12th spaces with 5ml of 0.5% ropivacaine in each space under fluoroscopy. Postoperatively patients were followed for 24hrs for pain by using visual analog scale (VAS) and Dynamic VAS on deep breathing and coughing. Rescue analgesia was with inj. tramadol 1mg/kg IV to maximum of 300mg/day when pain score exceeded 4.Time to first rescue analgesic, number of doses and patient satisfaction were noted in all patients.

RESULTS: Pain scores were low in both the groups but the mean time to first rescue analgesia was significantly more in G I (p-0.000) and also the number of demands and the amount of analgesia consumed were also less in G I. (table 1, 2a, 2b)

CONCLUSION: Both intercostal nerve block and peritubal infiltration of nephrostomy tract provide postoperative analgesia but ICNB is more efficient and also provides longer duration of analgesia following PCNL than peritubal infiltration.

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Table 1 Patient Characteristics

Parameter	Group P(n-30)	Group I(n-26)	P value
Age (years)	42.5±11.6	41.3±13.4	0.738
Gender	21:9	19:7	
Duration of surgery (hrs)	1.56±0.29	1.43 ±0.37	0.79
Analgesia(hrs)	7.167±3.92	13.22±4.07	0.000*
No. of demands	2.2±0.594	1.3±0.451	0.016*
Patient satisfaction	3.27±0.6	5.76±0.76	0.001*

Table 2a Visual analog pain score at 4hrly intervals

	VAS 0 Median[IQR]	VAS 4 Median[IQR]	VAS 8 Median[IQR]	VAS 12 Median[IQR]	VAS 16 Median[IQR]	VAS 20 Median[IQR]	VAS 24 Median[IQR]
Group P	2[1-3]	2[1-3]	4[4-5]	5[4-6]	4[2.75-5]	2[2-4]	3[2-4]
Group I	1[0-2]	1[0.75-2]	1[0.75-2]	2[1-3]	4[3-5]	4[3-5]	2[1.75-3]
p value	0.12	0.005*	0.00*	0.00*	0.306	0.004*	0.268

Table 2 b DVAS Pain score at 4th hourly Intervals

	DVAS 0 Median[IQR]	DVAS 4 Median[IQR]	DVAS 8 Median[IQR]	DVAS 12 Median[IQR]	DVAS 16 Median[IQR]	DVAS 20 Median[IQR]	DVAS 24 Median[IQR]
Group p	2.5[1-4]	3[2-4]	5[4-6]	6[4.75-7]	4[3-5]	3[1.75-4]	3[1.75-4]
Group I	1[1-2]	1[1-2]	2[1-3]	2.5[1-3]	5[4-6]	4[3-5]	3[2-3.25]
P value	0.09	0.000*	0.000*	0.000*	0.318	0.009*	0.737

S-319.

EFFECT OF NERVE STIMULATION USE ON THE SUCCESS RATE OF ULTRASOUND-GUIDED SUBSARTORIAL SAPHENOUS NERVE BLOCKADE

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BACKGROUND: Ultrasound-guided subsartorial saphenous nerve blockade is a commonly used technique to provide complete surgical anesthesia of the foot and ankle in combination with popliteal sciatic nerve blockade. However, in part due to its small caliber and absence of a prominent vascular landmark in the subsartorial plane distal to the adductor canal, the saphenous nerve is more difficult to reliably block than the sciatic nerve in the popliteal fossa.[1-3] Although the saphenous nerve is a sensory nerve only, neurostimulation can be used to elicit a "tapping" sensation on the anteromedial aspect of the lower leg extending towards the medial malleolus.[4,5] Hence, our objective was to test the hypothesis is that the addition of nerve stimulation use to an ultrasound-guided technique will increase the success rate of subsartorial saphenous nerve blockade.

METHODS: With institutional human ethics board approval and written informed consent, we enrolled 80 patients undergoing foot and ankle surgery in a randomized, single-blinded, parallel-group clinical trial. Patients were randomly assigned to receive ultrasound-guided subsartorial saphenous nerve blockade alone (US group) or with the use of additional nerve stimulation (time limit, 5 min; NS group). For saphenous blockade, all patients received 10 mL of 0.5% ropivacaine. The primary endpoint was complete absence of sensation to pinprick at 30 min at two different anatomic areas in the distribution of the saphenous nerve (10 cm distal to the medial tibial condyle and 2 cm proximal to the medial malleolus). Secondary endpoints included decreased sensation at 30 min and block failure (normal sensation) at 30 min.

RESULTS: All 80 patients completed the trial (each group, n = 40). Twenty-two patients (55%) in the NS group versus 18 (45%) in the US group had complete absence of sensation to pinprick at 30 min (Fisher's exact test, P = 0.50; 95% confidence interval of difference in proportions, -11.9% to 31.9%]). The percentages of patients with any evidence of blockade (decreased or complete absence of sensation) at 30 min were 92.5% (NS) and 97.5% (US), respectively (P = 0.62); corresponding failure rates (normal sensation) were 7.5% (NS) and 2.5% (US).

CONCLUSIONS: The addition of the use of nerve stimulation did not improve the success rate of ultrasound-guided subsartorial saphenous nerve blockade. This trial was registered at Clinicaltrials.gov: NCT02382744.

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S-320.

UNIPORT AND MULTIPORT EPIDURAL CATHETERS IN POST-SURGICAL PATIENTS

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INTRODUCTION: A properly functioning epidural is the gold standard analgesic modality for many thoracic and abdominal procedures post-operatively. However, epidural analgesia has been studied almost exclusively in the lumbar spaces of parturient[1-4] and not the thoracic spaces of post-surgical patients. Integral to the spread of local anesthetic within the epidural space, and ultimately providing pain relief, is whether the catheter design has one end-hole, or multiple side holes. These two catheter designs provide equivalent analgesia in laboring patients[1]. However, this may not be true in post-surgical patients wherein lower volumes are typically used for longer duration and the thecal sac is thinner and narrower. We hypothesize that flexible multi-port thoracic epidural catheters will provide superior analgesia when compared to flexible uniport catheters for post-surgical patients as measured by epidural failure rate (primary outcome defined as the need to use adjunctive opioids, replacing or removing the epidural) and pain scores (secondary outcomes).

METHODS: This is an IRB approved randomized, double-blind, prospective trial registered with clinicaltrials.gov. Patients undergoing thoracic or abdominal surgery, requesting a thoracic epidural expected to be in place >24 hours, and ages 18 to 75 were approached by an investigator. Exclusion criteria included any chronic pain/opioids, BMI >40, delirium and dementia. Using α=0.05, β=0.80 and an analgesic failure difference of 20%, power analysis predicted 91 patients would be needed per group. The placement team was unblinded to catheter type but the acute pain service that followed the patient post-op and recorded outcomes was blinded (the catheters appear identical). Ultimately, a blinded interim analysis was performed after the first 100 patients due to significant pushback to end the study from our acute pain service citing time constraints. A t-test was used to compare continuous pain score data and Kaplan-Meier curves displaying epidural "survival" were calculated for each catheter.

RESULTS: 100 patients were enrolled and underwent randomization. A significant number of patients were excluded from data analysis because the epidural was never used (post-op intubation, hemodynamic instability). 31 patients received the "green" and 35 patients received the "blue" catheter.

CONCLUSIONS: One of the catheter designs appears to provide superior analgesia (although both have a higher incidence of failure than typically seen in obstetrics). VNAS scores at PACU admit and discharge and on POD 1 and 2 are all lower, but only PACU discharge and POD 1 are statistically significant. The Kaplan Meier curves demonstrate that more epidurals are functioning appropriately in the blue group at all time points. This interim analysis provided us the necessary data to convince our acute pain service to continue enrollment until criteria was reached.

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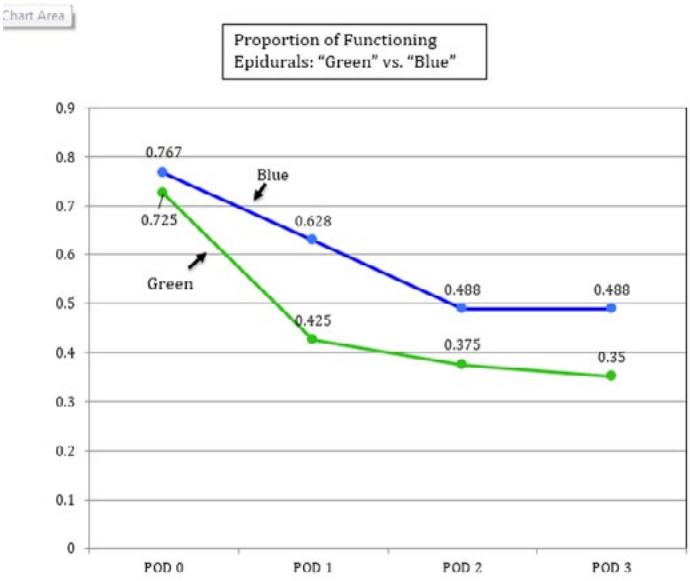
Verbal Numeric Analog Pain Scores (0-10)

	PACU Admit	PACU D/C	POD 1	POD 2	POD 3
"Green" Average VNAS	5.533	3.708	3.250	2.460	1.625
"Blue" Average VNAS	4.236	2.272	2.0	1.70	1.188
t-test	p=0.096	*p=0.005	*p=0.049	p=0.246	p=0.484



S-321.

ACCURATE NEEDLE ENTRY POINT AND ANGULATION IS CRUCIAL IN USING PREDETERMINED DEPTH TO LOCATE THE THORACIC PARAVERTEBRAL SPACE (TPVS)

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INTRODUCTION: Thoracic paravertebral block (TPVB) is an advanced technical procedure due to its difficulty in achieving a consistent local anesthetic spread pattern, difficulty in recognizing correct target endpoint, and risk of pneumothorax. The authors propose a technique that takes advantage of the consistent relationship between the transverse process (TP), superior costotransverse ligament (SCTL), and TPVS.

The authors examine 50 chest CTs to make multiple soft tissue and bony measurements in order to provide data for the proceduralist to more accurately locate the TPVS. The authors propose that TP thickness is consistent. Using the measured distances and the mixed virtual reality simulator of the thoracic spine, we speculate that predetermined depth in combination with precise needle entry point and needle angulation is crucial in consistently guiding the needle into the TPVS.

METHODS: After obtaining IRB approval, 50 adult chest CTs were used to retrieve the following information (Fig 1): thickness of the TP, thickness of the rib, anterior-posterior distance from skin to TP, skin to pleura, TP to pleura, skin to vertebral lamina (VL) and lateral distance from spinous process (SP) to tip of TP, SP to edge of VL. Measurements were performed at 3 different thoracic levels, T2, T5-6, and T9-10. The patient's height and weight were collected.

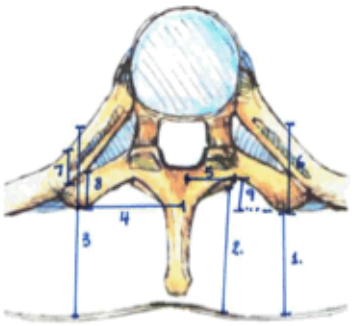
Means and standard deviations were calculated for each of the measurements (Table 1).

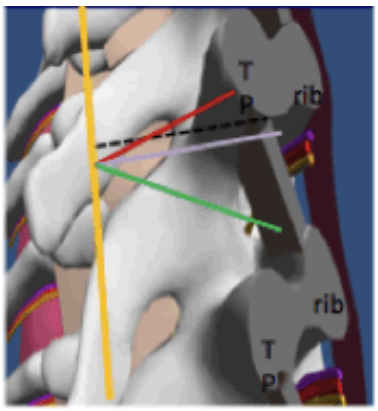
RESULTS: The thickness of the TP was consistent across different BMI ranges and at different thoracic levels (average 9-12mm). In addition, depth of TP to pleura averages 20mm, but none is less than 15 mm. From SP to the lateral and posterior aspect of TP is an average of 30mm, 28mm and 25mm at T2, T5-6, and T9-10 respectively.

DISCUSSION: If the proceduralist advances the needle perpendicular to skin (no medial or lateral, caudad or cephalad angulation) at a predetermined depth of 10mm caudad to the TP, the TPVS should be reliably located without risk of pneumothorax. This 10mm needle advancement should be adequate because the SCTL attachment to the TP is approximately midway between the anterior and posterior aspect of the TP.

However, predetermined depth must be paired with thoughtful needle entry point placement and needle angulation. The lateral needle entry point must be at the skin projection at the lateral edge of the TP, but not on rib (approximately 5mm from the most lateral aspect of TP) and 3 mm caudad to the inferior aspect of the TP (Fig 2 and 3). With this entry point, TP can be encountered using a slightly cephalad needle angulation, and when the needle is walked caudad to the TP, its angle is perpendicular to skin. Then, predetermined depth can be very reliable as an endpoint for TPVS localization.

Furthermore, the SCTL runs obliquely from the inferior aspect of the TP above to the superior aspect of the rib below, making the AP dimension of the TPVS widest and the SCTL more superficially engaged when the needle enters caudad to the TP. Walking cephalad once bony contact is made is not recommended since the rib tends to be cephalad to the corresponding TP, introducing unpredictability in depth of TPVS from bone.





Yellow line-skin,
Black dashed line-projection of TP lower border on the skin
Red line-safe landing trajectory (start 3 mm below projection of TP lower border and aim slightly up (15-30 degree from perpendicular)
Purple line-initial advancement-15-30 degree down from safe landing or perpendicular to skin
Green line- incorrect initial advancement pass

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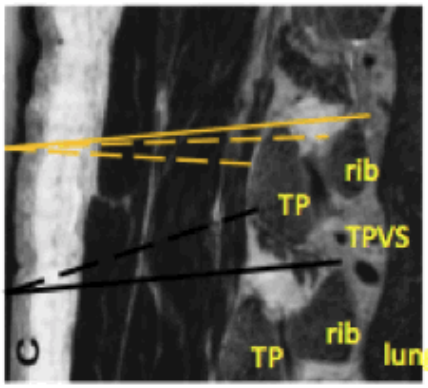

Predetermined depth is unreliable when walking needle cephalad once bony contact is made

	T2	T5-6	T9-10	T2	T5-6	T9-10	T2	T5-6	T9-10
Skin-TP	42	23	21	53	35	33	72	52	56
Skin-VL	47	33	30	58	43	42	76	61	66
Skin-pleura	68	43	43	74	54	57	94	72	81
SP-TP	30	28	24	31	28	25	30	27	25
SP-VL	20	17	18	21	17	19	20	17	18
TP-pleura	22	20	24	21	20	24	21	20	26
Thickness rib	10	16	17	9	16	17	10	15	16
Thickness TP	11	8	11	11	8	11	12	9	12
AP (TP-VL)	10	11	10	9	9	10	10	9	10

Table 1. Mean distance (in millimeters) between anatomic landmarks of the thoracic spine in patients with BMI <20, 20-40, and >40.

LEGEND.
BMI <20
BMI 20-40
BMI >40

TP = transverse process. VL = vertebral lamina. SP = spinous process. AP = anterior-posterior

S-322.

ADDUCTOR CANAL BLOCKS: CHANGING PRACTICE PATTERNS AND ASSOCIATED QUALITY PROFILE

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INTRODUCTION: Peripheral regional anesthesia involving the femoral nerve has been the gold standard approach for post-operative analgesia following total knee arthroplasty.[1] However, an alternative, the adductor canal block, has recently gained popularity since it is thought to result in less block-induced quadriceps muscle weakness.[2-4] The primary aim of this time-series analysis was to identify, through a multi-institution clinical registry, whether or not practice changes have occurred around the performance of femoral versus adductor canal blocks. Furthermore, if practice changes have occurred, our secondary aim was to assess for possible associated changes in safety and quality.

METHODS: Using a 20-member clinical registry, we conducted a time-series analysis examining the practice patterns and safety around the performance of adductor canal blocks for primary total knee arthroplasty between July 18, 2011 to October 9, 2015. To obtain a more granular insight into possible changes (good or bad) in quality associated with a transition to an adductor canal block intensive practice, we analyzed clinical outcomes data from a single member institution.

RESULTS: 4,382 patients had 6,921 blocks performed for 4,822 unilateral total knee arthroplasties. Across the registry, adductor canal block utilization increased from 0% during the first three months to 50.1% during the last three months. This increase in utilization was not associated with any increases in immediate or recovery room related complications. When analyzing the largest surgical volume center, the worst reported numeric rating scale pain score decreased from 5.5 to 4.9 ($p = 0.005$), length of stay decreased from 3.2 to 2.9 ($p = 0.03$), and 30-day hospital revaluations for pain increased from 3.3% to 6.7% ($p = 0.001$).

CONCLUSIONS: The large increase in the utilization of adductor canal blocks among the participating members of the International Registry of Regional Anesthesia (IRORA) was not associated with changes in safety. However, we found conflicting quality information when comparing a before and after period around adoption of adductor canal blocks for the largest contributing member hospital.

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Figure 1: Adductor canal blocks as a proportion of all blocks

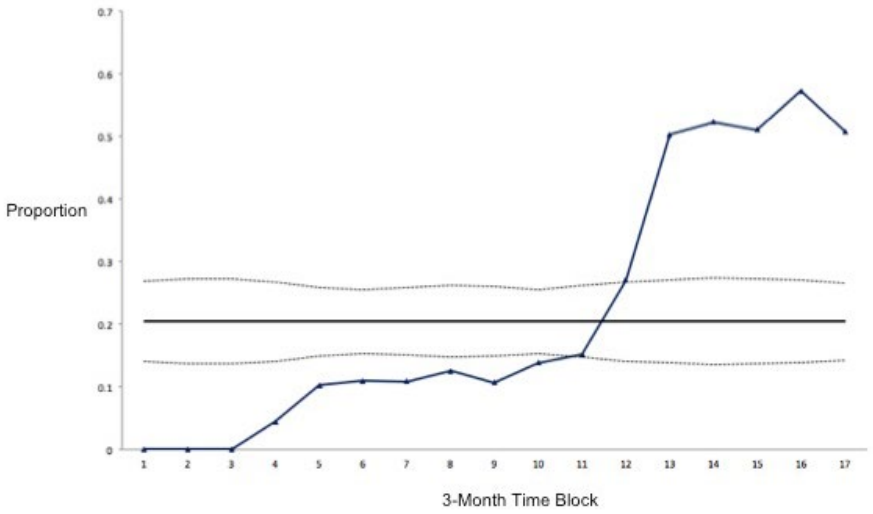

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Figure 2: Immediate and PACU complications over time

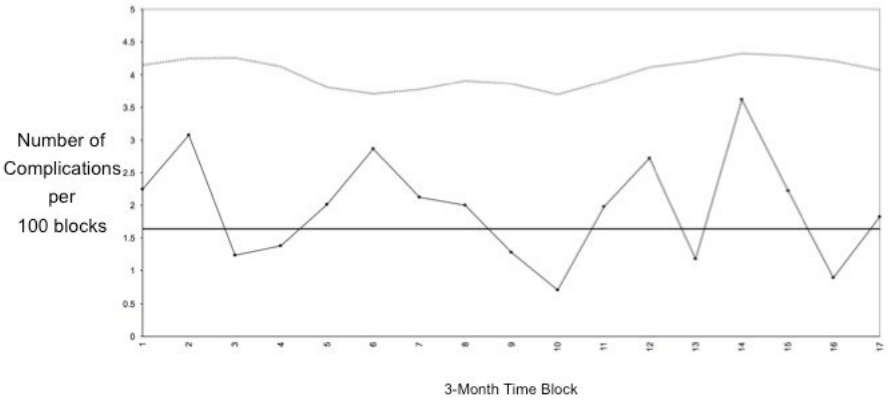

Figure 3: Pain scores over time for DHMC

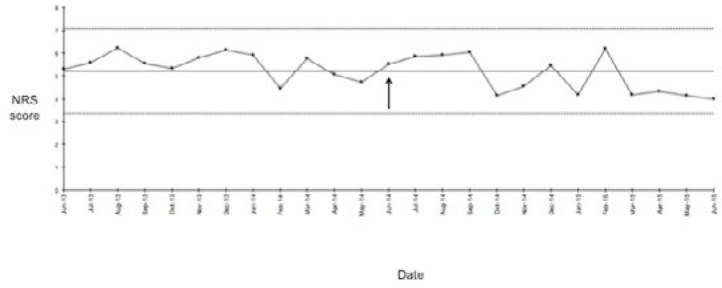

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Table 1: Characteristics of regional anesthesia for TKA by hospital (2011-2015)

Hospital	TKA *n* (%)	Adductor *n* (%)	Femoral *n* (%)	Sciatic [π] *n* (%)	Other [¥] *n* (%)	Catheter [Δ] *n* (%)
1	1,307 (27.1)	169 (11.9)	1,224 (30.6)	549 (54.7)	253 (49.7)	1,188 (39.6)
2	2 (0.04)	0 (0)	2 (0.05)	0 (0)	0 (0)	1 (0.03)
3	427 (8.9)	177 (12.5)	280 (7.0)	4 (0.39)	1 (0.19)	442 (14.8)
4	221 (4.6)	63 (4.5)	165 (4.1)	147 (14.6)	21 (4.1)	122 (4.1)
5	129 (2.7)	1 (0.07)	128 (3.2)	7 (0.69)	7 (1.4)	1 (0.03)
6	19 (0.39)	0 (0)	21 (0.52)	0 (0)	2 (0.39)	1 (0.03)
7	3 (0.06)	0 (0)	3 (0.08)	0 (0)	0 (0)	1 (0.03)
8	67 (1.4)	4 (0.28)	53 (1.3)	8 (0.79)	15 (2.9)	49 (1.6)
9	71 (1.5)	0 (0)	54 (1.4)	1 (0.09)	18 (3.5)	42 (1.4)
10	16 (0.33)	0 (0)	13 (0.32)	2 (0.19)	3 (0.58)	6 (0.20)
11	352 (7.3)	202 (14.3)	266 (6.7)	181 (18.0)	99 (19.4)	310 (10.4)
12	189 (3.9)	138 (9.8)	179 (4.5)	93 (9.3)	37 (7.3)	189 (6.3)
13	60 (1.2)	2 (0.14)	53 (1.3)	3 (0.29)	5 (1.0)	3 (0.10)
14	2 (0.04)	0 (0)	2 (0.05)	1 (0.09)	0 (0)	0 (0)
15	1,664 (34.5)	599 (42.4)	1,328 (33.2)	2 (0.19)	22 (4.3)	517 (17.2)
16	114 (2.4)	6 (0.42)	108 (2.7)	0 (0)	0 (0)	63 (2.1)
17	42 (0.87)	14 (0.99)	30 (0.75)	0 (0)	0 (0)	42 (1.4)
18	122 (2.5)	26 (1.8)	83 (2.1)	6 (0.59)	26 (5.1)	10 (0.33)
19	2 (0.04)	1 (0.07)	1 (0.03)	0 (0)	0(0)	1 (0.03)
20	13 (0.27)	12 (0.84)	1 (0.03)	0 (0)	0 (0)	7 (0.23)
Total	4,822 (100)	1,414 (100)	3,994 (100)	1004 (100)	509 (100)	2,995 (100)

TKA = total knee replacement (unilateral), includes revision surgery
[π] Sciatic block includes any approach from popliteal fossa to proximal gluteal region
[¥]Other block includes lateral femoral cutaneous, obturator, and lumbar plexus
[Δ]Catheter refers to a continuous peripheral nerve block administered through a catheter

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S-322 • continued

Table 2. Practice comparision between pre and post adductor canal policy change for DHMC

	n	Pre-policy·	Post-policy·	p value¬
Adductor Canal ¶	1,060	0.86%	85.7%	<0.001
Femoral¢	1,060	97.9%	14.0%	<0.001
NRS score ¥	1,060	5.5 (3.4)	4.9 (3.7)	0.005
30-day hospital re-evaluation following TKA∆	1,060	3.3%	6.7%	0.001
30-day hospital re-evaluation following THA∆	1,057	0.84%	0	0.05
Length of stay£	1,060	3.2 (2.1)	2.9 (1.8)	0.03

DHMC = Dartmouth-Hitchcock Medical Center, TKA = total knee arthroplasty (primary and revision), THA = total hip arthroplasty (primary and revision)

¶ Percentage of all blocks that were adductor canal blocks

¢ Percentage of all blocks that were femoral nerve blocks (includes either continuous or single shot)

¥ Numeric Rating Scale score for pain, max recording in recovery room, mean (sd)

∆ Percentage of patients who experienced a hospital visit following discharge for pain related reasons

£ Length of stay in days, mean (sd)

· Pre-policy June1, 2013 to May 31, 2014; Post-policy June 1, 2014 to June 18, 2015

¬ Comparing pre-policy with post-policy; chi square for proportional data; two sample t-test for continuous data

S-323.

EFFECT OF DEXAMETHASONE AS AN ADJUNCT ON PERIPHERAL NERVE BLOCK DURATION: A RETROSPECTIVE STUDY UTILIZING A QUALITY ASSURANCE DATABASE

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INTRODUCTION: Dexamethasone is commonly used as an adjunct in perineural injections with the goal of increasing peripheral nerve block duration. Its impact has been examined predominately with larger doses (8 mg) and in limited nerve block locations. This study examines peripheral nerve block duration in patients who received nerve blocks with or without perineural dexamethasone, at lower doses and in multiple block locations, utilizing a quality assurance database.

METHODS: Greater than 2,100 peripheral nerve blocks performed over an 8 month period were reviewed. Multiple data were analyzed in relation to nerve block duration including patient demographics, nerve block location, and dexamethasone use. Exclusion criteria included continuous catheters, local anesthetics other than ropivacaine, and block locations with less than 15 patients. Nerve block duration was defined as the patient's self-report of block cessation during postoperative telephone follow-up interview on postoperative day 1-3, depending on block duration. Linear regression models were used to examine univariate associations between nerve block duration and variables of interest. Additionally, a subgroup analysis was conducted among individual block types with and without dexamethasone using 2-sample t-tests.

RESULTS: Over 1000 subjects were included in the study with a mean perineural dexamethasone dose of 3.5 mg. Univariate analysis revealed an increased block duration with dexamethasone use ($P=0.026$) and placement of two blocks ($P<0.0001$). Both factors remained significant in multivariate analysis.

CONCLUSION: Addition of perineural dexamethasone demonstrated prolonged nerve block duration after adjustment for other variables. Increased block duration correlated with patient satisfaction.

S-324.

WITHDRAWN.

S-325.

PECTORAL BLOCKS AS AN ALTERNATIVE FOR PAIN MANAGEMENT AFTER VIDEO ASSISTED THORACOSCOPIC SURGERIES AND ITS POTENTIAL ROLE IN ENHANCING POSTOPERATIVE RECOVERY

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INTRODUCTION: Optimal pain control is an important aspect of care in thoracic surgery patients and is critical to avoid undesired pulmonary complications i.e. pneumonia. Many methods of pain management, each with attendant problems, have been tried with varied success, including intercostal nerve block, intrapleural analgesia, cryoanalgesia, thoracic epidural, paravertebral block, Intravenous or intrathecal narcotics, and NSAIDS. Regional anesthesia of the pectoral, some intercostal and long thoracic nerves can be obtained with a recently described PEC 1 and 2 block. We retrospectively reviewed the efficacy of this block for pain management after video assisted thoracoscopic surgeries (VATS).

METHODS: In this retrospective observational study, 10 patients who received PEC 1 and 2 blocks for postoperative pain control after VATS were studied. 10 cc of 0.5% ropivacaine was injected between the pectoralis minor and major (PEC 1) and 15 cc injected between pectoralis minor and serratus anterior muscle at the level of the 4th rib (PEC2) before extubation. Pain scores were observed for 24 hours post procedure, and the amount of rescue intravenous narcotic requirements were monitored.

RESULTS: Pain scores were in the range of 0-6 (On a scale 0 to 10) in patients who received PEC 1, 2 blocks and duration of analgesic effect lasted between 18-24 hours. Out of 10 patients, four patients did not require any intravenous narcotics. No complications including pneumothorax, hematoma, intravascular injection or local anesthetic toxicity were observed in any patients.

CONCLUSION: PEC blocks may be useful as a novel approach to pain management after VATS and may contribute to enhance recovery by decreasing the amount of systemic narcotics and lesser side effects compared to traditional pain management techniques.

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	Age	Gender	Procedure	Pain score (first 24hrs)	Frequency of IV Narcotics (first 24hrs)
1	82	Male	VATS	3-5	Two
2	53	Female	VATS, Mediastinoscopy	4-5	None
3	20	Male	VATS	4-6	Four
4	21	Male	VATS	0-3	None
5	24	Female	VATS	0-3	Once
6	68	Male	VATS	0-4	None
7	71	Female	VATS	0-3	None
8	66	Male	VATS	3-6	Four
9	35	Female	VATS	2-4	Three
10	88	Female	VATS, Mediastinoscopy	3-6	Once

S-326.

SINGLE-SHOT SUPRACLAVICULAR CATHETERS: A MATCHED CASE-CONTROL ANALYSIS OF A NEW TECHNIQUE IN PEDIATRIC REGIONAL ANESTHESIA

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INTRODUCTION: Supracondylar fractures of the humerus are the most common fracture in children under 7. Regional anesthesia is difficult to provide for this population, since a nerve block performed intra-operatively could confound the clinical post-operative neurovascular examination and many children do not tolerate block placement post-operatively. Described in a letter to the editor in *Paediatric Anaesthesia*[1], clinicians chose to place a supraclavicular intravenous angiocatheter under ultrasound guidance intra-operatively and to dose the catheter a single time in the recovery unit following neurologic evaluation by the orthopedic surgeon.

We hypothesized patients who receive a supraclavicular block via the aforementioned technique would require less cumulative opioids as our primary endpoint. Our secondary endpoints included acetaminophen and anti-emetic administration, length of PACU/hospital stay, and evidence of catheter related neurovascular deficits or development of compartment syndrome.

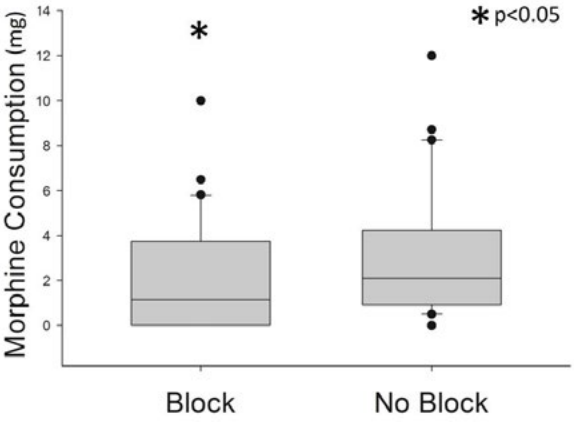
METHODS: Following IRB approval, medical records of patients undergoing surgery for supracondylar fractures at a pediatric tertiary care hospital between 2009 and 2013 were reviewed from the time of pre-operative evaluation through the first orthopedic surgery visit using a standardized data collection form. Children receiving a regional block were matched to no-block case controls based on gender, age, ASA status, and procedure.

RESULTS: A total of 30 supracondylar catheter cases and 30 control patients were identified from 335 reviewed charts, with no differences in patient characteristics.

We observed a statistically significant difference in total morphine consumption at 24 hours between the block and no block group; 1.1 mg (0-3.6) vs. 2.1 mg (0.9 - 4.2), P=0.04, respectively. Similarly, patients receiving a regional block received less post-operative acetaminophen on average: 150 mg (0-261) vs. 234 mg (114-360), P=0.06, and significantly less when adjusted for body weight; 6.7 mg/kg (0-12.3) vs. 11.8 mg/kg (6.6-21), P=0.01.

There were no abnormal post-operative neurovascular examinations, catheter complications, or evidence of compartment syndrome in either group. Difference in rates of post-operative anti-emetic medication administration (2 vs. 5 doses, P=0.42), length of PACU (64 vs. 59 min, P=0.32) and hospital (7 vs. 8 hrs, P=0.31) stay did not reach statistical significance.

CONCLUSIONS: The single-shot supraclavicular catheter technique is technically easy to perform, allows for post-operative neurologic examination, decreases supplemental analgesia requirements, and is not associated with major risk of complications. Additional studies should further investigate the block's efficacy and detect risk of minor complications.



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S-327.

A DOUBLE BLINDED, RANDOMIZED TRIAL COMPARING CONTINUOUS VERSUS SINGLE INJECTION FEMORAL NERVE BLOCK ANALGESIA AFTER TOTAL KNEE ARTHROPLASTY: PATIENT OUTCOMES, LENGTH OF STAY AND PRACTICALITY IN A COMMUNITY HOSPITAL SETTING

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Femoral nerve block (FNB) is a clinical best practice analgesic technique in comparison to PCA opioid or epidural following Total Knee Arthroplasty (TKA)[1]. But the superiority of continuous versus single injection femoral nerve block is not clear[2,3] and there have been very few controlled trials that evaluate this question[4]. We compared single shot FNB (sFNB) with continuous FNB (cFNB) analgesia as part of a standardized TKA pathway. This study was conducted in a community hospital with one surgeon and three anesthesiologists. The parameters investigated included pain control, physical therapy (PT) goals met, length of stay in hospital and complications out to 12 weeks post discharge.

METHODS: Patients having TKA were prospectively randomized in a double blinded fashion either to the sFNB or cFNB block groups. Patients had an Ultrasound and Nerve stimulator guided FNB. 0.5% Ropivacaine was used for both groups, with sFNB group blocked through the needle and cFNB group injected through the catheter. The sFNB had a sham catheter taped to the skin under an opaque dressing and connected to the infusion pump which was turned off, while the cFNB group received a continuous infusion of 0.2 % Ropivacaine. All patients had a successful subarachnoid block. All pumps were covered with opaque bags so the patients, nursing staff and physical therapists were blinded. The pumps were turned off at 4 am next morning. The patients had both standardized as well as rescue analgesics available, and all engaged in the PT pathway as per protocol.

RESULTS: 85 patients were enrolled in the study with 44 patients in catheter and 41 patients in single shot groups. Both groups were comparable from demographic stand point. Pain free time and mean pain scores for 6 hrs, 12 hrs, 18 hrs, 24 hrs, 36 hrs and 48 hrs were similar in both groups. Pain scores with PT were the same and there was no difference in pain scores at the three month follow-up. Rescue opioid for the time intervals and average cumulative opioid consumption was similar in the two groups. There was no difference between the two groups in participation in PT, distance walked, assistive device and knee immobilizer discharge. No difference in complication rates, nausea and vomiting or infection rate was noted. Average hospital stay for both groups was about 2 days.

CONCLUSIONS: Continuous femoral nerve catheter does not offer any advantage over single shot femoral nerve block in terms of pain control, opioid consumption, PT, length of stay or long term rehabilitation.

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S-328.

GENERAL ANESTHESIA OR PARAVERTEBRAL BLOCK: RETROSPECTIVE INCIDENCE OF URINARY RETENTION AFTER INGUINAL HERNIA REPAIR

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INTRODUCTION: Inguinal hernia repair and general anesthesia are known risk factors for urinary retention and thus delayed time to discharge. The optimal anesthetic management of patients undergoing inguinal hernia repair remains controversial from a surgical and anesthetic perspective. Regional anesthesia such as paravertebral blocks are fundamental to multimodal analgesia techniques, and can facilitate enhanced recovery after surgery, by lowering the need for additional pain medication, potentially avoiding urinary retention and its complications, obviating the need for prolonged hospital stay, possible consultation, and the incurred excess cost.

METHODS: The incidence of urinary retention after inguinal hernia repair performed under regional or general anesthesia was assessed retrospectively at our institution from 2010 to 2015. Repairs were performed by 4 surgeons with either general anesthesia or paravertebral block with sedation as the primary anesthetic. Urinary retention was defined as an inability to void with a bladder scan of greater than or equal to 200mL, requiring placement of a straight cath or indwelling foley catheterization. Time to first void and time to discharge were also assessed.

RESULTS: Among 480 patients undergoing hernia repair under general anesthesia, 92 developed urinary retention (19%), with an average time to first void of 301minutes, and average time to discharge of 23.7 hours. Out of 152 patients receiving a paravertebral block with sedation, 6 patients experienced urinary retention (3.9%), with an average time to first void of 172 minutes and average time to discharge of 5.9 hours. The difference was statistically significant.

CONCLUSIONS: Urinary retention complicating inguinal hernia repair can be a significant source of cost and labor. Paravertebral block appears to lower the risk of urinary retention, decreasing the time to first void and time to hospital discharge.

Subspecialty Abstracts

Sleep Medicine

S-329.

COMPARISON OF PERIOPERATIVE COMPLICATIONS BETWEEN HIGH STOP-BANG SCORE (>3) AND LOW STOP-BANG SCORE (0-2) PATIENTS. A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Surgical patients with obstructive sleep apnea (OSA) are associated with increased risk of perioperative complications. The STOP-Bang questionnaire are useful tools to identify the high-risk OSA (STOP-Bang ≥3) patients during the perioperative period. We conducted this meta-analysis to compare the perioperative complications in patients with high STOP-Bang score (≥3) versus low STOP-Bang score (0-2).

METHODS: A search of the literature databases MEDLINE (from 2008 to January 2016), Medline-in-Process & other non-indexed citations (up to January 2016), Embase (from 2008 to January 2016), Cochrane Central Register of Controlled Trials (up to January 2016), Cochrane Databases of Systematic Reviews (from 2008 to January 2016), Google Scholar, Web of Sciences (from 2008 to January 2016), Scopus (2008 to January 2016) and PubMed (from 2008 to January 2016) was carried out. The search yielded 119 citations. Irrelevant papers were excluded by title, abstract and full-text review, leaving 11 manuscripts for analysis. Inclusion criteria were: 1) Studies that used STOP-Bang questionnaire as a screening tool to identify the high-risk and low-risk for OSA in adult surgical population (>18 year); 2) studies that mentioned the perioperative complications associated with high STOP-Bang score (≥3) and low STOP-Bang score (0-2). 3) Publications in the English language. The perioperative complications were cardiac events or respiratory events or any complication requiring ICU admission. The study quality was evaluated using the Cochrane risk of bias tool. Statistical analysis was carried out using the Review Manager 5.3 software. The pooled odds ratio for perioperative complications was estimated.

RESULTS: The meta-analysis was carried out in 11 studies including a total of 20,482 patients (High STOP-Bang score group, n=7,598 and low STOP-Bang score group, n= 12,884). Overall, the odds of having perioperative complications was higher in high STOP-Bang score patients compared to low STOP-Bang score patients (OR 3.83; 95% CI: 1.75-8.36; P=0.0008)

CONCLUSION: This meta-analysis suggests that patients with high STOP-Bang score (>3) are associated with increased risk of perioperative complications. STOP-Bang questionnaires can identify the high-risk OSA patients and implementing the evidence based perioperative precautions may decrease the risk of postoperative complications. This further justifies the implementation of STOP-Bang tool as a screening tool to identify the high-risk OSA patients during the perioperative period.

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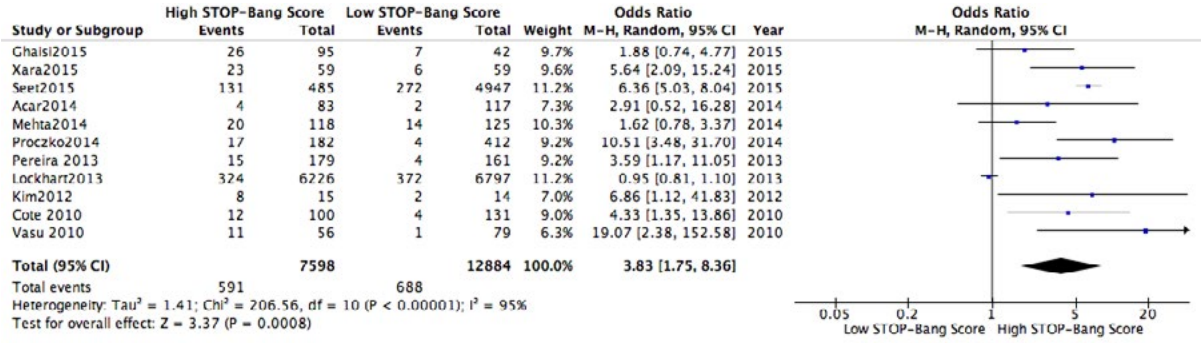

S-330.

DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE SLEEP APNEA DURING PREGNANCY, A SYSTEMATIC REVIEW

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INTRODUCTION: The incidence of obstructive sleep apnea (OSA) is higher during pregnancy compared with the nonpregnant population. The currently screening tools for OSA may not perform well in the obstetric population. OSA is directly linked to an increase in maternal and fetal morbidity. The goal of this systematic review is to determine the best OSA screening tool and the effect of OSA on maternal and fetal outcomes.

METHODS: A search of the literature databases Medline (from 1946 to 2015), Medline in-process and other non-indexed citations, Embase (from 1947 to 2015) was carried out. The search strategy yielded 71 citations. Irrelevant papers were excluded by title and abstract review, leaving 33 manuscripts. We reviewed the studies that included: 1) A target population of obstetric patients with obstructive sleep apnea; 2) OSA screening tools; 3) Maternal and fetal outcomes.

RESULTS: A number of sleep apnea screening tools have been evaluated for its use in the pregnant population. These screening tools are less accurate in the pregnant population (Table 1). There is growing literature reporting the impact of OSA on adverse maternal and fetal complications. OSA in pregnancy is associated with greater risk of preeclampsia, gestational hypertension, gestational diabetes, pulmonary embolism, preterm birth, and unplanned caesarean sections. OSA in pregnancy is also associated with increased risk of fetal heart rate deceleration with maternal desaturations (SPO_2 < 90%), lower Apgar score, low birth weights, still birth, small for gestational age and increased NICU admissions. Overall OSA is directly linked to an increase in maternal and fetal morbidity (Table 1). Treatment of OSA with CPAP in pregnancy has been shown to improve outcomes in a limited number of small studies.

CONCLUSION: Further work is needed to detect and treat OSA in pregnancy to decrease the maternal and fetal outcomes.

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Lockhart et al. Obstet Gynecol. 2015;126: 93-102.

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Table 1 - Maternal and fetal outcomes

Study ID	Study Type	n	Result
Edward[2001]	Prospective cohort	10	**Pressor responses to obstructive respiratory events** • Control OSA vs. Preeclamptic OSA 21±2/12±1 mm Hg and 38±5/25±4 mm Hg (0.005/0.005) • No difference in heart rate responses 34±5 beats/min vs. 49±13 beats/min (P=0.326)
Sahin[2008]	Prospective observational study	35	Pregnant OSA (11.4%) • Fetal heart rate deceleration with maternal ↓SPO_2 (75%) • Lower Apgar score • Low birth weights • NICU admission
Champagne[2009]	Case-control study	50	**Hypertensive (17) vs. Normotensive pregnancy (33)** • Apnea Hypopnea Index (AHI) 39±37 vs. 18±12 events/h • OSA in HTN OR 7.5, 95% CI: 3.5–16.2
Louis[2010]	Retrospective cohort study	114	**OSA pregnant (57) vs. non-OSA pregnant (114)** • Preeclampsia 19.3% vs. 7%; P=0.02 • Preterm birth 29.8% vs. 12.3%; P=0.007 • Cesarean sections aOR 8.1; 95% CI 2.9-22.1 • Maternal morbidity aOR 4.6; 95% CI 1.5-13.7
Tauman[2011]	Preliminary study	132	Habitual snorers vs. non-snorers • ↑nRBCs, p = 0.03 • ↑EPO, P = 0.005 • ↑IL-6, P = 0.01
Chen[2012]	Retrospective study	4746	Pregnant OSA vs. pregnant non-OSA • LBW 1.76 (95% [CI], 1.28 –2.40) • Preterm birth 2.31 (95% CI, 1.77–3.01) • SGA infants1.34 (95% CI, 1.09 –1.66) • CS1.74 (95% CI, 1.48– 2.04) Preeclampsia 1.60 (95% CI, 2.16 –11.26)
Louis[2012]	Prospective observational study	175	**OSA vs. non-OSA** • Body mass index (BMI) 46.8 ±12.2 vs. 38.1± 7.5 kg/m^2, P=0.002 • Chronic hypertension 55.6 vs. 32.4%, p=0.02 • Cesarean delivery 65.4 vs. 32.8%, p=0.003 • Preeclampsia 42.3 vs. 16.9, p=0.005 • NICU admission 46.1 vs. 17.8, p=0.002
Balserak[2013]	Case-control study	104	**Maternal hyperglycemia** • Sleep disordered breathing OR 2.85; 95 % CI 1.50–5.41; P=0.001 • Daytime napping OR 1.48; 95 % CI 0.96–2.28; P=0.08
Fung[2013]	Prospective cohort study	371	**OSA vs. Control** • Respiratory Disturbance Index (RDI) 7.9 (6.1–13.8) vs. 2.2 (1.3–3.5) (P<0.001) • Impaired fetal growth 43% vs. 11% (RR 2.67; 1.25–5.7; P = 0.04) • Fetal growth regulators decreased in cases (n.s,)
Reutrakul[2013]	Observational case-control study	45	**P-GDM vs. P-NGT** • Lower total sleep time median 397 vs. 464 min, *P* = 0.02 • Apnea Hypopnea Index (AHI) Median 8.2 vs. 2.0, *P* = 0.05 • OSA prevalence 73% vs. 27%, *P* = 0.01 • Diagnosis of GDM was associated with a diagnosis of OSA OR, 6.60; 95% CI, 1.15 - 37.96
Ding[2014]	Systematic Review	24 studies	**Moderate to severe OSA in pregnancy associated with** • Gestational diabetes mellitus OR=1.78; 95 % CI, 1.29 to 2.46 • Pregnancy-related hypertension OR=2.38; 95 % CI, 1.63 to 3.47 • Preeclampsia OR=2.19; 95 % CI, 1.71 to 2.80 • Preterm delivery OR=1.98; 95 % CI, 1.59 to 2.48 • Low birth weight OR=1.75; 95 % CI, 1.33 to 2.32 • NICU admission OR=2.43; 95 % CI, 1.61 to 3.68 • Intrauterine growth restriction OR=1.44; 95 % CI, 1.22 to 1.71 • Apgar score of <7 at 1 min OR=1.78; 95 % CI, 1.10 to 2.91
Louis[2014]	Retrospective cross sectional study	55 million	• Preeclampsia OR, 2.5; 95% CI, 2.2–2.9 • Eclampsia OR, 5.4; 95% CI, 3.3–8.9 • Cardiomyopathy OR, 9.0; 95% CI, 7.5–10.9 • Pulmonary embolism OR, 4.5; 95% CI, 2.3–8.9 • In-hospital mortality OR 5.0, 95% CI: 2.4–11.5
O'Brien[2014]	Cohort study	181	**Hypertensive (51) vs. Normotensive (16)** • Obstructive sleep apnea (OSA) 41% vs. 19% (P=0.05) • Snores vs. Non-snorers Apnea Hypopnea Index (AHI) 19.9±34.1 vs. 3.4±3.1, P = 0.013 Hemoglobin Oxygen saturation (SPO_2) 86.4±6.6 vs. 90.2±3.5, P = 0.021 Obstructive sleep apnea (OSA) RR 2, 95% CI 1.4 – 2.8
Pamidi[2014]	Systematic review & meta-analysis	21 studies	• Gestational hypertension/preeclampsia OR, 2.34; 95%CI, 1.60 - 3.09; 5 studies • Gestational diabetes OR, 1.86; 95% CI, 1.30 - 2.42; 5 studies
Xu[2014]	Meta-analysis	977	• Preeclampsia RR 1.96; 95% CI 1.34 to 2.86 • Preterm birth RR 1.90; 95%CI 1.24 to 2.91 • Cesarean delivery RR 1.87; 95% CI 1.52 to 2.29 • Neonatal ICU RR 2.65; 95% CI 1.86 to 3.76 • Gestational diabetes RR 1.40; 95% CI 0.62 to 3.19 • Small gestational age RR 0.64; 95%CI 0.33 to1.24

S-331.

UNDERSTANDING PHENOTYPES OF OBSTRUCTIVE SLEEP APNEA: APPLICATIONS IN ANESTHESIA, SURGERY AND PERIOPERATIVE MEDICINE – A LITERATURE REVIEW

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INTRODUCTION: Obstructive Sleep Apnea (OSA) is a common sleep related breathing disorder affecting up to 4% of the adult population. OSA is now recognized to be a heterogeneous disorder with both anatomical (upper airway) and non-anatomical determinants. The relative dominance of each pathophysiological factor varies largely between individuals defining various phenotypes. Additionally, a phenomenon called 'phenotypic plasticity' is applicable to OSA which is the ability of the organism with a given phenotype to change its phenotype in response to changes in the environment. Although CPAP is the gold standard treatment for OSA, it can be unsatisfactory due to non-compliance. Hence there is a potential and need to individualize treatment of OSA to the particular phenotypes. The purpose of this review is to educate anesthesiologists on the different phenotypes of OSA to optimize perioperative management of these patients.

METHODS: A search of the literature databases Medline, Medline-in-Process & other non-indexed citations (1946 to present) was carried out. The search yielded 237 citations. Irrelevant papers were excluded by title and abstract review. Eighteen articles were included in this narrative review, where various OSA phenotypes in adult males and females were described.

SUMMARY OF THE REVIEW: OSA phenotypes can be classified based on pathophysiology, demographics, ethnicity, sleep and position (Table 1). The pathophysiological phenotypes are also described as intermediate/component phenotypes which are assessed in terms of their relative contribution to the overall phenotype. These component phenotypes include craniofacial morphology, obesity, arousal threshold, upper airway muscle activity and ventilatory control stability (loop gain). Increased susceptibility to upper airway collapse during REM sleep and while supine was also identified. The elderly patients with OSA are a unique phenotype when compared with their younger counterparts and are a typical example of phenotypic plasticity. For a given level of OSA, the elderly OSA patients report less daytime sleepiness than their younger counterparts. It is important to recognize the individual phenotypes to target therapy based on the specific mechanism involved in OSA pathogenesis for a particular patient. From the anesthetic perspective, it is vital to identify the OSA phenotype with high arousal threshold. In the postoperative period, a subset of OSA patients with high arousal threshold are at a greater risk of opioid-related respiratory events because these patients rely heavily on arousal to restore airflow. The OSA phenotypes of high and low arousal threshold are compared in Table 2.

CONCLUSION: OSA is a multi-factorial disease with various individual phenotypes. With the increasing ability to identify many of the OSA phenotypes from sleep studies, we may be able to provide better perioperative management of these patients in our practice.

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Table 1. Classification of OSA Phenotypes

Intermediate phenotypes	Anatomical	Physiological (Nonanatomical)	
	Obese	Low arousal threshold	
	Craniofacial	High loop gain Hyporesponsive genioglossus	
Demographics	OSA in old age	OSA in males	Postmenopausal OSA
Based on Ethnicity	African Americans	Asians	Caucasians
REM OSA	REM predominant OSA	REM isolated OSA	
Based on Sleep quality	EDS	Insomnia	
Based on position	Supine predominant OSA	Supine isolated OSA	

OSA – Obstructive sleep apnea

REM – Rapid eye movement

EDS – Excessive daytime sleepiness

Table 2. OSA phenotypes of low and high arousal threshold

Low arousal threshold	High arousal threshold
Higher propensity to wake up from sleep	Lower propensity to wake up from sleep
More likely to have mild to moderate OSA	Predominantly associated with severe OSA
Sedatives are beneficial	Sedatives can evoke a respiratory arrest
Associated with less hypoxia due to reduced apnea duration	More prone to hypoxia due to prolonged apneas

OSA – Obstructive sleep apnea

S-332.

ANESTHETIC CONSIDERATIONS FOR PATIENTS WITH CONGENITAL CENTRAL HYPOVENTILATION SYNDROME: A SYSTEMATIC REVIEW OF THE LITERATURE

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INTRODUCTION: Congenital central hypoventilation syndrome (CCHS) is a form of sleep disordered breathing characterized by a diminished drive to breathe during sleep despite progressive hypercapnia and hypoxia. The condition results from mutations in the paired-like homeobox 2B (PHOX2B) gene.[1] It is crucial for anesthesiologists to be aware of possible late presentations of the condition, to have a clinical suspicion and understand how CCHS is diagnosed and managed. The aim of this review is to examine the current data on CCHS as it relates to perioperative considerations.

METHODS: A systematic search of all Medline, EMBASE, Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Trials was done up to October 2015. The results were limited to human studies published in the English language. Study titles and abstracts were screened initially to identify studies relating to CCHS relevant to anesthetic care. All study designs including randomized controlled trials, observational studies, case reports, or case series were included. Two of the authors identified the relevant literature independently with the third author as arbitrator for disagreements.

RESULTS: The searches yielded 7367 titles with at least one key word. Reference to CCHS was found in 165 articles, of which 45 were relevant to perioperative considerations. There were 14 relevant case reports categorised as pertaining to the following: (1) Novel presentations of the condition following sedation/ anesthesia (2) Anesthetic techniques used in patients with established CCHS (3) Patients with CCHS who experienced anesthetic complications. Review of the case reports showed patients ranged from neonates up to age 59 years. Known CCHS patients had anesthetic techniques that involved gaseous induction with sevoflurane, avoidance of long acting sedatives, opioids and muscle relaxants. There appeared to be few post-operative complications. Regional techniques were used where possible with close monitoring postoperatively. Novel presentations of the disease following sedation or anesthesia often led to diagnosis. Patients had minor procedures such as dental extraction, tonsillectomy or adenoidectomy and then failed to breathe adequately at the end of surgery or in recovery. The sequelae of undiagnosed CCHS led to complications such as hypoxia, desaturations, apneas, seizures, unplanned intensive care admissions, prolonged hospital stays and long-term tracheostomies.

CONCLUSION: Anesthesiologists need to be aware of undiagnosed late onset CCHS, and include this condition in the differential diagnosis of patients with unexplained postoperative respiratory depression. Anesthetic techniques should minimize use of agents that further depress respiration post-procedure and ensure adequate monitoring to detect postoperative apneas.

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S-333.

IMPROVEMENT OBSERVED IN HOME SLEEP TESTING PARAMETERS IN AMBULATORY ORTHOPEDIC SURGICAL PATIENTS WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Obstructive sleep apnea (OSA) is an independent risk factor for perioperative complications.[1] Suitability of ambulatory surgery in patients with OSA or at risk for OSA remains controversial.[2-3] Although recently evaluated among inpatients, this study addresses the fundamental question of what sleep changes occur in the postoperative setting to ambulatory patients.[4] To date, no prospective study examining the fundamental changes in sleep parameters among ambulatory surgical patients has been conducted.

METHODS: Consecutive adults scheduled for elective ambulatory orthopedic surgery were recruited. Study subjects completed the STOP BANG questionnaire and three unattended 5-channel Home Sleep Tests (HST): baseline within a month before surgery, night of surgery (NOS), and third night after surgery (POD3). Study participation and all study data were blinded to the surgical and anesthesia teams. The primary outcome was post-operative adverse outcomes including unplanned admission, difficult airway management, post-operative respiratory complications, and arrhythmias.

RESULTS: Two hundred three subjects were recruited. One hundred eighty four completed the baseline HST (71% male, mean age 39.8±9.6, BMI 28±5.2), 171 completed both the baseline and NOS and 164 completed all three. Twenty percent had baseline AHI > 5. Eighty nine percent of enrolled subjects received general anesthesia. Eighty seven percent of enrolled subjects used opioids for post-operative pain management. Thirty-three patients had a previous diagnosis of OSA with 21 CPAP compliant. There was a statistically significant improvement observed for AHI and ODI for those with baseline AHI < 5 (AHI baseline 3.1±1.5, NOS 1.9±1.6p< 0.0001). There were 20 unplanned admissions with 1 due to hypoxemia, 6 due to the recognition of an existing history of OSA prompting admission for observation, and 13 due to surgical or social issues. No mortality, acute respiratory failure, or readmission was observed. There was no difference in adverse events between patients with the preoperative diagnosis of OSA and those without the diagnosis or risk for undiagnosed OSA. AHI, ODI, SPO2 nadir, and CT90 did not change significantly for those with AHI > 5 or > 15.

CONCLUSION: This study advances the understanding of sleep changes that occur with ambulatory surgery in both patients with and without OSA. These findings suggest that ambulatory orthopedic surgical patients with an existing diagnosis of OSA or those with clinical risk factors for OSA may not be at increased risk for perioperative complications and/or adverse outcomes and may not require extended observational periods or more intensive monitoring post-operatively.

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S-334.

DOES SEVERITY OF OBSTRUCTIVE SLEEP APNEA AFFECT POSTOPERATIVE COGNITION?

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BACKGROUND: Obstructive Sleep Apnea (OSA) is a sleep-breathing disorder that affects roughly 25% of adults and 70% of these individuals are undiagnosed. In the perioperative setting, OSA patients are at increased risk for postoperative cognitive decline (POCD). We aim to determine which cognitive functions are impaired in the early postoperative period in OSA patients.

METHODS: We recruited volunteers aged ≥50 years undergoing non-cardiac and non-pulmonary surgery. After obtaining informed consent, all patients were asked to wear a portable sleep apnea monitoring device to gather baseline apnea-hypopnea index (pAHI). Cognitive functions were assessed using the Digit Symbol Substitution Tests (DSST), verbal fluency, word list, Memorial Delirium Assessment Scale (MDAS - three words recall), digit span forward and digit span backward. Cognitive functions were completed once preoperatively and once postoperatively (POD1). An independent t-test was performed comparing cognitive performance of patients with moderate to severe OSA (pAHI>30) with patients with mild or no OSA (pAHI ≤30) at preoperative and POD1.

RESULTS: 28 patients who completed the portable sleep monitoring device and cognitive assessments were included. The average age was 62.4 ± 8.2 years and 46% were male. 21% of patients had a pAHI>30 (Table1). Preoperatively, pAHI >30 patients reported they had history of OSA (p=0.050), lung problem (p=0.031), and hypertension (p=0.013) (Table 1). They performed better than pAHI ≤30 patients on Digit Span Maximum, Forward (p=0.030) and Digit Span Maximum, Backward (p=0.005) (Table 2).Postoperatively, pAHI >30 patients tended to perform worse than pAHI ≤30 on all neurocognitive tests on POD1 (Table 3).However, these tendencies disappeared when preoperative and postoperative changes in neurocognitive status were compared between two groups (Table 4).

DISCUSSION: There are some significant differences or tendencies noted in preoperative and postoperative neurocognitive status in patients with severe OSA (pAHI >30) and patients with no to moderate OSA (pAHI ≤30). However, in this preliminary data, severity of OSA did not affect degree of cognitive status changes perioperatively. A future study with a larger sample size and longer observation to monitor cognitive status are needed to confirm these results.

Baseline apnea-hypopnea index (pAHI) was used to define obstructive sleep apnea (OSA): OSA is defined as pAHI > 30 on either preop day 1 or day 2.

The subjects who cancelled surgery transferred to ICU; withdrew consent were removed. Fisher's exact test was used for categorical variable and two sample t test was used for continuous variable. There are 6 patients (21%) whose pAHI > 30.

Table 1. Subject Characteristics and Medical History by OSA Status

		OSA, n (%)		
Variable	**Total (n=28)**	**pAHI ≤ 30 (n=22)**	**pAHI > 30 (n=6)**	**p-value**
Sex, Female	15 (54%)	12 (55%)	3 (50%)	1.000
Race, White	19 (68%)	14 (64%)	5 (83%)	0.630
Age, mean ± SD, year	62.4 ± 8.2	62.1 ± 8.0	63.5 ± 9.6	0.717
BMI, mean ± SD, kg/m2	30.6 ± 7.1	29.5 ± 6.8	34.9 ± 7.4	0.102
BMI > 35 kg/m2	5 (18%)	3 (14%)	2 (33%)	0.286
TICS Score, mean ± SD	35.1 ± 2.7	34.9 ± 2.7	35.7 ± 2.4	0.545
CES-D Score, mean ± SD	9.6 ± 6.2	8.7 ± 5.8	13.6 ± 7.0	0.114
CES-D ≥ 16	5 (20%)	3 (15%)	2 (40%)	0.252
History of OSA	5 (18%)	2 (9%)	3 (50%)	0.050*
History of Lung Issue	4 (16%)	1 (5%)	3 (50%)	0.031*
History of Hypertension	10 (36%)	5 (23%)	5 (83%)	0.013*
Use of CPAP	4 (14%)	2 (9%)	2 (33%)	0.192

*p<0.05

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Table 2. Preop Neurocognitive Testing by OSA Status

	OSA, mean ± SD			
Variable	**Total (n=28)**	**pAHI ≤ 30 (n=22)**	**pAHI > 30 (n=6)**	**p-value**
Digit Symbol	51.5 ± 13.1	51.9 ± 14.4	50.3 ± 6.9	0.805
Verbal Fluency Trial 1, No. Correct	12.1 ± 4.4	12.1 ± 4.8	12.0 ± 1.3	0.948
Verbal Fluency Trial 1, No. Incorrect	0.5 ± 0.7	0.5 ± 0.7	0.3 ± 0.8	0.611
Verbal Fluency Trial 1, 10 Second Response	3.5 ± 1.2	3.3 ± 1.2	4.2 ± 1.2	0.128
Verbal Fluency Trial 2, No. Correct	12.9 ± 3.9	13.1 ± 4.1	12.5 ± 3.3	0.769
Verbal Fluency Trial 2, No. Incorrect	0.5 ± 0.7	0.6 ± 0.8	0.2 ± 0.4	0.223
Verbal Fluency Trial 2, 10 Second Response	4.0 ± 1.3	3.8 ± 1.4	4.7 ± 0.8	0.171
Total Verbal Fluency, No. Correct	25.0 ± 7.7	25.2 ± 8.2	24.5 ± 5.7	0.851
Word List Delay Count	6.9 ± 2.0	6.7 ± 2.1	7.7 ± 1.2	0.307
Word List Learning Trials Count	21.8 ± 3.2	21.7 ± 3.3	21.7 ± 3.1	0.944
3 Words Repeat	3.0 ± 0.0	3.0 ± 0.0	3.0 ± 0.0	NA
3 Words 5 Minute Recall	1.4 ± 1.4	1.5 ± 1.3	1.0 ± 1.5	0.481
Digit Span Maximum Forward	5.8 ± 0.5	5.7 ± 0.6	6.0 ± 0.0	0.030*
Digit Span Maximum Backward	5.6 ± 0.6	5.5 ± 0.7	6.0 ± 0.0	0.005*
MDAS, None	28 (100%)	22 (100%)	6 (100%)	NA

*p<0.05

Table 3. POD 1 Neurocognitive Testing by OSA Status

	OSA, mean ± SD			
Variable	**Total (n=28)**	**pAHI ≤ 30 (n=22)**	**pAHI > 30 (n=6)**	**p-value**
Digit Symbol	44.6 ± 11.7	46.2 ± 11.8	38.4 ± 10.1	0.190
Verbal Fluency Trial 1, No. Correct	10.7 ± 3.7	11.1 ± 3.8	9.3 ± 3.2	0.306
Verbal Fluency Trial 1, No. Incorrect	0.6 ± 0.8	0.5 ± 0.8	1.0 ± 0.6	0.172
Verbal Fluency Trial 1, 10 Second Response	3.4 ± 1.5	3.3 ± 1.4	3.8 ± 2.0	0.427
Verbal Fluency Trial 2, No. Correct	12.5 ± 3.8	13.1 ± 3.8	10.0 ± 2.9	0.074
Verbal Fluency Trial 2, No. Incorrect	0.3 ± 0.7	0.2 ± 0.5	0.7 ± 1.2	0.422
Verbal Fluency Trial 2, 10 Second Response	3.8 ± 1.0	3.7 ± 1.0	4.0 ± 0.6	0.485
Total Verbal Fluency, No. Correct	23.2 ± 6.7	24.2 ± 7.0	19.3 ± 3.7	0.116
Word List Delay Count	6.3 ± 2.5	6.6 ± 2.0	5.0 ± 3.6	0.162
Word List Learning Trials Count	20.2 ± 3.4	20.6 ± 3.2	18.7 ± 3.9	0.226
3 Words Repeat	2.9 ± 0.3	2.9 ± 0.3	2.8 ± 0.4	0.639
3 Words 5 Minute Recall	1.1 ± 1.2	1.1 ± 1.2	0.8 ± 1.3	0.576
Digit Span Maximum Forward	5.9 ± 0.5	5.8 ± 0.5	6.0 ± 0.0	0.104
Digit Span Maximum Backward	5.6 ± 0.7	5.5 ± 0.7	5.7 ± 0.5	0.667
MDAS, None	25 (93%)	19 (90%)	6 (100%)	1.000

*p<0.05

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Table 4. Change between Preop and POD 1 Neurocognitive Testing by OSA Status

	OSA, mean ± SD			
Variable	**Total (n=28)**	**pAHI ≤ 30 (n=22)**	**pAHI > 30 (n=6)**	**p-value**
Digit Symbolx	-6.0 ± 11.0	-5.0 ± 11.5	-10.0 ± 8.3	0.374
Verbal Fluency Trial 1, No. Correct	-1.4 ± 5.1	-1.0 ± 5.2	-2.7 ± 4.7	0.499
Verbal Fluency Trial 1, No. Incorrect	0.1 ± 1.1	0.0 ± 1.1	0.7 ± 1.0	0.185
Verbal Fluency Trial 1, 10 Second Response	-0.1 ± 1.7	-0.0 ± 1.4	-0.3 ± 2.7	0.725
Verbal Fluency Trial 2, No. Correct	-0.5 ± 4.5	0.1 ± 4.8	-2.5 ± 2.7	0.218
Verbal Fluency Trial 2, No. Incorrect	-0.2 ± 0.9	-0.4 ± 0.8	0.5 ± 0.3	0.036*
Verbal Fluency Trial 2, 10 Second Response	-0.3 ± 1.5	-0.1 ± 1.6	-0.7 ± 0.5	0.200
Total Verbal Fluency, No. Correct	-1.9 ± 7.7	-1.0 ± 8.3	-5.2 ± 3.6	0.243
Word List Delay Count	-0.7 ± 2.0	-0.4 ± 1.9	-2.0 ± 2.2	0.158
Word List Learning Trials Count	-1.8 ± 3.3	-1.4 ± 3.4	-3.5 ± 1.9	0.252
3 Words Repeat	-0.1 ± 0.3	-0.1 ± 0.3	-0.2 ± 0.4	0.639
3 Words 5 Minute Recall	-0.3 ± 1.6	-0.2 ± 1.8	0.0 ± 0.0	0.845
Digit Span Maximum Forward	0.0 ± 0.6	0.0 ± 0.7	0.0 ± 0.0	0.771
Digit Span Maximum Backward	-0.1 ± 0.9	0.0 ± 0.9	-0.3 ± 0.5	0.421
MDAS, difference from None to Mild	2 (7%)	2 (10%)	0 (0%)	1.000

Change = POD1 - Preop. *p<0.05 xThe sample size is 25 because 3 subjects were outpatients so that they did not do.

S-335.

DIFFERENCE BETWEEN WRIST AND ANKLE ACTIGRAPHY TO ESTIMATE SLEEP-WAKE CYCLE IN CRITICALLY-ILL PATIENTS

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INTRODUCTION: Critically-ill patients suffer from disruption of circadian rhythm and sleep loss, which may play an important role in the pathogenesis of ICU-acquired delirium[1] Actigraphy, a watch accelerometer that measures activity, has been used to monitor activity in the ICU.[2] However, movement in critically-ill patients can be limited due to the use of physical restraints that may reduce the range of motion at the wrist. We sought to determine if detection of movement at the upper or lower extremity is representative of the actual patient activity and which of the two locations has a higher correlation with a nursing reported sleep diary.

METHODS: We conducted a prospective observational study, enrolling patients receiving mechanical ventilation and admitted to the cardiovascular ICU after elective surgery. Upon admission to the ICU, wrist and ankle actigraphy recordings were initiated for 24 hours. Concurrently, nurses recorded hourly observations of sleep. Wrist and ankle actigraphy were used to determine the proportion of total sleep time (TST) in 24 hours during nighttime (defined as 22:00 to 05:59), TST in 24 hours, and arousal index (number of arousals/hour) during nighttime.

RESULTS: 10 patients were enrolled (2 female, 8 male, average age 64.4, SD: 11.4). From the actigraphy data, TST at night was 354 minutes (SD: 354) at the wrist and 402 minutes (SD: 86) at the ankle. TST in 24 hours was 672 minutes (SD: 271) at the wrist and 883 minutes (SD: 278) at the ankle. The mean arousal index was 5.8 (SD: 3.5) at the wrist and 2.7 (SD: 1.7) at the ankle. Of patients with complete nursing logs (n=6), TST at night was 288 minutes (SD: 248) and TST in 24 hours was 480 minutes (SD: 197). The proportion of TST in 24 hours at night was 53% from wrist recordings, 58% from ankle recordings, and 75% from nurse observation. There was no correlation between wrist actigraphy and nurse observation (correlation coefficient 0.56), while there was a higher correlation between ankle actigraphy and nurse observation (correlation coefficient 0.80).

CONCLUSIONS: There were substantial discrepancies between wrist and ankle actigraphy data, compared with nurse observation. While sleep measured at the ankle seemed to overestimate nurse-reported sleep, there was a stronger correlation between nurse observation and ankle activity. These preliminary data suggest that when comparing actigraphy to the nursing sleep diaries, although ankle actigraphy overestimates sleep at night, ankle recordings might be more representative of nursing observation than wrist activity data. These data also confirm previous findings that ICU patients' sleep patterns can be disrupted at night and that a substantial amount of sleep occurs during the daytime.

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S-336.

POSTOPERATIVE OXYGEN THERAPY: AN EFFECTIVE THERAPY FOR PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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INTRODUCTION: Untreated obstructive sleep apnea (OSA) is associated with an increased incidence of postoperative complications. Surgical patients with newly diagnosed OSA are frequently not compliant with postoperative continuous positive airway pressure (CPAP) – the mainstay of treatment for OSA. Supplemental oxygen therapy may be a more acceptable treatment modality, but the effectiveness of postoperative oxygen therapy in patients with OSA has not been studied. The objective of this randomized controlled trial is to determine if postoperative oxygen therapy reduces the number of apneic and hypopneic events in surgical patients with newly diagnosed OSA.

METHODS: After obtaining Research Ethics Board approval, surgical patients over 18 years were approached for consent. Patients with elevated bicarbonate (HCO_3-) (> 30mEq/l) were excluded. Patients underwent a home polysomnography (PSG) with a 10-channel portable device (Embletta X-100). A certified PSG technologist scored the PSG recordings. Patients with Apnea Hypopnea Index (AHI) >5 were randomized into oxygen therapy (O2 group) or no oxygen therapy (Control group). Patients in O2 group received oxygen at 3 l/min by nasal prongs for 3 postoperative nights. In both groups, patients were managed according to their routine care. The perioperative care team could give study patients CPAP therapy or oxygen as needed clinically. Patients underwent an overnight PSG on the 3rd postoperative night and were monitored for oxygen saturation with oximetry.

RESULTS: Of the 722 patients who were screened, 195 patients consented for a home PSG. One hundred and twenty-three patients with AHI >5 were randomized, O2 group: 62 and Control group: 61. Twenty patients withdrew due to postoperative pain, nausea and vomiting. A total of 103 patients (oxygen: 54, Control: 49) underwent PSG on postoperative night 3. The gender, age, body mass index (BMI), neck circumference and preoperative AHI between the O_2 group and Control group were similar. All of the patients in the O_2 group were compliant with oxygen therapy. In the control group, 85% of patients on postoperative night 1, 42% on postoperative night 2, and 20% on postoperative night 3 received oxygen therapy. No patients received CPAP treatment. On the 3rd postoperative night, the oxygen desaturation index (ODI), average overnight oxygen saturation (SpO_2, lowest SpO_2 and percentage of time with SpO_2 <90(CT90) significantly improved in the O_2 group vs. the Control group (Table). Patients in the O_2 group had a significantly decreased AHI, central apnea index, hypopnea index and respiratory arousal index (Table). Oxygen therapy did not prolong the duration of apnea-hypopnea events.

CONCLUSIONS: Postoperative oxygen therapy reduced the number of apneic and hypopneic events - primarily be decreasing the central apnea index and hypopnea index, and improved oxygenation. Postoperative oxygen therapy may be an effective alternative to CPAP in patients with newly diagnosed OSA.

Table: The effect of oxygen therapy on sleep disordered breathing

Variable	Preoperative Baseline			Postoperative night 3		
	Oxygen	Control	p	Oxygen	Control	p
N	62	61		54	49	
Apnea Hypopnea Index	16.9(8.5, 29.5)	16.1(9.5, 32.8)	>0.1	3.5(1.3, 19.4)	15.8(8.3, 55.9)	<0.01
Obstructive Apnea Index	7(2.5, 17.0)	8.1(2.4, 19.1)	>0.1	3.1(0.8, 14.1)	3.8(1.1, 17.3)	>0.1
Central Apnea Index	0(0,0.6)	0(0, 0.8)	>0.1	0(0, 0.2)	0.2(0, 3.0)	<0.01
Mixed Apnea Index	0(0, 0.1)	0(0, 0)	>0.1	0(0, 0)	0(0, 0.1)	0.07
Hypopnea Index	6.9(5.0, 10.5)	7(4.0, 11.4)	>0.1	0(0, 2.5)	7.3(2.1, 16.0)	<.01
Respiratory Arousal Index	3.7(1.6, 10.8)	5.1(2.4, 9.9)	>0.1	0.9(0.1, 5.6)	3.2(0.7, 5.6)	0.03
Mean AH Duration, s	23.2(18.8, 27.5)	23.1(19.8, 25.6)	>0.1	16.9(15.1, 20.9)	18.1(16.1, 22.3)	>0.1
Longest AH Duration, s	56.2(44.6, 70.8)	59.1(46.0, 73.7)	>0.1	33.7(22.3, 47.0)	46(30.5, 63.2)	0.02
ODI	16.1(10.3,27.8)	14.1(9.5, 31.8)	>0.1	0.7(0, 5.7)	20.9(8.2, 58.1)	<.01
Average SpO_2	93.5(92.5, 94.4)	93.2(91.8, 94.6)	>0.1	96.7(95.4, 97.8)	92.2(89.8, 93.7)	<.01
Lowest SpO_2	83(77.0, 85.0)	81(75.0, 87.0)	>0.1	91(84.0, 94.0)	79(74.0, 85.0)	<.01
Cumulated time SpO_2 <90%	1.9(0.5, 8.0)	3.4(0.6, 9.2)	>0.1	0.13(0, 2.7)	10.2(2.1, 31.0)	<.01

Subspecialty Abstracts

Technology, Computing and Simulation, Equipment Monitoring

S-337.

INTELLIGIBILITY IN THE OPERATING ROOM: SIZE MATTERS

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AFFILIATION: [1]Department of Anesthesiology, University of Miami, Miami, FL, [2]Music Engineering, University of Miami, Coral Gables, FL

INTRODUCTION: Noise in healthcare settings have been increasing since 1960[1] and represents a significant source of dissatisfaction among staff and patients and risk to patient safety.[2] Operating rooms (ORs), in which effective communication is integral to patient care, are particularly noisy. In addition to background noise, speech intelligibility is impacted by room architecture and acoustics.[2] For example, sound reverberation time (RT_{60}) is predicted to increase with room size and is known to negatively impact intelligibility. We set out to test the hypothesis that increasing room size has a negative impact on speech intelligibility as measured by a set of validated psychoacoustical descriptors referenced to optimal ranges for a classroom.

METHODS: We studied our ORs during times of non-use (after hours or between cases). Room content at the time of analysis was assessed by quantifying and assigning items into 5 volume categories to arrive at an adjusted room content volume metric (V_C). Detailed room dimensions were measured to calculate room spatial volumes (V_R). Psychoacoustic analysis was performed by playing a series of sweep-tones of ascending pitch from a speaker and recording the impulse responses (i.e. resulting sound fields) from three locations in each room (Figure 1). The recordings were analyzed using custom Matlab scripts to calculate 6 psychoacoustic descriptors of intelligibility (Table 1). Multiple linear regression was performed using V_R and V_C as predictor variables and each psychoacoustic descriptors as an outcome variable.

RESULTS: 40 ORs were studied. Average V_R in cubic meters was 130.7 (SD = 33.7) and ranged from 71.2 to 195.4. Principle component analysis of the 6 outcome variables indicated high redundancy (79.42% of variance was explained by 1 factor) and suggests that all outcome variables were predicted similarly. Considering RT_{60}, the regression model with V_R and V_C as predictors produced adjusted $R^2 = 0.612$, $F(2, 40) = 31.69$ and $p < 0.0001$ (regression results for the other outcome variables are shown in Table 2). V_R was positively correlated with RT_{60} and V_C was negatively correlated with RT60. The regression equation was $RT_{60} = 3.00 \times V_R - 0.48 \times V_C + 532.53$.

Conclusions: Our results suggest that an OR's size and contents (e.g., anesthesia machine, carts, tables and garbage cans) can predict a range of psychoacoustic descriptors of speech intelligibility. Specifically, increasing OR size correlated with worse speech intelligibility while increasing amounts of OR contents correlated with improved speech intelligibility—the latter is understandable in that contents necessarily subtract volume from a room. This study provides a method for identifying existing ORs that may benefit from acoustic modifiers (e.g., sound absorption panels). Additionally, it suggests room dimensions and projected clinical use should be considered during the design phase of OR suites to optimize acoustic performance.

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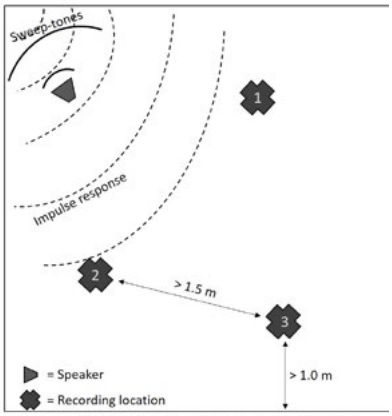

Figure 1. Diagram of setup used to perform acoustical analysis of operating rooms.

Table 1. Psychoacoustical descriptors used to measure intelligibility

	Relevance	Description	Unit	Optimal range (classroom)
RT60	Reverberation	Time for sound in room to disappear	Milliseconds (ms) (lower is better)	< 600
C50	Speech clarity	Measure of the impact of early sound reflections on speech clarity	Decibels (dB) (higher is better)	> 0 dB
STI	Speech clarity	Quality of speech transmission between source and listener	Index (0-1) (higher is better)	Minimum value between 0.62 - 0.66
STI noise	Speech clarity	Same as STI, except typical noise sound levels are used in calculation	Index (0-1) (higher is better)	Minimum value between 0.62 - 0.66
D50	Speech definition	Early energy fraction	Decibels (dB) (higher is better)	> 0 dB
Dmax	Speech intelligibility	Maximum source-listener distance for % of articulation loss of consonants < 15%	Meters (m) (higher is better)	> distance between source and listener

Table 2. Descriptive results of outcome variables

	Mean	SD	Minimum	Maximum
RT_{60}	862.8	119.9	536.7	1073.3
C_{50}	2.02	0.64	1.18	4.92
STI	0.81	0.03	0.76	0.89
STI noise	0.70	0.02	0.66	0.75
D_{50}	0.65	0.06	0.54	0.83
D_{MAX}	1.51	0.12	1.28	1.80

Table 3. Regression model results with two predictors

	Adjusted R Squared	Model fit: F(2, 40)	p
RT_{60}	0.612	31.69	< 0.0001
C_{50}	0.357	11.84	< 0.0001
STI	0.524	22.46	< 0.0001
STI noise	0.511	21.41	< 0.0001
D_{50}	0.410	14.56	< 0.0001
D_{MAX}	0.572	27.06	< 0.0001

S-338.

ADVERSE EVENT REPORTING SYSTEMS IN A NON OPERATING ROOM SETTING

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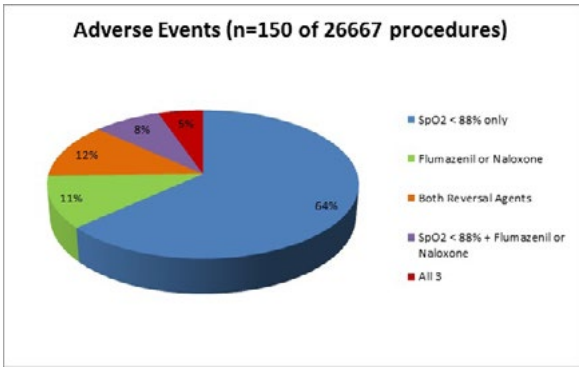
BACKGROUND: With the growth of procedures outside the operating room (OR), the use of sedation in a non-OR environment has increased considerably. While anesthesiologists have traditionally been the physicians tasked with providing safe and effective sedation in these settings, non-anesthesiologist administration of sedation has become more prevalent. While adverse outcomes from sedation delivery within the OR are fairly well studied, much less is understood regarding sedation protocols in nontraditional settings. With the expanding scope of procedural conscious sedation, there has not been the concomitant development of quality assurance systems to ensure the delivery of safe sedation care. We sought to develop a system to provide quality assurance for sedation cases.

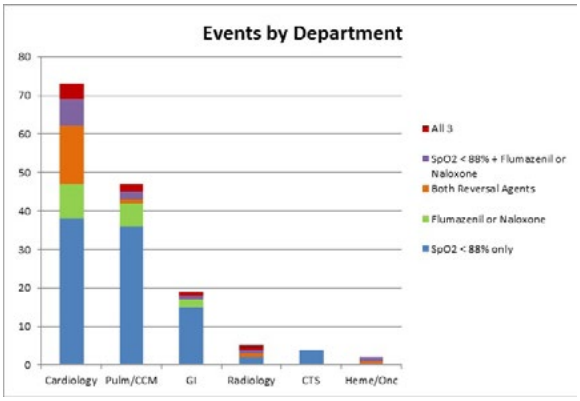
OBJECTIVE: This retrospective study aims to examine the utility of the electronic medical record (EMR) system in comparison to a self-reporting system in identifying the incidence of oxygen desaturation and/or use of reversal agents during non-OR procedural sedation at a university-based hospital setting.

METHODS: The Emory Healthcare data warehouse was used to identify all case encounters linked to the "moderate sedation" electronic order set and all case encounters linked to a CPT and or ICD-9 code for TEE, cardioversion, bronchoscopy, EGD, colonoscopy, or ERCP procedures performed by Emory Healthcare faculty from June 2013-July 2014. Demographic and clinical data were collected describing the type of procedure, department, SpO_2, use of supplemental oxygen, and use of sedation reversal agents during the intra- and or post-procedural setting. The incidence of oxygen desaturation and or use of reversal agents were identified through the EMR system and compared to those identified via the current electronic incident reporting system within the same cohort.

RESULTS: A total of 26,667 were identified and reviewed. Of the 26,667 cases reviewed, 150 were significant for oxygen desaturation and or use of reversal agents. Of these 150 cases, 95 (63.3%) resulted in desaturation only (SpO_2 < 88%), 17 (11.3%) required administration of either flumazenil or naloxone, 18 (12.0%) resulted in administration of both flumazenil and naloxone, 12 (8.0%) resulted desaturation and administration of either flumazenil or naloxone, and 8 (5.3%) of cases resulted in desaturation and administration of both flumazenil and naloxone. Overall, the incidence of events identified via the EMR was 0.56% in comparison to 0.003% from the current electronic incident reporting system.

CONCLUSIONS: Significantly more sedation-related adverse events were identified via the EMR system rather than the self-reporting system. Despite potential limitations, the use of an EMR based system appears to be more sensitive for adverse events compared to a self-reporting system. It is possible the EMR system may more accurately capture the incidence rate of adverse events during non-OR procedural sedation. If so, an improved adverse event monitoring system would be crucial in the development of the quality assurance systems needed for delivering safe sedation care for a given healthcare system.





S-339.

DECREASING MATERNAL MORTALITY IN SUB-SAHARAN AFRICA: CAN SIMULATION AND OBSTETRIC CRISIS CHEKCLISTS MAKE AN IMPACT?

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INTRODUCTION: The WHO reports that one out of 40 women in Sub-Saharan Africa (SSA) die in childbirth with a large proportion due to preventable causes such as failure to follow standard management protocols.[1,4]

Current data shows surgical safety checklists reduce mortality across economic backgrounds and improve adherence to evidence based guidelines in simulation.[2,5,6] Obstetric crisis simulation has demonstrated improvement in adherence to evidence based guidelines in high resource settings[3] and the South Africa Saving Mothers Reports recommends obstetric "fire drills" for maternity unit training in SSA.[7] There is however, a paucity of literature on the impact of simulation training on the management of obstetric crisis and maternal mortality in low income countries (LIC). Accordingly, we will test the hypothesis that small group didactics and obstetric crisis checklists will improve adherence to published guidelines as compared to memory alone in the management of high fidelity simulations of Cesarean Section (C/S) complicated by preeclampsia and peripartum hemorrhage.

METHODS: After informed consent and institutional approval, 10 Kenyan Registered Nurse Anesthetist students managed environment appropriate high fidelity simulation scenarios of severe preeclmapsia and peripartum hemorrhage during C/S. Performance was assessed based off a Safe Anesthesia C/S Checklist developed through a modified Delphi technique. Following baseline sessions, participants underwent individual debriefing, Safe C/S Checklist introduction, and small group didactics . Two weeks later, post intervention simulation testing was performed using the Safe C/S Checklist. Primary outcome measured was percentage (%) correct steps completed for scenario management pre and post intervention. Data was analyzed using a paired t-test and reported as a mean +/- 95% CI.

RESULTS: Our results show statistically significant improvement in mean % steps correct for both scenarios, mean delta for PPH 47.3% and for Pre-E 56.5% (p value's <0.02) . The mean % steps correct for post intervention PPH was 69% and 75% for Pre-E. A poor performance from memory alone was highlighted in the pre intervention mean % steps correct for PPH (22%) and Pre-E (22.6%).

CONCLUSION: This pilot study examined the effect of small group didactics and checklist use on anesthetist performance managing obstetric emergencies in a LIC. We found significant improvement however, the effect of repeated experiential learning exercises and didactic sessions cannot be isolated from effects of checklist use. Future studies should randomize participants to different educational interventions to isolate the most effective pedagogical approach and to evaluate whether obstetric crisis checklists and simulation education can have lasting results on maternal mortality in SSA.

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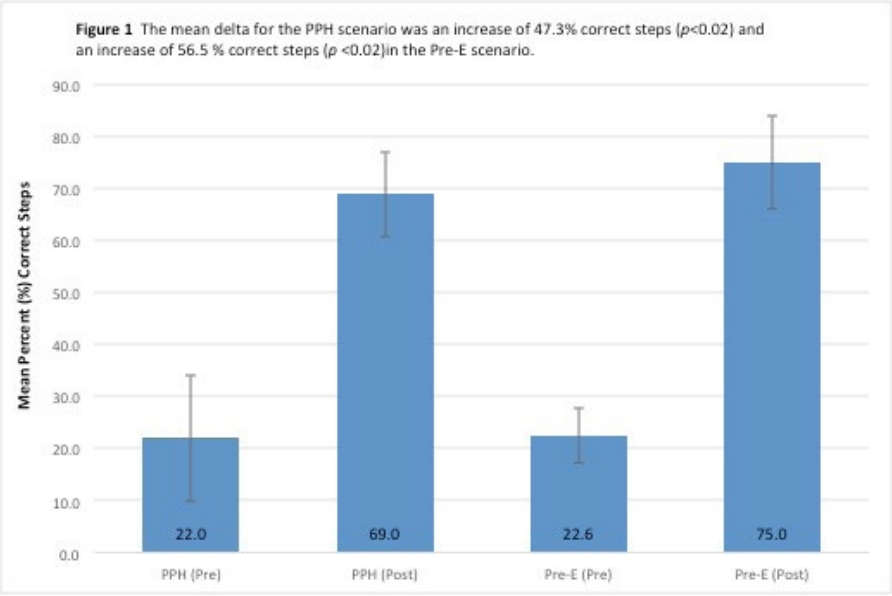

Figure 1 The mean delta for the PPH scenario was an increase of 47.3% correct steps (p<0.02) and an increase of 56.5 % correct steps (p <0.02)in the Pre-E scenario.

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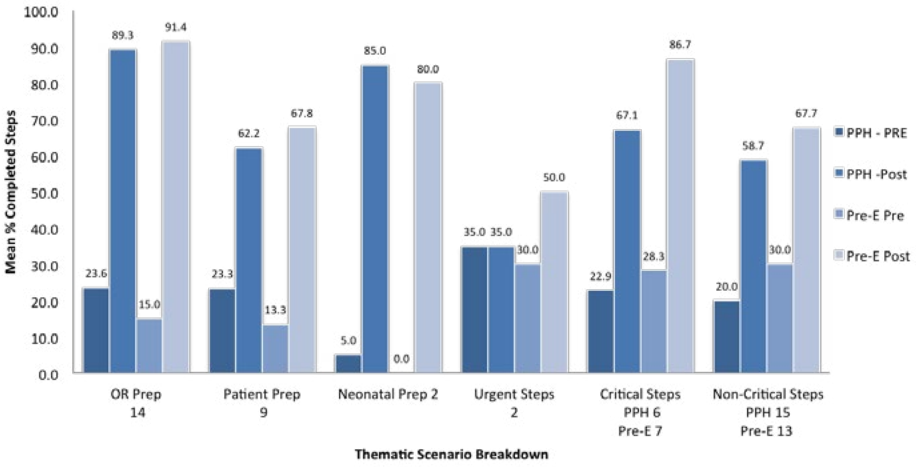
Figure 2 Mean % Correct steps is reported for differents stages of the scenario. The checklist items for OR prep, Patient Prep, and Urgent Steps were the same for both scenarios while the critical steps and management steps differed for PPH and Pre-E.



S-340.

USE OF A STANDARDIZED CHECKLIST INCREASES THE COMPLETION RATE OF CRITICAL ACTIONS IN DISASTER EVACUATION FROM THE OPERATING ROOM: A RANDOMIZED CONTROLLED SIMULATION STUDY

AUTHORS: Y. A. Acar[1], N. Mehta[2], M. Rich[1], M. Careskey[3], J. R. Generoso[1], R. L. Fidler[4], J. Hirsch[2]

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INTRODUCTION: Since 2006, over 600 major disasters were counted in the United States, some requiring hospital evacuations[1]. It was reported that 22% of hospitalized patients would have special needs[2]. In 2014, the American College of Chest Physicians released its first consensus statement on the evacuation from the ICU, mainly based on expert opinion[3]. It focused on improving education, emphasising simulation and checklists[3,4]. Our group was interested in evacuation from the OR, from where evacuation poses unique challenge[5]. Therefore, we developed evacuation checklists, and prospectively tested these in high fidelity simulations.

METHODS: This prospective, randomised study was approved by the IRB of our institution and informed consent was obtained from all participants. Scenarios were set up in a real operating room (OR). The setup included a ventilated Laerdal SimMan™ manikin undergoing a simulated open appendectomy. Initially, a hypotensive episode was simulated. Subsequently, the team was asked via loudspeaker to immediately evacuate the patient out of the hospital. Confederates staffed the surgical team. The circulating nurse was staffed by a confederate if no nurse was available. Participants were randomized to two groups. The checklist group (CG) was given a checklist at the beginning of the evacuation and the non-checklist group (NCG) was not. Checklists for anesthesiologist and circulating nurse were evaluated. The confederates did not make comments, but executed orders and assisted with tasks. Timelines and critical endpoints were recorded. Main outcomes were the completion of critical actions and total evacuation time. Descriptive statistics were presented as frequency (percentage) for categorical variables. Data were presented as mean ± SD (standard deviation) and minimum-maximum for non-normally distributed data. Mann-Whitney U tests were used for continuous , Chi-Square tests for categorical variables using SPSS 15.0 (SPSS Inc. Chicago, IL). A p value of less than 0.05 was considered statistically significant.

RESULTS: Fourteen scenarios were run, 7 with and 7 without checklist. Time from scenario start to out-of-OR was longer in CG (372 vs 317 seconds, p=0.456). The airway was reinforced with tape in 3 vs 0 for CG and NCG, respectively. Participants in CG brought drug supplies in 6 cases and equipment in 6 cases compared to 0 cases in NCG. (Table 1). All subjects commented that they felt uncomfortable during evacuations and 19 of 21 deemed that checklists useful in a real evacuation.

CONCLUSIONS: A checklist for anesthesiologist and circulating nurse has the potential to increase the completion rate of pre-defined key parameters. There was no significant difference in evacuation times between the checklist and non-checklist group.

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1. Table 1

	Parameters	Checklist group	Without checklist group	All	p
Demographics	Scenarios (n)	7	7	14	
	Participants (n)	12	9	21	
	Mean age (years)	30,2±2.8 (26-35)	31,7±6.6 (27-48)	30.9±4.9 (26-48)	.968*
	Profession (n)	12	9	21	.972*
	- Physician	8	6	14	
	- Nurse	4	3	7	
	Previous evacuation training experience positive (n)	1	1	2	.830**
Timeline	Total time (sec)	590,4±68.9 (494-704)	581,9±100.8 (455-776)	586.1±83.1 (455-776)	.620*
	Start-Out of OR (sec)	372,2±83.9 (304-518)	317,4±87.3 (207-460)	344,8±87.0 (207-518)	.456*
	Stairs door-Stairs begins (sec)	64,8±15.9 (39-80)	95,4±49.1 (39-165)	82,7±40.7 (39-165)	.343*
	Stairs begins-Ends (sec)	95,6±36.9 (66-158)	88,4±8.5 (75-100)	92,0±25.9 (66-158)	.318*
Final Assessment	Oxygen tank positive	7	5	12	.127**
	Secure IV positive	2	0	2	.127**
	Secure airway positive	3	0	3	.051**
	Drug supply positive	6	2	8	.031**
	Equipment supply positive	6	0	6	.001**
	Dropped material positive	2	2	4	1.00**

*: Mann-Whitney U test, **: Chi-Square test

S-341.

SEER SONORHEOMETRY VERSUS ROTATIONAL THROMBOELASTOMETRY IN LARGE VOLUME BLOOD LOSS SPINE SURGERY

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Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry is a novel technology that uses acoustic deformation of the developing clot to measure its visco-elastic properties and extract functional measures of coagulation (Figure 1). Multi-level spine surgery is associated with significant perioperative blood loss and coagulopathy occurs frequently. In this study we compared SEER Sonorheometry results to equivalent rotation thromboelastometry (ROTEM®) and laboratory parameters obtained during deformity correction spine surgery.

METHODS: Four independent SEER Sonorheometry hemostatic indices (Clot Time, Clot Stiffness, Fibrinogen and Platelet Contribution) were measured. SEER Sonorheometry Clot Time, utilizing kaolin as an activator, was compared to ROTEM® intrinsic temogram (INTEM) clotting time and the activated partial thromboplastin time (aPTT). For Clot Stiffness thromboplastin was the primary activator and this was compared against ROTEM® external temogram (EXTEM) amplitude at 10 minutes (A10). The assay for the Fibrinogen Contribution was similar to Clot Stiffness but abciximab was added to inhibit platelet function. The Fibrinogen Contribution assay was correlated with the ROTEM® fibrinogen temogram (FIBTEM) A10. Finally, the SEER Sonorheometry Platelet Contribution was calculated by subtracting the Fibrinogen Contribution from the Clot Stiffness. This variable was compared to both absolute platelet counts and ROTEM determined clot elasticity attributable to platelets. Results Fifty-one patients were enrolled in this prospective observational study. SEER Sonorheometry Clot Stiffness, Fibrinogen and Platelet Contribution had a high degree of correlation with ROTEM EXTEM A10 (r = 0.93), FIBTEM A10 (r = 0.92) and platelet counts (r = 0.81) respectively (Fig 2-4). The correlation between Platelet Contribution and ROTEM-determined clot elasticity attributable to platelets was 0.9 (Fig. 5). SEER Sonorheometry Clot Time exhibited a high degree of concordance with ROTEM INTEM A10 and aPTT, however the majority of values were with a narrow normal range.

CONCLUSION: SEER Sonorheometry demonstrates a high level of correlation with ROTEM for determining clot stiffness and assessing fibrinogen and platelet contribution to clot strength. An advantage of SEER Sonorheometry is direct measurement of clot elasticity with no need to transform amplitude oscillation to elasticity.

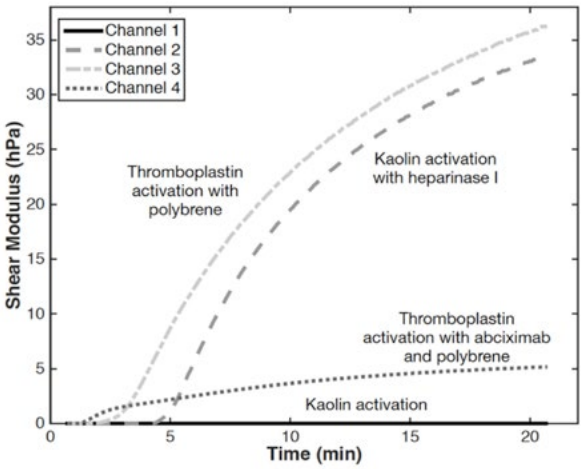

Figure 1. Typical SEER Sonorheometry shear modulus curves obtained with the Quantra Surgical Cartridge. Measurements were performed with a whole blood sample from a healthy donor spiked with 6 IU of unfractionated heparin. Estimates of clot time and clot stiffness are generated from these curves within 15 minutes of test initiation..

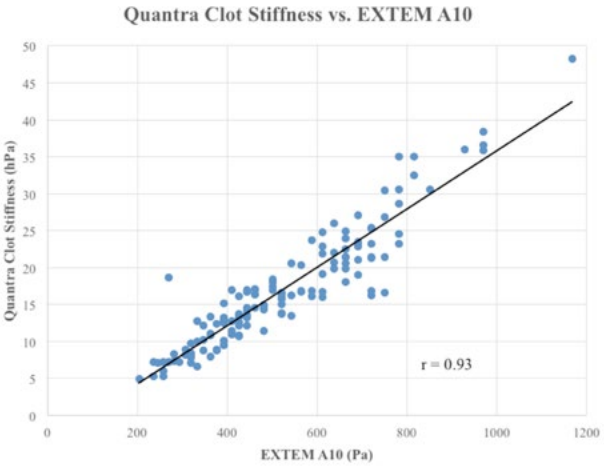

Figure 3. Scatter plot between the Quantra Clot Stiffness and the ROTEM-EXTEM A10. A10-Amplitude at 10 minutes, hPa-hecto Pascal, Pa-Pascal, EXTEM-external temogram.

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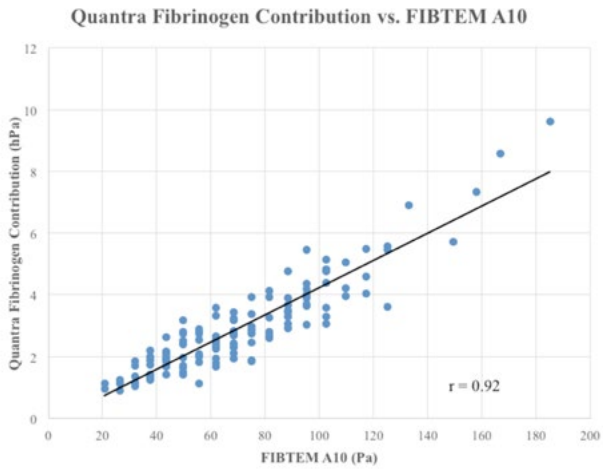

Figure 5. Scatter plot between the Quantra Fibrinogen Contribution and the EXTEM-FIBTEM A10. A10-Amplitude at 10 minutes, hPa-hecto Pascal, FIBTEM-fibrinogen temogram.

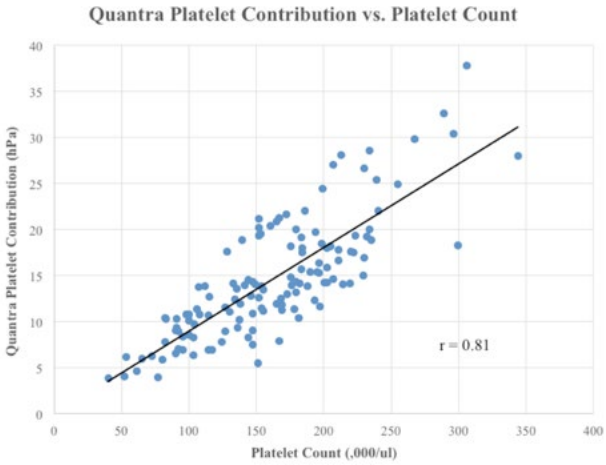

Figure 7. Scatter plot between the Quantra Platelet Contribution and Platelet count. hPa-hecto Pascal.

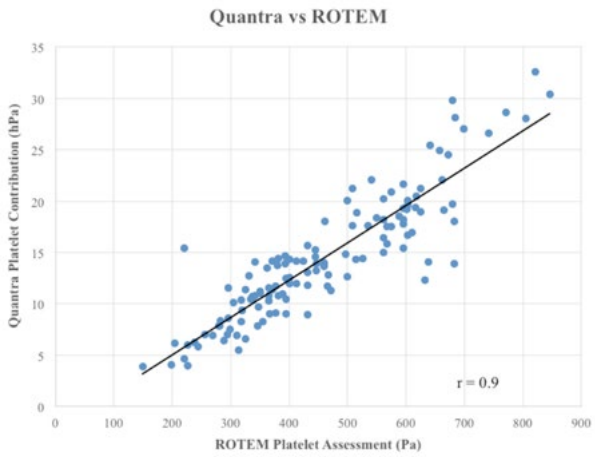

Figure 9. Scatter plot between ROTEM platelet attributable elasticity against Quantra Platelet Contribution. hPa-hecto Pascal, Pa-Pascal.

S-342.

ACUTE CHANGES IN PERFUSION INDEX HAD AN IMPACT ON THE ACCURACY OF NON INVASIVE CONTINUOUS HEMOGLOBIN MEASUREMENTS DURING INDUCTION OF ANESTHESIA IN HUMAN

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INTRODUCTION: Non invasive continuous hemoglobin (SpHb) measurement had some advantages in the perioperative period. We have previously reported that perfusion index (PI) increased significantly and PI had a moderate correlation with SpHb-total hemoglobin (tHb) during anesthesia induction[1]). Accordingly, we have proposed the hypothesis that maintaining PI using with continuous intravenous infusion (civ) of phenylephrine during anesthesia induction improves the accuracy of SpHb measurement.

METHODS: This study protocol was approved by our university ethics committee and registered in a publicly accessible database, the UMIN Clinical Trial Registry (UMIN000011231). Patients were divided into two groups; the control group (C group) and the phenylephrine group (P group). Anesthesia in all patients was induced and maintained with propofol, remifentanil, ketamine. In the P group phenylephrine civ (0.5 μg/kg/min) was started simultaneously when general anesthesia was induced. SpHb were measured using a Masimo Radical 7 device running Masimo SET V7.6.0.1 using a finger sensor (R2-25, Rev K). SpHb and PI were measured twice; before and 15-20 min after anesthesia induction. Simultaneously arterial blood samples were also drawn from the femoral artery or the invasive arterial line. tHb was measured with the ABL800 blood gas analyzer (Radiometer GmbH, Copenhagen, Denmark). Primary outcome was SpHb-tHb after anesthesia induction and correlation between SpHb and tHb. Secondary outcome was changes in SpHb, tHb and PI. According to our previous study, 14 patients in each group were needed. The Student's t test and Pearson's correlation were used to compare parameters. All data are presented as mean±SD. A $p<0.05$ indicates significant difference. Results Thirty four patients were enrolled this study and 4 patients were excluded because SpHb could not be measured before induction. Patients' demographic data is shown in Table 1. *Primary outcome* SpHb-tHb increased significantly in both groups after anesthesia induction (Table 2). However, SpHb-tHb was not significantly different between the groups (Fig 1A). SpHb had a linear correlation with tHb in both groups (Fig 1B). *Secondary outcome* Before anesthesia induction PI in the P group was significantly higher than those in the C group (Table 2). PI increased significantly in both groups after anesthesia induction but changes in PI in the P group was significantly smaller than those in the C group [3.1±2.5 vs. 0.8±1.4, $p<0.01$] (Fig 2). SpHb did not change after anesthesia induction in both groups (Fig 3A and B). tHb decreased significantly after anesthesia induction in both groups but changes in tHb in the P group was significantly smaller than those in the C group [-0.96±0.38 vs. -0.42±0.25, $p<0.01$] (Fig 3C and D).

CONCLUSIONS: Phenylephrine civ did not change SpHb-tHb nor improve correlation between SpHb and tHb. However, it decreased changes in PI and those in tHb. These results suggest that maintaining PI decreased changes in tHb and has an impact on the accuracy of SpHb measurement.

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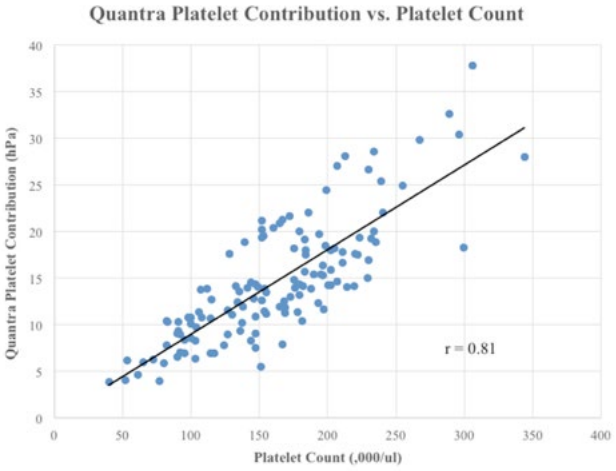

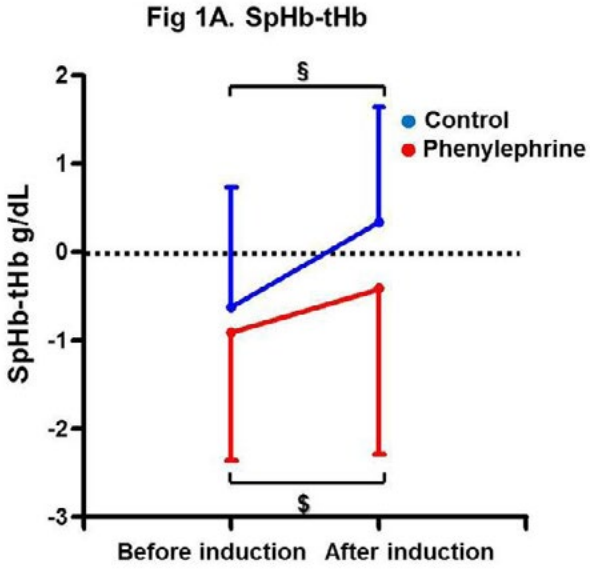

SpHb-tHb was not significantly different between the groups during anesthesia induction.
SpHb: non-invasive continuous hemoglobin ;
tHb: total hemoglobin measured in laboratory;
§ : p<0.01 Before vs. After induction;
$: p<0.05 Before vs. After induction;

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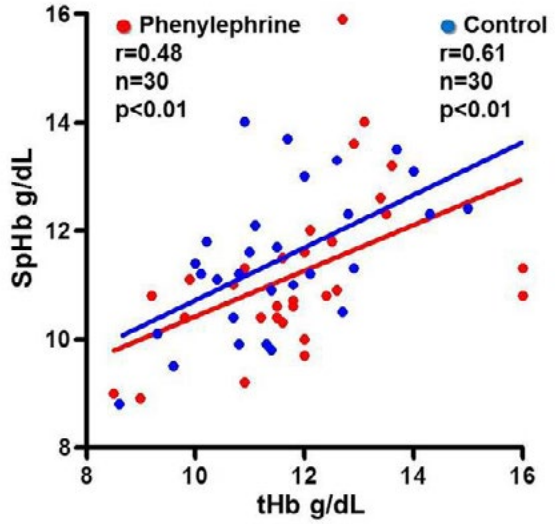
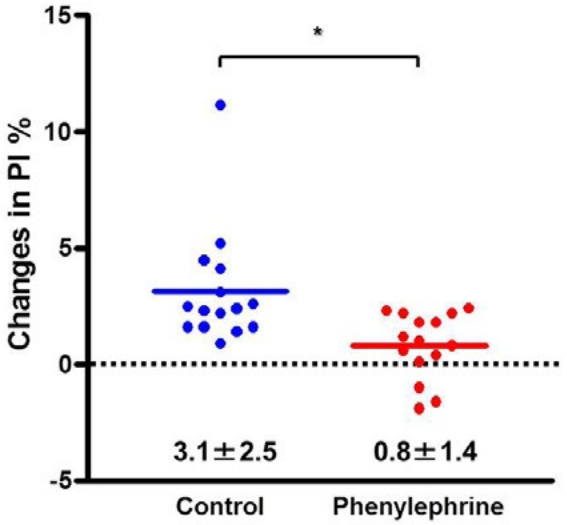
Fig 1B. Correlation between SpHb and tHb



SpHb had a linear correlation with tHb.
SpHb: non-invasive continuous hemoglobin ;
tHb: total hemoglobin measured in laboratory;

Fig 2. Changes in PI



PI: perfusion index;
*: p<0.01 Control vs. Phenylephrine group;

Fig 3A. SpHb

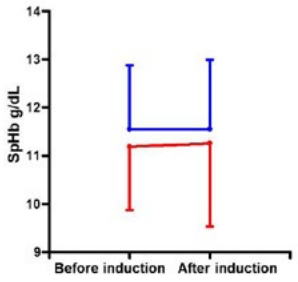


Fig 3B. Changes in SpHb

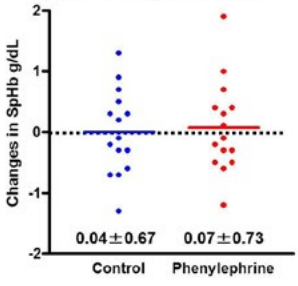


Fig 3C. tHb

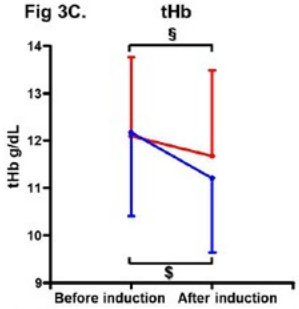
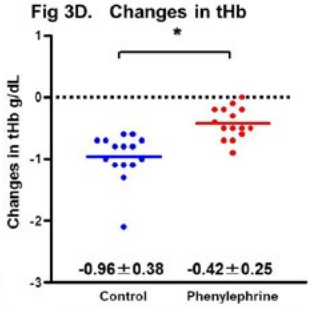


Fig 3D. Changes in tHb



SpHb did not change significantly after anesthesia induction (Fig 3A and B).
tHb decreased significantly after anesthesia induction (Fig 3C), and changes in tHb in the phenylephrine group was significantly smaller than those in the control group (Fig 3D).
SpHb: non-invasive continuous hemoglobin;
tHb: total hemoglobin measured in laboratory;
§ : p<0.01 Before vs. After induction; $: p<0.05 Before vs. After induction;
*: p<0.01 Control vs. Phenylephrine group;

Table 1. Patients' demographic data

	Control	Phenylephrine	P value
Male/Female, n	7/8	8/7	
Age, years	54 (16)	58 (14)	0.3663
Height, cm	161 (8)	161 (5)	0.9558
Body weight, kg	62 (15)	58 (8)	0.3574
ASA PS	2 (1, 3)	2 (1, 3)	0.9830

Mean (SD) or Median (range)

S-343.

ASSESSING IMAGE ACCURACY IN SIMULATION-BASED TRAINING OF TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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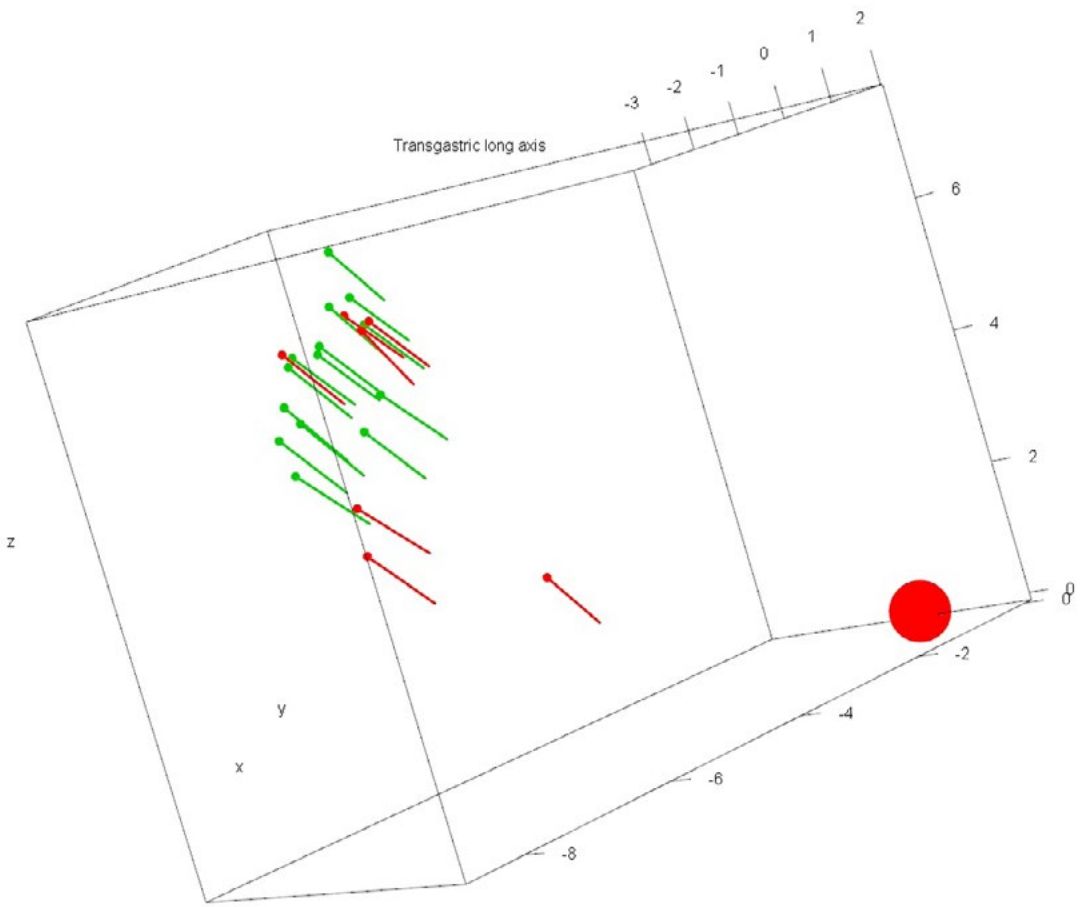
INTRODUCTION: Simulation-based training is an effective educational tool for teaching transesophageal echocardiography (TEE). Use of a TEE simulator allows manual dexterity to be tracked during image acquisition, but assessing the accuracy of an acquired image currently relies on subjective visual grading. Data on ultrasound probe position and orientation in three-dimensional (3D) space have not yet been used to evaluate image accuracy. The offset between a trainee-captured image plane and an expert-captured "ideal" plane can be measured, but this method of accuracy assessment neglects the fact that similar appearing images can be acquired with various scan plane rotations and probe manipulations. In this study, the variability among multiple known TEE experts was used to assess the accuracy of ultrasound probe position and orientation in TEE trainees.

METHODS: This study was conducted as part of an ongoing Foundation for Anesthesia Education and Research (FAER) grant project. 14 attending anesthesiologists (all diplomates of the National Board of Echocardiography in Advanced Perioperative TEE) and 7 interns participated in the study. The interns were ultrasound novices who had completed a 13-day basic multi-modal ultrasound course, during which 3 days were focused on TEE. Participants captured 12 standardized TEE windows on a Vimedix TEE simulator (CAE Healthcare, Montreal, Canada). The simulator recorded real-time 3D data on probe position and orientation and exported the data for each subject in a comma-separated values (.csv) file, which was then imported to R (R Core Team, Vienna, Austria) for analysis. Each subject's TEE probe position and beam direction was plotted in 3D space as a unit vector. An intern's unit vector was deemed acceptable if its start and end points appeared to come from the same distribution as the corresponding 14 expert points. The random variable defined was point-to-centroid distance, which was assumed to be normally distributed. Z-scores and p-values were therefore calculated for the start and end points of an intern unit vector.

RESULTS: The average z-scores for the point-to-centroid distance of the start and end points were 0.460 and 0.474, respectively. Of the aggregate 83 intern beams recorded, 69 were deemed acceptable under this methodology. The poorest performing intern captured 8 of 12 windows. The best performing interns captured 11 of 12 windows. The midesophageal ascending aorta short axis and midesophageal right ventricle inflow-outflow were the easiest windows for interns, with every intern capturing them. The transgastric long axis was most difficult, with only 4 out of 7 interns capturing this window.

CONCLUSION: Using the variability among known TEE experts to define an acceptable range of ultrasound probe positions and orientations for a particular window is not only possible, but also feasible. This can be used to objectively assess a trainee's echocardiography ability, and can be incorporated into studies that compare the efficacy of different trainings or track trainee improvement over time.



S-344.

PULSE-INDUCED CONTINUOUS CARDIAC OUTPUT (PICCO) VERSUS TRANS-ESOPHAGEAL DOPPLER MONITOR (TED) FOR OPTIMIZATION OF FLUID MANAGEMENT IN PATIENTS UNDERGOING MAJOR ABDOMINAL SURGERY. A COMPARATIVE STUDY

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INTRODUCTION: Perioperative fluid management is essential to the practice of anesthesia.[1] Outcomes may be improved if fluid therapy is individualized according to the patient's fluid responsiveness.[2] PiCCO is an invasive device that quantifies several parameters, including continuous cardiac output (CO), stroke volume variation (SVV).[3] Trans-esophageal Doppler monitoring (TED) is a minimally invasive form & has the benefit of providing beat to beat analysis.[4]

This prospective, randomized study evaluates the use of PiCCO system from the fluid & hemodynamic point of view in comparison to TED in order to maintain an adequate circulatory volume ensuring end-organ perfusion & oxygen delivery.

SUBJECTS & METHODS: After research ethics' committee approval & patients' written informed consents, this study was performed on 72 patients (ASA I-II), aged >18 years old, undergoing major abdominal surgery (duration >120 min & blood loss >1000 ml). Patients were randomly allocated into 2 groups; PiCCO group (n=36); whenever SVV rises >10, we gave 200 ml bolus of HES130/0.4 over 5 min to establish a SVV ≤10, and continued giving it keeping SVV≤ 10 & no increase in SV >10%, TED group (n=36); HES Colloid was infused when systolic flow time corrected (FTc) <0.35 sec. If SV was maintained or increased & FTc remained <0.35 sec, fluid challenge would be repeated. If SV raised >10% but FTc >0.35 sec, fluid challenge would be repeated until no further SV rise. If FTc > 0.40 sec with steady SV; no further fluid would be administered until FTc or SV fell by 10%.

Patients' demography, HR & MAP, PiCCO & TED derived measurements, CVP, Arterial PH, Central venous oxygen saturation $S_{CV}O_2$, Serum lactate, Urine output, Blood loss, Intravenous fluid, RBCs, platelets & FFP transfused were all recorded after induction of anesthesia & at the end of surgery.

8 & 24 hours postoperatively; same laboratory data were recorded. Patients were monitored for infectious & organ complications. ICU length of stay & number of mortalities were recorded.

RESULTS:

The two studied groups were comparable demographically (table 1).

Table 2 shows the hemodynamic variables of the studied groups.

Intraoperative blood loss, crystalloids, blood & plasma transfusion are shown in table 3.

Intraoperative hypotensive events, need of IV norepinephrine & urine output are shown in table 4.

Regarding arterial PH, serum HCO3-, lactate, ScvO2 readings; they are shown in tables 5, 6, 7, 8 respectively.

Postoperative complications were significantly lower in the PiCCO (pneumonia, wound infection, arrhythmias & UTI) compared to TED (pneumonia, sepsis, mechanical ventilation need, decubitus infection, ARF & wound infection) (table 9).

CONCLUSIONS: During major abdominal surgery; intraoperative fluid optimization using PiCCO monitor shows more hemodynamic stability and is associated with a lower rates of postoperative complications, organ dysfunction & infection with a tendency to decrease ICU length of stay in comparison to TED monitor.

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2. Cleve Clin J Med 2009; 76:S28-31

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Table-1: Demographic features of the two studied groups

	PiCCO *(n=36)*	TED *(n=36)*	P-value
AGE (yrs)	63.39±4.57	63.3±5.13	0.4
SEX (F/M)	18/18 (50/50%)	17/19 (47.2/52.8%)	0.5
ASA (I/II)	27/9 (75/25%)	29/7 (80.6/19.4%)	0.3

Data were expressed as mean ±SD or Number (%)

Table-2: hemodynamic variables in the two studied groups.

	PiCCO *(n=36)*	TED *(n=36)*	P-value
Baseline			
HR (beat/min)	74.08±8.23	74.11±6.48	0.09
MAP(mmHg)	103.14±7.78	103.33±9.49	0.1
CVP (mmHg)	8.03±1.73	9.06±2.41	0.04*
End of Surgery			
HR (beat/min)	70.17±7.35* ***(p= 0.04 vs. baseline)***	73.39±9.39	0.06
MAP(mmHg)	92.39±7.89**	91.19±9.19** ***(p= 0.001 vs. baseline)***	0.3
CVP (mmHg)	10.083±2.19** ***(p= 0.001 vs. baseline)***	10.00±2.00	0.3

*Data were expressed as mean ±SD. *P< 0.05= significant; **P<0.01= highly significant.*

Table-3: Intraoperative blood, blood, crystalloids, and plasma transfusion in the two study groups

	PiCCO *(n=36)*	TED *(n=36)*	P-value
Blood loss (ml)	1452.8 ± 443.68	900 ± 352.95	0.001**
Blood transfusion (ml)	1326 ± 468	638 ± 238	0.001**
Colloid (ml)	1390.3± 182.37	883.33±221.04	0.001**
Crystalloids (ml)	***3150±758.3***	3052±392.4	0.4
Plasma (n)	14(38.9%)	***5(13.9)***	0.01*

*Data were expressed as mean ±SD or Number (%).*P< 0.05= significant; **P<0.01= highly significant.*

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Table-4: Intraoperative events in the two study groups.

	PiCCO *(n=36)*	TED *(n=36)*	P-value
Hypotensive events (n)	1.61 ± 0.49	3.39±1.1	0.001**
I.V.Noradrenaline (n)	5 (13%)	13(36.1%)	0.03*
Urine output (ml)	2097±476.58	1538±347.46	0.001**

*Data were expressed as mean ±SD or Number (%).*P< 0.05= significant; **P<0.01= highly significant.*

Table-5: Mean value of PH for cases in the study groups at beginning and on follow up

PH	PiCCO *(n=36)*	TED *(n=36)*	P-value
PH-Begin	7.41±0.04	7.41±0.03	0.4
PH-End	7.37±0.03* *(p= 0.01 vs. baseline)*	13(36.1%) *(p= 0.01 vs. baseline)*	0.1
PH-8hrs	7.4±0.03	7.4±0.03	0.2
PH-24hrs	7.41±0.02	7.42±0.03	0.1

*Data were expressed as mean ±SD.*P< 0.05= significant; **P<0.01= highly significant.*

Table-6: Mean value of HCO3 for cases in the study groups at beginning & on follow up

HCO_3	PiCCO *(n=36)*	TED *(n=36)*	P-value
HCO3--Begin	24.06±1.33	23.25±1.18	0.01*
HCO3--End	23.03±0.99** *(p= 0.001 vs. baseline)*	22.28±1.41** *(p= 0.002 vs. baseline))*	0.01*
HCO3--8hrs	24.28±1.00	24.67±2.24** *(p= 0.001 vs. baseline)*	0.3
HCO3--24hrs	25.58±1.89** *(p= 0.001 vs. baseline)*	25.36±1.38** *(p= 0.001 vs. baseline)*	0.5

*Data were expressed as mean ±SD.*P< 0.05= significant; **P<0.01= highly significant.*

Table-7: Mean value of ScvO2 for cases in the study groups at beginning & on follow up

$ScvO_2$	PiCCO *(n=36)*	TED *(n=36)*	P-value
$ScvO_2$-Begin	71.89±4.7	72.08±4.15	0.8
$ScvO_2$-End	80.28±4.39** *(p= 0.001 vs. baseline)*	80.55±3.38** *(p= 0.001 vs. baseline))*	0.7
$ScvO_2$-8hrs	68.69±4.7** *(p= 0.0005 vs. baseline)*	69.67±4.94* *(p= 0.02 vs. baseline)*	0.3
$ScvO_2$-24hrs	67.33±3.83** *(p= 0.001 vs. baseline)*	67.44±4.8** *(p= 0.001 vs. baseline)*	0.9

*Data were expressed as mean ±SD.*P< 0.05= significant; **P<0.01= highly significant.*

Table-8: Mean value of serum Lactate in the study groups at beginning & on follow up

Lactate	PiCCO *(n=36)*	TED *(n=36)*	P-value
Lactate-Begin	1.39±1.24	1.44±0.31	0.5
Lactate-End	1.79±0.49** *(p= 0.001 vs. baseline)*	2.26±0.6** *(p= 0.001 vs. baseline))*	0.01*
Lactate-8hrs	1.81±0.52** *(p= 0.0005 vs. baseline)*	2.12±0.59** *(p= 0.001 vs. baseline)*	0.02*
Lactate-24hrs	1.24±0.29* *(p= 0.02 vs. baseline)*	1.42±0.34	0.04*

*Data were expressed as mean ±SD.*P< 0.05= significant; **P<0.01= highly significant.*

Table-9: postoperative outcome and complications

	PiCCO *(n=36)*	TED *(n=36)*	P-value
Mortality (n)	**0**	**0**	**N.A**
ICU Stay (Day)	**3**	**7**	**0.01***
Pts. With Complications (n)	**4**	**9**	**0.01***
Total Complications (n)	**4**	**9**	**0.01***

*Data were expressed as Number.*P< 0.05= significant; **P<0.01= highly significant.*

S-345.

COMPARISON OF STATISTICAL METHODS FOR METHODS COMPARISON STUDIES WITH REPEATED MEASUREMENTS: A SIMULATION STUDY

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INTRODUCTION: New tests or devices are often studied in a 'method comparison study' before introduction in daily clinical practice. If a new device is used to measure a clinical parameter repeatedly, e.g. a new blood pressure measuring device, the performance of this device may differ between subjects and within subjects. This should be taken into account in the methods comparison study. However, available statistical methods handle the repeated nature of these measurements differently. It is unclear which method performs best. Therefore, we compared the performance of available statistical methods directly in a simulation study based on empirical data. We compared the classic Bland-Altman method (BA CLASSIC), the Bland-Altman method for repeated measurements (BA REPEAT) and the mixed effect model approach by Myles (MYLES) in different scenarios.

METHODS: A simulation study was conducted comparing the performance of 3 statistical methods in bootstrap samples from an empirical data set with repeated measurement pairs. Details of the 3 statistical methods are listed in Table 1. The empirical data set contained consecutive systolic blood pressure (sBP) readings with the non-invasive EV-Nexfin (index device) and the Compact S5 arterial line based monitor (reference). We constructed ten scenarios with variation in the number of sBP pairs and time-intervals between consecutive measurements and sampled 10,000 bootstrap samples with replacement for each scenario. For each method we calculated mean SD and performance, which was defined as the proportion of simulated data sets in which the index device would pass the predefined limits of agreement of - 20 mmHg until 20 mmHg based on the Association for the Advancement of Medical Instrumentation (AAMI) criteria.

RESULTS: The empirical dataset contained 42 subjects with 151 sBP measurement pairs each. Table 2 provides the mean SD from the 3 statistical methods for the ten different scenarios. The SDs for BA CLASSIC differed on average -.02 from the BA REPEAT. The SDs for MYLES were 2.76-3.44 mmHg smaller. With MYLES 16.16-97.62% of the simulated data sets passed. The data sets passed in 2.00-12.36% and 1.97-12.09% with the BA CLASSIC and BA REPEAT, respectively.

CONCLUSIONS: Our simulation study comparing 3 statistical methods revealed two interesting phenomena: 1) The BA CLASSIC and BA REPEAT method differed only slightly. This may be due to a relatively low variance ratio (between subject-/total variance) compared to the original BA paper. 2) The MYLES SDs were considerably smaller than from the BA methods, resulting in an increased proportion of simulated data sets passing the AAMI criteria.

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Table 1. Description of the classic Bland-Altman method (BA CLASSIC), the Bland-Altman method for repeated measurements (BA REPEAT) and the mixed effect model approach by Myles (MYLES), used in methods comparison studies.

Statistical method	Technique to allow for replicate measurements	Bias calculation	LoA calculation
BA CLASSIC	-	Mean (B) of all differences between index and reference device	$B \pm 1.96$* standard deviation (B)
BA REPEAT	Analysis of variance (ANOVA)	Mean (B_i) of the subject means	$B_i \pm 1.96$* standard deviation (B_i), between subject error is corrected for the number of observation per subject.
MYLES	Mixed effect model #	Mean (B_i) of the subject means	$B_i \pm 1.96$* standard deviation (B_i), random residual variances from the mixed effect model for the index and reference device are added to the within subject variances

MYLES allows for potential limitations of the reference device by including the mean of each measurement pair as explanatory variable.

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Table 2. Performance and average standard deviations derived from 10,000 Monte Carlo simulations with repeated systolic blood pressure measurements by the index device and the reference device in ten different scenarios with varying number of measurements (*m*) and time-intervals between consecutive measurements (Δt).

Scenario	*m*	Δt (sec)	SD [mean(SD)] BA CLASSIC	SD [mean(SD)] BA REPEAT	SD [mean(SD)] MYLES	Performance BA CLASSIC	Performance BA REPEAT	Performance MYLES
1	151	10	11.62 (1.11)	11.64 (1.11)	8.20 (.77)	3.01 %	2.80 %	97.62 %
2	51	30	11.54 (1.09)	11.56 (1.09)	8.21 (.77)	3.33 %	3.26 %	97.06 %
3	26	60	11.76 (1.31)	11.78 (1.32)	8.54 (1.00)	4.48 %	4.38 %	89.16 %
4	6	300	14.61 (2.61)	14.63 (2.61)	11.59 (1.95)	2.00 %	1.97 %	16.16 %
5	6-151	10	11.65 (1.41)	11.68 (1.41)	8.70 (1.02)	5.83 %	4.87 %	69.62 %
6	6-26	60	11.52 (1.70)	11.56 (1.70)	8.86 (1.16)	9.43 %	8.45 %	58.18 %
7	26	10-1260	11.60 (1.26)	11.63 (1.26)	8.30 (.93)	4.87 %	4.76 %	91.93 %
8	6	10-1460	11.52 (1.72)	11.54 (1.72)	8.70 (1.36)	12.36 %	12.09 %	75.51 %
9	6-151	10-1460	11.61 (1.27)	11.64 (1.28)	8.25 (.86)	5.14 %	5.12 %	94.87 %
10	6-26	60-1260	11.75 (1.51)	11.77 (1.52)	8.65 (1.16)	7.34 %	7.45 %	81.74 %

S-346.

GDT-2D-VISUALIZER: THE DEVELOPMENT OF ON-LINE TWO-DIMENSIONAL SVV-SVI PLOTTING SYSTEM

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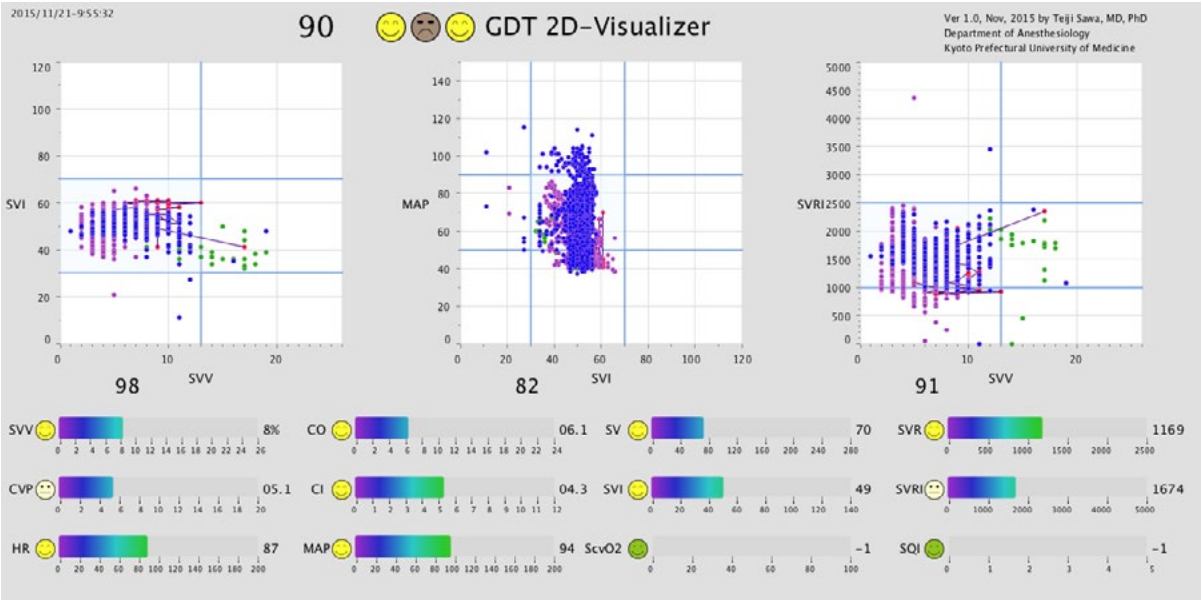
The arterial pulse waveform analysis (APWA) with semi-invasive cardiac output monitoring device, such as FloTrac/Vigileo system (Edwards Lifescience), has become popular in perioperative hemodynamic and fluid management by anesthesiologists. In goal-directed therapy, the target goal in hemodynamic parameters is set up by measuring cardiac output, estimated preload and afterload. Forrester hemodynamic classification has been commonly used to categorize hemodynamic stages, and guides the therapeutic strategies depending on classified stages. However, in semi-invasive arterial pulse waveform analysis, stroke volume variation (SVV) is utilized as an index of preload, instead of pulmonary capillary wedge pressure. In APWA, using SVV and CI or stroke volume index is probably appropriate to categorize hemodynamic stages as a substitute for Forrester subsets. In this study, we developed the on-line evaluation software named GDT-2D-visualizer. 2D-GDT-visualizer can display the hemodynamics data such as SVV and strike volume index (SVI) as two-dimensional XY plot graphs, and works as a simple hemodynamic management support system to visualize intraoperative goal-directed fluid therapy.

METHODS: To make the 2D-GDT-visualizer, we used "Processing" which is a Java-based programming language developed by MIT Media Lab for the visual design in specialized graphic arts. By using this system, SVV and SVI values are on-line recorded at every twenty seconds from FloTrac/Vigileo system, and all data are real-timely plotted in a XY-graph. In addition, we performed arithmetical estimation of the SVV-SVI relationship in a XY-plot and applied measured values into the estimation. Finally, we applied the 2D-GDT-visualizer to eight liver transplantation cases, and compared the measured data plots with the arithmetical estimation of SVV-SVI plots.

RESULTS: The arithmetical estimation was close to the real movement of SVV-SVI interaction. Especially, clamping the inferior vena cava caused significant changes of SVV (145%+125%), while it caused only smaller changes of SVI, CVP, and systolic BP 24%+26%, 46%+24%, and 11%+11%, respectively(mean+SD), and the 2D-plot visualized these acute hemodynamic changes well. The system seems useful to visualize the relationship between SVV and SVI helped the goal-directed hemodynamic management during anesthesia.

CONCLUSIONS: The arithmetical estimation was close to the real movement of SVV-SVI interaction. The 2D-GDT-visualizer is educationally useful to visualize the relationship between SVV and SVI helped the goal-directed hemodynamic management during anesthesia.



S-347.

OBJECTIVE MEASUREMENT OF PAIN PERCEPTION IN LABORING WOMEN

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INTRODUCTION: In many clinical situations it would be desirable to have an objective way to assess pain perception. We have tested a new device that uses functional near-infrared spectrometry (fNIRS) to measure the cerebral hemodynamic response to painful stimuli in real time (RTCHR) and tested for correlation wit patient-reported numeric rating scale (NRS) pain ratings. RTCHR is a measure of frontal lobe cortical activity, driven by regional changes in oxygenated and deoxygenated hemoglobin concentration, which has been shown to correlate with pain or nociception[1].

METHODS: After IRB approval and obtaining informed consent, we enrolled 5 patients for this study. Women were asked to fill out a pain sensitivity questionnaire and then connected to the RTCHR device using a commercial adhesive forehead reflectance sensor (Covidien Nellcor OxiMax Max-Fast Forehead Sensor, Mansfield, MA). Patients were asked for a NRS pain rating after each contraction and at various time points during interventions (spinal block or placement of epidural catheter) by an independent investigator. The study started at setup for epidural analgesia and ended with achievement of analgesia (NRS ≤2 with contractions). Analysis of RTCHR data was performed in a blinded manner, i.e. no event times were disclosed. Data was tested for normal distribution and the appropriate correlation coefficients were calculated (Pearson vs. Spearman rank vs. Kendall Tau). A p level of less than 0.05 was considered to be significant. Receiver-operating characteristic (ROC) curves were calculated to determine appropriate RTCHR thresholds for clinically meaningful differentiations.

RESULTS: The study protocol was successfully applied to all subjects and the RTCHR measurement device was well tolerated. A representative patient dataset showing overlay of events during the study period, fetal heart rate (FHR), uterine contractions (TOCO), and RTCHR measurements is shown in Fig. 1A. The correlation between measured RTCHR and patient-reported pain NRS was statistically significant (0.81, p less than 0.001, Fig. 1B).

CONCLUSIONS: Our results indicate a good correlation between RTCHR based objective pain measurements and patient-reported NRS pain ratings. Whether an objective pain assessment provides a clinical advantage in a patient population that is capable of providing immediate feedback remains to be determined. For other patient populations such as sedated/anesthetized patients or research applications, however, an objective pain measurement device could become a valuable asset.

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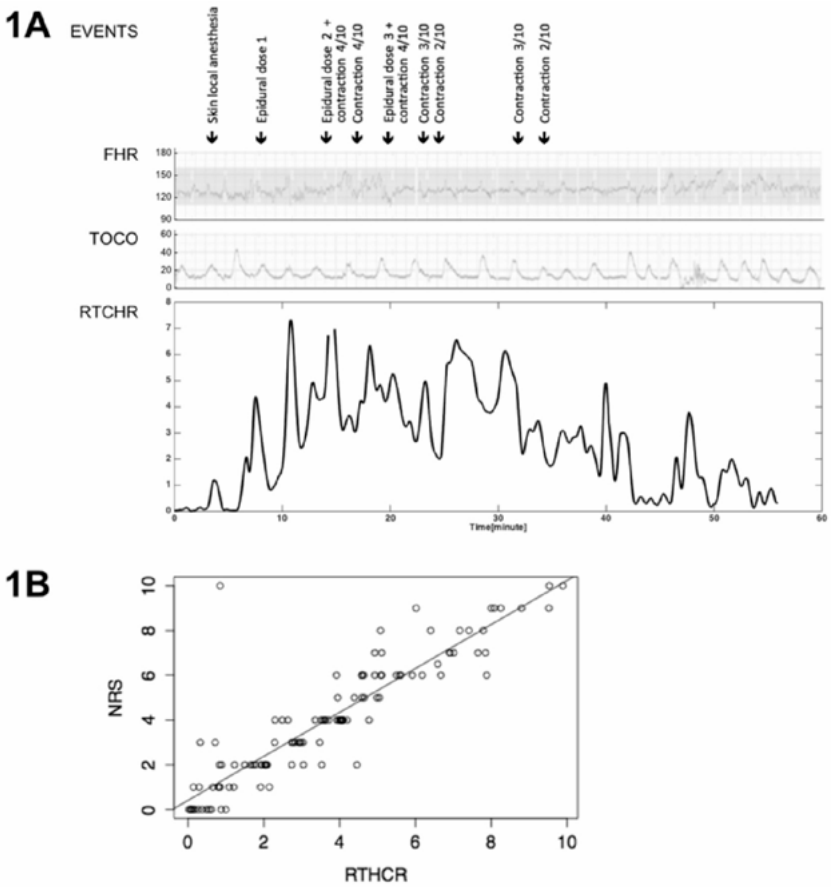

Figure 1A: Representative patient dataset showing events with patient-reported numerical rating scores (NRS) pain ratings, fetal heart rate (FHR) tracing, contraction tracing (TOCO), and Real-Time Cerebral Hemodynamic Response (RTCHR) data. Figure 1B: Correlation between NRS pain ratings and RTCHR scores (Kendall-Tau 0.81, p<0.001).

S-348.

TRENDING ABILITY OF CARDIAC OUTPUT MEASUREMENT BY LIDCORAPID™ AND TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN ELECTIVE CARDIAC SURGERY: A COMPARISON WITH THERMODILUTION

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BACKGROUND: Measurement of cardiac output (CO) is considered an important hemodynamic parameter in cardiac surgery. The current gold standard for CO measurement, the pulmonary artery catheter (PAC), has come into question of its safety and efficacy.[1] A replacement for the PAC in the intraoperative setting would be a step forward in safety in an already high-risk setting. Over the past decades new, less invasive techniques and monitors such as Transesophageal Echocardiography, LiDCO™ and Flotrac™ have been developed as alternatives to the PAC. Studies showing the efficacy of these technologies in cardiac surgery, especially for intraoperative management, are lacking. We compared the ability of the LiDCOrapid™ and TEE to measure CO directly and also the trending ability of these devices to that of the PAC.

METHODS: 100 patients undergoing elective cardiac surgery were enrolled for this prospective observational study. There was no change in the routine anesthetic care. We measured CO at five different times during the study period: immediately after induction, five minutes after placing in Trendelenburg position, immediately after incision, 15 minutes after weaning from bypass, and the last after chest closure. The specific values from the supine of each device were compared to each other and sorted into good (difference <30%) or poor correlation (difference >30%). The demographic and clinical data of the good and poor groups were then compared by using an independent t-test (for normal distribution) or a Mann-Whitney rank sum test (for unknown distribution). We used box plots to compare the gross distributions of data and medians from each device. Polar plot analysis was performed to measure trending ability of each monitor, radial limits of agreement (RLoAs) within ±30° were considered as acceptable error at any quadrant.[2]

RESULTS: Overall 1500 data points in 100 subjects were analyzed. Only 24 subjects showed good relation between all three devices at the after induction measurement (Table 1), and 41 out of 100 from the post chest closure measurement (Table 2). Except for preoperative EF (P 0.006) and HR in post chest closure (P .04), none of the demographic and clinical conditions showed statistical significant difference between good and poor correlation. The box plots showed the PAC with a consistently higher median. The TEE had narrow interquartile ranges while the PAC and LiDCO™ were more dispersed (Fig. 1). Polar plot analyses (Fig. 2) showed RLoAs ±61°, ±66°, ±63°, for PAC v. LiDCO™, PAC v. TEE and LiDCO™ v. TEE respectively for all data points. The RLoAs were calculated by converting all data points into positive changes and calculating what angle (above and below the x-axis) included 95% of all data points.[3]

CONCLUSIONS: Both LiDCOrapid™ and TEE correlated poorly with the PAC. Both devices showed limit of agreement well outside the limit when compared to PAC, showing poor trending ability, therefore should not be considered as a suitable alternative monitoring tool during cardiac surgery.

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Good Correlation (24 subjects)			Poor Correlation (76 subjects)			
	Median	SD/IQ Range		Median	SD/IQ Range	P Value
Age (years)	64	±14.1*	Age (years)	62.5	±11.4*	0.99
Gender‡	Male 18 (75%)	-	Gender‡	Male 54 (71%)	-	0.96
BMI (kg/m^2)	30.8	±4.3*	BMI (kg/m^2)	30.9	(25.8 to 35.6)†	0.45
HR	58.5	±7.4*	HR	60	(50 to 67)†	0.84
MAP	72	±10.4*	MAP	74	(71 to 77) †	0.39
PASP	30.5	±11.8*	PASP	34	(18 to 60) †	0.24
EF%	64%	(58% to 65%)†	EF%	55%	(53% to 60%)†	0.0062

Table 1. Demographic and hemodynamic data. * :data that had a normal distribution according to the Shapiro-Wilks test, represented as a median with a ± SD. †: data that did not have a normal distribution according to the Shapiro-Wilks test, represented as a median with 1st to 3rd interquartile range.. ‡: Categorical data p value determined with Chi-Square test. Gender given as number of males with percentage of males.

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Good Correlation (41 Subjects)			Poor Correlation (59 Subjects)			
	Median	SD/IQ Range		Median	SD/IQ Range	P-value
Age	64	10.8*	Age	62	12.9*	0.92
Gender‡	Male 30 (73%)	-	Gender‡	Male 42 (71%)	-	0.78
BMI	31.4	(26.5-34.8)†	BMI	30.5	(26.6-35.7)†	0.99
HR	82	11.5*	HR	87	11.1*	0.04
MAP	70	8*	MAP	71	(64-77)†	0.08
PASP	32	(27.8-36.5)†	PASP	36	8.1*	0.14
EF	55%	9.30%*	EF	59%	(55%-64.5%)†	0.4
CPB time	121	(101-160)†	CPB time	130	38*	0.54
Drugs‡-	Pts given inotropes: 37		**Drugs‡-**	Pts given inotropes:59		0.84
- Norepi	2		- Norepi	3		-
- Epi	1		- Epi	2		-
- Norepi/Epi	11		- Norepi/Epi	19		-
Norepi/GTN	2		- Norepi/GTN	8		-
- Epi/GTN	3		- Epi/GTN	4		-
-3 or more inotropes	18		-3 or more inotropes	23		-
Surgery‡-	41(total)		**Surgery‡-**	59(total)		.94
- CABG	27		- CABG	37		-
- AVR	6		- AVR	11		-
- MVR	1		- MVR	2		-
Combined	7		- Combined	9		-

Table 2. Demographic and hemodynamic data taken from the post-chest closure measurement. Also includes surgery undergone, time on cardioplegic bypass, and drugs given.*: Shapiro-Wilks test showed normal distribution, represented as a median with a ± standard deviation. †: Shapiro-Wilks test did not show normal distribution, median with 1st to 3rd interquartile range. ‡: Categorical data, p-value obtained with Chi-Square test. Gender represented by number of males with percentage. Combined surgery includes any combination of the listed or with AAA repair, atrial myoma, or MAZE.

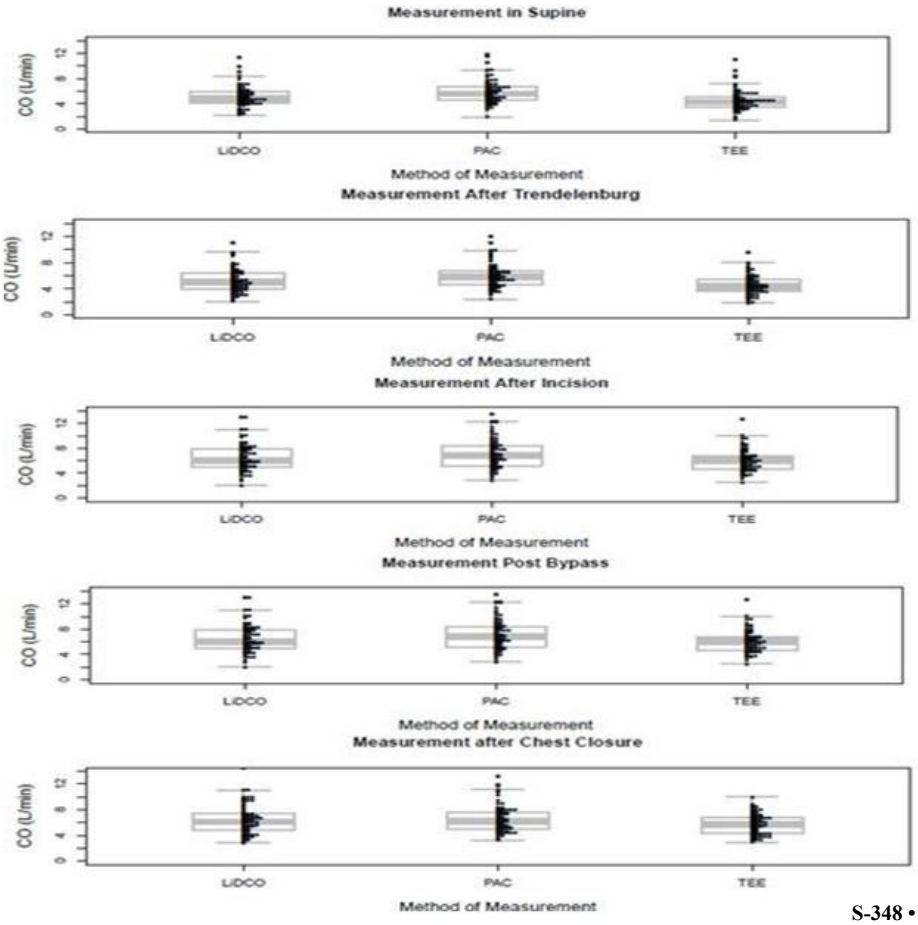

Figure 1. Box plots with dot plot overlay of data from each device at each measurement.

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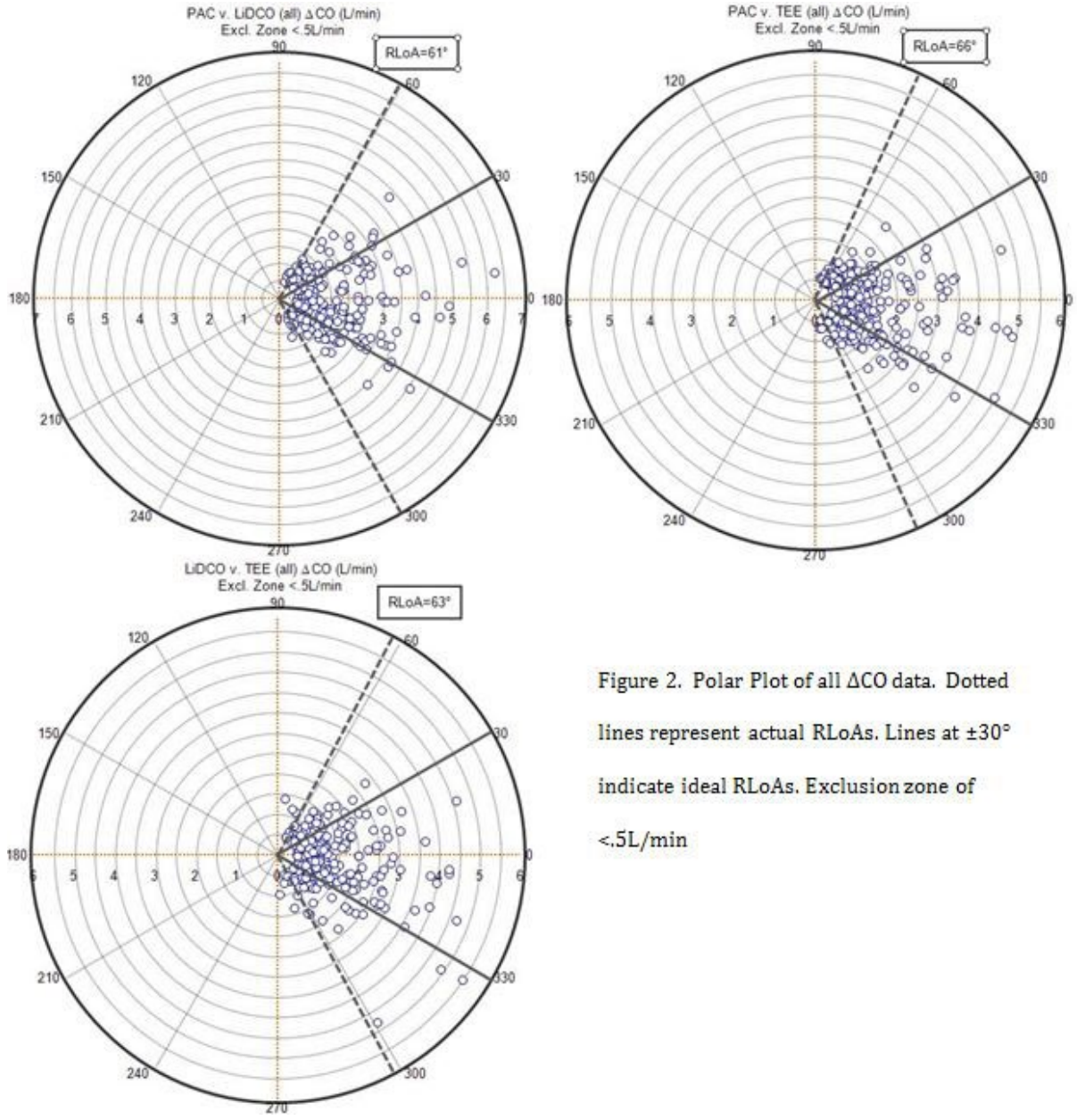

Figure 2. Polar Plot of all ΔCO data. Dotted lines represent actual RLoAs. Lines at ±30° indicate ideal RLoAs. Exclusion zone of <.5L/min

S-349.

CLINICAL EVALUATION OF THE VIOS MONITORING SYSTEM - INITIAL REPORT OF A PILOT STUDY

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INTRODUCTION: Continuous vital sign (VS) monitoring with stand alone bedside monitors is standard practice in ICUs and operating rooms; however, these systems are expensive and constrained to certain environments. The Vios System (VMS, Vios Medical, Inc. St. Paul, MN, USA) is the first FDA-cleared platform to utilize commercially available hardware for wireless patient monitoring in low, mid, or high acuity settings. The VMS system allows for flexible and low-cost monitoring through a wireless (Bluetooth) sensor placed on a patient's chest. VMS has capability for real-time analysis and display on a bedside or central station monitor, and synchronized for remote viewing from any global location. In this pilot study we evaluated the accuracy of VMS as compared to gold-standard bedside monitoring systems.

METHODS: After IRB approval and informed consent 1 physician and 8 nurses were trained on the VITALS1 protocol. 55 adult patients indicated for monitoring within the cardiac step-down unit following cardiac catheterization were enrolled into the study.

VS data was acquired simultaneously by the VMS (figure 1) and the existing bedside monitor. Specifically, ECG (lead I and II morphology/artifacting), HR, RR, SPO2, pulse rate, axillary temperature, and posture were captured by each system.

Each patient was monitored for a minimum of 10 minutes, during which 5 comparative data points were captured for each VS. For patient posture, the nurse recorded a visual assessment of the patient. The nurses and patients each completed a questionnaire about the VMS system after use. The data was analyzed using regression analysis and Bland-Altman plots with $p < 0.05$ considered significant

RESULTS: The patients had a mean age of 55 years (range 19-82), mean weight 65kg (range 48-90), and mean BMI 26.2 kg/m2 (range 20-67). None were unstable. The comparative data was highly correlated for ECG, HR, RR, pulse rate and SPO_2 with significant agreement between the traditional and VMS (Table). Patient posture was accurately reflected 100% of the time. The nurses and patients were favorably impressed and preferred the VMS to the existing system.

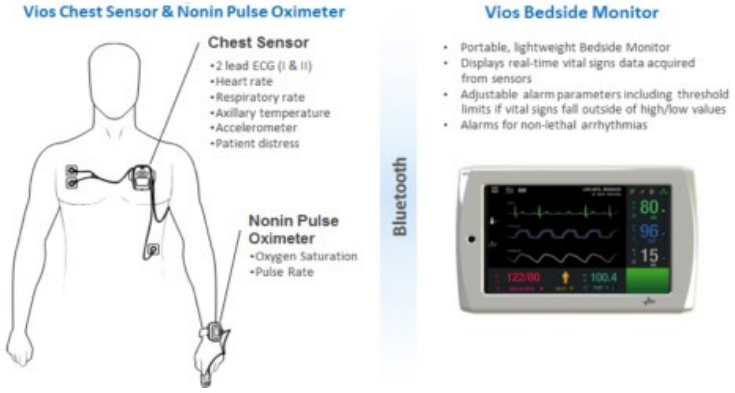
DISCUSSION & CONCLUSIONS: This pilot study confirmed the successful transmission, analysis, and accuracy of the VMS that was well-received. Several studies are being planned to evaluate its acceptance into standard clinical practice and its capability to extend vigilance into environments beyond the hospital allowing remote patient management services. Monitoring patient orientation and activity are additional value points of the VMS system. Benefits of this new clinical metric are: 1) ability to monitor neurological status, 2) potential to decrease pressure ulcers and DVT, and 3) be used as a readiness for discharge tool.

Table: Correlation and Bland-Altman plot results

Parameter	*Heart Rate	*Respiratory Rate	SPO_2 (%)	*Pulse Rate	Posture	ECG morphology & artifacting
†Relationship between the two systems (95% confidence)	$r^2 = 0.99$	$r^2 = 0.81$	$r^2 = 0.71$	$r^2 = 0.98$	100%	Equivalent (qualitative analysis)
†Bland-Altman agreement (95% confidence)	±1.1%	±4.2%	±2.8%	±1.4%	N/A	N/A

*beats or breaths per minute; † $p < 0.00$ for heart rate, respiratory rate, pulse oximetry and pulse rate (for pulse rate n=17)

Figure . The Vios Monitoring System



S-350.

ANOMALY DETECTION THEORY PREDICTS EMERGENCY BLOOD TRANSFUSION AND INTENSIVE CARE UNIT STAY

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OBJECTIVES: Hemorrhage remains a leading cause of preventable trauma death. Acute resuscitation protocols advocate early transfusion of blood and blood components but these products require > 30 minutes for the blood bank to prepare. Thus, methods to enable earlier alerting of the blood bank for impending blood product requirement are urgently needed. Most of the vital signs (VS) derived blood transfusion and mortality prediction algorithms use regression methods[1]. Hyperspectral image analysis methodologies employ anomaly detection theory (ADT)[2], to discriminate hundreds of contiguous spectral bands by wavelength. We hypothesize that treating the trauma patient VS features as distinct wavelengths using principles of ADT, the prediction power of early transfusion and intensive care unit (ICU) stay could be improved in comparison to traditional logistical regression (LR).

METHODS: From all adult (>17 years old) patients admitted directly from point of injury to a level one trauma center, we identified those transfused within the first 4 hours (pRBC) after admission, and days in ICU. Patients dying <15 min after admission were excluded. Seven Pre-hospital VS were analyzed using both LR and ADT to predict pRBC and ICU stay, including systolic (SBP), diastolic blood pressure, pulse pressure, respiration rate, heart rate (HR), Shock Index (SI=HR/SBP) and SI*Age. Area under the receiver operating characteristic curve (AUROC) was used to evaluate the predictive power of the methods. The AUROC (p-value <0.05 significant) were compared with Delong's method. The accuracy and reliability of the models was assessed by 60%-20%-20% training (60%) and testing (20%) methods, and validation (20%) which was repeated 100 times.

RESULTS: In two years (2009 to 2010), 4,202 trauma patient data met inclusion criteria, 6% patients received pRBC in 4 hours, 10% had > 3 day ICU stay and 2.9 % died. Patients were male (67%), mean age 43 years, suffering blunt (83%) and penetrating (12%) trauma (Table 1). Admission Injury Severity Score was >=16 in over one quarter of the admissions. ADT testing AUROC was better than LR for prediction of pRBC 0-4 hours after admission (0.74 v 0.63, p=0.006), and for ICU stay > 3 days (0.71 v 0.66 p< 0.04).

CONCLUSION: ADT method performed significantly better than LR at predicting early blood use, and prolonged ICU stay. Improved prediction by ADT principles may occur when data are skewed (small % positive outcomes to predict), and because of non-linearity of the trauma patient VS data during initial resuscitation. ADT analyses, used previously to detect incoming missile trajectories in real-time (1), may be useful to expedite discrimination of hemorrhaging from non-hemorrhaging trauma patients and those likely to need prolonged ICU stay, even when VS appear stable.[1]

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Patient Demographics		
	Total Cases	Testing Case (20%)
	4202 cases	840 cases
Age, mean (SD)	42.6 (19.0)	42.3 (19.2)
Sex, n (%)		
Male	2833 (67.4)	566 (67.4)
Female	1369 (32.6)	274 (32.6)
ISS, mean (1Q,3Q)	10.8 (4,16)	11.4 (4,17)
GCS, mean (SD)	14.1 (2.5)	14.1 (2.6)
Injury type, n (%)		
Blunt	3473 (82.7)	694 (82.6)
Penetrating	501 (11.9)	101 (12.0)
Missing	101 (2.4)	17 (2.0)
Others	127 (3.0)	28 (3.3)

Table 1: Trauma Patient Demographics for 4202 total cases and 840 testing cases used for validation. ISS= Injury Severity Score; GCS= Glasgow Coma Scale. IQ= Inter-Quartlie range, SD = standard deviation; % = percent

S-351.

NON-INVASIVE QUANTITATIVE AIRFLOW MEASUREMENT DEVICE

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INTRODUCTION: Anesthesia and sedation show an increased morbidity in non-intubated and spontaneously breathing patients due to delayed detection of upper airway obstruction[1]. Current monitoring techniques are ineffective in directly measuring airflow changes. A commercial hotwire anemometer sensor[2] for open circuit flow measurement was used to develop an open-circuit flow system (OCFS). The OCFS was compared to a calibrated pneumtograph sensor for accuracy during volume measurements. The OCFS provides a volume measurement by sensing flow through a facemark. The device is intended to be used with pediatric patients during inhalation induction to assess provider response to airway management with and without the use of the OCFS. The connection site of the OCFS will be between the facemark and the elbow of the circuit.

METHODS: Measured volumes of the pneumotach (Medgraphics Express Series Pneumotograph) and the OCFS were compared. The sensors were connected in series as shown in Figure 1. Volumes of 1000 ml, 100 ml, and 60 ml were delivered manually using pre calibrated syringes. Each syringe volume was delivered over periods of 0.5, 1 and 2 seconds. 17 trials with the 1000ml syringe were conducted (4 times greater then 2s periods, 6 times 2s periods, 4 times 1s periods, 3 times 0.5s periods). 19 trials with a 100 ml syringe were conducted (11 times 1.5s periods, 8 times 0.5s periods). 13 trials with a 60 ml syringe were conducted (1 times 2s period, 8 times 1 second periods). The volumes measured by both the OCFS and the pneumotach were recorded.

RESULTS: The measured values from the pneumotach and OCFS are listed in Table 1 and summarized and illustrated in Table 2 and Figure 2. The accuracy of the two measurement methods were analyzed using a standard t-test at a 95% significance level. The null hypothesis of the analysis was defined as no measurement difference between the pneumotach and OCFS. While the pneumotach more accurately measured the 1000 mL tests ($p = 0$), the systems showed no significant difference when measuring 100 ml ($p = 0.6378$) and 60 mL ($p = 0.2793$) airflow volumes. Using the two one-sided test (TOST), both methods met equivalence (equivalence margin of 10%). The similar results achieved by the first iteration of the OCFS illustrate the system's potential.

CONCLUSION: The insufficiencies of current modalities to detect upper-airway obstruction of non-intubated patients in the intra-operative environment suggest a need for a device, which directly measures airflow and notifies of an obstructive event. Results from the OCFS show stable data. More consistency is seen in the 60 ml and 100 ml volumes compared to the pneumotach. This supports further development of this product for the clinical setting. Further testing will involve pneumatic-simulated respiration followed by healthy human subject testing. This OCFS illustrates the potential for flowmeters in open-circuit obstruction detection.

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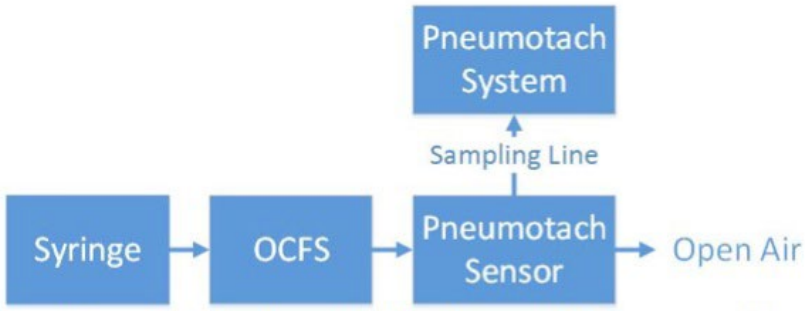

Figure 1. Sensor Connection Diagram. The OCFS and Pneumotach Sensor were connected in series with the calibrated syringe. The Pneumotach Sensor had a sampling line.

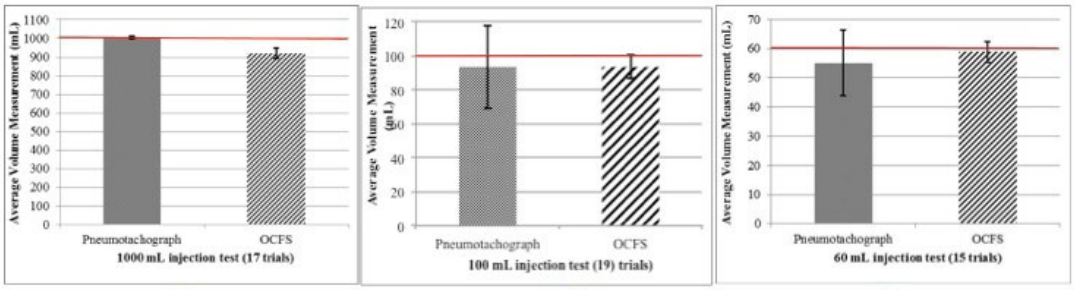

Figure 2. Average Volume Measurement of Pneumotachograph and OCFS with (a) 1000 mL delivered from syringe (b) 100 mL delivered from syringe and (c) 60 mL delivered from syringe. At a 95% significance level, only the 1000 mL trials showed a significant difference ($p = 0$).

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Table 1. Compared In-line volumes

Syringe Volume (mL)	Speed (s)	Pneumotachograph (mL)	OCFS (mL)
1000	Over 2	1016	942
1000	Over 2	999	932.8
1000	Over 2	997	904.2
1000	Over 2	996	905.8
1000	2	1017	925
1000	2	1019	900.3
1000	2	1006	899.5
1000	2	1007	943.1
1000	2	1007	980.8
1000	2	1006	893.1
1000	1	1012	917.4
1000	1	1011	955.2
1000	1	999	895.1
1000	1	1003	882.1
1000	0.5	995	876
1000	0.5	998	957
1000	0.5	995	937.8
100	1.5	23	80.86
100	1.5	36	87.48
100	1.5	105	92.19
100	1.5	105	89.48
100	1.5	103	89.57
100	1.5	105	97.38
100	1.5	102	95.67
100	1.5	103	89.9
100	1.5	104	87.19
100	1.5	104	90.43
100	1.5	104	100.8
100	0.5	102	93.62
100	0.5	103	107.3
100	0.5	104	103.8
100	0.5	103	95.24
100	0.5	102	83.62
100	0.5	64	97.71
100	0.5	102	91.62
100	0.5	103	104.1
60	1	62	57.67
60	1	60	59.81
60	1	67	52.14
60	1	60	55.24
60	1	60	54.67
60	1	59	55.52
60	1	34	63.38
60	1	60	61
60	2	59	63
60	0.5	61	61.29
60	0.5	62	63
60	0.5	61	55.43
60	0.5	53	62.24

Table 2. Average Values and Standard Deviations

Syringe Volume (mL)	Pneumotachograph Average (mL)	Pneu. Standard Deviation (mL)	OCFS Average (mL)	OCFS Standard Deviation (mL)
1000	1005	8	920.4	29.4
100	94	24	93.6	7.1
60	55	11	58.8	3.6

S-352.

OBJECTIVE MEASUREMENT OF PAIN PERCEPTION IN VOLUNTEERS AND ANESTHETIZED PATIENTS

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INTRODUCTION: Pain is per definition a subjective perception. In certain clinical or research scenarios however, it is desirable to be able to objectively assess pain/nociception. We have tested a new device that uses functional near-infrared spectrometry (fNIRS) to measure the cerebral hemodynamic response to pain stimuli in real time (RTCHR) and compared its performance with other available heart rate variability (HRV) based obj ective measures of pain perception, e.g. analgesia-nociception index (ANI).

METHODS: After IRB approval and obtaining informed consent, we enrolled 20 volunteers and 10 patients for this study. Subjects were connected to the RTCHR device and to an ECG monitor. For the volunteers, heat pain threshold (HPTr, corresponding to a visual analog rating scale (VAS) pain rating of 1) and heat pain tolerance (HPTo, corresponding to VAS pain rating of 10) was established using a Peltier thermode. Then additional stimuli were presented with intensities between HPTr and HPTo. For all stimuli, subjective pain was continuously (500Hz) reported by volunteers. ECG data was stored (500Hz) for further offline analysis. ANI was computed according to Logier et al1 using MATLAB. In order to investigate whether it is possible to record a meaningful signal from anesthetized patients, we have enrolled patients undergoing craniotomy and captured the pinning of the skull with the Mayfield clamp, which is known to be a nociceptive stimulus of high intensity and usually treated preemptively with IV narcotics. Anesthetic management was left at the discretion of the anesthesiologist. ECG was recorded continuously (500Hz) as well as fNIRS data for further analysis. ANI was calculated as described above. Data was tested for normal distribution and the appropriate correlation coefficients were calculated. A p level of <0.05 was considered to be significant. Receiver-operating characteristic (ROC) curves were calculated to determine appropriate RTCHR thresholds for clinically meaningful differentiations.

RESULTS: We observed a significant ($r=0.23$, $p<0.001$) correlation between volunteer-reported NRS pain ratings and pain levels as measured by RTCHR. Correlation between RTCHR and heart rate variability based ANI was not significant ($r=0.024$, $p=0.63$). RTCHR score and ANI were significantly correlated ($r=-0.14$, $p=0.006$). When using a RTCHR threshold of 4.8, one could differentiate between NRS ≥ 7 and NRS < 7 with 71% sensitivity and 66% specificity. We were able to record RTCHR signal in anesthetized patients.

CONCLUSIONS: Our results suggest that RTCHR might be a useful addition to the perioperative monitoring armamentarium of anesthesiologists. Current clinical practice mostly relies on surrogate parameters such as heart rate or blood pressure changes, which all have certain limitations. Whether the RTCHR technology can be used to predict hemodynamic or movement responses to surgical noxious stimulation remains to be determined and will be investigated in future studies.

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S-353.

A NEW LOOK INTO THE TRAIN-OF-FOUR (TOF) RATIO: IS T4/TREF THE BETTER INDICATOR FOR NEUROMUSCULAR RECOVERY?

AUTHORS: D. Schmartz[1], A. C. Reis[1], C. Baumann[2], I. Clerc-Urmes[2], T. Fuchs-Buder[1]

AFFILIATION: [1]Anesthesiology & Intensive Care, CHRU de Nancy, Vandoeuvre-les-Nancy, France, [2]ESPRI-BIOBASE Unit - PARC, CHRU de Nancy, Vandoeuvre-les-Nancy, France

INTRODUCTION: The TOF is the most frequently used stimulation pattern.[1] The "normal" TOF-ratio (i.e. T4/T1) may overestimate the neuromuscular recovery. Indeed, as long as the T1 response did not recover to its initial value, the quotient of T4/T1 will overestimate the degree of neuromuscular recovery. Referring the 4th response to a reference value taken before curarization may overcome this limitation of the TOF. TofScan® is a new quantitative neuromuscular monitoring. Along the classical TOF-ratio, it also indicates the T4/Tref; where Tref (for reference) is the mean amplitude of the four TOF responses before administration of the neuromuscular blocking agent. Both quotients are displayed simultaneously.The pertinence of this T4/Tref ratio has not yet been studied. The aim of our study was to compare neuromuscular recovery assessed by bothTOF-ratios of the TofScan® (i.e; the normal TOF-ratio and T4/Tref) and the "normal" TOF-ratio displayed by the TOF-WatchSX®, which is still considered the gold standard for quantifying neuromuscular recovery in clinical routine. Primary endpoint was the interclass correlation (ICC), secondary endpoint was the negative predictive value of T4/T1 and T4/Tref to detect residual paralysis.

METHODS: After ethics committee approval and informed consent, we included 41 patients. Anesthesia was induced and maintained with propofol and remifentanil, endotracheal intubation was facilitated by a single bolus dose of 0.6 mg/kg of rocuronium without any reinjection. Neuromuscular block was assessed concomitantly with TOF-WatchSX® on one hand and TofScan® on the other hand, attribution to the dominant hand was done by randomization. We calculated sample size with a confidence level of 0.99, expected intraclass correlation of 0.9 and distance from correlation to limit of 0.09 for the intraclass correlation coefficient. The agreement between both measurements was compared by calculating ICC and a Bland-Altman analysis. Negative predictive value (NPV) to detect residual neuromuscular blockade was calculated as the % of patients with either a T4/T1 on the TofScan ≥ 0.9 or a T4/Tref on the TofScan® that do not have a residual paralysis on the TOF-WatchSX®, defined as a TOF ratio ≥ 0.9.

RESULTS: Table 1 shows the ICC and NPV, the figures a Bland-Altman plot for T4/T1 ratio ≥ 0.9 and T4/Tref ratio ≥ 0.9; as well as time to neuromuscular recovery.

DISCUSSION: Overall agreement between TofScan® and TOF-WatchSX® in measuring neuromuscular recovery was good. The "normal" TOF ratio may be interchangeable between TofScan® and TOF-WatchSX®. ICC for T4/Tref was lower than ICC for T4/T1 (table 1), but the NPV of the T4/Tref was much better (76% vs 34%).

CONCLUSIONS: TofScan® and TOFWatchSX® show a good agreement in assessing neuromuscular recovery and may be used interchangeable. The new T4/Tref ratio, as built into the TofScan®, has a better predictive accuracy for excluding residual neuromuscular paralysis. Based on these first, preliminary data, we suggest T4/Tref as a new clinical useful indicator for neuromuscular recovery.

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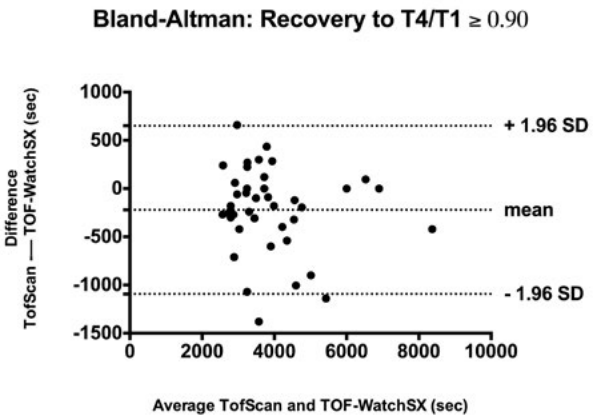
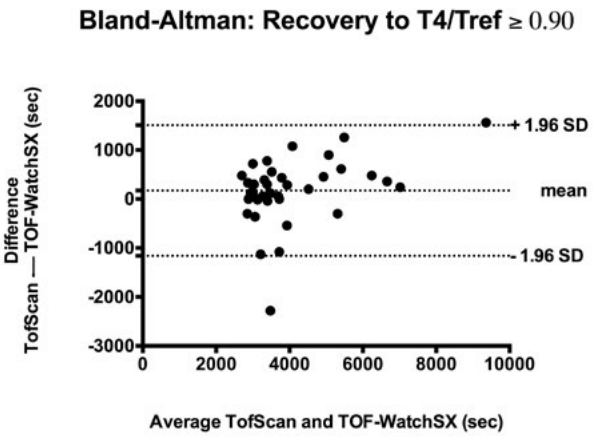
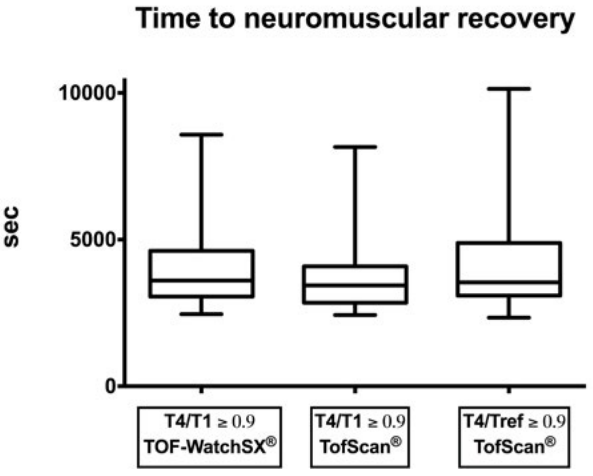
Table 1

	T4/T1 ≥ 0.9	T4/Tref ≥ 0.9
ICC	0.929	0.881
ICC, CI 95%	0.873-0.961	0.784-0.936
NPV (%)	34	76

ICC: intraclass correlation coefficient; CI: confidence interval; NPV: negative predictive value to detect residual paralysis







S-354.

BATTERY DURATION OF A TRANSPORT VENTILATOR WITH OXYGEN CONCENTRATOR

AUTHORS: D. F. Szpisjak[1], J. O'Neil[2], N. Lahvic[2]

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INTRODUCTION: A portable, battery powered patient monitor, ventilator, and O_2 concentrator has been designed for the transport of critically ill patients. If the patient requires an increased FiO2, the energy required by the O_2 concentrator may affect battery duration. The purpose of this study was to determine battery duration when the O_2 concentrator was off or running continuously.

METHODS: The battery duration of the MOVES Portable ICU (Thornhill Research Inc., Toronto, Ontario, Canada) was measured when ventilating the Training Test Lung (TTL) (Michigan Instruments, Grand Rapids, MI). The TTL compliance setting was 0.1 L/cm H_20. The methodology was similar to an previous study from our lab.1 Adult tracheal and bronchial resistances were simulated with manufacturer supplied tubing. No additional airway resistor was used. The ventilator and its circle airway circuit were assembled per manufacturer instructions and all system tests were successfully completed. The ventilator settings were intermittent mandatory ventilation, RR=10, I:E = 1:2, PEEP = 5 cm H_20, and FiO_2 = 0.21 or 0.60. Pressure control mode was used with pressure adjusted from 10 to 11 cm H_2O as needed to achieve a target VT of 800 ± 50 mL. There were five runs for each FiO_2 group. Respiratory parameters were recorded with the series 3700 Research Pneumotach (Hans Rudolph Inc., Shawnee, KS) after calibration with the series 5530 calibration syringe (Hans Rudolph Inc.). To simulate the battery drain of non-invasive monitoring, the MOVES EKG, non-invasive blood pressure (NIBP), and pulse oximeter (SpO_2) were attached to the signal replicators of a high fidelity human patient simulator (HPS) (CAE Healthcare USA, Sarasota, FL). The HPS vital signs settings were those of a normal adult, approximating NIBP = 120/80, HR = 80, and SpO_2 = 98%. The NIBP was cycled every five minutes. The temperature probe sampled ambient air. When ventilating with FiO_2 = 0.21, the MOVES gas sampling tube was attached to the Y-piece of the circuit. When ventilating with FiO_2 = 0.60, the MOVES gas sampling tube sampled ambient air, simulating high metabolic O_2 consumption and causing the O_2 concentrator to run continuously. Delivery of an FiO2 = 0.60 was confirmed by the Philips IntelliVue G5-M1019A (Philips Healthcare, Boeblingen, Germany) attached to the Y-piece of the circuit. Battery duration was analyzed with Kaplan-Meier curves and the log-rank test with Holm-Šidàk correction. Data were reported as mean (±SD), and $P < 0.05$ was considered significant.

RESULTS: The battery duration with FiO_2 = 0.21 exceeded that with FiO_2 = 0.60 [10.35 (± 0.16) vs. 3.48 (± 0.02) h, respectively, P = 0.0018]. The mean difference was 6.87 (± 0.16) h.

CONCLUSIONS: When running continuously in a high metabolic oxygen demand simulation, the O_2 concentrator decreased MOVES battery duration by > 6 h when compared to ventilating with room air. Battery duration with only intermittent demand of the O_2 concentrator requires further testing.

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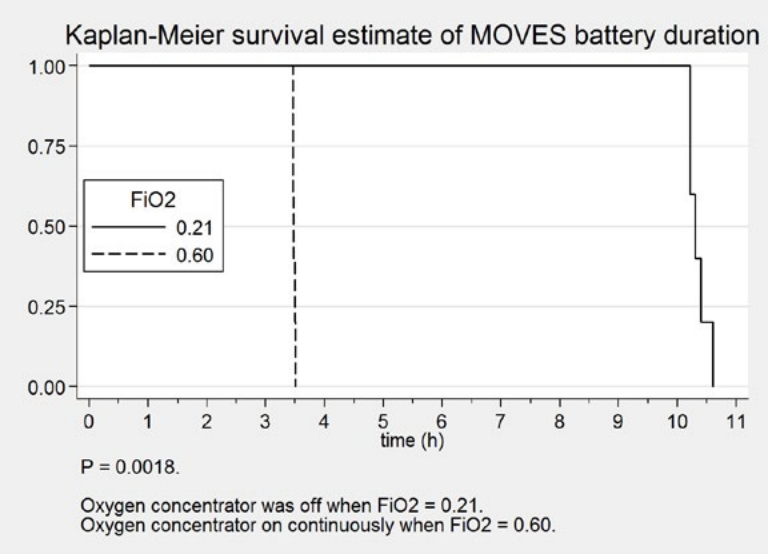

S-355.

EVALUATION OF NONINVASIVE CARDIAC OUTPUT MONITORING IN SHEEP WITH HEMODYNAMIC INSTABILITY

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INTRODUCTION: Noninvasive cardiac output monitoring (NICOM) uses bioreactance technology to measure the phase shift between an applied alternating current and voltage measured across the thorax; phase shifts are tightly coupled to changes in thoracic pulsatile blood flow, and hence stroke volume.[1] This technology has been validated in several patient populations, but not in the setting of acute hemorrhagic shock. In this study, we evaluated the precision and accuracy of NICOM against thermodilution-based cardiac output (T-CO) under hemodynamically unstable conditions. The objective was to compare the effect of intravascular volume depletion on measurements obtained by NICOM versus the gold standard PAC. The hypothesis was that bioreactance measured CO was able to follow very low CO when PA catheter monitoring might be unable to obtain data.

METHODS: After IACUC approval, twenty male juvenile Dorset sheep were studied for a hemorrhagic shock model of resuscitation. Animals were anesthetized with isoflurane after initial induction, intubation, and ventilation. Animals were continuously monitored with cut downs on the femoral artery (BP) and the femoral vein (CO). NICOM required placement of four electrode stickers on the thorax, forming a box around the heart. Animals were stabilized then hemorrhaged to a MAP <33 mmHg and held at that level for 1 hr prior to resuscitation. Resuscitation was IV infused hetastarch, equal volume to blood loss, as animals were stabilized at a MAP >55 mmHg. Animals were observed for 1 hr after resuscitation. The data collected included CO and MAP every 20 min from the acutely hemorrhaged sheep from baseline to 1 hr post-resuscitation. Data were compared between measures and over time.

RESULTS: MAP at baseline averaged 68 mmHg; avg baseline CO was 2.0 and 2.9 L/min for PAC and NICOM respectively. NICOM measurements were consistently higher than PAC (0.85 L/min; SE 0.16 L/min; $p<0.0001$; limits of agreement -1.6, 3.3 L/min). The greatest differences between methods occurred at the end of shock, coinciding with the greatest variability in hemodynamic stability (MAP σ=23 mmHg). The correlation between PAC and NICOM over the entire process was moderate ($r = 0.65$); although 14/20 animals showed excellent congruence between methods (cross correlation $r>0.89$ at zero lag), PAC readings for 6/20 sheep consistently lagged behind NICOM. Although NICOM readings had higher intrinsic variability (NICOM = 0.98; versus PAC = 0.13), PAC readings were less reliable with 24 dropped or out-of-range observations (CO < 0.1 L/min) during shock, versus none with NICOM.

CONCLUSION: NICOM outperformed PAC when measuring CO in hemodynamically unstable subjects with rapidly changing MAP. NICOM responses were consistently reliable with acceptable accuracy in a clinically realistic shock model. Availability of such a tool will allow clinicians to have information about CO in patient when the T-CO method is not feasible to help diagnose and guide therapy.

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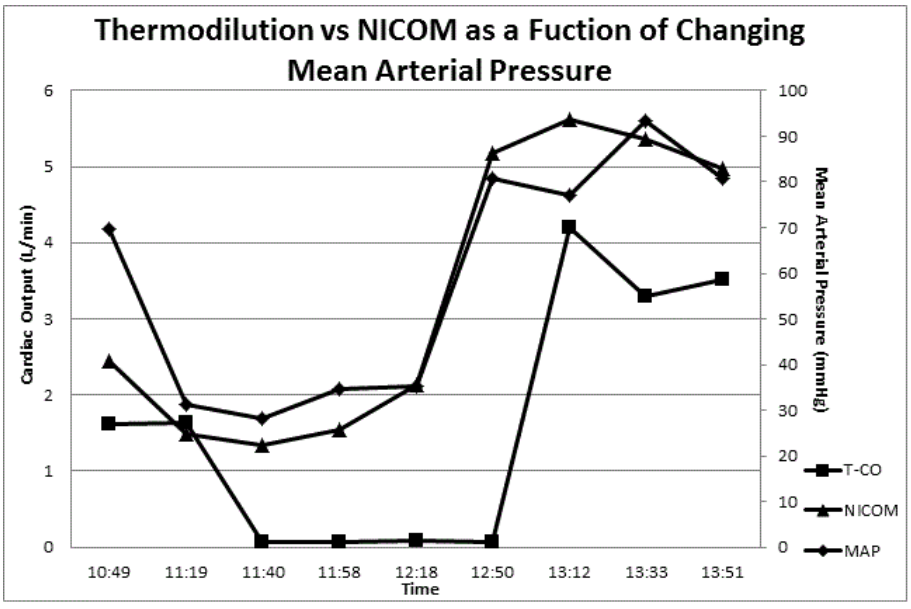

Figure I: MAP and corresponding CO over a period of hemorrhage and resuscitation, demonstrating the unreliable nature of thermodilution at low intravascular volume.

S-356.

DEFINITION OF NORMAL VORTEX AND ENERGY LOSS REFERENCE VALUE IN LEFT VENTRICLE USING VECTOR FLOW MAPPING

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INTRODUCTION: Now pathophysiology of various cardiovascular disease and relative merits of each cardiovascular surgery are becoming clear owing to Vector Flow Mapping® (Hitachi-Aloka) by analyzing left ventricular vortex pattern and energy loss. Although energy loss reference value of children was defined by Itatani et al[1]), that of adults has not been defined yet. It is imperative to define the normal left ventricular vortex pattern and the energy loss reference value.

METHODS: Transthoracic echocardiography was performed in 50 healthy adults. 3-chamber view was analyzed by Vector Flow Mapping offline, and left ventricular vortex pattern and energy loss were calculated. Fisher's exact test, multivariate analysis and stepwise multivatiate linear regression analysis were performed using the following variables: age, heart rate, transmitral E wave and A wave peak velocity, e', and BSA.

RESULTS: Left ventricular vortex pattern was counterclockwise rotation (posterior wall to anteroseptal) in all subjects. On multivariate analysis, heart rate was independent predictor of systolic energy loss, while heart rate and transmitral E wave peak velocity were independent predictors of diastolic energy loss. Moreover, based on the multivariate linear regression analysis, the regression equations for systolic energy loss and diastolic energy loss were derived.

CONCLUSION: Normal pattern vortex of left ventricle minimizes energy loss and enables left ventricle to eject blood effectively. Definition of adult energy loss reference value in left ventricle is supposed to improve the diagnosis and treatment of cardiovascular diseases.

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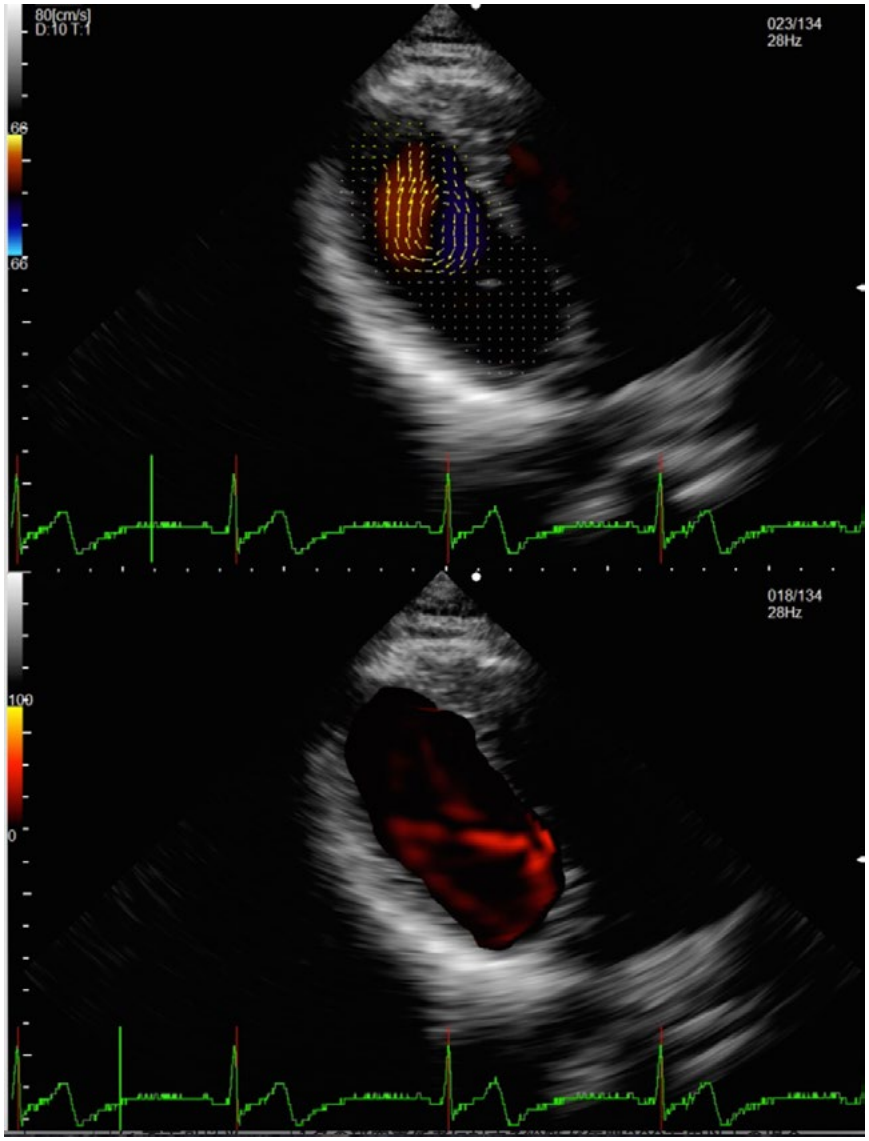

S-357.

TRANSPORT VENTILATOR BATTERY DURATION IN A MECHANICAL LUNG MODEL OF ARDS

AUTHORS: J. Stockton[1], D. F. Szpisjak[2]

AFFILIATION: [1]F. Edward Hebert School of Medicine, Uniformed Services University, Bethesda, MD, [2]Anesthesiology, Uniformed Services University, Bethesda, MD

INTRODUCTION: Battery powered portable ventilators are designed for the transport of critically ill patients. Previous studies of portable ventilator battery duration did not use a lung model consistent with adult respiratory distress syndrome (ARDS)[1] or a respiratory rate (RR) > 10[2,3]. The purpose of this investigation was to determine the battery duration of a portable ventilator at the extremes of compliance, airway resistance, and RR.

METHODS: The battery duration of the Uni-vent 731 EMV+ transport ventilator (Zoll Medical Corp., Chelmsford, MA) was measured when ventilating the Training Test Lung (TTL) (Michigan Instruments, Grand Rapids, MI) as a model of high compliance (HC) - low resistance (LR), and low compliance (LC) - high resistance (HR). The HC and LC settings were 0.1 and 0.02 L/cm H_20, respectively. HR was provided by the Rp20 resistor (Michigan Test Instruments). For the LR setting, no resistor was added. The ventilator had been recently serviced and its airway circuit assembled per manufacturer instructions. The ventilator settings were assist control, V_T = 800 mL, I:E = 1:2, PEEP = 5 cm H_20, and FiO2 = 0.21. The HC-LR and LC-HR lung settings were tested at RR = 10, 20, and 30 bpm for a total of 6 groups. There were five runs for each group. Respiratory parameters were recorded with the series 3700 Research Pneumotach (Hans Rudolph Inc., Shawnee, KS) after verifying pressure calibration against a column of water and calibrating flow with a calibration syringe. Battery duration was analyzed with Kaplan-Meier curves and the log-rank test with Holm-Šidàk correction. Data were reported as mean (±SD), and $P < 0.05$ was considered significant.

RESULTS: Battery duration ranged from 5.6 (± 0.11) to 10.4 (± 0.07) h in the LC-HR-30 and HC-LR-10 groups, respectively (table).

CONCLUSION: If RR is constant, worsening lung compliance and resistance decreases battery duration by approximately 0.62 h. If RR ≤ 30, planning for no more than five hours battery duration from a fully charged battery met all testing conditions while providing > 30 min safety margin.

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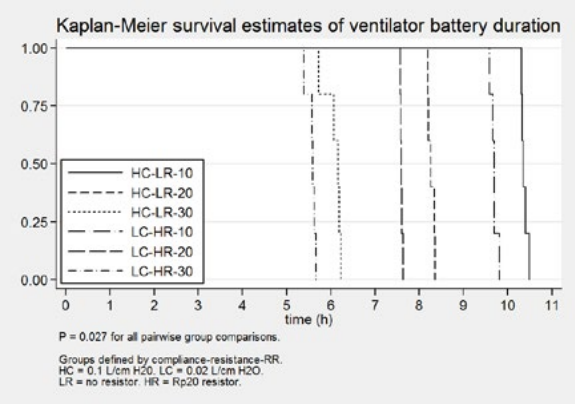
Transport ventilator battery duration in hours

Respiratory Rate	HC-LR Lung Model Battery Duration (h)	LC-HR Lung Model Battery Duration (h)	Difference (h)
10	10.38 (± 0.07)	9.69 (± 0.08)	0.69
20	8.27 (± 0.08)	7.60 (± 0.020)	0.67
30	6.07 (± 0.20)	5.57 (± 0.11)	0.50
HC = 0.1 L/cm H_2O	LR = no resistor	LC = 0.02 L/cm H_2O	HR = Rp20

The mean difference in battery duration between the HC-LR and LC-HR groups for like RR was 0.62 (± 0.10) h (figure). The pairwise differences between all groups were statistically significant (P = 0.027).



S-358.

COMPARATIVE ANALYSIS OF MEDICAL USE AND SPORTS AND AVIATION USE PULSE OXIMETERS REVEALS NO MEANINGFUL DIFFERENCE

AUTHORS: A. J. Hudson[1], J. Benjamin[2], T. Jardeleza[2], C. Bergstrom[3], W. A. Cronin[2], M. Mendoza[4], L. Schultheis[5]

AFFILIATION: [1]Anesthesiology, Uniformed Services University of the Health Sciences, Bethesda, MD, [2]Anesthesiology, Walter Reed National Military Medical Center, Bethesda, MD, [3]Anesthesiology, University of Maryland School of Medicine, Baltimore, MD, [4]Center for Devices and Radiological Health, Anesthesia Devices Branch, U.S. Food and Drug Administration, Silver Spring, MD, 5Bioengineering, University of Maryland, College Park, MD

INTRODUCTION: All pulse oximeters are regulated as prescription medical devices for non-invasive measurement of arterial oxygen saturation of hemoglobin. The Food and Drug Administration (FDA) reviews data from human volunteers undergoing hypoxemic challenge before a new oximeter can be cleared for medical use through a Premarket Notification [510(k)] under 21 CFR § 870.2700 with the product code "DQA".[1,2] Pulse oximeters that are specifically labeled for use only in sports and aviation, rather than for medical monitoring, also fall under 21 CFR § 870.2700, but the regulatory product code for these types of oximeter is "OCH".[2] Sports and aviation oximeters are not typically reviewed by FDA even though they are widely marketed and sold without prescription. The purpose of this clinical investigation was to compare accuracy of pulse oximeters that have been cleared by the FDA for medical use to oximeters for sports use when spot checking oxygen saturation (SpO_2).

METHODS: A randomized, concurrent controlled, comparative study of pulse oximetry in the perioperative setting was conducted. Surgical patients who had an indwelling arterial catheter and managed post-operatively in the surgical ICU were enrolled. Eight commercially available sports and recreational use pulse oximeters were compared to an FDA-cleared pulse oximeter. Sampling of pulse oximeter data was obtained as clinically convenient. Comparison of SpO_2 by pulse oximetry versus hemoximetry was obtained when blood gas analysis was medically necessary.

RESULTS: Sixty (60) enrolled patients were each randomized to 2 test devices and 1 medical device. Two patients were withdrawn due to atrial fibrillation. Approximately 100 samples per oximeter ranged between 79-99% SpO_2. Modified Bland Altman analyses did not detect a clinically meaningful difference, on average, between non-medical and medical grade pulse oximeters when SpO_2 ranged between 90-99%.

CONCLUSIONS: Our study did not reveal a clinically significant difference, on average, between the medical and sports oximeters in SpO2 from 90-99%. FDA review of peripheral pulse oximeter accuracy in the 90-99% may be unnecessary, but should increase focus on evaluating accuracy at lower SpO_2 values, i.e. between 70-89%. Additional study in human beings undergoing hypoxemic challenge is warranted.

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Scholars' Abstracts

Airway Management

S-400.

INDEPENDENT RISK FACTORS FOR POSTOPERATIVE PULMONARY COMPLICATIONS IN A RURAL TERTIARY ACADEMIC MEDICAL CENTER

AUTHORS: S. Belenkiy, D. Sizemore, M. Mueller, O. M. Elzamzamy, A. Attaallah, M. C. Vallejo

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INTRODUCTION: We aimed to determine the incidence of postoperative pulmonary complications (PPCs) and identify risk factors for postoperative reintubation in a rural tertiary academic medical center.

METHODS: This protocol was reviewed and approved by our Institutional Review Board. We conducted a time matched, case control analysis from September 2010 through December 2013, where 98 patients with PPCs were identified and matched to a control group of 4055 patients from the institutional Integrated Data Repository quality assurance medical record database. Data is presented as mean ± SD with 95% CI, median with range in parenthesis, or percentage with Odds Ratio (OR) and analyzed using Mann-Whitney or Chi-square tests. A $P < 0.05$ is significant.

RESULTS: The overall incidence of PPC was 2.4%. No differences were noted with respect to BMI, gender, and anesthesia type (general, regional, or local). Significant differences did occur with age 61.63 ± 14.25 yr. PPC (95% CI: 58.79-64.46) vs. 54.02 ± 17.38 yr. control (95% CI: 53.48-54.55, $P < 0.001$) and median ASA status III (II-IV) PPC vs. III (I-V) control ($P < 0.001$). Table 1 lists additional independent risk factors for reintubation.

CONCLUSIONS: In addition to age and ASA status, we found the following independent risk factors including an elective procedure, preoperative in-patient status, surgical duration > 2 hr., and a pre-operative diagnosis of hypertension and COPD all significantly increased the odds for a PPC.

Table 1. Independent predictors for PPCs

Variable	PPC (n=98)	Control (n=4055)	*P* value	OR	95% CI	
Elective procedure (%)	97.9%	82.7%	< 0.001	10.0	2.5	40.5
Pre-op In-Ptient status (%)	97.9%	65.40%	< 0.001	25.1	6.2	102.1
Surgical Duration >2 hr. (%)	90.7%	38.7%	< 0.001	15.5	7.8	30.9
Pre-op Hypertension (%)	69.8%	52.0%	< 0.001	2.1	1.4	3.3
Pre-op COPD (%)	30.9%	10.6%	< 0.001	3.8	2.4	5.9

Scholars' Abstracts

Ambulatory Anesthesia

S-401.

INCIDENCE AND PREDICTORS OF HOSPITAL READMISSION AFTER AMBULATORY CHOLECYSTECTOMY

AUTHORS: E. B. Rosero[1], G. P. Joshi[2]

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Introduction: Currently, 65-70% of all surgical procedures in the United States are performed on an outpatient basis. However, data on outcomes after ambulatory surgery are scanty[1,2]. The aim of this study was to evaluate the incidence and predictors of readmission after ambulatory surgery using large outpatient and inpatient state administrative data.

METHODS: The 2009 to 2011 State Ambulatory Surgery and Services Databases (SASD) from California, New York, and Florida were analyzed to identify patients undergoing ambulatory cholecystectomy. Appropriate Current Procedural Terminology (CPT) codes were used to identify the procedures. The primary outcome was any hospital readmission (defined as a hospitalization within 30 days post-surgery) linked to the index outpatient procedure. Data on hospital readmissions were extracted from the State Inpatient Databases (SID) from the corresponding states. Variables common to the SASD and SID allow tracking patients across outpatient and inpatient visits and calculation of the number of days between encounters. Univariate analyses and logistic regression models were conducted to assess predictors associated with increased odds of readmission. Finally, table analyses were used to describe the most frequent causes of readmission after ambulatory cholecystectomy.

RESULTS: A total of 230,839 ambulatory cholecystectomies were identified. Of those, 99.6% were done via laparoscopy. Median (interquartile range) age of patients was 49 (36-62) years. Most patients (74.6%) were women (Table). A total of 127 patients (0.06%) were transferred from the ambulatory center to a hospital (unplanned hospital admissions). In addition, 4,678 patients (2.03%) were readmitted to the hospital. Of those, 11.7% were admitted within 24 hours (unexpected admissions) and 53.3% 1 to 7 days after surgery. Logistic regression models revealed the following factors associated with increased odds of readmission: surgery done on weekend (OR, 1.32; 95% CI, 1.03 - 1.70; P < .026), age > 75 years (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.29-1.76; P < .0001), male sex (OR, 1.12; 95% CI, 1.05 - 1.20; P < .001), diabetes (OR, 1.11; 95% CI, 1.01 - 1.22; P < .043), chronic renal failure (OR, 1.38; 95% CI, 1.08 - 1.75; P < .009), white race vs. Hispanic (OR, 1.67; 95% CI, 1.12 - 2.50; P <0.0001), and type of health insurance (Medicare vs. Private OR, 1.19; 95% CI, 1.06 - 1.34; Medicaid vs. Private OR, 1.20; 95% CI, 1.08 - 1.33; P < .0001). The most frequent causes of hospital admission included surgical complications (33.4%), acute pain (11.8%), infection (10.3%), postoperative nausea/vomit (5.4%), surgical or gastrointestinal bleeding (4.0%), cardiac (3.6%) and respiratory complications (3.3%).

CONCLUSIONS: Our analysis reveals that the incidence of readmission after ambulatory cholecystectomy is low (~ 2%). In addition to patient demographics and comorbidities, performance of surgery on a weekend is a significant independent predictor of readmission.

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TABLE. BASELINE CHARACTERISTICS OF PATIENTS HAVING AMBULATORY CHOLECYSTECTOMY

CHARACTERISTIC	Number	Percent
Age, years		
18 to 39	72,541	31.42
40 to 64	112,863	48.89
65 to 74	29,799	12.91
75+	15,636	6.77
Female sex	166,835	74.58
Race/ethnicity		
White	134,771	64.52
Black	12,022	5.76
Hispanic	48,998	23.46
Other	13,087	6.26
Primary Insurance		
Medicare	48,808	21.14
Medicaid	25,975	11.25
Private Insurance	143,616	62.22
Other	12,427	5.38
Procedure performed on weekend	2,818	1.22
Hypertension	63,345	27.44
Heart failure	1,084	0.47
Chronic lung disease	20,412	8.84
Diabetes	21,312	9.23
Chronic renal failure	2,208	0.96
Obesity	28,045	12.15

S-402.

SAME-DAY CANCELLATION IN OUTPATIENT SURGERY: A RETROSPECTIVE REVIEW AT A LARGE ACADEMIC TERTIARY REFERRAL CENTER

AUTHORS: L. K. Licatino, J. A. Hyder, M. M. Smith, W. Mauermann, M. E. Warner, D. W. Barbara;

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INTRODUCTION: Same-day surgical or procedural cancellations can incur significant personnel and facility costs and be detrimental to optimal patient care. This study was undertaken to determine the frequency and causes of same-day cancellations, as well as to examine several associated factors.

METHODS: We performed retrospective review of all same-day cancellations at an outpatient surgery center at a large academic tertiary referral center from 2010-2013. Cancellations were classified as foreseeable, unforeseeable or indeterminate. Data regarding interval between cancellations and visiting a non-surgeon provider, time to performance of procedure, and location of performed procedure were collected and analyzed.

RESULTS: 211 same-day cancellations were identified out of 41,389 cases performed during the study period (0.5%). Of the cancelled procedures, 36% were deemed foreseeable while 50% were unforeseeable and 13% were indeterminant. General reasons for cancellation included medical (48%), patient non-compliance (17%), unknown (12%), procedure no longer required (7%), patient cancellation (6%), administrative/scheduling (4%), preincisional complication (4%), and patient not appropriate for outpatient facility (2%). Of the 77 foreseeable cases, 47% were due to patient non-compliance. Other reasons included medical (36%), administrative/scheduling (9%), patient not appropriate for outpatient center (5%), and procedure no longer required (3%). The mean time from most recent visit with a non-surgeon provider was 44.3 ± 75.3 days. 183 (87%) of the cancelled procedures were eventually performed. 64% of these procedures were performed at the outpatient center while 36% were done at an inpatient facility. On average, these procedures were performed 24.5 ± 68.3 days following cancellation.

CONCLUSIONS: Same-day cancellation of outpatient procedures was an infrequent occurrence at our outpatient center. Only the minority of canceled cases were deemed to be foreseeable. The most common cause of foreseeable cancellation was patient non-compliance with preoperative instructions. Though infrequent, a renewed focus on foreseeable cancellations of outpatient procedures could offer opportunities for practice improvement and improved quality of care.

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S-403.

VENTILATORY EFFECTS OF GASTROENTEROLOGIST-ADMINISTERED SEDATION FOR COLONOSCOPY

AUTHORS: K. Kristiansen[1], J. T. Mathews[1], D. M. Mathews[1], J. Vecchio[2]

AFFILIATION: [1]Anesthesiology, University of Vermont College of Medicine, Burlington, Vermont, [2]Medicine-Gastroenterology, University of Vermont College of Medicine, Burlington, Vermont

INTRODUCTION: Procedural sedation is frequently practiced by non-anesthesiologists. As these procedures are associated with some degree of pain, a combination of opiates and benzodiazepines is often administered to ensure adequate sedation.[1,2] It is well established that these medications can cause respiratory depression.[3-5] To date, no studies have investigated the degree of respiratory depression in patients undergoing colonoscopy with sedation given by non-anesthesiologists. In this observational study, we utilized a noninvasive ventilatory monitor to quantify the degree of respiratory depression in patients undergoing colonoscopy with gastroenterologist-administered sedation.

METHODS: The ExSpiron™ (Respiratory Motion Inc, Waltham MA) monitor was utilized for the study. The sensor padset was placed in the preprocedural area according to the manufacturer's specifications. The monitor was calibrated utilizing a Wright's spirometer. A baseline measurement of respiratory rate (RR) minute ventilation (MV) and tidal volume (TV) was determined in the procedure room prior to sedation. Both the procedural nurse and the gastroenterologist were blinded to the device. Routine patient monitoring included sidestream capnography. Medication administration, midazolam with meperidine, adverse events, and the need for intervention were recorded for each patient. Respiratory changes were analyzed including the nadir of minute ventilation and time below 40% of baseline MV.

RESULTS: 31 patients were recruited and the data from 25 was suitable for analysis. Following sedation administration, MV decreased, on average, to approximately 60% of baseline. The figure shows the average (+ S.D.) MV values for 15 minutes following the first dose of sedation which was midazolam 2 mg and meperidine 50 or 75 mg. During the procedure 19 patients (76%) had periods of minute ventilation below 40% of baseline value, with an average time below 40% of 5.8 minutes. 5 patients had MV nadirs below 20% of baseline and 2 had nadirs below 10%. There were no adverse clinical outcomes; one patient required a jaw thrust.

CONCLUSION: Gastroenterologist-administered sedation for colonoscopy resulted in a degree of ventilatory depression. Based on ARDSnet extubation criteria, 40% of baseline MV has been established as an "unsafe" level .6 It is interesting that 76% of patients fell below 40% and that routine care and monitoring in these patients resulted in only 1 intervention (jaw thrust).There were no adverse outcomes despite this degree of ventilatory depression. Further work is necessary to determine the utility of non-invasive ventilatory monitoring in such cases.

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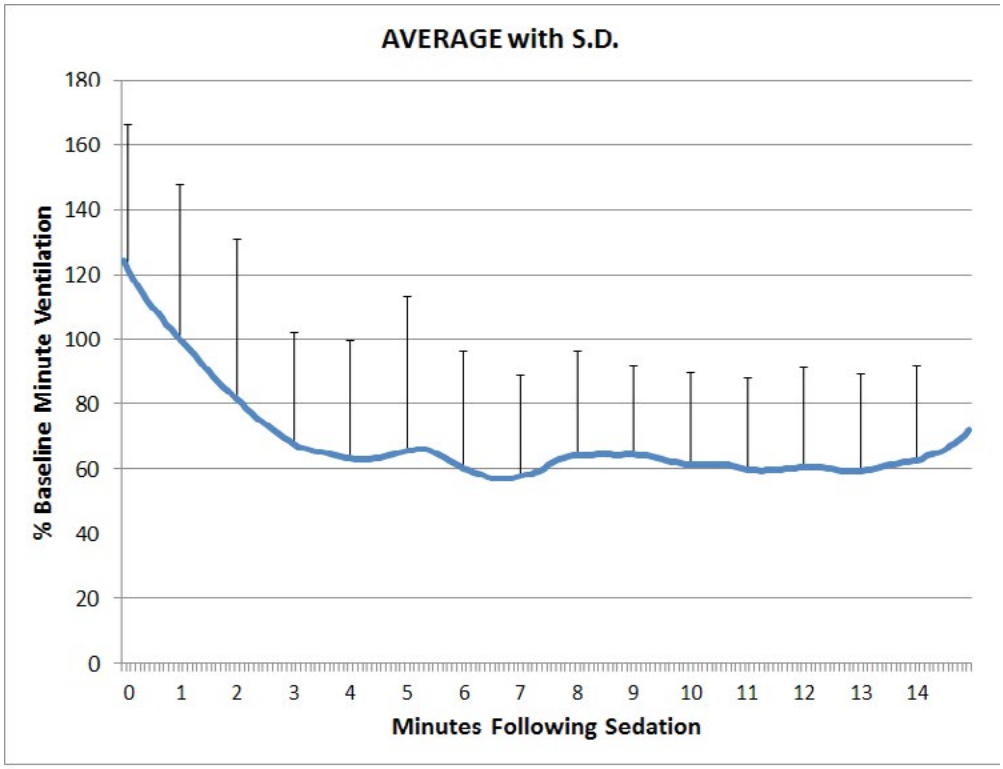

S-404.

PREOPERATIVE FALLS AND THEIR ASSOCIATION WITH FUNCTIONAL DEPENDENCE AND QUALITY OF LIFE

AUTHORS: V. L. Kronzer, R. Tang, A. P. Schelble, F. Sadiq, M. S. Avidan

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INTRODUCTION: Falls are widely recognized as a major public health problem,[1,2] and evidence suggests they are relevant to patients' health.[3] No study has rigorously explored the characteristics of surgical patients with recent preoperative falls. Our objective was to describe the essential features of preoperative falls and determine whether they are associated with preoperative functional dependence and poor quality of life.

METHODS: A substudy of the ongoing registry, SATISFY-SOS (NCT02032030), this observational study involved 15,060 surveys from adult patients undergoing elective surgery. Surveys were collected between January 2014 and August 2015, with a response rate of 92 percent. Data from the patient's electronic medical record supplemented the survey data. RESULTS: In the six months prior to surgery, 26% (99% CI. 25% to 27%) of patients fell at least once, and 12% (99% CI. 11% to 13%) fell at least twice. The proportion of patients who fell was highest among neurosurgical patients (41%, 99% CI. 36% to 45%). At least one fall-related injury occurred in 58% (99% CI. 56% to 60%) of those who fell. Falls were common in all age groups, but surprisingly they did not increase monotonically with age (Figure 1). Middle-aged patients (45 to 64 years) had the highest proportion of fallers (28%), recurrent fallers (13%), and severe fall-related injuries (27%) compared to younger age (18-44) and older age (65+) patients ($p < 0.001$ for each). Number of preoperative falls exhibited a dose-response relationship with preoperative functional dependence and poor physical quality of life (Figure 2). Moreover, multivariable logistic regression showed that a history of preoperative falls is an independent predictor of each (OR 1.94; 99% CI. 1.68 to 2.24; OR 2.18; 99% CI. 1.88 to 2.52). This association was stronger than that of other metrics for preoperative assessment such as the American Society of Anesthesiologists (ASA) physical status score and the Charlson Comorbidity Index.

CONCLUSIONS: This study is the first to specifically investigate preoperative falls. It found that preoperative falls are common and often injurious, across all ages. These results challenge existing belief that falls increase monotonically with age and invite investigation of middle-age and younger-age falls. Finally, a history of falls enhances assessment of preoperative functional dependence and quality of life.

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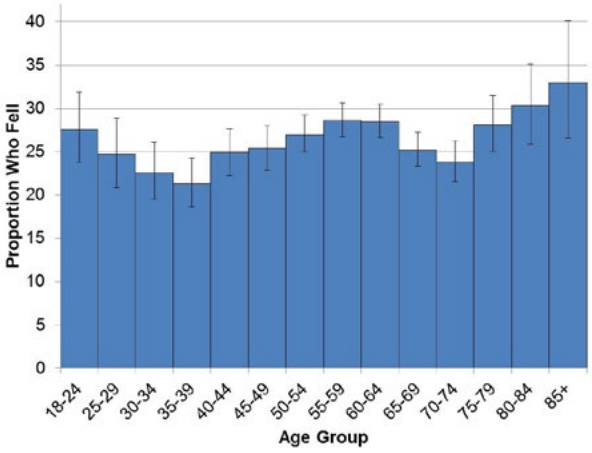

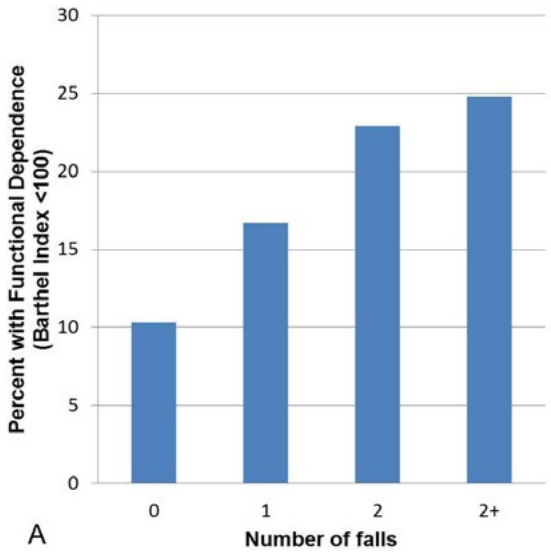

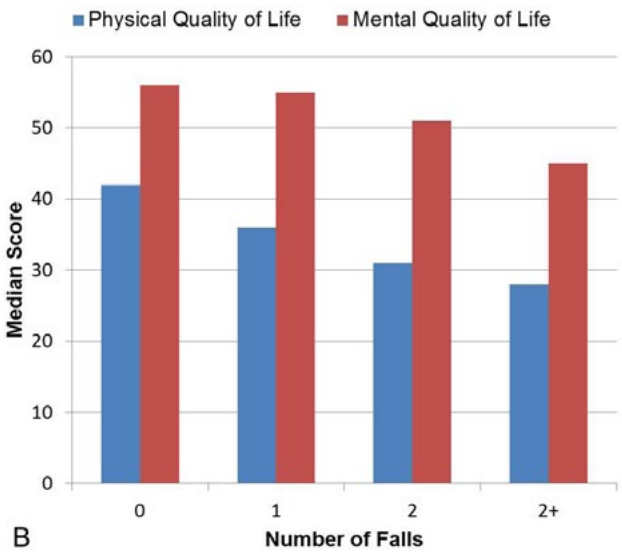

Scholars' Abstracts

Anesthetic Pharmacology

S-405.

INHIBITION OF FREE FATTY ACID RECEPTOR GPR40 ABOLISHES CARDIOPROTECTION CONFERRED BY INTRALIPID IN TWO RODENT MODELS OF BUPIVACAINE CARDIOTOXICITY AND ISCHEMIA REPERFUSION INJURY

AUTHORS: S. Umar, J. Li, P. Partownavid, A. Mahajan, M. Eghbali

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INTRODUCTION: We have previously shown that Intralipid (ILP) protects the heart against ischemia/reperfusion (I/R) injury and Bupivacaine cardiotoxicity. However the underlying mechanism of this protection is not fully understood. Free fatty acid receptor-1 or GPR40 is expressed in the heart and is activated by medium and long chain fatty acids. We explored whether cardioprotective effects of ILP are mediated, at least in part through GPR40 in two animal models of I/R injury and Bupivacaine cardiotoxicity.

METHODS: Bupivacaine cardiotoxicity: Sprague-Dawley rats were used. Continuous Echo and ECG were performed. In protocol-1 (n=3) rats received Bupivacaine bolus (10mg/kg, IV) to induce asystole. Resuscitation with ILP 20% (5ml/kg bolus, and 0.5ml/kg/min maintenance) and chest compressions were initiated. In protocol-2 (n=3) rats were pre-treated with GPR40-antagonist GW1100 (200uM, IV) 30-min before inducing asystole. Heart rate (HR) and ejection-fraction (EF) were measured before and 30 min after GW. In both protocols, HR, EF and fractional shortening (FS) were measured before asystole (baseline) and at 1, 5 and 10 min after ILP. I/R: Mice hearts were perfused on Langendorff with Krebs Henseleit (KH) buffer. Aorta was clamped for 20 min to induce global ischemia at 370C, followed by 40 min reperfusion with KH (CTRL), 1% ILP (ILP), or with 1% ILP together with GW (10μM, ILP+GW). A catheter was inserted into LV to measure LV systolic pressure (LVSP), LV end-diastolic pressure (LVEDP) and HR. The LV developed pressure (LVDP) was calculated as LVSP-LVEDP and rate pressure product (RPP) as HRxLVDP. The dP/dtmax and -dP/dtmin were calculated. IACUC approval obtained, n=3-7/group and data expressed as mean±SEM. Results: Bupivacaine cardiotoxicity: In protocol-1, baseline HR and EF were 321±21 beats/min and 72.3±4.6%. Bupivacaine resulted in asystole and ILP improved HR gradually; HR was 86±13 at 1 min (27% recovery), 216±10 at 5 min (67% recovery), and 228±14 at 10 min (71% recovery). LV function fully recovered within 5 min of ILP as EF and FS were similar to baseline (EF=72±5%, FS=42±4%). In protocol-2, there were no significant differences between HR and EF before (HR=316.6±3.3, EF=68.0±2.3%) and 30 min after GW (HR=330±5.7, EF=71.6±1.5%) excluding GW effects on hemodynamics. GW pre-treatment however prevented ILP rescue, with no recovery of cardiac function even after 10 min. I/R: ILP significantly improved RPP from 2349±1824 in CTRL to 10213±1217 in ILP. GW prevented protective effect of ILP since the RPP in ILP+GW was significantly lower than ILP (2186±674, n=7). LVDP was also lower in ILP+GW compared to ILP alone (22.6±3.9 in ILP+GW, 70.6±13.2 in ILP, 11.9±6.7 in CTRL, $p<0.01$ ILP+GW vs. ILP). ILP+GW also had much lower LV dP/dtmax and LV dP/dtmin compared to ILP (dP/dtmax=749.1±14.6 in ILP+GW, 2127.4±408 in ILP, 338.4±248 in CTRL $p<0.01$ ILP+GW vs. ILP; dP/dtmin=-443±99 in ILP+GW, -1464±206 in ILP, -243±168 in CTRL, $p<0.01$ ILP±GW vs. ILP).

CONCLUSIONS: GPR40 is involved in ILP's cardioprotection against Bupivacaine cardiotoxicity and I/R injury, as pre-treatment with a selective GPR40 antagonist prevents ILP's rescue.

S-406.

VALIDATION OF ANESTHETIC BINDING SITES WITHIN THE GABAA RECEPTOR VIA *IN SILICO* DOCKING SCORES OF PROPOFOL DERIVATIVES AND NONIMMOBILIZER CONTROLS

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INTRODUCTION: General anesthetics are thought to potentiate the inhibitory currents of ligand-gated ion channels (LGIC) through drug-specific binding sites. Although the exact molecular structure of the heteropentameric GABAa LGIC remains unknown, molecular modeling has allowed significant advancements in understanding anesthetic binding and action. Novel three-dimensional models of the GABAa receptor (GABAaR) recently constructed via homology modeling techniques revealed putative anesthetic binding cavities within the α/β and β/γ intersubunit spaces. The binding affinities for propofol derivatives docked into these cavities were calculated and correlated with experimentally measured GABAaR EC50 values in order to verify model reliability.

METHODS: The α/β and β/γ subunits were individually extracted from the previously constructed GABAaR homology model via Discovery Studio 4.1 software. The binding cavity within each intersubunit space was defined from the convergence of three residues notable for anesthetic activity.[1] A propofol molecule was manually docked within the selected binding spaces utilizing 3D technology to avoid steric hindrance and ensure proper orientation within the cavities. The automated Flexible docking algorithm surveyed the protein conformational space in relation to varied propofol ligand poses to achieve an energetically optimized binding cavity. The rigid CDOCKER algorithm was then applied to each cavity configuration to dock a series of propofol derivatives. The calculated binding affinities were correlated with their known EC50's at the GABAaR. The cis and trans forms of the non-immobilizer compound 1,2-dichlorohexafluorocyclobutane (F6), which lack anesthetic activity, were included in these docking trials as negative controls.

RESULTS: The Flexible docking algorithm produced an energetically favorable binding pocket for propofol at the essential residue convergence site within both the α/β and β/γ intersubunit space. The calculated binding affinities for the propofol derivatives docked into these sites showed strong log-linear correlation with EC50 data (α/β R2 =0.93, β/γ R2 =0.90). The docking scores for cis-F6 and trans-F6 within the α/β binding cavity were 30.84 kcal/mol and 28.19 kcal/mol, respectively, with very similar results obtained within the β/γ binding cavity.

CONCLUSIONS: The in silico binding affinities for propofol derivatives docked within the α/β and β/γ intersubunit cavities showed log-linear correlation with experimentally derived GABAaR potentiation, suggesting binding sites that may be important for receptor activation. The F6 molecule displayed unfavorable docking energies within both cavities, indicating a lack of affinity for these binding sites in accordance with its clinical profile. While these results validate the structure of this model, further exploration of potential binding sites within the GABAaR is necessary to better understand receptor modulation.

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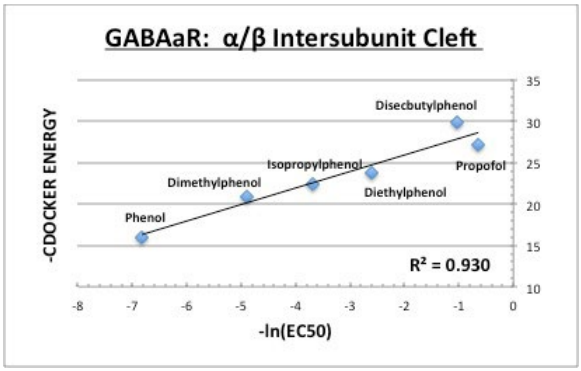

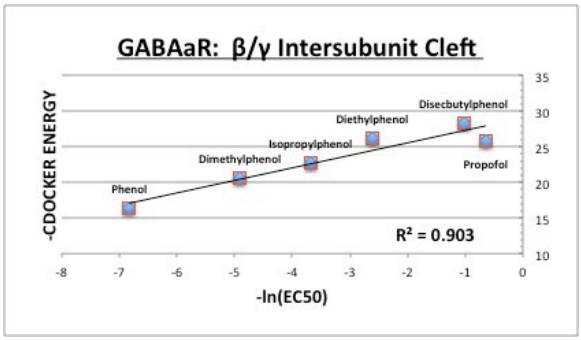

S-407.

THE IMPACT OF INTRAOPERATIVE NITROUS OXIDE ON PATIENT-CENTERED OUTCOMES AND HOSPITAL UTILIZATION

AUTHORS: K. Ruscic[1], S. Grabitz[1], T. Kurth[2], M. Eikermann[1]

AFFILIATION: [1]Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, MA, [2]Institute of Public Health, Charité Universitätsmedizin Berlin, Berlin, Germany.

INTRODUCTION: Nitrous oxide (N_2O) is often avoided as an anesthetic due to potential side effects. Using a dataset of more than 100,000 patients, we explored effects of N_2O on patient-centered outcomes. Prior smaller studies failed to show a significant effect of N_2O use on change in hospital length of stay[1], risk of death or CV complications[2]. Indeed, N_2O use has been associated with decreased mortality and respiratory complications[3]. We tested the hypothesis that N_2O use decreases adverse discharge disposition (death or discharge to a nursing facility without preoperative nursing home residence), hospital length of stay, costs, and hospital readmission rate.

METHODS: We studied 108,264 adults undergoing general anesthesia with endotracheal intubation for non-cardiac surgery (Table 1). The age-adjusted minimal alveolar concentration (MAC) of N_2O during surgery (mean end-tidal concentration averaged over surgery duration) was divided into equal tertiles: 0 (0-0), 0.195 (0.100 - 0.347), 0.564 (0.502-0.632) (median, (interquartile range)). Covariates were defined a priori to control for potential confounding in regression models, including gender, age, BMI, admission type, emergency surgery, ASA class, SPORC and CII index, duration of surgery, vasopressor equivalents, morphine equivalents, NMBA dose, hypotensive minutes, intraoperative fluid, volatile anesthetics, work RVU, and FiO_2. Primary outcome was adverse discharge disposition. Secondary outcomes included hospital length of stay, healthcare costs, and hospital readmission.

RESULTS: Adverse discharge disposition occurred in 6,140 cases and did not correlate with N_2O use (Table 2, Fig 1A). In accordance with our hypothesis, hospital length of stay, healthcare cost, and readmission rate were lower at high compared with low N_2O doses (Table 2, Fig 1 B-E). The association between N_2O dose and postoperative outcomes remained significant in several sensitivity analyses.

CONCLUSIONS: Intraoperative N_2O use is associated with lower hospital length of stay, total hospital costs and hospital readmission rate without increasing adverse discharge disposition for patients.

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Table 1: Characteristics of the Study Population, by median effective dose equivalent of nitrous oxide.
Values are presented as mean (standard deviation) unless stated otherwise.

Characteristics	Median effective dose equivalent of nitrous in tertiles median [interquartile range]			Total
	1 0 [0-0.01] n = 36 088	2 0.19 [0.10-0.35] n = 36 088	3 0.56 [0.50-0.63] n = 36 088	0.19 [0.01-0.50] n = 108 264
Frequency (percentage) gender, male	14893 (41.27)	16769 (46.47)	17162 (47.56)	48824 (45.1)
Age, years	53.83 (16.24)	52.6 (16.63)	57 (15.99)	54.48 (16.4)
Body mass index kg/m²	28.54 (7.47)	28.95 (7.32)	28.27 (6.31)	28.59 (7.06)
Frequency (percentage) American Society of Anesthesiologists (ASA) physical status classification				
1	2958 (8.2)	3752 (10.4)	3280 (9.09)	9990 (9.23)
2	20468 (56.72)	21380 (59.24)	22542 (62.46)	64390 (59.47)
3	12001 (33.25)	10441 (28.93)	9820 (27.21)	32262 (29.8)
4	661 (1.83)	515 (1.43)	446 (1.24)	1622 (1.5)
Duration of surgery, minutes	171 (119)	166 (122)	192 (115)	176 (120)
Relative value units	15.33 (10.78)	16.25 (11)	17.63 (10.32)	16.41 (10.74)
Frequency (percentage) emergent/urgent	1466 (4.06)	1800 (4.99)	1217 (3.37)	4483 (4.14)
Frequency (percentage) ambulatory procedure	10529 (29.18)	9154 (25.37)	5905 (16.36)	25588 (23.63)
Frequency (percentage) neuraxial anesthesia	2914 (8.07)	3871 (10.73)	1029 (2.85)	7814 (7.22)
Total fluids administered, mL	1692 (2079)	1682 (2648)	1821 (2767)	1732 (2517)
Morphine equivalent dose, mg	5.32 (7.24)	5.87 (7.59)	6.98 (8.31)	6.06 (7.76)
Non-depolarizing NMBA dose, ED95/kg/h	2.56 (2.51)	2.66 (2.36)	2.95 (2.43)	2.72 (2.44)
Volatile anesthetics, age-adjusted MAC	0.68 (0.36)	0.61 (0.28)	0.46 (0.21)	0.58 (0.31)
Time MAP<55 mmHg, minutes	1.97 (9.39)	2.42 (13.63)	2.1 (15.22)	2.17 (12.98)
Vasopressor equivalent	0.26 (3.28)	0.26 (8.08)	0.29 (17.25)	0.27 (11.16)
Charlson Comorbidity Index (1)	1.23 (1.42)	1.19 (1.4)	1.05 (1.28)	1.15 (1.37)
Score for prediction of postoperative respiratory complications (2)	1.84 (2.12)	1.82 (2.15)	1.78 (2.21)	1.81 (2.16)

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S-407 • continued

Table 2: Primary and secondary unadjusted and adjusted outcomes, by median effective dose equivalent of nitrous oxide.

Characteristics	Median effective dose equivalent of nitrous in tertiles median [interquartile range]			Total
	1 0 [0-0.01] n = 36 088	2 0.19 [0.10-0.35] n = 36 088	3 0.56 [0.50-0.63] n = 36 088	0.19 [0.01-0.50] n = 108 264
OUTCOMES				
Frequency (percentage) adverse discharge disposition	1597 (4.43)	1816 (5.03)	2727 (7.56)	6140 (5.67)
Mean (SD) postoperative hospital length of stay, days	4.26 (6.25)	4.39 (5.65)	4.15 (5.06)	4.27 (5.68)
Frequency (percentage) readmission within 30 days	3280 (9.09)	2896 (8.02)	2597 (7.2)	8773 (8.1)
Frequency (percentage) postoperative major respiratory complications within 7 days	1479 (4.1)	1578 (4.37)	937 (2.6)	3994 (3.69)
ADJUSTED OUTCOMES				
Adjusted frequency (95% CI) adverse discharge disposition	351 (289-414)	358 (296-421)	355 (290-419)	
Adjusted mean (95% CI) postoperative hospital length of stay, days	3.35 (3.32-3.38)	3.28 (3.25-3.31)	3.09 (3.06-3.12)	
Adjusted frequency (95% CI) readmission within 30 days	2437 (2321-2553)	2271 (2175-2368)	2129 (2007-2251)	
Adjusted frequency (95% CI) postoperative major respiratory complications within 7 days	590 (539-641)	565 (518-612)	478 (429-527)	

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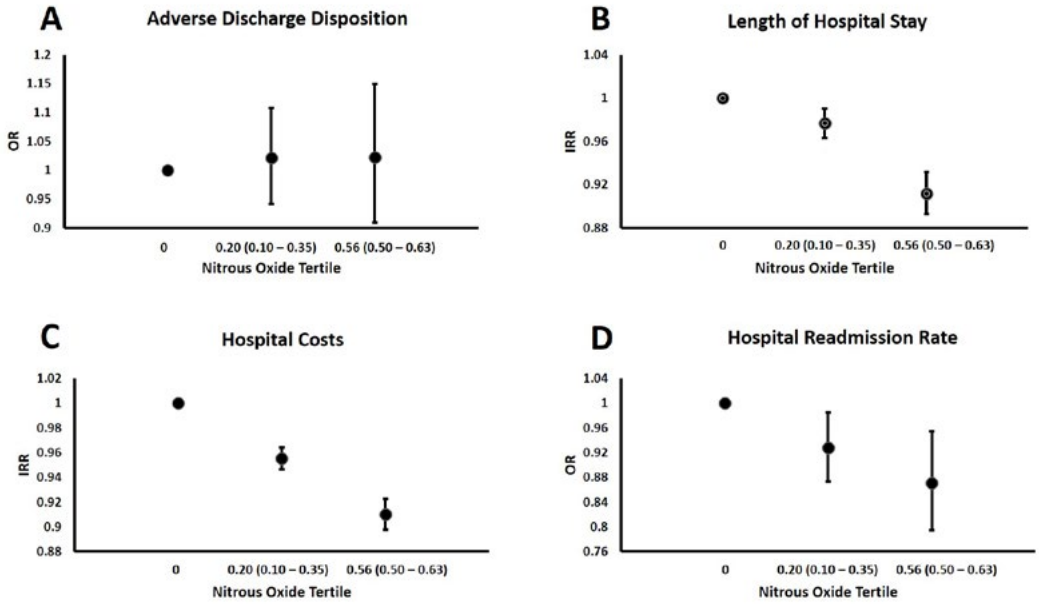

Figure 1: Odds ratio (OR) or incidence rate ratio (IRR) for each nitrous oxide tertile for adverse discharge disposition (A), length of Hopital stay (B), hospital costs (C), and hospital readmission rate (D). Error bars represent 95% confidence intervals. Nitrous oxide tertiles are age-adjusted MAC median (interquartile ranges).

S-408.

TOP DOWN MASS SPECTROMETRY OF THE BETA-3 HOMOPENTAMERIC GABA RECEPTOR

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INTRODUCTION: The GABA receptor is highly regulated by post-translational modifications (PTMs), which determine channel function, trafficking and pharmacology. While the sites of multiple PTMs have been identified in several subunit isoforms, the exact amino acid sequence and combination of PTMs that make up the protein species expressed in cells, also known as proteoforms, remain unknown. It is likely the case that proteoforms, and not just a single PTM, determine the structure of the GABA receptor, and thus how it interacts with regulatory proteins and drugs. Top down mass spectrometry permits the determination of proteoforms by the analysis of intact proteins with high resolution mass spectrometry followed by fragmentation to determine amino acid sequence and localize PTMs.

METHODS: We have developed a recombinant doxycycline-inducible expression system for a TAP (tandem affinity purification)-tagged His8x-FLAG-TEV-beta3 human GABA receptor in HEK cells. The protein was solubilized in DDM/CHS, and purified with a FLAG M2 antibody column and Ni-NTA column. Bottom up mass spectrometry was performed on an Elite LTQ-Orbitrap mass spectrometer as previously described[1]. For top-down mass spectrometry, chloroform/methanol precipitation was performed prior to direct injections into the Elite, and fragmentation performed with CID and HCD.

RESULTS: High levels of expression of His8x-FLAG-TEV-beta3 GABA receptor have been obtained, and orthogonal purification resulted in better purity than FLAG purification alone. Bottom-up mass spectrometry yielded greater than 80% sequence coverage, and deglycosylation with PNGase F identified three known N-glycosylation sites. We have optimized sample preparation and instrument capability for high resolution top down mass spectrometry by utilizing KirBac1.1, which is a more tractable bacterial membrane protein easily produced in high abundance. High resolution scans on an Elite LTQ-Orbitrap demonstrated multiple KirBac1.1 proteoforms with isotopic resolution and fragmentation by CID and HCD yielded more than 30% sequence coverage. We are currently in the process of characterizing the full complement of beta-3 GABA receptor proteoforms.

CONCLUSIONS: We have optimized methodology for top down mass spectrometry of membrane proteins, and this effort applied to the GABA receptor represents a novel and key step towards better understanding GABA receptor biology. In addition, the ability to characterize the GABA receptor by top down mass spectrometry may help overcome challenges associated with identifying photolabeled adducts of hydrophobic ligands as well as reveal ligand binding stoichiometry.

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S-409.

AGE DEPENDENT TRENDS IN ANESTHETIC ADMINISTRATION, AND THE AGE DEPENDENT DECREASE IN MAC: A SINGLE CENTER RETROSPECTIVE STUDY AND REGRESSION ANALYSIS OF PUBLISHED STUDIES

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INTRODUCTION: Previous studies have shown anesthetic sensitivity (i.e. MAC) changes with age,[1] and excessive anesthetic administration increases the incidence of postoperative cognitive dysfunction[2] and delirium.[2,3] However, the last meta-analysis to measure the extent of age-dependent MAC changes was published in 1996,1 and many new studies have since been published. Further, only one prior study has examined the extent to which extent anesthesiologists alter anesthetic administration in older patients.[4] We conducted a meta-regression analysis to determine how much MAC changes with age, and a single center retrospective study to determine the extent to which the mean delivered MAC changed with age. We also analyzed the relationship between MAC, brain response (as measured by mean Bispectral Index scores), and age.

METHODS: We used Mapleson's meta-regression technique[1] to analyze age dependent MAC changes. We combined the studies previously analyzed,[1] and any new human studies identified in a Pubmed search for the keywords "minimum alveolar concentration" and a named anesthetic gas.[3]

For the single center retrospective study, we used a similar regression model to examine all surgical cases at our institution during a 2-year period in patients over age 30 who received a single inhaled anesthetic. We excluded cases with continuous IV anesthetic infusions, and those in which the core temperature dropped below 34 degrees C.

RESULTS: In our regression model of published studies containing 1245 patients, MAC declined by 5.92% per decade of age (95% CI=[4.82%-7.00%]). 17167 surgical/anesthetic cases from our center met inclusion criteria for our retrospective study, and the average end tidal MAC decreased by an estimated 3.75% per decade, 95% CI=[3.52%-3.98%]. There was a signficant difference in the model predicted end tidal MAC decrease in our cases versus the published age dependent MAC decrease ($p < 0.0001$). Older patients at our center received a higher age adjusted MAC fraction, and displayed higher mean BIS values.

CONCLUSIONS: We conclude that MAC decreases by ~6% per decade, similar to Mapleson's prior estimate.[1] Our data provide further evidence that anesthesiologists do not fully decrease anesthetic administration by this amount in older patients. Older patients received increased age adjusted MAC administration, but paradoxically displayed higher BIS values.

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Scholars' Abstracts

Cardiovascular Anesthesiology

S-410.

FTY720 PREVENTS OXLDL INDUCED MACROPHAGE TRAPPING VIA REDUCTION OF HEME OXYGENASE 1 EXPRESSION IN ATHEROSCLEROTIC BURDEN MICE

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: The mortality rate of perioperative myocardial infarction is high and preventive strategies are scarce[1]. Macrophages (MØ) recruited from the circulation destabilize atherosclerotic lesions[2]. Thus, induction of MØ egress out of atherosclerotic lesions into the circulation or into lymphatics may be a potential therapeutic strategy to stabilize atherosclerotic plaques[3]. High expression of heme oxygenase 1 (HO-1) is associated with MØ accumulation and predicts an unstable plaque phenotype[4]. The Sphingosin-1-phosphate (S1P) receptor system regulates the expression of HO-1[5].

METHODS: After IRB approval thioglycolate elicited MØ were stimulated with oxLDL (oxMØ) or vehicle (MØ). The S1P-analogue FTY720 (Sigma) was used at 10 and 50ng/ml (in vitro) and 1µg/g bw p.o. (in vivo). HO-1 mRNA and protein levels were measured after FTY720 stimulation by RT-PCR and Western Blot. In vivo, MØ egress from sites of inflammation was studied after cell injection into the peritoneal cavity. Mice were treated with vehicle or FTY720 one day before till 24 hrs after cell injection. Remaining MØ and MØ that homed into regional lymph nodes (LN) or blood were quantified by flow cytometry. To study MØ egress from atherosclerotic plaques DiR (Invitrogen), labeled MØ were injected into the tail vein of ApoE-/- mice fed a high-cholesterol diet for 16 weeks. MØ were allowed to home into plaques for 2 days before 4-day FTY720 treatment was started. Egressing MØ in the adventia of the innominate artery were quantified on immunohistochemistry stainings for CD68 (clone MEC 13.3). MØ remaining in atherosclerotic lesions were measured via 2D Fluorescence reflectance imaging of dissected aortas. Data were analyzed by Mann-Whitney-U- or Kruskal-Wallis-Test followed by Dunn's post test.

RESULTS: Exposure of oxMØ to FTY720 led to reduced HO-1 mRNA ($n=7$, $p<0.05$) and protein levels ($n=7$, $p<0.05$). After injecting MØ into the peritoneum of mice to quantify egress in vivo, lavage of the abdominal cavity had quantitatively more MØ in the oxMØ group than in controls ($n=3/4$, $p<0.05$). Oral FTY720 treatment reduced the number of oxMØ in lavage ($p<0.001$) but increased in blood ($p<0.05$) and LN ($p<0.001$) ($n=8/9$) indicating increased egress. Ex vivo induction of HO-1 led to opposing results ($n=5$, $p<0.05$). More egressing MØ were detectable in the adventitia of the innominate artery after a 2 day FTY720 treatment compared to vehicle ($n=7$, $p<0.03$) Fluorescence reflectance imaging for quantification of MØ remaining inside the lesion showed less signal in the 4 day FTY720-treatment group compared to vehicle ($n=9/10$, $p<0.01$).

CONCLUSIONS: FTY720 prevented the oxLDL mediated MØ trapping via reduced HO-1 expression in vivo. In mice suffering atherosclerosis FTY720 induced MØ egress from plaques and rapidly promoted a more stable plaque phenotype offering potential perioperative treatment strategies for high-risk patients.

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S-411.

TRPA1 ACTIVATION REDUCES MYOCARDIAL INJURY IN RODENTS

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INTRODUCTION: The transient receptor potential ankyrin 1 (TRPA1) is traditionally viewed as a nociceptor responding to temperature, electrophiles, and noxious stimuli[1]. However, TRPA1 may also be an intracellular sensor for oxygen tension and perhaps an important regulator responding to hypoxia and hyperoxia[2]. In this study, we determined whether TRPA1 is present in the heart and further if TRPA1 activation reduces myocardial infarct size. We also determined whether TRPA1 is important for mediating opioid-induced cardioprotection.

METHODS: After obtaining IACUC approval, the study consisted of both in vivo and in vitro studies of myocardial injury and biochemical analysis.

Initially, left ventricle-derived H9C2 cells and left ventricle from male Sprague-Dawley rats were used to characterize TRPA1 presence at the heart by PCR, western blot, and immunofluorescence. Further, isolated adult rat primary cardiomyocytes (n=3 biological replicates) were also subjected to 2 hypoxia followed by 4 hours reoxygenation. After 4 hours, cell death was measured by trypan blue exclusion. A subset of these groups received either vehicle (DMSO) or a TRPA1 activator (Opotovin 1μM or ASP7663, 3μM) immediately before hypoxia.

For the in vivo studies, male Sprague-Dawley rats (n=6 per group) were anesthetized, instrumented, and subjected to 30 min of ischemia followed by 2 hours of reperfusion. The TRPA1 activators, opotovin, (1mg/kg) or ASP7663 (3mg/kg) were given through the internal jugular vein 5min before ischemia. In additional groups, rodents were given morphine (MOR, 0.3mg/kg) 5min before ischemia. Sub-sets of these rodents received either the TRPA1 inhibitors TCS5861528 (1mg/kg) or AP18 (1mg/kg) 15min before morphine. Infarct size was assessed by triphenyltetrazolium staining.

RESULTS: By western blot and qPCR, TRPA1 was identified in H9C2 cells and the left ventricle. Immunofluorescence revealed TRPA1 was also in primary adult cardiomyocytes. The two selective TRPA1 activators given before hypoxia reduced cardiomyocyte cell death (optovin, 23±2*%, ASP7663, 27±3*% versus control, 37±1%, *P<0.01 versus control).

For in vivo studies, the two selective TRPA1 activators reduced myocardial infarct size (Figure 1, optovin: 44±3%, ASP763: 45±2%, versus control 66±2%, *P<0.01). Selective inhibition of TRPA1 also blocked morphine-induced infarct size reduction (TCS5861528: 62±2%, AP18: 65±3% versus morphine: 44±2*% and control: 66±2%, *P<0.01 versus all other groups).

CONCLUSIONS: Our results suggest TRPA1 is present in the cardiac myocyte and activation can reduce myocardial injury for both isolated cardiomyocyte and in vivo rodent models. This is the first study, to our knowledge, to show that TRPA1 is present in the cardiac myocyte and serves a role in protection from ischemia-reperfusion injury. This is important for anesthesiologists since drugs inhibiting TRPA1 for pain control may block pathways which protect from ischemia-reperfusion injury.

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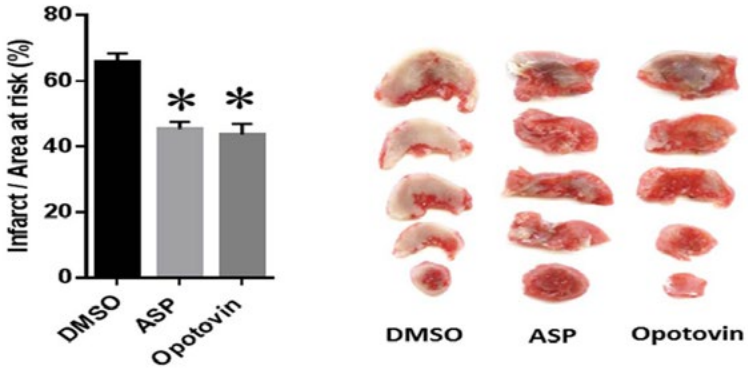

Figure. Infarct size results showing either ASP or Opotovin, two TRPA1 activators, given 5 min prior to ischemia, can reduce infarct size.

S-412.

PATHOPHYSIOLOGY OF PERIOPERATIVE ACUTE CORONARY SYNDROMES: A CORONARY ANGIOGRAPHIC INVESTIGATION

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INTRODUCTION: Approximately 5% of patients age 45 or older undergoing noncardiac surgery experience a cardiac complication, with perioperative myocardial infarction (PMI) being most prevalent. The pathophysiology of PMI remains poorly understood. Although mismatch in myocardial blood supply-oxygen demand (type 2) has classically been believed to antecede many perioperative MIs, strong evidence to support this hypothesis remains lacking. Other studies have suggested that plaque rupture (type 1) may be an underappreciated etiology of PMI. While a plethora of studies have focused on risk assessment and prevention of myocardial ischemia in the perioperative period, limited evidence exists regarding the etiology of PMI.

METHODS: Following IRB approval, we reviewed hospital records and coronary angiograms of adult patients who underwent angiography for acute coronary syndrome (ACS) within 30 days of noncardiac surgery at a major tertiary hospital between 1/2008-12/2015. Angiograms were retrospectively reviewed independently by an interventional cardiologist and an interventional cardiology fellow who were initially blinded to clinical data and outcomes, and when interpretation was discordant, electrocardiogram, procedure note and/or echocardiogram findings were reviewed to reach consensus. Based on the findings, the etiology was classified as type 1 (plaque rupture), type 2 (supply/demand mismatch), or type 4b (stent thrombosis).

RESULTS: 145 patients were identified. More than half of patients (51%) had pre-existing CAD and 44% were on beta-blockers at the time of surgery. The distribution of MI types 1 (plaque rupture), 2 (supply/demand mismatch), and 4b (stent thrombosis) was 26.9% (39/145), 71% (103/145), and 2.1% (3/145), respectively. Thirty-day mortality was 3.4% (5/145); one patient died following type I MI, and four patients following type II. Median peak post-operative troponin I was 3.2 ng/ml (IQR 0.9-8.2), and median time to peak troponin was 1.8 days (IQR 0.8-2.9). The median hospital length of stay was 9.3 days (IQR 6.3-14.3).

CONCLUSIONS: In this single center cohort, nearly 3 out of 4 patients who underwent coronary angiography for ACS following noncardiac surgery had supply/demand mismatch compared to a primary coronary event as the etiology. To date this is the largest angiographic series of patients with perioperative ACS.

S-413.

HIGH-SENSITIVITY CARDIAC TROPONIN FOR THE DIAGNOSIS OF PERIOPERATIVE MYOCARDIAL INJURY AND INFARCTION: A COMPARISON OF DIFFERENT APPROACHES

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INTRODUCTION: A particularly notable feature of recently introduced high-sensitivity cardiac troponin (hscTn) assays is the ability to detect preoperative baseline values, which allows the comparison with postoperative values and the quantification of relative and absolute change. Change metrics for hscTn have been advocated by experts for the diagnosis of acute MI. However, for the diagnosis of perioperative myocardial injury or infarction (MI) no evidence exists as to which metrics may be optimal.

METHODS: In an ancillary study to the Vitamins in Nitrous Oxide Trial, we compared several approaches to diagnose perioperative MI according to the Third Universal Definition of MI. Myocardial injury was defined as cardiac troponin elevation without ischemic ECG changes. Patient had serial 12-lead ECGs and standard cTnI as well as hscTnT obtained preoperatively and on the first 3 postoperative days. To diagnose MI, two conditions had to be met: (1) ECG changes indicative of myocardial ischemia and (2) cTn elevation >99th percentile URL.

RESULTS: Out of 607 study patients, 70 patients developed ischemic changes on postoperative ECGs (11.5%). 82 patients (13.5%) developed new postoperative cTnI elevation using a standard assay. 351 patients (57.8%) developed a new hscTnT elevation >99th percentile; 177 patients (29.2%) had a >50% hscTnT increase, and 89 patients a >100% increase (14.7%). Using standard cTnI plus ischemic ECG signs as criteria, 35 patients (5.8%) met the criteria for postoperative MI. Using hscTnT plus ischemic ECG signs as criteria, up to twice as many patients met the criteria for acute MI (max: n=63, 10.4%; Table 1). Based on the hscTnT metric, the incidence rate of postoperative myocardial injury was between 7.9% (n=48) and 52.6% (n=319).

CONCLUSIONS: The adoption of novel hscTn assays has the potential to substantially increase the number of patients who meet the criteria for postoperative MI and myocardial injury compared to standard cardiac troponin assays. The choice of hscTn metric will have a substantial influence on incidence rates.

Table 1: Patients who meet Diagnosis of MI by Day

Standard cardiac- Troponin I	EOS	POD1	POD2	POD3	Total Number of MI
New Postop is >=99th %tile (>=0.07 ug/L)	4	13	17	11	35 (5.8%)
New Postop is >=99th %tile and baseline cTnI is <99th %tile	1	9	15	10	29 (4.8%)
cTnI increase >=50% from baseline and baseline is <99th%tile, or cTnI increase >=20% from baseline and baseline is >99th%tile **(ACCF 2012 definition)**	3	15	18	11	37 (6.1%)
High sensitivity- cardiac Troponin T (hs-cTnT)	**EOS**	**POD1**	**POD2**	**POD3**	**Total Number of MI**
Postop hs-cTnT >=99th%tile	17	37	26	12	63 (10.4%)
Postop hs-cTnT >=99th%tile if baseline <99th percentile	2	10	6	5	18 (3.0%)
Postop hs-cTnT increased >=50% from baseline	5	19	16	9	39 (6.4%)
Postop hs-cTnT increased >=50% from baseline and baseline hs-cTnT <99th%	2	9	7	5	16 (2.6%)
Postop hs-cTnT increased >=100% from baseline	4	12	13	9	33 (5.4%)
Postop hs-cTnT increased >=100% from baseline and baseline hs-cTnT <99th%	2	6	6	5	15 (2.5%)
Postop hs-cTnT increased by >=100% if baseline <99th%, or increased by >=50% if baseline hs-cTnT >99th%	5	17	15	9	39 (6.4%)
Postop increased by 5µg/L or more compared to baseline hscTnT	7	23	19	10	44 (7.2%)
Postop increased by 10 µg/L or more compared to baseline hscTnT	7	18	16	9	37 (6.1%)

S-414.

HEPARINIZED FIBRINOGEN LEVEL VERSUS POST-PROTAMINE REVERSAL FIBRINOGEN LEVEL WHILE ON CARDIOPULMONARY BYPASS: IS THERE A DIFFERENCE?

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INTRODUCTION: The purpose of this study was to determine the accuracy of using intraoperative heparinized fibrinogen levels to identify patients needing cryoprecipitate while undergoing cardiac surgery. If accurate, this information could help anesthesiologist preemptively treat with cryoprecipitate earlier leading to decreased postoperative bleeding and blood products. Presently, an acute bleeding profile (Ie Fibrinogen) is submitted to the laboratory after protamine reversal and rewarming. By attaining the fibrinogen level earlier, one can begin the cryoprecipitate thawing process earlier, (typical time is about 20 minutes) and therefore, administer the product earlier.

METHODS: This was an observational prospective study involving consecutive fifty patients undergoing cardiac surgery requiring cardiopulmonary bypass. For the purpose of this analysis, the treatment criterion for fibrinogen levels was set to < 200 for administering cryoprecipitate. McNemar test was used with significance level of .05 to test whether or not intraoperative heparinized fibrinogen levels could accurately identify patients needing cryoprecipitate (those with fibrinogen level < 200) compared to fibrinogen levels in protamine-reversed heparin samples.

RESULTS: A total of forty-seven patients were included in the final analyses; values for three patients were identified as extreme outliers and were excluded. Based on intraoperative heparinized fibrinogen levels, 46.8% of the patients were identified having fibrinogen levels less than 200. Post-protamine-reversal fibrinogen levels indicated 51.1% of the patients with less than this critical value. The McNemar test showed no statistically significant difference for intraoperative heparinized fibrinogen levels' accuracy in identifying patients needing cryoprecipitate compared to that of fibrinogen levels in protamine-reversed heparin samples (P=0.804).

CONCLUSIONS: The results show that the heparinized samples are representative of an accurate test result prior to protamine reversal. Therefore, we conclude that cryoprecipitate therapy to mitigate further blood loss can be initiated earlier as opposed to waiting for protamine reversal before attaining a fibrinogen sample.

S-415.

NON-CARDIAC SURGERY IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES: AN INSTITUTIONAL OUTCOMES STUDY

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INTRODUCTION: Within the healthcare system, LVADs have become increasingly commonplace.[1] Patients with LVADs have endured successful recoveries and have become managed as outpatients. Over time, such patients have presented for a wide array of non-cardiac procedures.[2,3] This population presents unique perioperative challenges, including management of anticoagulation, hemodynamics, and limits to physiologic monitoring. These challenges are described in numerous studies; additionally, current studies analyze several outcomes and management strategies.[2-4] However, studies are lacking in sample size and are limited in outcome scope. We hypothesize that perioperative complications within this population are currently underreported, and that our study will more specifically elucidate management challenges.

METHODS: Within the anesthesiology database available at our tertiary care academic institution, we investigated adult patents with LVADs undergoing non-cardiac surgery over a ten-year period. Variables studied included medical history, surgical, and anesthetic characteristics for each case, as well as physiologic monitoring data. Outcomes studied included hemodynamic instability, bleeding complications, and organ-system based major perioperative complications.

RESULTS: We describe 247 LVAD patients undergoing 703 non-cardiac procedures at our institution (Table 1). Most commonly, cases involved endoscopy and cardiology procedures; however 158 cases were performed outside of these procedural units. Perioperative bleeding complications were common and management of anticoagulation was variable (Table 2). Hemodynamic monitoring proved problematic; over half of cases exhibited a >20 minute blood pressure monitoring gap, and multiple cases had no blood pressure recording (Table 3). Hypotension and malignant dysrhythmias occurred in a significant number of cases. Most common complications included acute kidney injury, thrombosis, myocardial ischemia, stroke, and seizure; postoperative mortality within 30 days occurred in 14 patients.

Table 1: Case Characteristics

ASA Class3	/ 3E	92 (13%)
	4 / 4E	603 (85%)
	5 / 5E8	(1.1%)
Admission Status	IP/AP	586 (83%)
	OP1	17 (17%)
Anesthetic Technique	General	177 (25%)
	Regional	6 (0.9%)
	MAC	520 (74%)
Common Surgical Services	Cardiology	284 (40%)
	Gastroenterology	261 (37%)

Table 2: Anticoagulation/Bleeding Management

Preoperative Blood Products	PRBCs	26 (3.7%)
	Platelets3	(0.4%)
	FFP	83 (12%)
Intraoperative Blood Products	PRBCs	30 (4.3%)
	Platelets	14 (2.0%)
	FFP	21 (2.9%)
Intraoperative EBL >500cc		10 (1.4%)
Postoperative Blood Products	PRBCs	78 (11%)
	Platelets2	(0.3%)
	FFP	27 (3.8%)

Table 3: Intraoperative Hemodynamics

Arterial Line Used	142 (20%)
Central Line Used	32 (4.6%)
PA Catheter Used1	1 (1.6%)
Transesophageal Echocardiography Used	10 (1.4%)
Blood Pressure Monitoring Gap >20 Minutes	387 (55%)
No Blood Pressure Recorded for Intraoperative Period	31 (4.4%)
MAP <70 mmHg for >20 Minutes	176 (26.5%)
MAP <60 mmHg for >20 Minutes	43 (6.5%)
MAP <50 mmHg for >20 Minutes	10 (1.5%)
Intraoperative Malignant Dysrhythmia9	(1.3%)

Table 4: 30-Day Postoperative Complications

Mortality	14 (2.0%)
Thrombosis (LDH >480 U/L)	41 (5.8%)
Acute Kidney Injury	111 (16%)
Elevated Troponin >0.10 ng/mL	17 (2.4%)
Acute DVT	3 (0.4%)
Seizure	2 (0.3%)
Stroke	5 (0.7%)

S-416.

MORPHINE ACTIVATES ENDOTHELIAL CELLS AND PROMOTES MONOCYTE ADHESION IN VITRO

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I**NTRODUCTION:** Morphine is the most common opioid worldwide. It is well known to protect from myocardial reperfusion injury. However, recent studies suggest that morphine can also promote myocardial infarction (MI).[1-3] The exact mechanism of perioperative MI is obscure, but proteolytic enzymes released from macrophages (MØ) recruited from the circulation can destabilize atherosclerotic plaques.[4] At predilection sites for atherosclerotic plaques endothelial cells (EC) proliferate more frequently and are more adhesive for leukocytes.[5] Morphine but not sufentanil signals via the μ3-opioid receptor.[6] We tested whether morphine activates EC and promotes monocyte adhesion, the prerequisite for infiltration into atherosclerotic lesions.

METHODS: Human EC (fEnd.5) were activated by oxidized low-density lipoprotein (oxLDL) either in the presence of 20ng/ml morphine, 0.02 to 1ng/ml sufentanil or vehicle. In subgroups 1μg/ml naloxone or 1μM atorvastatin were added. We quantified proliferation and after IRB approval measured adhesion of thioglycolate elicited fluorescently labeled MØ to EC in a 30min adhesion assay. Mitomycin was used in some experiments to prevent adhesion. Data following Gaussian distribution were tested using student's t-test or ANOVA with bonferroni test. Data are presented as mean ± SEM. $p<0.05$ was considered significant.

RESULTS: Morphine promoted EC proliferation (125% of control, n=5, $p<0.05$). Morphine induced MØ adhesion to oxLDL activated EC (237±15.3% of control, n=9, $p<0.05$). Naloxone normalized adhesion (87.2±4.1, n=6, p=n.s.) and atorvastatin treatment abolished morphine mediated increased adhesion (135.5±216.1% of control, n=6, $p<0.01$). Incubation with different doses of sufentanil had no statistically significant effect on adhesion. Blocking EC proliferation by mitomycin did prevent morphine-induced adhesion.

CONCLUSIONS: Morphine induced EC proliferation and promoted MØ adhesion. This observation might induce MØ accumulation in atherosclerotic plaques and could thereby explain morphine mediated MI.[1-3] Induction of adhesion is likely mediated via the μ3-opioid receptor, as sufentanil was ineffective. Atorvastatin represents a potential therapeutic strategy. Studies in animal models of atherosclerosis are required to investigate opioid effects on plaque stability.

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Figure 1. Calculated parameters for first 6 hours of monitoring separated by GOS groups.

S-417.

SAFETY OF RAPID RIGHT VENTRICULAR PACING FOR CONTROLLED HYPOTENSION DURING ENDOVASCULAR AORTIC ARCH REPAIR

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INTRODUCTION: Thoracic endovascular aortic repair (TEVAR) is a modern approach for repair of aortic pathology including aneurysm, dissection, and trauma.[1] Stents must be precisely deployed at narrow proximal landing zones near the arch vessels.[2] Deployment is complicated by the hydrodynamics of aortic blood flow that force the stent distally ("wind-sock" effect). Controlled hypotension (SBP < 60 mmHg) is required during deployment to limit stent migration. Various drugs have been used to induce hypotension,[3,4] but rapid right ventricular pacing (RRVP) is emerging as a preferred technique.[5] Small studies have shown efficacy and safety,[6-8] but deaths related to RRVP have been reported.[9] In this study, we seek to determine factors predictive of safe and successful RRVP, with a focus on cardiovascular comorbidities.

METHODS: Approval was obtained from the Committee on Human Research. We reviewed the medical records of patients undergoing RRVP for TEVAR, and gathered details about medical history, aortic disease, the endovascular procedure, hemodynamics, medications, lab values, and imaging studies.

RESULTS: Four cases of TEVAR with RRVP were identified. Patients were elderly (72 ± 9 y) and comorbidities included CAD, history of CHF, aortic valve stenosis, CKD, history of CVA, and COPD. The indications for TEVAR are shown in Figure 1. Central venous sheaths were placed in the right internal jugular or subclavian vein by the anesthesia team, and temporary pacing wires (5 Fr) were placed by a cardiologist. In one case, oozing was noted around a pacing wire passed through the hemostasis valve of a multi-lumen access catheter, likely due to size mismatch.

Stent grafts were placed in the aortic arch in three cases and the ascending aorta in one case. Two cases required arch debranching with carotid-carotid-subclavian bypass, and two cases required secondary stents in the arch vessels (Figure 2). Patients required 2 ± 1 episodes of RRVP. In one case, IV adenosine was first attempted, but unsuccessful. RRVP was performed at 172 ± 11 bpm, and each episode of hypotension lasted less than one minute. All operations were technically successful, there were no intraoperative complications, and 30-day mortality was zero.

CONCLUSIONS: RRVP is a safe and effective method to achieve controlled hypotension during TEVAR. In this study, patients with aortic stenosis, mildly depressed ejection fraction, pulmonary hypertension and non-occlusive CAD tolerated RRVP well. Future work must determine whether patients with more severe CAD, valvular lesions, systolic and diastolic heart failure, and cardiac rhythm disturbances can safely undergo RRVP. Vascular access for TEVAR requires careful consideration. Mismatch between the pacing catheter and sheath was observed to cause oozing in one case, and the risk of air embolus or infection may be increased.

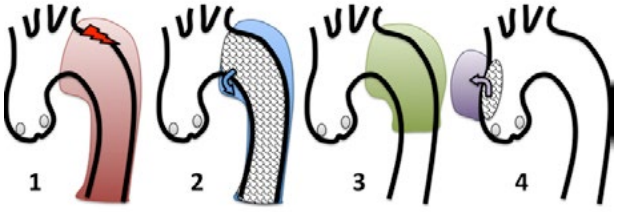

Figure 1. Schematic of aortic arch pathology in patients undergoing TEVAR with rapid right ventricular pacing in this study. (1) Aneurysm with chronic Type B dissection, (2) aneurysm enlarging due to endoleak after prior TEVAR, (3) isolated arch aneurysm, and (4) ascending aortic pseudoaneurysm due to leaking patch at prior aortic cannulation site in a patient with a history of CABG.

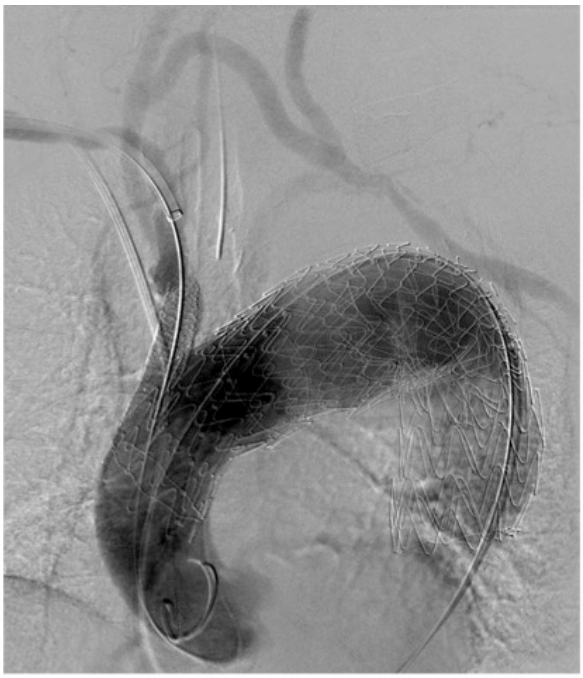

Figure 2. Aortic arch stent, innominate artery "snorkel" stent, and patent carotid-carotid-subclavian bypass after RRVP and deployment of stents.

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S-475.

ALTERING BUFFER Ca2+ AND pH STIMULATES ACTIVATION OF MITOCHONDRIAL Ca^{2+}/H^{+} EXCHANGER

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Calcium overload in mitochondria (m) is well known to contribute to myocyte damage in cardiac ischemia and reperfusion injury. Integral proteins across the inner mitochondrial membrane facilitate transmembrane influx and efflux of Ca^{2+}. Influx of Ca^{2+} occurs primarily by the mitochondrial Ca^{2+} uniporter (mCU) and efflux by the Na^{+}/Ca^{2+} exchanger (NCE). Evidence for activation of Ca^{2+}/H^{+} exchange (CHE), an additional mechanism for Ca^{2+} influx or efflux tied to trans-matrix pH, has been investigated recently but requires further mechanistic understanding. We hypothesized that altered buffer (extra-matrix) pH and $[Ca^{2+}]$ can induce CHE activity as demonstrated by reciprocal changes in matrix pHm and $[Ca^{2+}]$m when mCu Ca^{2+} influx is in equilibration and NCE is prevented by using Na+ free buffer and an NCE blocker (CGP 37157). Our aim was to determine if changing extra-matrix buffer pH alters $[Ca^{2+}]_m$, inferring CHE activity, when Na^{+} and ADP are absent to prevent Ca^{2+} efflux through NCE and hydrogen (H^{+}) uptake through complex V, respectively. To do so, mitochondria were isolated from guinea pig hearts using differential centrifugation, suspended in isolation buffer, and loaded with fura-4-AM, a fluorescent probe used to measure $[Ca^{2+}]$m. Isolated mitochondria were placed in one of 3 experimental buffers (acidic, pH 6.9; physiologic, pH 7.15; or alkaline, pH 7.6). Mitochondria were charged with the Na+-free substrate pyruvic acid (0.5 mM). Matrix levels of Ca2+ were monitored spectrofluorometrically before and after adding a bolus of 40 μM CaCl2 (EGTA ~38-40 μM) to the mitochondrial buffer. Matrix Ca^{2+} levels were monitored for 30 min to permit primary uptake through the mCU and to attain equilibrium. Matrix pH and mitochondrial membrane potential (ΔΨm) were also measured using the fluorescent probes BCECF-AM and rhodamine 123, respectively. We found that mitochondria suspended in pH 6.9 buffer exhibited a delayed, secondary increase in $[Ca^{2+}]$m precluded by a reciprocal decrease in matrix pH. These changes were absent in mitochondria suspended in pH 7.15 and 7.6 buffers. ΔΨm was unaffected by any protocol suggesting that changes in pH and Ca^{2+} were not due to a change in ΔΨm. Although changing buffer pH and $[Ca^{2+}]$ caused changes to pHm and $[Ca^{2+}]_m$, there may be other factors in addition to CHE that explain these observations. Assessment of mitochondrial respiration and proton pumping by blocking complexes I, III, IV, V, and mCU may be necessary to fully evaluate CHE independent of other causes of H^{+} and Ca^{2+} flux. A better understanding of mitochondrial Ca^{2+} uptake, including the role of CHE, may be helpful in treating and reducing cardiac ischemia and reperfusion damage in patients.

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Scholars' Abstracts

Critical Care

S-418.

GOAL DIRECTED EARLY MOBILIZATION REDUCES ICU LENGTH OF STAY AND IMPROVES FUNCTIONAL MOBILITY: AN INTERNATIONAL MULTI CENTER, RANDOMIZED, CONTROLLED TRIAL (SOMS TRIAL)

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INTRODUCTION: ICU-acquired weakness (ICUAW) affects short- and long-term patient outcomes.[1] Immobilization leads to ICUAW. In medical ICU patients, early mobilization resulted in improved patient outcomes,[2] but barriers to early mobilization (pain, open wounds, unstable fractures) might exist in the Surgical Intensive Care Unit (SICU).

We tested the SICU Optimal Mobilization Score (SOMS)3-5 approach to goal-directed early mobilization in a prospective, multicenter, international, randomized, controlled trial.6

METHODS: Following IRB approval and informed consent, mechanically ventilated patients (< 48h at enrollment) expected to require mechanical ventilation for another 24h or more, showing adequate functional independence (Barthel Score ≥ 70) prior to the acute event, were randomly allocated to receive SOMS guided early mobilization (Figure 1) or standard of care.

The primary outcome was the mean daily SOMS level achieved, key secondary outcomes were SICU length of stay (LOS), and mini functional independence measure (mmFIM) score representing functional mobility in the domains locomotion and transfer mobility at hospital discharge. We also quantified hospital length of stay and SICU discharge readiness, in-hospital and 3-month mortality as well as discharge disposition.

RESULTS: 200 patients were randomized and included in the intention to treat analysis (Table 1). There were significant differences in the main primary outcome (mean achieved SOMS 2.2 vs 1.5, $p < 0.001$), and in the key secondary outcomes SICU length of stay (10 vs 14 days, $p = 0.03$), and mmFIM at hospital discharge (6 vs 5, $p < 0.001$). In addition, more patients in the intervention group were discharged home (51% vs. 27%, OR 2.8, $p = 0.001$) (Table 2).

CONCLUSION: Goal directed early mobilization shortened SICU length of stay, and improved functional mobility at hospital discharge. In addition, the exploratory analysis revealed that more patients in the intervention group were discharged home.

Table 1: Baseline Demographic and Clinical Characteristics, According to Study Group.

Variable	Control Group	Intervention Group
	(N = 96)	(N = 104)
Age - yr	59 ± 20	60 ± 17
Male sex - no. (%)	61 (64)	65 (63)
height (inch)	67 ± 6	67 ± 4
weight (lbs)	179 ± 52	177 ± 44
Race - no (%)		
White	84 (88)	91 (88)
Black	5 (5)	4 (4)
Other	7 (7)	9 (9)
Hispanic ethnic group - no. (%)	2 (2)	5 (5)
Characteristics of functional status		
GCS	9 ± 3	10 ± 3
APACHE II	17 ± 7	17 ± 8
Barthel Score	98 ± 6	98 ± 7
Admission Diagnosis - no (%)		
Post-Operative Observation	41 (43)	55 (53)
Trauma	32 (33)	21 (20)
Sepsis	14 (15)	13 (13)
Respiratory Failure	20 (21)	24 (23)
Hemodynamic instability	23 (24)	30 (29)
Bowel obstruction	6 (6)	6 (6)
Pancreatitis	1 (1)	3 (3)
Other	24 (25)	30 (29)
Reasons for Mechanical Ventilation - no (%)		
ARDS/ALI	16 (17)	13 (13)
Pneumonia	6 (6)	8 (8)
COPD/Asthma	6 (6)	4 (4)
Altered mental status	24 (25)	35 (34)
Post operative volume	29 (30)	31 (30)
Cardiogenic	5 (5)	9 (9)
Non-cardiogenic edema	4 (4)	6 (6)
Other	44 (46)	42 (40)
Admission Comorbidities - no (%)		
Diabetes mellitus	18 (19)	19 (18)
CAD (Coronary Artery Disease)	25 (26)	19 (18)
COPD/Asthma	18 (19)	17 (16)
PVD (Peripheral Vascular Disease)	9 (9)	3 (3)
Chronic renal disease	9 (9)	4 (4)
Psychiatric	5 (5)	17 (16)
Musculoskeletal	2 (2)	4 (4)
Other	54 (56)	60 (58)
None	13 (14)	9 (9)
Admission Lab - mean ± SD		
Admission Hb	11.5 ± 2.2	11.2 ± 2.1
Admission Creatinine	1.4 ± 1.1	1.4 ± 1.3
Admission INR	1.3 ± 0.3	1.3 ± 0.4

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Table 2: Primary and Secondary Outcomes.

Variable	Control Group	Intervention Group	Absolute difference	P Value
	(N = 96)	(N = 104)		
Primary Outcome: mean achieved SOMS level over the course of the ICU stay	1.5 ± 0.8	2.2 ± 0.9	0.7 (0.5 to 1.0)	<0.001
Key Secondary Outcomes				
ICU LOS	14 ± 11	10 ± 9 #	-3 (-6 to 0)	0.03
mmFIM at hosptial discharge	5 ± 3	6 ± 2	1 (1 to 2)	<0.001
Secondary Outcomes				
Quality of Life at 3 months after hospital discharge	108 ± 10	107 ± 11	-1 (-6 to 4)	0.68
Muscle weakness defined by MRC scale <48 (%)	69	69	OR: 1.0 (0.5 to 2.1)	0.95
Exploratory secondary Outcomes				
ICU LOS until discharge readiness	13 ± 11	10 ± 9	-3 (-6 to 0)	0.02
Hospital LOS	**25 ± 17**	**22 ± 20**	**-3 (-8 to 3)**	**0.34**
In-hospital mortality (%)	8	16	OR 2.1 (0.9 to 5.2)	0.09
3-month mortality (%)	17	22	OR 1.4 (0.7 to 3.0)	0.35
Discharged Home (%)	27	51	OR 2.8 (1.5 to 5.0)	0.001

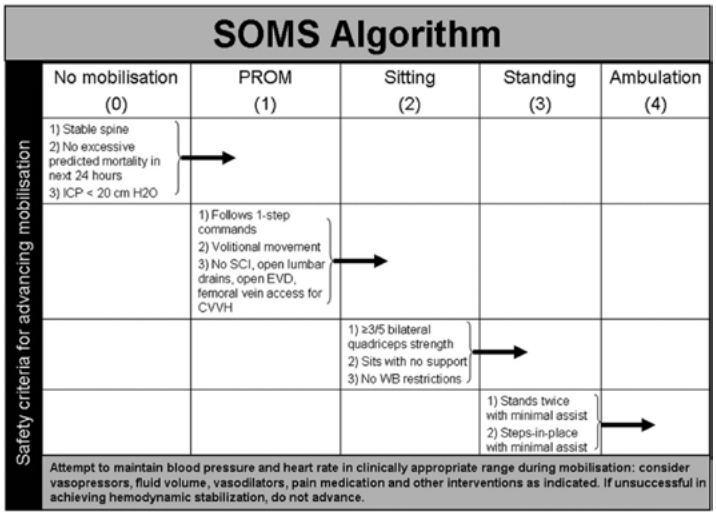

Figure 1. Surgical ICU Optimal Mobilization Score (SOMS) algorithm for goal-directed early mobilization.

S-419.

CONTRIBUTION OF MITOCHONDRIAL OXIDATIVE STRESS IN THE FORMATION OF ENDOTHELIAL-DERIVED MICROVESICLES

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INTRODUCTION: Endothelial-derived microvesicles (eMVs), small membrane-bound particles released from the vascular endothelium in response to various stimuli, are known to be elevated and actively involved in many pathological processes including atherosclerosis, acute kidney disease, and sepsis.[1] We have recently shown that ceramide, a sphingolipid formed during cellular stress[2], is a potent stimulus for eMV formation when administered to human cardiac microvascular endothelial cells (HMVECs). Further, these ceramide-derived eMVs have detrimental effects on the human microvasculature. When given intraluminally to human adipose arterioles, they initiate a switch in the mediator of flow-induced dilation (FID) from anti-inflammatory nitric oxide (NO) to pro-inflammatory, pro-thrombotic, hydrogen peroxide (H_2O_2), the same transition that occurs between health and disease. We have also shown that eMVs generated from plasminogen-activator inhibitor 1 (PAI-1), a known eMV stimulus, are capable of initiating this same switch in vasoactive mediator. Tandem mass spectrometry (MS/MS) analysis revealed that despite protein composition differences, proteins identified in ceramide- and PAI-derived eMVs exhibited strong correlations to mitochondrial dysfunction and oxidative stress. To determine if reactive oxygen species are necessary for the development of ceramide- and PAI-1-generated eMVs, *we hypothesized that suppression of cellular and mitochondrial-derived ROS during PAI-1 or ceramide treatment would impair eMV formation.*

METHODS: HMVEC-Cs were treated with vehicle (DMSO), C2 Ceramide (15 μM), PAI-1 (20 ng/mL), or a mitochondrial pro-oxidant (antimycin A; 10μM) for 3hrs in the presence or absence of the cytosolic antioxidant L-phenylalanine-4'-boronic acid (FBA; 10 μM), or the mitochondria-targeted phenylboronic acid (mitoPBA; 100 μM). To quantify eMV formation, flow cytometry was utilized to count CD31/Annexin V+ vesicles. All data is presented as fold change ± SEM versus vehicle.

RESULTS: eMV formation was significantly increased in all three treatment groups (3.4±0.7, 2.7±0.6, and 3.7±0.9 in ceramide, PAI-1, and antimycin A, respectively, n=4 all groups, $p<0.05$, one-way ANOVA). In FBA-treated cells, eMV generation was only decreased in cells treated with antimycin A (1.3±0.1 vs. 3.7±0.9, n=3 and 4, respectively), whereas mitoPBA significantly decreased the number of eMVs produced in all treatment groups (0.45±0.1, 0.44±0.1, and 0.55±0.1, in ceramide, PAI-1, and antimycin A, respectively, n=3 all groups).

CONCLUSIONS: These data suggest that mitochondrial-derived ROS play a critical role in the formation of eMVs generated by ceramide and PAI-1. We conclude that suppression of mitochondrial ROS and subsequent formation of eMVs may mitigate endothelial dysfunction observed in acute and chronic disease.

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S-420.

REVERSAL OF BURN INJURY-INDUCED INFLAMMATORY RESPONSES AND MUSCLE WASTING BY A NOVEL TARGET, THE NICOTINIC α7ACHRS IN MICE

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INTRODUCTION: Systemic inflammatory response of critical illness (e.g., burn injury [BI]) leads to skeletal muscle wasting (MW) where increased muscle proteolysis plays a critical role[1]. MW in these patients is a major risk factor affecting prognosis[2]. JAK/STAT-pathway activation (phosphorylation) as well as FoxO-mediated transcription has recently been evidenced as a pivotal mediator of inflammatory response-induced protein catabolic processes[3]. We and others have reported that α7 acetylcholine receptors (α7AChRs) are upregulated in macrophages and peripheral tissues including skeletal muscle during denervation, BI and disuse atrophy, and that stimulation of α7AChRs mitigates inflammatory responses[4,5]. This study tested the hypothesis that stimulation of α7AChRs with specific α7AChRs agonist, GTS-21, attenuates inflammation-induced MW in muscle distant to the BI site by modulating JAK/STAT signaling in mice.

METHODS: The study was approved by Institutional Animal Care Committee. 30% total body surface area BI was produced in the trunk under anesthesia. The BI mice received either GTS-21 10mg/kg IP, b.i.d. (Burn-GTS) or saline (Burn-Saline). Sham-burned mice served as controls. Tibialis anterior muscle was harvested on post-burn day 1 or 3 (Day 1 or 3). After weighing muscle, RNA and protein were extracted. Real-time polymerase chain reaction and immunoblots were performed to characterize molecular signals related to inflammatory and proteolytic pathways.

RESULTS: At Day 1, mRNA expression of muscle-specific proteolytic molecules, MuRF1 and atrogin-1, were significantly increased 2.9 and 2.3 fold, respectively, in Burn-Saline mice compared to sham-burned mice (n=8 -16, $p<0.05$) (Fig.1). Compared to Burn-Saline group, Burn-GTS mice had significantly decreased MuRF1 and atrogin-1 expression (MuRF1: Burn-Saline and Burn-GTS: 2.9 and 1.6, atrogin-1; Burn-Saline and Burn-GTS: 2.3 and 1.8, respectively, $p<0.05$) (Fig. 1). Similarly, protein expression of inflammatory and muscle atrogenic proteins, FoxO1 and phosphorylated Stat3 were upregulated in Burn-Saline mice, both of which were significantly decreased in Burn-GTS mice. At Day 3, percent tibialis anterior muscle mass loss normalized to body weight was significantly decreased in Burn-Saline mice, but GTS-21 treatment ameliorated muscle mass loss (Sham-burn vs. Burn-Saline vs. Burn-GTS: 100 vs. 87 vs. 96%, respectively, $p<0.05$) (Fig. 2).

CONCLUSION: These data for the first time document that specific stimulation of α7AChRs with GTS-21, by modulating multiple catabolic molecular signals including decreased expression of MuRF1, atrogin-1, FoxO1 and phosphorylated Stat3, can attenuate protein wasting as evidenced by reversal of muscle mass loss seen in distant muscle of BI mice treated with GTS-21. Thus, α7AChRs stimulation can be a novel, potent therapeutic target for reversal of BI- induced MW.

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Fig. 1a

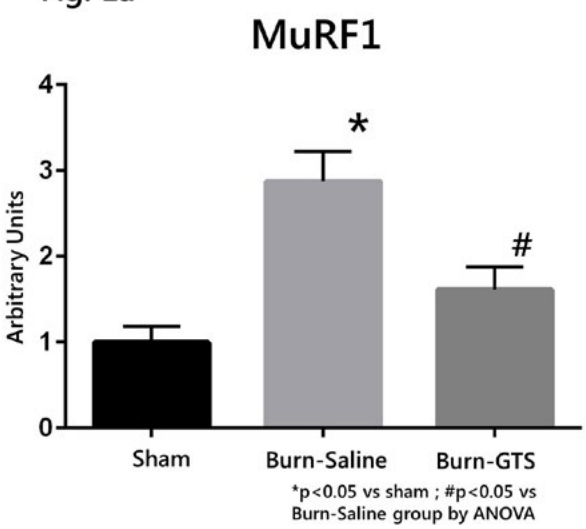

Fig. 1b

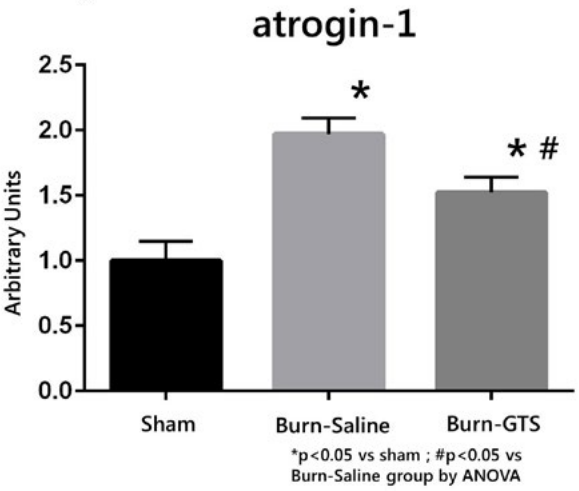

Fig. 2a

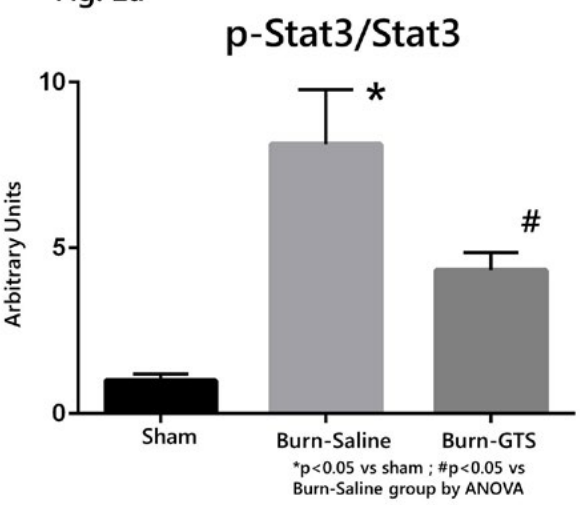

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Fig. 2b

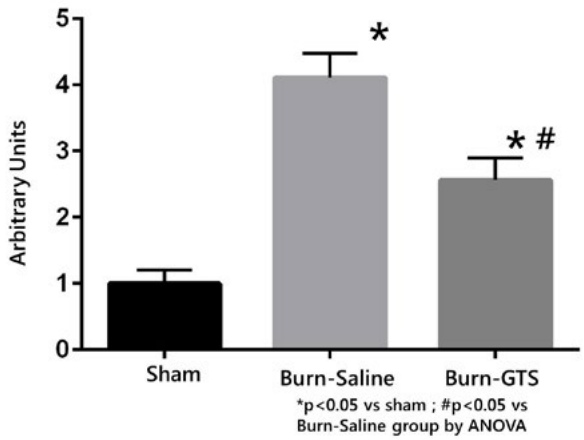
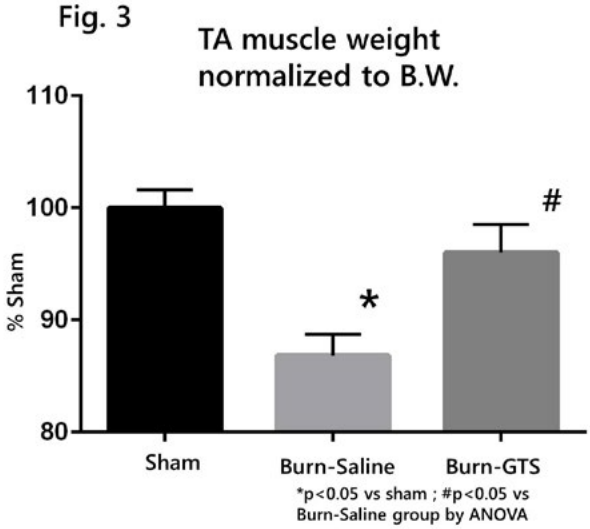


Fig. 3



S-421.

PREVALENCE OF SPIRITUAL NEEDS AMONG CRITICALLY ILL ADULTS AND THEIR FAMILY MEMBERS

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INTRODUCTION: Quality care, even in the most technically sophisticated environments, involves more than just the physical needs of the patient. Since JCAHO recognized the need for addressing not only the physical but also the spiritual aspects of care[1], hospitals and medical personnel are struggling with how best to address these undeniably important needs. Our aims were to discover how often critically ill patients and/or their family members identify spiritual beliefs as important and whether those spiritual needs are being addressed adequately by home faith community and/or hospital chaplaincy resources.

METHODS: Cross-sectional survey of adult Intensive Care Unit (ICU) patients and their family members between October 2015 and December 2015. Two study team members surveyed patients and their family members in four adult intensive care units - two surgical ICUs, a medical ICU, and a cardiac care unit which together are comprised of 68 total beds - at a single academic, urban, tertiary care center. Of note, the tertiary care center has a chaplaincy training program and all ICUs had their own assigned chaplain and there was also an in-house, on-call chaplain available 24 hours a day. The study questionnaire was based on the FICA spiritual history tool©[2] and assessed demographic information, including age, race, ethnicity, gender, and faith tradition, as well as the respondent's perceived spiritual needs.

RESULTS: There were a total of 144 survey respondents (50% male and 50% female), with the majority of survey participants being Caucasian or African American (68% and 21%, respectively). The most common religious identifications were Christian, Jewish, or no faith tradition (76%, 8%, and 11%, respectively). In total, 123 (85%) of the respondents identified that spirituality was important to them in times of crisis and of these 123 respondents, 111 (90%) were satisfied with the spiritual care they received while in the ICU, be it from hospital chaplaincy services or their home faith community. Of note, 12 respondents were identified as having spiritual needs that were not being met by their home faith community or the hospital chaplaincy service and of these respondents, all identified as Christian and 75% identified as Caucasian.

CONCLUSION: A high prevalence (85%) of critically ill patients and family members identified having spiritual needs during the period of critical illness, though the vast majority (90%) felt that their spiritual needs were being met with current resources at a hospital with assigned ICU-based chaplains and an always available, on-call, in-house chaplain. Future research is needed into how the spiritual support provided by a community pastor or religious community differs in content or effectiveness from that provided by the hospital chaplain. The high prevalence of spiritual needs of critically ill patients and their family members emphasizes the importance of having chaplaincy resources available in critical care units.

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S422.

WITHDRAWN.

Figure 1. Calculated parameters for first 6 hours of monitoring separated by GOS groups.

S-423.

MONDAY MORNING: ICU PHYSICIANS' PERSPECTIVES ON HOW ATTENDING HANDOFFS IMPACT PATIENT FAMILIES

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INTRODUCTION: The families of patients admitted to the intensive care unit (ICU) interact with different attending physicians during the course of prolonged critical illness. Previous research on ICU care team/family interactions has identified relationships with physicians as an important aspect of family-centered care. The objective of the present study was to generate hypotheses about the impact that attending physician handoffs might have on the family ICU experience, to enable the development of interventions aimed at promoting care continuity and family-centered care.

METHODS: We re-analyzed transcripts from a qualitative interview study about ICU attending handoffs1 in which 30 semi-structured interviews were conducted with intensivists practicing in United States adult academic ICUs (Table 1). Using a grounded theory constant comparative approach, each transcript was coded independently by two coders to characterize themes relating to families' experience of attending handoffs. Given the hypothesis-generating nature of the study, inter-coder reliability was not calculated; rather, a consensus coding approach was used with adjudication by a third investigator. NVivo software was used to facilitate data management and coding.

RESULTS: There were no apparent associations between physician attributes (years in practice, gender, specialty, geographic region of practice) and perceptions about the family impact of attending handoffs. Attendings conceptualized the family impact of handoffs in terms of (1) the family-attending relationship, (2) family awareness of care transitions and (3) continuity of care (Table 2). (1) Relationships: Patients' families sometimes developed deep bonds with particular attending physicians, and expressed concern for a degradation of the family-attending relationship with end-of-service attending handoffs. On the other hand, if there was not a meaningful relationship between the attending and family, the attending handoff offered an opportunity for a new, potentially better, relationship. (2) Awareness of care transitions: 13/30 attendings related that some families had no clear understanding that these handoffs were occurring, and that families were at times surprised to meet new attending physicians at the start of a rotation. (3) Continuity of care: Some attendings reported warning families of the upcoming transition and deliberately complimenting the incoming attending to instill confidence in their colleagues' capability.

CONCLUSIONS: Attending handoffs may have positive, negative, or neutral effects on ICU families depending on the dynamics of the family-attending relationship and families' preparedness for the attending transition. Additional research is needed to elucidate the physician- and family-level factors that impact the family experience of critical illness and to develop interventions to support these vital caregivers.

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Table 1. Demographic Characteristics of Study Participants

Participant	Sex	Age	Years in practice	Region	Specialty	ICU Type
1	Male	36	7	Northeast	Anesthesia	CTICU
2	Male	40	2	Northeast	Anesthesia	STICU; CTICU
3	Male	50	16	Northeast	Surgery	STICU
4	Male	39	8	Midwest	Anesthesia	STICU; CTICU; Other ICU
5	Male	54	20	Northeast	Medicine	MICU
6	Female	36	1	Northeast	Medicine	MICU
7	Female	36	2	Northeast	Medicine	MICU
8	Male	36	4	Northeast	Surgery	STICU
9	Male	51	21	Northeast	Medicine	MICU
10	Male	45	20	Northeast	Anesthesia	SICU; CTICU
11	Female	55	23	West	Anesthesia	CTICU
12	Male	65	35	Northeast	Anesthesia	MICU; STICU
13	Male	34	4	Northeast	Anesthesia	STICU; CTICU
14	Male	40	7	West	Anesthesia	STICU; CTICU
15	Male	37	6	Northeast	Anesthesia	STICU; CTICU
16	Female	44	6	Northeast	Surgery	STICU
17	Female	42	10	South	Surgery	STICU
18	Male	40	9	South	Medicine	MICU
19	Male	49	18	South	Surgery	STICU
20	Male	38	3	Midwest	Medicine	MICU
21	Female	37	4	Northeast	Medicine	MICU
22	Male	35	1	Northeast	Medicine	MICU
23	Male	48	14	West	Medicine	MICU
24	Male	58	26	Midwest	Medicine	Other ICU
25	Female	50	20	South	Surgery	STICU
26	Female	45	10	Midwest	Emergency	STICU
27	Female	39	6	South	Emergency	STICU
28	Male	49	17	Northeast	Medicine	MICU
29	Male	43	6	Northeast	Anesthesia	STICU; CTICU
30	Male	60	29	Northeast	Anesthesia	Other ICU

CTICU: Cardiothoracic intensive care unit
MICU: Medical intensive care unit
STICU: Surgery/trauma intensive care unit

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Table 2. Selected Illustrative Quotations

Concept	Positive Impact	Negative Impact	Neutral
Family-attending relationship	"If there are issues with the interaction between the previous attending and the family, you are notified of that and you can take steps to correct the ongoing interactions" *Participant #3*	"I think one of the jobs of the attending physician is to carry the weight of uncertainty and some of the weight of sadness for families I spend a lot of time trying to get them intentionally to trust me, so that when I tell them if I have to, that there's not more to be done or it's time to stop, that they don't feel they're killing their loved one but they're agreeing to what this physician they trust said. And so I feel it's hard- It's very hard to hand that off" *Participant #20*	"It varies a lot. Some families are used to the attending turning over and it neither disturbs them or is something they look forward to they don't really know who their attending is or have a clear understanding of it." *Participant #5*
Awareness about attending transitions	"I'll let [the patient] know that, listen we provide a 24/7 operation here, but in order to do that means you are not going to see just me...because people have no [idea] what it is we do. It's not Grey's Anatomy." *Participant #17*	"Every time you have a new physician coming in, the family has no idea who you are, why you're even changing. And you're kind of looked at as the guy who has no idea what's going on." *Participant #2*	"So, I will say [to families] I am the attending on for the week. I don't think families know what the difference is, because I think that also the people they see on a regular basis are the residents and the nurse practitioners, So I think their state of who they associate with care many times is the resident or the NP or the fellow." *Participant #28*
Continuity of care	"When you go in and introduce yourself and say 'I am the person who was [here] yesterday in a different form'. And they [family/patient] understand that you know what's going on. Like you're talking about the case rather than asking them from scratch to explain what went on." *Participant #21*	"I think obviously for patients, the serious concern, especially given the complexity of the MICU is that things are going to get missed, inappropriate medications are going to be given, recreate the wheel with doing another billion tests And I think sometimes when I come on-service I'm a young female and if they had my chair who is 60 with grey hair, I think there are immediate perceptions as far as the person, what they look like, and so that obviously could maybe potentially create anxiety until they get to know the person too." *Participant #6*	"I think it effects them a lot in the sense that the patient's families have a loved one in the ICU and they are interested in their ultimate outcome from their ICU experience not- Sunday to Monday transition. What means something is coming to the ICU and leaving the ICU. So I think they expect, and rightfully so, that there is a good handoff between people who are going to be taking care of their family member." *Participant #13*

S-424.

SURVEYING ICU NURSES REGARDING PERSPECTIVES ON PATIENT COMMUNICATION

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INTRODUCTION: ICU patients have a concerning incidence of depression, anxiety, and post-traumatic stress disorder.[1] For mechanically ventilated (MV) patients, these issues may be compounded by the inability to speak. Some data suggest that engaging in communication with MV patients is also frustrating for caregivers, particularly ICU nursing staff.[2] As part of a project to develop advanced communication technology for these patients, we delivered a survey to ICU nurses across several settings about provider needs and perceptions.[3] The results of this survey will contribute to the final design of a proposed communication system.

METHODS: After IRB approval and an introduction to the project through a brief presentation, a total of 334 bedside nurses in 6 ICU settings (2 Neuro ICUs, 1 Medical/Surgical ICU, 1 Surgical ICU, 1 Medical ICU, and 1 Respiratory Acute Care Unit) at 2 tertiary care academic medical centers are being administered a 10-12 minute anonymous online survey (REDCap[4]). The survey remains open for two weeks. The questions in the survey include whether nurses could understand MV patients (and have sufficient time to do so); whether these patients and their family members are satisfied with existing communication methods; and whether nurses experience avoidance or frustration when engaging with these patients. Future potential design features of a novel communication system are also a focus of the survey.

RESULTS: Analysis from the first surveyed hospital (n=204 nurses in 4 settings) is presented here. Thirty percent of nurses overall started the survey, and 25.5% of nurses completed it. The nurses were highly experienced (17.3 +/- 12.2 years of experience), with the majority of work experience in critical care (14.0 +/- 11.3 years on average).

Nurses were dissatisfied with their ability to communicate with and understand MV ICU patients. Eighty percent of nurses disagreed with the idea that communication methods in use for intubated ICU patients were sufficient. Forty-two percent of nurses disagreed with the statement "I can understand most ICU patients who are unable to speak", while only 2.0% strongly agreed. Eighty percent of nurses agreed with the statement: "Most ICU patients have difficulty communicating their needs when unable to speak", and 63% disagreed with the statement that "Most non-speaking ICU patients are satisfied with the methods of communication used in the ICU" (with another 31% not sure).

Fewer than 40% of nurses agreed that they were completely comfortable communicating with a non-speaking patient, and more than half noted that they avoided some contact with patients who were difficult to understand.

CONCLUSIONS: There is an urgent need to improve the ability for patients on mechanical ventilation to communicate with their ICU caregivers. Future research should be directed at the development of assistive communication technology, including how this technology might improve patient outcomes.

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S-425.

ANALYSIS OF ADMISSION/DISCHARGE CRITERIA ADHERENCE AMONG CLOSED AND OPEN ICU'S ON WEEKEND VS WEEKDAYS

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INTRODUCTION: Intensive Care Units in the United States consume up to 10 % of all hospital beds, utilize up to one third of hospital resources, and generate 1% of the gross domestic product or almost $64 billion each year.[1] The growing demand for critical care beds is demonstrated by the 50,000 – 100,000 patients that hold ICU beds on any given day in the US.[1] The goal of this study is to assess how strictly ICU admission criteria are followed in closed ICUs versus open ICUs. Hypothesis: Unwarranted ICU bed occupancy rates will be higher in the open unit and higher on weekends for both units.

METHODS: This retrospective observational study incorporated the review of medical records of consecutive patients ages 18 and older located in the closed Neurocritical Care Unit (NCCU) and open Medical Intensive Care Unit (MICU). Medical records came from four random weekdays and two random weekends between July 1, 2015 and July 31, 2015. Nationally recognized criteria set by the Society of Critical Care Medicine[2] were applied to patients located in these ICU's by two researchers and the results were cross-analyzed by the third researcher. Consensus categorizations of the three researchers were used in the analysis. A set of chi-square tests was used to test the hypothesis. Included cases provided >80% power for a chi square test of 2×2 contingency tables with medium effect size (0.3).

RESULTS: A total of 202 patient charts were reviewed (118 MICU and 84 NCCU). For MICU, unwarranted bed occupancy was found to be 43% on weekdays (36/84), 41% on weekends (14/34), and 42% overall (50/118). For NCCU, unwarranted bed occupancy was 20% on weekdays (11/54), 27% on weekends (8/30), and 23% overall (19/84). A chi-square test of independence was performed to examine the relation between the type of ICU (MICU vs. NCCU) and number of unwarranted beds occupied overall. The relationship between these variables was significant, $X2$ (2, N = 202) = 8.51, p = .004. Results also indicated significantly higher unwarranted bed occupancy during the weekdays for MICU compared to NCCU, $X2$ (2, N = 138) = 7.40, p = .007. Within each ICU types, weekend vs. weekday bed occupancies were not significantly different.

CONCLUSIONS: Overall and weekday unwarranted bed occupancy was significantly higher for the open ICU. This data suggests that ICU admission/discharge criteria are more strictly adhered to by closed intensive care units on weekdays. Reasons for unwarranted ICU bed occupancy need further exploration given the potential impact on patient care and cost to hospitals and patients.

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S-473.

COMPLICATIONS OF TRAUMA PATIENTS ADMITTED TO LEVEL 1 AND 2 TRAUMA HOSPITALS IN THE UNITED STATES

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INTRODUCTION: Traumatic injury is a leading cause of morbidity and mortality worldwide[1]. Although pre-hospital systems[2,3] and hospital characteristics (e.g. specialized trauma centers)[4-6] have been studied to improve outcomes, there is a shortage of epidemiological data describing the clinical course of trauma patients after hospital admission. The primary aim of this study was to describe clinical characteristics of patients admitted to the hospital after traumatic injury, including an assessment of in-hospital complications. The secondary aim was to evaluate the relationship between the development of complications and in-hospital mortality.

METHODS: This was a retrospective cohort study of adults admitted to the hospital after trauma in 2013, using the National Trauma Database (NTDB). The NTDB is a nationally representative sample of 100 Level 1 or 2 trauma centers. Logistic regression analyses were performed to determine independent predictors for in-hospital complications and in-hospital mortality.

RESULTS: Of the 153,613 patients studied, 21,496 (13.7%) developed in-hospital complications. The most common complications were pneumonia (4.6%), urinary tract infection (3.2%), and Acute Respiratory Distress Syndrome (2.4%). In-hospital complications were associated with higher injury severity score, older age, and male gender. Additionally, preexisting medical comorbidities including coronary disease, congestive heart failure, diabetes, stroke, peripheral vascular disease, chronic pulmonary disease, chronic kidney disease, and alcoholism were associated with higher in-hospital complication rates, as was ICU admission (adjusted OR 7.33) and mechanical ventilation (adjusted OR 10.03). Overall in-hospital mortality was 4.8%. The development of in-hospital complications was associated with higher in-hospital mortality (adjusted OR 4.49 for 1 complication, 5.13 for 2-4 complications, and 9.11 for 5-9 complications).

CONCLUSIONS: Amongst patients admitted to the hospital after traumatic injury, in-hospital complications were significantly associated with the presence of medical comorbidities, which may represent modifiable risk factors. Additional risk factors including age, gender, and injury severity may not be modifiable, but may help identify patients at high risk for in-hospital complications and associated mortality.

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S-476.

VASOACTIVE DRUG INFUSION ARCHITECTURE IMPACTS THE ABILITY OF ICU NURSES TO MAINTAIN HEMODYNAMIC STABILITY IN A LIVING ADOLESCENT SWINE MODEL

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BACKGROUND: Meticulous and constant titration of pharmacological agents is mandatory to maintain target hemodynamic stability in an intensive care setting. Experienced ICU nurses (RN) achieve this goal by rapid adjustments in drug and sometimes crystalloid carrier rate. However the time to achieve desired steady state plasma drug concentrations depends on infusion system architecture, specially the common volume (V) defined as the volume between the point where drug and inert carrier streams meet to the patient's blood. We hypothesized that low V infusion systems allow better hemodynamic control by ICU RNs than larger V infusion systems.

STUDY DESIGN: Endo occlusion balloons in the IVC and Aorta of a live swine simulator were used to surreptitiously manipulate blood pressure while experienced ICU RNs tried to maintain mean arterial pressure (MAP) between specified limits (70-90 mm Hg) using either sodium nitroprusside (SNP) or norepinephrine (NE) infusions.

PARTICIPANTS:8 live anesthetized adolescent swine models were used. Experienced ICU RNs from SEMC volunteered to participate for each animal.

METHODS: The carrier rate was fixed at 10 ml/hour. RNs had access to continuous hemodynamic data but were blinded to the use of small (0.2ml-Edelvaiss multiline drug infusion manifold) or large (3.5ml- 4 gang high flow stopcock) V catheters as well as blood pressure manipulations. The aorta or IVC was occluded for 5 minutes followed by 15-minute observations. Six manipulations were performed in 8 animals yielding 12 data points each for IVC/ Aorta occlusion.

RESULTS: Time to restore MAP to target range, time out of MAP range, and area out of range (integral of MAP over time) were all lower with smaller V for both IVC and Aortic occlusions. After aortic occlusion, the time to restore mean arterial pressure to range (t1: 2.4±1.4 vs. 5.0±2.3min, P = 0.003, average ± SD), time-out-of-range (tOR: 6.2±3.5 vs. 9.5±3.4min, P = 0.028), and area-out-of-range (pressure–time inte- gral: 84±47 vs. 170±100 mmHg·min, P = 0.018) were all lower with smaller common volumes. After IVC occlusion, t1 (3.7±2.2 vs. 7.1±2.6min, P = 0.002), tOR (6.3±3.5 vs. 11±3.0min, P = 0.007), and area-out-of-range (110±93 vs. 270 ± 140 mmHg·min, P = 0.003) were all lower with smaller common volumes. Common-volume size did not impact the total amount infused of either drug.

CONCLUSIONS: Nurses did not respond as effectively to hemodynamic instability when drugs flowed through large common- volume infusion systems. The data show that despite very different practice styles and infusion techniques, the infusion system configured with low dead volume results in better hemodynamic stability. ICU RNs were better able to maintain MAP stability with a low V infusion system in this simulator. These data imply that drug infusion system common volume should be minimized to the extent possible.

LIMITATIONS: Owing to potential tachyphylaxis we set a ceiling limit on the dose of the infusions (0.5 and 3 mcg/kg/min for NE and SNP, respectively). Furthermore we did not allow the RN to manipulate the carrier flow as they might in clinical practice.

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Scholars' Abstracts

Economics, Education and Policy

S-426.

INCREASING UPTAKE OF COGNITIVE AIDS IN CRITICAL EVENTS

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INTRODUCTION: Crises in the operating room (OR) during a pediatric case are fortunately rare with the incidence of cardiac arrest in non-cardiac patients being 2.7/10000[1]. This rarity means that increasingly few anesthesiologists can claim personal experience of the full range of potential OR emergencies. In order to address this, the Society for Pediatric Anesthesia developed cognitive aids in the form of Critical Event Checklists (SPA CECs). Several studies have demonstrated the benefit of cognitive aids in improving adherence to guidelines, performing critical tasks and improved Anesthesia Non-Technical Skills[2,3]. However, despite the presence of cognitive aids, individuals often do not use the aids frequently or use them incorrectly[4,5]. The way that trainees utilize cognitive aids can potentially be augmented through improved education/orientation surrounding the tool. The objective of the study was to investigate whether the presence of SPA CECs improve the performance of anesthesiology trainees during simulations and whether the mode of orientation (e-module vs. didactic) results in improved uptake of the cognitive aids.

METHODS: IRB approval was attained from the local institution. A randomized, 2 x 2 factorial design was used. Subjects were randomized twice. The first randomization was whether the SPA CEC was available to the participant during the simulations. The second randomization was the mode of orientation (e-module vs. didactic). The simulations were videotaped and will be rated by two Pediatric Anesthesiologists using the Managing Emergencies in Pediatric Anesthesia (MEPA) scenario specific checklist and GRS.

RESULTS: In this work in progress, we have conducted 36 MEPA simulations. Preliminary results demonstrate that in 28% of simulated scenarios, residents use a cognitive aid when it is available to them. Of the seven MEPA scenarios that residents were exposed to, cognitive aids were utilized exclusively on two scenarios (Malignant Hyperthermia and Local Anesthetic Toxicity). The uptake rate of cognitive aids in these two specific scenarios was 62.5% amongst residents that underwent the simulation and had cognitive aids available. Additional results, specifically performance impact of the CECs, will be available for presentation at the time of the conference.

CONCLUSIONS: Preliminary results suggest that uptake of the cognitive aid is dependent on the type of critical event occurring as opposed to the orientation that residents receive. Specifically, participants are more likely to use the SPA CEC in events that are task list oriented (i.e. Malignant Hyperthermia and Local Anesthetic Toxicity). The significance of these results is that they indicate that cognitive aids should be created for specific critical events; therefore, this lends insight into ways to improve currently existing resources (i.e. SPA CEC) and direction towards creation of future resources.

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S-427.

WITHDRAWN.

S-428.

HANDOFF CURRICULUM IN ANESTHESIA RESIDENCY PROGRAMS: A NATIONAL SURVEY OF PROGRAM DIRECTORS

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INTRODUCTION: The Accreditation Council for Graduate Medical Education (ACGME) requires that residency programs teach residents about handoffs as well as monitor and evaluate resident handoffs. The educational approaches used by anesthesia residencies to accomplish these goals are unknown. We conducted a cross-sectional survey in order to characterize handoff education and monitoring in United States anesthesia residency programs.

METHODS: In 2014, we developed and administered a 20-item electronic survey to anesthesiology program directors (PDs) or their designees. The survey addressed respondent attitudes about handoff training, evaluation, and satisfaction with handoff practices. The survey was administered via the Qualtrics platform, a web-based survey administration tool. All PDs of anesthesiology residency programs in the United States were eligible for participation. PDs were identified from publicly available information. Institutional Review Board (IRB) approval was obtained from each author's institution prior to conducting this survey. Participants were not paid for their participation. Descriptive statistics were used to characterize response frequencies and Mann-Whitney U tests were used to compare continuous data.

RESULTS: Responses were received from 46 of 130 (35%) residency PDs or their designees. We compared geographic region and residency program size in responders versus nonresponders to assess for response bias. There were no significant differences found. 42 of 46 (92%) respondents were PDs. While the majority (35; 76%) reported having an explicit handoff curriculum for residents, eleven (24%) respondents did not have such curriculum. There was variability in teaching methods used, with the two most frequently reported being "taught by faculty" (32; 70%) and "taught by senior residents" (28; 61%) in the clinical environment (Table). Only half of programs (23; 50%) reported that residents received formal training multiple times during residency and almost half (21; 46%) reported that residents did not receive any formal assessment of their handoff skills/competence. Regarding respondents' overall satisfaction with their program's handoff curriculum, mean and median satisfaction was 50 (scale of 1-100). For respondents who reported not having an explicit curriculum, mean satisfaction was statistically significantly lower (mean ± SD) (31± 22 vs 56 ± 20, p=0.003) when compared to those who had such a curriculum. We found similar results when we asked about the priority placed on handoff education (56 ± 25 for programs with a curriculum vs 36 ± 22 for programs without, p=0.03).

CONCLUSIONS: Most responding anesthesiology residency programs have handoff curricula in place, but there is variability in the timing and extent of handoff training, as well as in methods used to monitor and provide feedback about resident handoffs. More research is needed to understand effective approaches for handoff education in residency programs.

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Table: Anesthesiology Program Director or Designee responses about handoff practices, training, and evaluation

Question	N (%)
Response Options	
When do residents in your program learn about handoffs?*	
During Internship / PGY-1 year	27 (58.7)
During CA-1 orientation	35 (76.1)
In clinical environment	24 (52.2)
After CA-1 orientation, during dedicated teaching time	7 (15.2)
Select all handoff teaching methods used by your residency.*	
Didactics (lecture)	20 (43.5)
Small group exercises, including role playing	16 (34.8)
Simulation (either in situ or at simulation center)	17 (37.0)
Teaching by faculty in the clinical environment	32 (69.6)
Teaching by senior residents in the clinical environment	28 (60.9)
Educational readings (handbooks, guides, literature)	10 (21.8)
Online Modules	10 (21.8)
Please indicate if you are *satisfied/very satisfied* with the way that handoffs currently happen in each of the following settings.	
OR to PACU handoffs	38 (82.6)
OR to ICU handoffs	30 (65.2)
Intraoperative handoffs	29 (63.0)
ICU shift-to-shift handoffs	26 (56.5)
Other handoffs type	2 (4.4)
What barriers to teaching residents about handoffs have you encountered?*	
Variability in handoff practices of faculty	28 (60.9)
Faculty engagement/buy-in about handoffs	25 (54.3)
Competing curricular priorities	23 (50.0)
Time for teaching	22 (47.8)
Time for curriculum development	19 (41.3)
Variability in handoff practices of senior residents	15 (32.6)
Other barriers	3 (6.5)
None	8 (17.4)
How do you evaluate your residents' knowledge about handoffs?*	
Subjective testing by faculty	33 (71.7)
Subjective testing by senior residents	11 (23.9)
Objective testing (e.g. written or online tests)	3 (6.5)
Simulation	2 (4.4)
Other evaluation method	2 (4.4)
No formal evaluation	12 (26.1)
How do you assess your residents' handoff skills/competence?*	
Structured written assessment by faculty (e.g., CEX: Clinical Evaluation Exercise)	8 (17.4)
Structured written assessment by senior residents (e.g., CEX)	3 (6.5)
Unstructured written assessment by faculty	16 (34.8)
Unstructured written assessment by senior residents	5 (10.9)
Other assessment method	3 (6.5)
No formal evaluation	21 (45.7)
Does your residency program use any handoff mnemonics?	
Yes	16 (34.8)
No	3 (6.5)
Not sure	28 (60.9)
Which handoff mnemonics(s) do anesthesia residents use?*	
I-PASS	5 (10.9)
I-PASS-the-BATON	2 (4.4)
SBAR	20 (43.5)
SHARQ	1 (2.2)
PANDA	1 (2.2)
Other mnemonic	7 (15.2)
Which of the following handoffs use a standardized form, tool, or checklist?*	
OR to PACU handoffs	32 (70.0)
OR to ICU handoffs	28 (60.9)
Intraoperative handoffs	19 (41.3)
Shift-to-shift handoffs in the ICU	15 (32.6)
Other handoff type	3 (6.5)

*Multiple responses allowed.

S-429.

QUALITY IMPROVEMENT INITIATIVE; DEVELOP A STANDARDIZED HAND-OFF PROTOCOL FOR UTILIZATION AMONGST ANESTHESIA PROVIDERS TO ENHANCE INTRAOPERATIVE COMMUNICATION

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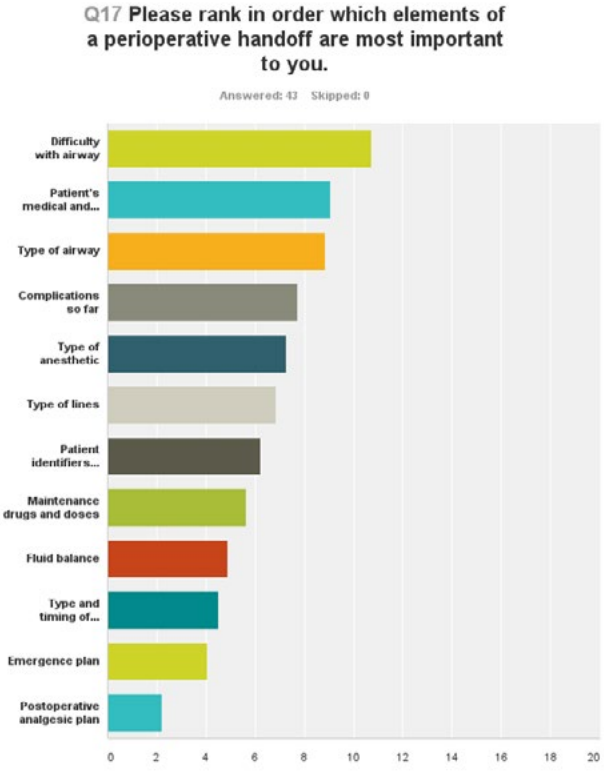
INTRODUCTION: The interest in hand-offs in medicine grew partly in response to The Joint Commission's National Patient Safety report in 2006, which required institutions implement a standardized approach to 'hand-off' communications, including an opportunity to ask and respond to questions. Studies have elucidated that hand-offs increased the risk of any major in-hospital morbidity or mortality by 8% – with similar effect size for attendings, residents, and CRNAs alike.[1] With a more systematic approach to hand-offs, a consequent decrease in mistakes that occur during the hand-off process is expected. The purpose of this study was to develop a standardized hand-off protocol to be used intraoperatively for transitions of care.

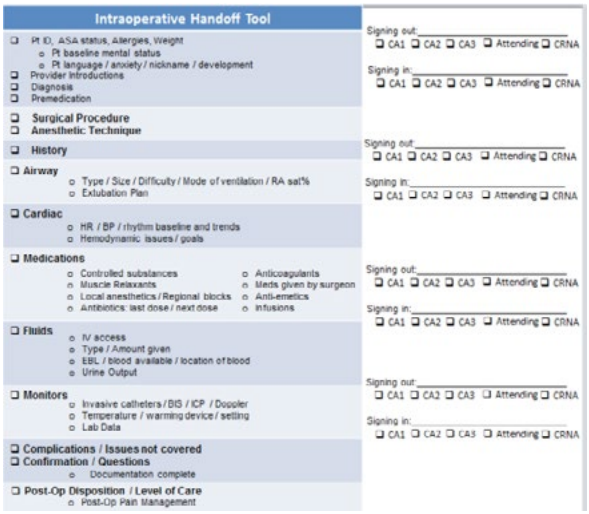
METHODS: Anesthesiologists were asked to rate the importance of a subset of twelve elements in regards to the hand-off process. After reviewing other institutions' hand-off models and comparing them to our current practice needs, we compiled and presented a prototype hand-off tool to our department. Subsequent feedback required reformatting which resulted in the construction of a formal tool.

RESULTS: 43 anesthesia providers (attending anesthesiologists, residents and CRNAs) responded to the survey. The major results were as follows:

Out of the 12 criteria queried, the top 5 ranking on a mean weighted scoring scale were: difficulty with airway (10.72), patient's past medical and surgical history (9.05), type of airway(8.84), intraoperative complications(7.72) and type of anesthetic (7.26). The general consensus revealed the following 5 criteria were relatively less crucial - maintenance drugs (5.65), fluid balance (4.88), antibiotics (4.53), emergence plan (4.05), and postoperative pain management (2.21). Respondents were divided with respect to the importance of patient identifiers with 27.91% ranking it the least important aspect and 25.58% the most important aspect. The majority of respondents ranked types of lines (72.08%) and drug maintenance/dosing (81.39%) between 5 and 9 (on a 12 point-scaled level of significance). Of the free form responses, 16 of the 25 providers requested a checklist tool to improve the hand-off process.

CONCLUSION: Assessing both provider and patient needs enabled the design of a concise, formatted checklist for intraoperative use. Compiling various components of existing hand-off tools and modifying according to provider feedback, the final tool included salient points found imperative to our practice. Based on collaborative efforts, the hand-off tool has been implemented during critical transitions of care between anesthesia providers. Consequently there will be an improvement in the overall hand-off process likely decreasing intraoperative complications and hand-off omissions. Further investigation entails compliance to the tool as measured across all anesthesia providers, ultimately engaging the utilization of a standardized method that addresses current practice needs.





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S-430.

LEARNING PREFERENCES OF ANESTHESIA RESIDENTS: A SINGLE INSTITUTION STUDY

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INTRODUCTION: Instructors and trainees alike may benefit from an understanding of the student's learning preferences. Learning inventories have been described by medical educators as a method to establish goals on medical education design[1-2]. One of these inventories, the VARK questionnaire, has been widely used in education and research and identifies four types of learning styles: visual, aural, read/write, and kinesthetic[3]. A number of recent studies have evaluated medical students' learning styles using the VARK model[4-5]; however, data on anesthesia residents' learning preferences remain scarce. The purpose of our study is to determine if anesthesia residents at our institution know their learning preference and to identify possible learning trends.

METHODS: This study was approved by our Institutional Review Board. VARK questionnaires were administered on paper to our residents and collected during the same encounter. Demographic information as well as perceived learning preferences were also collected prior to completing the questionnaire. Perceived and actual preferred learning styles were compared using STATA Data Analysis and Statistical Software and the exact McNemar's test.

RESULTS: Resident characteristics are shown in Table 1.

Out of 73 eligible residents, 29 (40%) completed the survey. Forty-three percent of respondents perceived that they had a multimodal learning style, which was significantly higher than visual (11%, p = 0.04), aural (4%, p = 0.003), and read/write (7%, p = 0.01). Thirty-six percent believed they had a kinesthetic learning style, which was significantly higher than aural (p = 0.01) and read/write (p = 0.04). Perceived learning styles are shown in Figure 1.

Based on the results from the VARK questionnaire, 48% of respondents actually had a multimodal learning style, which was higher than visual (14%, p = 0.03), aural (14%, p = 0.03), read/write (14%, p = 0.03), and kinesthetic (10%, p = 0.01). Actual learning styles are shown in Figure 2.

A lower percentage of respondents actually had a kinesthetic learning style than they perceived (p = 0.04). Overall, 21% of respondents correctly perceived their preferred learning styles.

CONCLUSION: Residents' preferred learning modality was multimodal, and they were particularly poor at predicting their exact learning style. Surprisingly, a lower percentage of individuals actually had a kinesthetic learning style than they perceived. These individuals may have focused more on "learning by experience," but could have in fact benefitted from learning through other modalities. A precise understanding could help learners focus on individual study strengths and adapt study habits to make learning sessions more valuable. Future investigations should explore potential multimodal curriculums for anesthesia residents so that they all may become their own best learners.

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Category	Participants
Age[a]	29.4 ± 3.7
Gender	Female: 14 Male: 14
Class	CA – 1: 22 CA – 2: 3 CA – 3: 4

Table 1: Resident Characteristics
[a]: Values are mean ± standard deviation

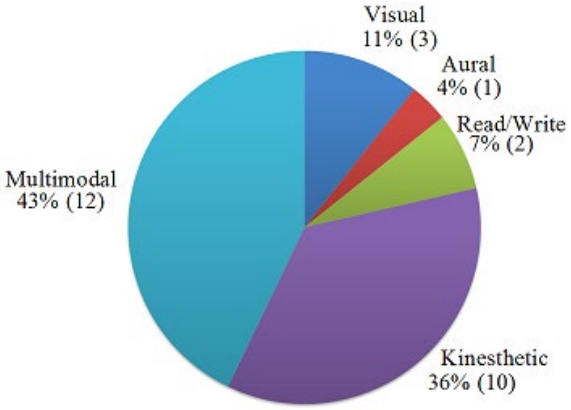

Figure 1: Perceived Preferred Learning Style

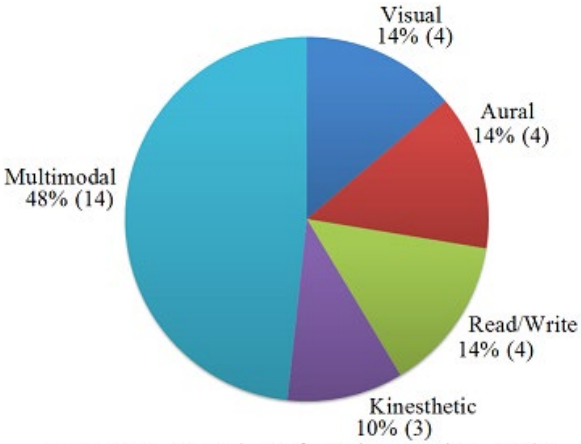

Figure 2: Actual Preferred Learning Style

S-431.

WITHDRAWN.

Scholars' Abstracts

Neuroscience in Anesthesiology and Perioperative Medicine

S-432.

TOWARDS NEUROPHYSIOLOGICAL BIOMARKERS OF BRAIN VULNERABILITY: FRONTAL ALPHA WAVES PREDICT THE PROPENSITY FOR INTRAOPERATIVE BURST SUPPRESSION

AUTHORS: Y. R. Shao[1], K. J. Pavone[2], O. Akeju[2], E. N. Brown[2], P. Purdon[2]

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INTRODUCTION: Post-operative delirium (POD) occurs frequently in elderly patients.[1] Recent studies show that EEG burst suppression during general anesthesia predicts POD and impairment of functional independence[2,3]. Aging is associated with significant neurobiological and neurophysiological changes that could render some elderly patients more vulnerable than others to burst suppression, subsequent POD, and cognitive dysfunction. In a previous study, we found that anesthesia-induced frontal alpha waves diminish significantly with age[4]. The generators of these frontal alpha waves overlap significantly with cortical regions that undergo profound neurodegeneration in aging and dementia[5,6]. We therefore hypothesized that frontal alpha power during general anesthesia could be related to the propensity for patients to develop intraoperative burst suppression.

METHODS: We analyzed EEG data from a previously reported cohort[4] in which 155 patients received propofol (n=60) or sevoflurane (n=95) as the primary anesthetic. We estimated the EEG spectrum and coherence from a 2 min period of stable anesthetic maintenance. We defined burst suppression operationally by the presence of at least three consecutive suppression events within a 1 min period occurring within a window beginning 10 minutes after induction through the end of the procedure[4]. We used logistic regression analysis to characterize the effects of age, anesthetic dose (propofol infusion rate and sevoflurane age-adjusted minimum alveolar concentration), alpha power, and alpha coherence on the probability of an episode of burst suppression. We used the Bayesian Information Criterion (BIC) to select the best statistical model (Figs. 1, 2).

RESULTS: After considering the effects of age, anesthetic dose, alpha power and alpha coherence, the best model for predicting the probability of burst suppression was a logistic regression with alpha power as the only explanatory variable (Fig. 3, $p = 0.00035$ for alpha power under propofol anesthesia; Fig. 4, $p = 0.005$ for alpha power under sevoflurane anesthesia). Based on these models, under propofol, the odds of experiencing burst suppression increases by 1.36 fold per dB decrease in alpha power, and the odds ratio of experiencing burst suppression for an individual at the 1st quartile vs. an individual at the 3rd quartile of alpha power is 5.79. Under sevoflurane, the odds of experiencing burst suppression increases by 1.23 fold per dB decrease in alpha power, and the odds ratio of experiencing burst suppression for an individual at the 1st quartile vs. an individual at the 3rd quartile of alpha power is 2.41.

CONCLUSIONS: Anesthesia-induced frontal alpha power, independent of age, is a strong predictor of burst suppression, and may help identify patients at risk of postoperative delirium. We hypothesize that alpha oscillations could serve as a neurophysiological biomarker for brain vulnerability under general anesthesia.

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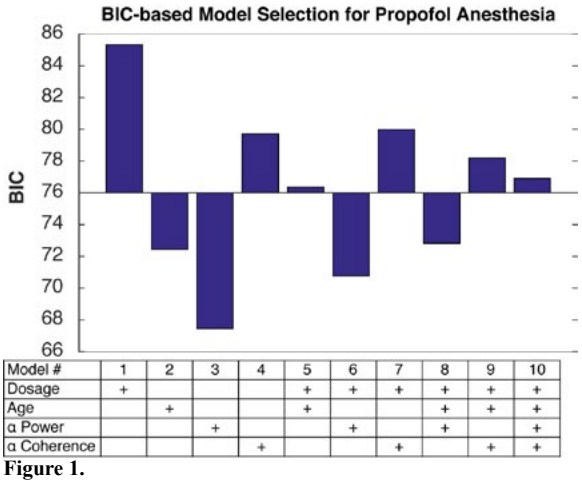

Figure 1.

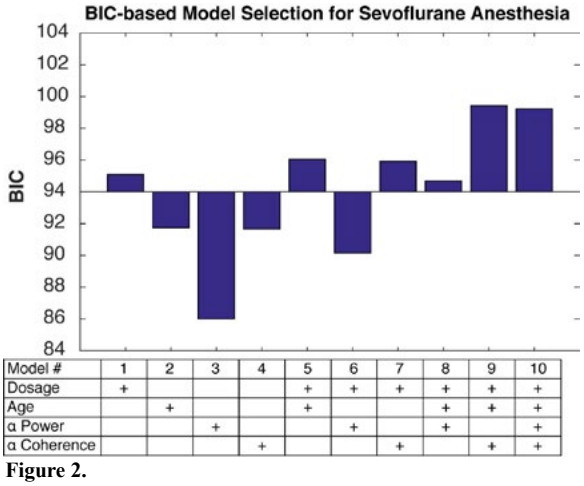

Figure 2.

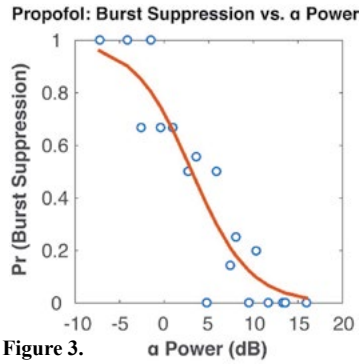

Figure 3.

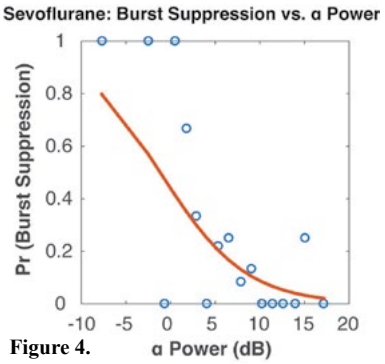

Figure 4.

S-433.

A NOVEL TREATMENT FOR MEMORY IMPAIRMENT AFTER CONCUSSION IN MICE

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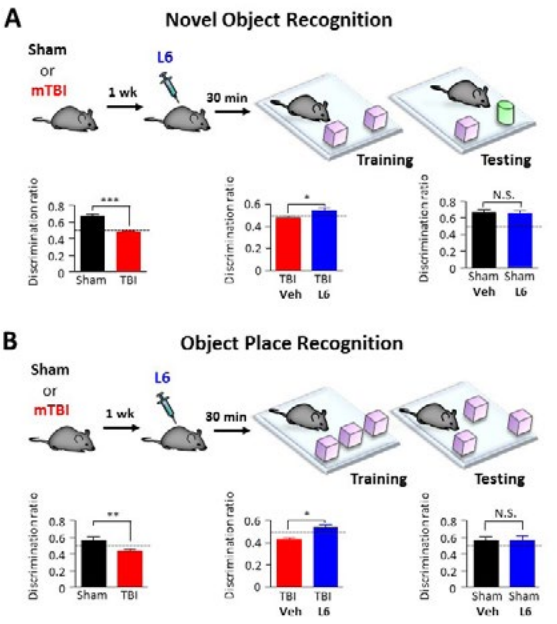
INTRODUCTION: Traumatic brain injury (TBI) is a leading cause of death and disability worldwide. Concussion or mild TBI (mTBI) accounts for more than 75% of all TBI, and has an estimated cost of over $17 billion per year in the United States alone. Cognitive impairments, particularly deficits in memory and executive function, are common after mTBI and strongly predict poor long-term functional recovery and loss of independence. The mechanisms underlying these cognitive deficits remain elusive and there are no effective treatments. Previous studies identified γ-aminobutyric acid type A receptors (GABAARs) that contain the α5 subunit (α5GABAARs) as key mediators of inflammation-induced memory deficits. TBI triggers an intense inflammatory response in the brain that can persist for years after the initial insult. Here, we test the hypothesis that post-traumatic cognitive deficits are caused by increased α5GABAAR activity and that inhibiting α5GABAARs will improve cognitive impairment after mTBI.

METHODS: Approval from the local Ethics Committee was obtained and investigators were blinded to the treatment groups. Under anesthesia, a modified free weight drop method was used to produce mTBI in the mice. Cognitive performance was tested in TBI and sham mice (anesthesia only) 1 week after the injury. Memory was assessed in a Novel Object Recognition (NOR) and an Object Place Recognition (OPR) assay. Executive function was assessed with a puzzle box (PB) assay. The role of α5GABAARs was tested by treating mice with a drug that selectively inhibits α5GABAAR function (L-655,708 0.5 mg/kg i.p.). Statistical analyses were conducted using GraphPad Prism 5.0. All values are expressed as mean ± SEM. Results: After a single brief concussive injury, mice recovered their righting reflex spontaneously and showed no overt impairment of behavior. One week after mTBI, mice exhibited impaired performance in both NOR (Sham: 0.67 ± 0.03; TBI: 0.48 ± 0.02, n = 12-23; p<0.0001, Fig 1A) and OPR (Sham: 0.54 ± 0.04; TBI: 0.41 ± 0.02, n = 7-17; p<0.001, Fig 1B) assays. In addition, mTBI mice demonstrated impaired executive function (F(3, 100)=2.78, p<0.05), short-term memory (F(2,75)=4.37, p<0.05) and long-term memory (F(1,45)=7.47, p<0.05) compared to sham animals (Fig 2B). Mice treated with L-655,708 showed improved memory performance in both NOR (Vehicle: 0.48 ± 0.02; L6: 0.54 ± 0.03, n = 20-23; p<0.05, Fig 1A) and OPR (Vehicle: 0.41 ± 0.02; L6: 0.52 ± 0.03, n = 14-17; p<0.05, Fig 1B) assays. Inhibiting α5GABAARs also improved short term memory (F(2,91)=4.13, p<0.05) but did not reverse executive function or long term memory impairment in the PB assay (Fig 2C).

CONCLUSIONS: One week after mTBI, mice exhibited impaired memory and executive function performance. Inhibiting α5GABAARs with L-655,708 reversed the memory impairment but not the executive dysfunction. These results suggest that α5GABAARs are novel targets for treatments that aim to improve memory performance after mTBI. The results also support the notion that radio-labelled α5GABAARs (e.g. with [11C]Ro15-4513) may serve as biomarkers in imaging studies for post-concussive memory deficits.

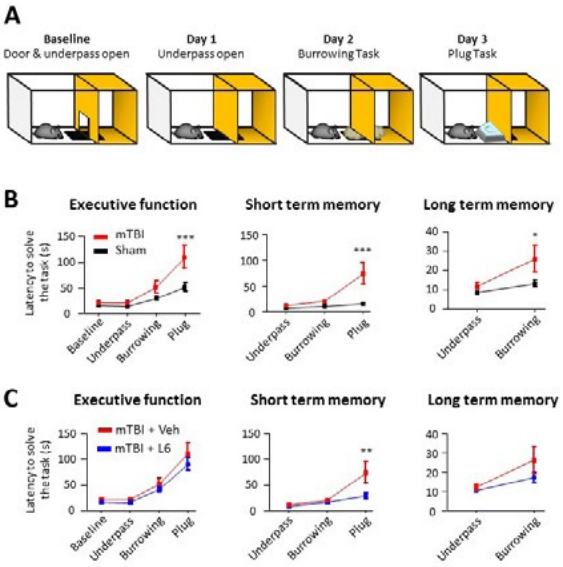
Fig. 1



Novel Object Recognition and Object Place Recognition memory is impaired 1 week after mTBI. L-655,708 after mTBI improves memory performance. (A) Performance on the Novel Object Recognition assay is impaired 1 week after mTBI. L-655,708 (L6) improves memory performance 1 week after mTBI but has no effect in Sham animals (n = 12-23, *** P < 0.001, * P < 0.05, Student's t-test). **(B)** Performance on the Object Place Recognition assay is impaired 1 week after mTBI. L6 improves memory performance 1 week after mTBI but has no effect in Sham animals (n = 12-23, ** P < 0.01, * P < 0.05, Student's t-test).

2

Fig. 2



mTBI impairs executive function and short term memory. L-655,708 improves short term memory after mTBI. (A) Diagram of the puzzle box assay. Each day the mice are exposed to progressively more difficult tasks which test their executive function and memory performance. **(B)** 1 week after mTBI mice show impairments on difficult executive function tasks and on short and long term memory. Specifically, they demonstrate increased latency to solve more difficult cognitive tasks such as the plug task. **(C)** L655, 708 (L6) improves short term memory after mTBI but does not improve executive function or long term memory (n = 12-23, *** P < 0.001, ** P < 0.01, * P < 0.05, one-way ANOVA).

3

S-434.

ACUTE EXPERIMENTAL PAIN AFFECTS LONG-TERM MEMORY OF AUDITORY CUES PRESENTED DURING SEDATION WITH DEXMEDETOMIDINE AND MIDAZOLAM

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AFFILIATION: [1]Anesthesiology, University of Pittsburgh, Pittsburgh, PA, [2]Psychology, University of Pittsburgh, Pittsburgh, PA, [3]Psychology, Carnegie Mellon University, Pittsburgh, PA

INTRODUCTION: Acute pain is an attention-demanding stimulus that impairs explicit memory in awake subjects.[1] This contrasts with conflicting evidence from patients under general anesthesia that opioid analgesia may reduce[2] or have no effect[3] on implicit memory. The purpose of this study was to determine if long-term memory for auditory stimuli would be modulated when paired with pain stimulation during infusion of saline versus low-dose midazolam (Mdz) or dexmedetomidine (Dex). Our hypotheses were that pain would impair memory under saline, but attenuate the memory-impairing effects of the anesthetic agents by transiently heightening arousal.

METHODS: This preliminary study includes 5 healthy adults (2 male), with mean (sd) age 23.2 (1.7) years. A list of 90 words was played 3 times (random order), and subjects made classifications (e.g. alive or not) about each. Thirty of the words were consistently followed by a 1 s painful (rated 7/10) electrical stimulation. Either drug was then administered via target-controlled infusion to effect site concentrations: 20 ng/ml for Mdz or 0.15 ng/ml for Dex. After steady-state was reached, the same experimental procedures were repeated with a new word list. During memory testing (24 hours later), previous words were intermixed with an equal number of novel words. Subjects responded using the Remember-Know-New procedure.[4] "Remember" indicated recall of specific (episodic) details. "Know" was for familiarity with no specific association recalled. "New" indicated no recognition. Subjects received the other drug during a subsequent visit (with different words). As in a similar study[5], d' (d-prime) was calculated for each condition; d' reflects the proportion of words correctly identified with the false-alarm rate incorporated to account for subject's discrimination threshold. Paired t-tests were performed on the d' values.

RESULTS: The group average memory results are shown in Table 1, and d' values displayed graphically in Fig. 1. Driven by large differences in "Remember" responses, d' was significantly lower with both Dex and Mdz, compared to saline. Under Mdz, pain significantly reduced "Remember" responses ($p = 0.006$). Fig. 2 demonstrates the inter-subject variability that characterizes our results, using the non-significant "remember" responses under Dex as an example. Subjects varied greatly in their sedated memory performance (notably Subj 2). Further, the effect of pain on memory varied between improvement (Subj 7), worsening (Subj 1), and no difference (Subj 5).

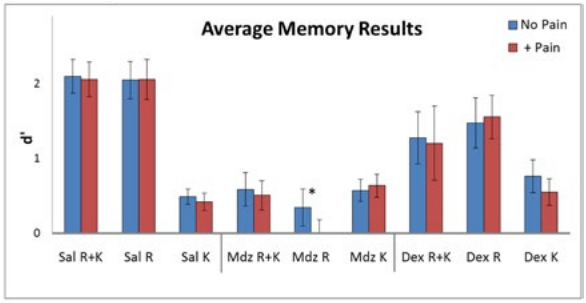
CONCLUSIONS: We have developed an experimental framework for determining how pain influences auditory memory at baseline and under sedation with two distinct anesthetic agents. Preliminary findings suggest decreased memory with pain, but demonstrate heterogeneity for memory performance as a function of both pain pairing and sedative given. Data from more subjects should allow more definitive conclusions.

Table 1. Memory testing results separated by response category, drug condition, and pair pairing.

Drug Condition & Pain Pairing	Remember + Know			Remember Only			Know Only		
	Average Hit Rate	Average FAR	Average d'	Average Hit Rate	Average FAR	Average d'	Average Hit Rate	Average FAR	Average d'
Saline									
No Pain	0.87	0.23	2.10	0.57	0.07	2.05	0.30	0.16	0.49
+ Pain	0.86	0.23	2.09	0.57	0.07	2.06	0.29	0.16	0.42
Midazolam									
No Pain	0.42	0.23	0.59	0.10	0.07	0.34	0.31	0.16	0.58
+ Pain	0.39	0.23	0.51	0.06	0.07	-0.01	0.33	0.16	0.64
Dexmedetomidine									
No Pain	0.63	0.23	1.19	0.31	0.06	1.48	0.42	0.17	0.77
+ Pain	0.62	0.23	1.29	0.33	0.06	1.56	0.35	0.17	0.55

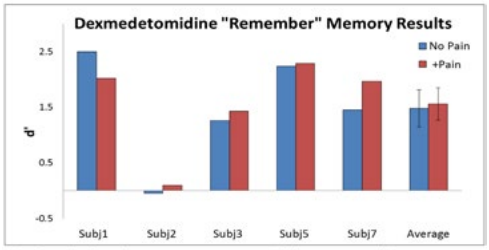
Hit Rate is number of words correctly identified in each response category. FAR = false-alarm rate. Statistically significant differences due to pain pairing are denoted by an asterisk (*).

Figure 1. All subject average memory response data by drug condition, showing differences due to pain.



Error bars represent standard error across subjects. Statistically significant difference due to pain pairing are marked with an asterisk (*). Abbreviation are: Sal = saline, Mdz = midazolam, Dex = dexmedetomidine, R = Remember, K = Know, R+K = combined results for both Remember and Know responses.

Figure 2. Example individual subject responses for "Remember" responses under dexmedetomidine.



Error bars for the subject average represent standard error across subjects.

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S-435.

INTRAVENOUS IMMUNOGLOBULIN ADMINISTRATION IS ASSOCIATED WITH REDUCED DELIRIUM RATE AND DECREASED DELIRIUM DURATION IN LUNG TRANSPLANT RECIPIENTS- A SINGLE CENTER RETROSPECTIVE STUDY

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INTRODUCTION: Preclinical studies have suggested that blocking neuroinflammation may decrease postoperative delirium and cognitive dysfunction.[1-3] However, there is limited human evidence to support this hypothesis.[4,5] Lung transplant recipients have a high incidence of postoperative delirium,[6] and often receive intravenous immunoglobulin (IVIG),[7] which suppresses antibody-mediated organ rejection and has anti-inflammatory effects.[8] We examined retrospectively whether IVIG administration was associated with decreased postoperative delirium in lung transplant recipients.

METHODS: We performed a secondary data analysis of lung transplant recipients enrolled in the NOBLE study[6] to examine the association between IVIG administration and delirium. Following transplant, the presence, duration, and severity of delirium were documented using the Confusion Assessment Method and the Delirium Rating Scale.

RESULTS: Twenty-seven patients with pre-transplant elevated Panel Reactive Antigens (PRA) received IVIG (mean dose 108 grams [SD = 71]) during and after transplantation.7 Patients receiving IVIG were less likely to be Caucasian (p=0.028) and tended to have pulmonary fibrosis as their native disease (p =0.097), but did not differ in other background characteristics. Among IVIG recipients, 7 (26%) developed postoperative delirium, compared to 17 (47%) of patients who did not receive IVIG. Controlling for native disease, primary graft dysfunction, and ethnicity, patients who received IVIG were less likely to experience delirium (OR = 0.26 [0.07, 0.95], p =0.041) and exhibited a shorter duration of delirium (3.9 days shorter [1.3, 11.6], p = 0.015). These findings were unchanged after controlling for factors we previously found to be associated with postoperative delirium, such as pre-transplant cognitive function6 and intraoperative cerebral perfusion.[9]

CONCLUSIONS: Lung transplant recipients who received IVIG were less likely to experience delirium and had shorter delirium duration. Prospective studies in larger lung transplant cohorts are needed to confirm this association and to determine the extent to which postoperative neuroinflammation may be altered following IVIG administration.

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S-436.

THE INCIDENCE OF AIRWAY COMPLICATIONS FOLLOWING POSTERIOR OCCIPITOCERVICAL SPINE FUSION

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INTRODUCTION: The management of the airway may be challenging in patients undergoing occipitocervical spine fusions (OCF). Limited information is available regarding the incidence, severity, the mechanism, and the risk factors for postoperative airway complications after OCF. Changes in the occipitocervical angle (dOC2A) of fusion after surgery may result in acute airway obstruction, dyspnea and/or dysphagia.[1,2] The aim of this study was to determine the incidence, nature, and risk factors for postoperative airway complications in patients undergoing OCF and to determine the relationship between the dOC2A and airway complications.

METHODS: After IRB approval, we retrospectively reviewed the charts of all patients who underwent OCF from 2005-2013. We excluded patients who had combined anterior/posterior or revision surgeries and those already intubated or with tracheostomy. Data collected included patient demographics, airway management, anesthesia and surgical data, and postoperative complications. Plain lateral radiographs or computed tomography were used to measure the dOC2A (Figure 1). Immediate postoperative airway complications included in the analysis were the need for reintubation and the delay of extubation in the operating room. Delayed complications were tracheostomy, pneumonia and mortality. Statistical analyses were done using unpaired t test, Mann-Whitney U test, Chi-square test and Fisher's exact test, as appropriate. P-value of <0.05 was considered significant.

RESULTS: Records of 59 patients were reviewed. Demographic data are shown in Table 1. Common indications for surgery included degenerative, rheumatoid arthritis, metastases and fracture. Following extubation in the operating room (OR), there were no complications in 43 (73%) patients (Group 1). Airway complications were seen in 16 (27%) patients (Group 2); 4 patients required re intubation (2 in the OR, 2 in post anesthetic care unit), and 12 had delayed extubation and were taken to the intensive care unit intubated. The number of vertebral levels fused, presence of difficult intubation and duration of surgery were significantly associated with airway complications. There was no significant difference in the dOC2A between the groups (-1.070±5.527 versus -4.375±10.788, p=0.127) (Table 2).

CONCLUSIONS: Airway management in patients undergoing OCF poses a challenge for anesthesiologists. The incidence of airway complications was 27%. The decision to extubate needs to be individualized, and factors such as difficult intubation, number of vertebral levels fused and the duration of the surgery has to be considered. We could not find a significant correlation between dOC2A and postoperative airway complications. The risk factors for postoperative airway complications are multifactorial and there is a need for prospective study to identify the risk factors.

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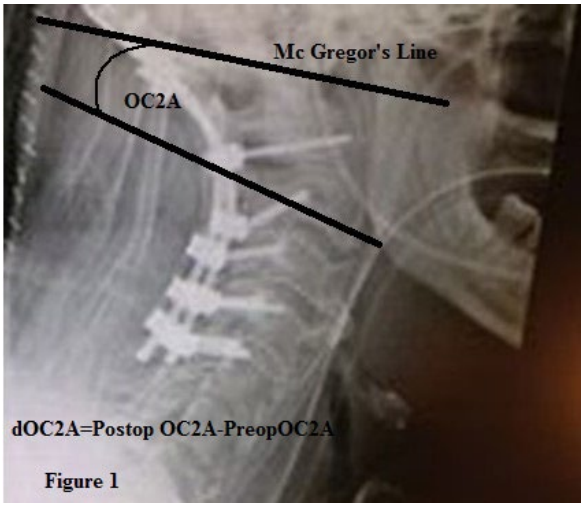

Figure 1

Table 1: Demography and Baseline Data

	No Complications n=43	Complications n=16	p value
Age (yrs) (mean±SD)	65.11±13.7	57.69±15.73	0.08
M:F (n)	22:21	10:6	0.333
Levels of vertebrae (n) ≤6 >6	29 14	5 11	0.012*
Duration of Surgery (min) (mean±SD)	333.87±83	493.12±138.11	0.0001*
Estimated blood loss (ml) (mean±SD)	726.97±1085.29	772.18±584.94	0.875
Fluid intake (ml) (mean±SD)	3927.30±1654.25	4572.5±1666.42	0.195
Difficult Intubation (n)	4	8	0.002*
*p<0.05			

S-437.

NOVEL WIRELESS DEVICES TO DRIVE OPTOGENTIC ACTIVATION OF THE LOCUS COERULEUS AND EVOKE AROUSAL AND ACTIVITY IN MICE

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INTRODUCTION: Optogenetic tools allow for anatomic and temporal control of neuronal activity. Use of optogenetic tools has provided fundamental insights into brain function. Optogenetics utilizes light to activate genetically encoded photosensitive ion channels expressed in neurons and alter neuronal activity. Canonically, these experiments require implantation of an optic fiber into the brain that must be connected to a light source via fiber optic cable. To make the connection requires that the animals be handled and then they are tethered via the optic cable introducing obvious confounds to experiments exploring neural circuits involved in sleep and arousal.

METHODS: In the experiments reported here, we utilized novel wireless LED devices to provide photostimulation to the locus coeruleus (LC) of mice in their home cage. The devices are miniaturized and flexible allowing for them to be implanted, affixed to the skull and the skin closed completely. The LED light source is controlled and powered via radiofrequency transmission. To explore the utility of these devices in the study of sleep/wake circuitry we carried out experiments targeting the LC, a nucleus important in driving arousal. Mice expressing Cre recombinase under control of the galanin promotor (Gal-Cre +) or wild type (Gal-Cre -), were stereotactically injected unilaterally in the LC with adeno-associated virus (AAV) encoding for recombinase dependent expression of channelrhodopsin (AV5-DIO-EF1a-ChR2). The galanin neuropeptide promoter restricted expression of Cre to a subset of neurons in the LC. The mice were subsequently implanted with devices and medially directed LED light sources were placed 1 mm lateral to previously injected LC nuclei. Injection and implantation sites were confirmed by immunohistochemistry once all experiments were completed. Mice were allowed to recover for a minimum of 2 weeks after surgery. A minimum of 48 hrs prior to recording, home cages were mounted on custom built adapters that held RF emitting antennas close (~5 cm) to the cage wall and floor. During a period of normally high sleep and inactivity (~10 am) the movement of each mouse was recorded over three successive 15 min epochs. During the first and last epoch activity was recorded and no optical stimulation was provided to the LC via the implanted device. During the second epoch the LC was optically activated at 10Hz. No contact or disturbance of the animals was required. All experiments were carried out in accordance with IRB approved protocols.

RESULTS: During the period of photostimulation, Gal-Cre + but not Gal-Cre - animals showed a marked increase in movement in their home cage and activity decreased to baseline when the stimulation was stopped.

CONCLUSIONS: These results demonstrate the utility of wireless optogenetic systems to further explore neural circuits regulating sleep and arousal. Further, the results support the role of LC neurons in driving behavioral arousal and the sufficiency of the galanin subpopulation to drive arousal.

S-477.

NEURON-TARGETED CAVEOLIN-1 DECREASES SEVERITY AND EXTENDS SURVIVAL IN THE hSOD1G93A MOUSE MODEL OF AMYOTROPHIC LATERAL SCLEROSIS

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BACKGROUND: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by a loss of somatic upper and lower motor neuron pathways that leads to diffuse muscle weakness, paralysis, and death. Interventions that protect neurons might decrease disease severity and increase survival. Caveolin (Cav) is a cholesterol-binding and scaffolding protein present in membrane/lipid rafts (MLR). Previous work from our group demonstrated that neuron-targeted Cav-1 over-expression (SynCav1) in vivo augments MLR formation, increases pro-growth and pro-survival signaling, promotes neuroplasticity, and improves behavioral function. It is therefore conceivable that Cav-1 over-expression might reduce motor neuron death and prolong survival in ALS. Transgenic (TG) mice expressing ALS-linked human superoxide dismutase 1 mutant protein (hSOD1G93A) exhibit an ALS-like neurodegenerative phenotype. In this study, we mated TG hSOD1G93A mutant mice (SOD1) with TG mice engineered to over-express Cav-1 in neurons (SynCav1) and evaluated disease onset, progression, and mortality in SOD1 positive and SOD1-SynCav1 double positive offspring.

METHODS: C57BL/6 wild type, SOD1, SynCav1, and SOD1-SynCav1 mice were utilized. Body weight was measured weekly between 6 and 17 weeks. Voluntary running wheel (VRW) test was performed at 8, 12, and 16 weeks. Motor-evoked potentials (MEP) in upper and lower limbs were evaluated weekly between 12 and 16 weeks. Spinal cord motor neurons were quantified histologically at 12 and 16 weeks. Survival analyses were performed using Kaplan-Meier estimator.

RESULTS: SOD1-SynCav1 mice had prolonged survival compared to SOD1 mice (median survival=182 vs 153 days, p=0.0006, n=18-19 mice/group). SOD1-SynCav1 mice had higher body weight at 16 and 17 weeks (p=0.003, n=20 mice/group). The dramatic and progressive weight loss observed in SOD1 mice was not seen in SOD1-SynCav1 mice (23% decline at 17 weeks from max weight at 10 weeks vs 5.3% decline at 17 weeks from max weight at 12 weeks). SOD1-SynCav1 mice performed better on the VRW test at 12 weeks (velocity and total distance, p=0.0045, n=9-10 mice/group). MEP amplitude was larger in upper and lower limbs in SOD1-SynCav1 mice at 14 weeks (p=0.003, n=9-10 mice/group). MEP latency was shorter in lower limb in SOD1-SynCav1 mice from 12-16 weeks ($p < 0.05$, n=9-10 mice/group). The number of motor neurons in the thoracic and lumbar spinal cord at 12 weeks was greater in SOD1-SynCav1 mice (p=0.02, n=4 mice/group).

CONCLUSION: These data demonstrate that neuron-targeted Cav1 over-expression leads to delayed onset, preserved neuromuscular function, and increased survival in the SOD1G93A mouse model of ALS. The increased number of motor neurons seen in SOD1-SynCav1 mice suggests that Cav1 affords neuroprotection. These proof-of-principle findings suggest that Cav1 over-expression as a novel therapeutic intervention to reduce disease severity and prolong survival in ALS warrants investigation.

Scholars' Abstracts

Obstetric Anesthesiology

S-438.

COMPARISON OF ANTIEMETIC AND OPIOID USE IN PATIENTS UNDERGOING CESAREAN SECTION WITH SPINAL ANESTHESIA CONTAINING FENTANYL VERSUS MEPERIDINE

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INTRODUCTION: Meperidine is a hydrophilic opioid with a lipid-H20 partition coefficient between fentanyl and morphine.[1] Based on this property, IT meperidine provides analgesia of intermediate duration with lower risk of respiratory depression.[2] At higher doses[3,4] and compared to placebo[5,6], meperidine causes more nausea and vomiting but this occurs with any opioid. Our aim is to retrospectively investigate the efficacy and side effect of 10mg meperidine combined with bupivacaine in Cesarean sections with spinal anesthesia. Our objective is to determine the amount of antiemetics used intraoperatively as a measure of nausea and vomiting, and evaluate the 24 hour postoperative opioid use.

METHODS: 211 (n=66 in meperidine and n=145 in fentanyl groups) ASA I-II women who underwent spinal anesthesia with 0.75% hyperbaric bupivacaine and 10mg meperidine or 0.75% hyperbaric bupivacaine and 15mcg fentanyl between Jan 2013-Dec 2014 for C-section were included. Analysis included antiemetic use (propofol, dexamethasone, ondansetron, metoclopramide, glycopyrrolate, diphenhydramine, droperidol, phenegran), 24 hour postoperative opioid use, highest and lowest SBP, vasopressor use, and total IV fluid.

RESULTS: More patients in the meperidine group received antiemetics (89.4% vs 65.5%, p<0.001). Propofol has many uses; we use it as a hypnotic, anxiolytic and antiemetic.7 Analysis without propofol suggests a trend towards more antiemetic use in the meperidine group but results were not significant (Table 1). There was a 10% decrease of 24-hour IV morphine equivalent use in the meperidine vs fentanyl group (33.8 mg vs 37.2 mg, p<0.05) (Table 1).

There was no difference in the incidence of hypotension (53.8% vs 66.7%, p=0.79) and vasopressor use (84.1% vs 87.9%, p=0.48) between the fentanyl and meperidine groups (Table 1). More IV fluid was given to: 1) the meperidine vs fentanyl group (1986ml 95%CI 1757-2215 vs 1545ml 95%CI 1406-1684, p<0.05), and 2) subjects who received antiemetics vs those who did not receive antiemetics (1908ml 95%CI 1764-2052ml vs 1623ml 95%CI 1397-1848, p<0.05)(Figure 1).

CONCLUSION: Our study shows IT 10mg meperidine is associated with more antiemetic use compared to IT 15mcg fentanyl, suggesting more nausea and vomiting with IT meperidine. IT meperidine was associated with a 10% decrease in postoperative opioid use. Further prospective, RCTs will be required to further delineate the risk-benefit of 10mg IT meperidine use.

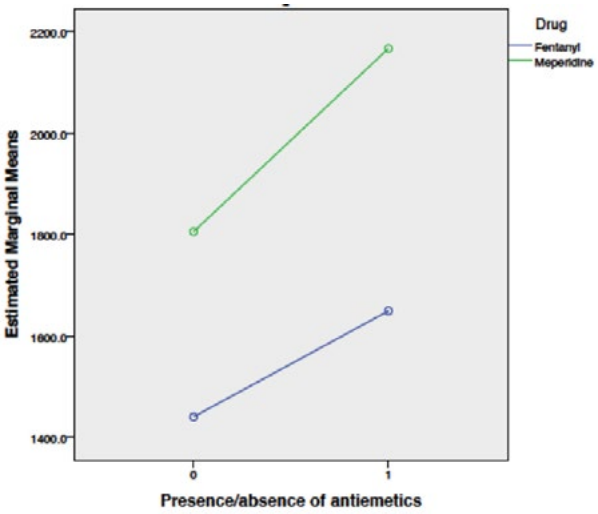

Table 1 - Outcome Measures

	Fentanyl	Meperidine	p-value
Use of Antiemetics	65.5%	89.4%	<0.001
Use of Antiemetics Excluding Propofol	62.1%	74.2%	0.08
Postoperative IV Morphine Equivalents (mg) [Mean(SD)]	37.2 (11.6)	33.8 (8.5)	<0.05
SBP Decrease >20%	53.8%	66.7%	0.79
Use of Vasopressor	84.1%	87.9%	0.48

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S-478.

MASSIVE CARDIAC THROMBOSIS AND DISSEMINATED INTRAVASCULAR COAGULOPATHY IN A PATIENT WITH RETAINED DEAD FETUS SYNDROME

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PATIENT PRESENTATION: A 30-year-old GA2014 at 24 weeks gestation presented to the ED with sudden onset chest pain, shortness of breath, and palpitations. Two days PTA, she was diagnosed with interauterine fetal demise; US revealed a 14-week-sized fetus and "surprisingly vascular" uterus. CT was negative for PE, but revealed signs for heart failure. Labs in the ED revealed BNP 2122, INR 1.1, fibroinogen 171, H/H 13.6/38.9, and plts 161. EKG showed sinus tachycardia, LAE. Formal TTE: global hypokinesis, EF 30-35%, dilated LA, MVP with regurgitation, and elevated RV pressure. Cardiology consult stated new onset HF may be due to DMD carrier status (recent diagnosis). MRI showed demised 14-week gestation with macerated products of conception, relatively unclear planes between the uterus and uterine contents, and prominent para-uterine vasculature. The patient was admitted and scheduled for a D&C/possible hysterectomy.

OR COURSE—D&C:

- 1842: IV induction, easy intubation, difficult arterial line placement
- 1909: Incision
- 1930: 1600 mlacute blood loss
- 1949: Open conversion, uterotonic agents
- 2015: Total of 2500 ml blood loss, epi gtt, TEE shows global hypokinesis, EF 20-25%
- 2153: TEE shows left ventricle completely filling with sludge causing near complete akinesis, compressions/ACLS started
- 2200: EBL 6L, Hct 23, PT 57.1, INR 6.1, fibrinogen <35
- 2217: Time of death

DISCUSSION: This case presents intraoperative death from a large cardiac thrombus associated with DIC in the setting of retained dead fetus syndrome in a patient with carrier status for Duchenne Muscular Dystrophy and new onset dilated cardiomyopathy. DIC is a disorder of hemostasis resulting in massive activation of the clotting cascade with consumption of pletelets and clotting factors in addition to massive thrombolysis, leading to both thrombosis and hemorrage.[3] This disorder is a rare but well-known complication of retained products of an intrauterine fetal demise.[4]

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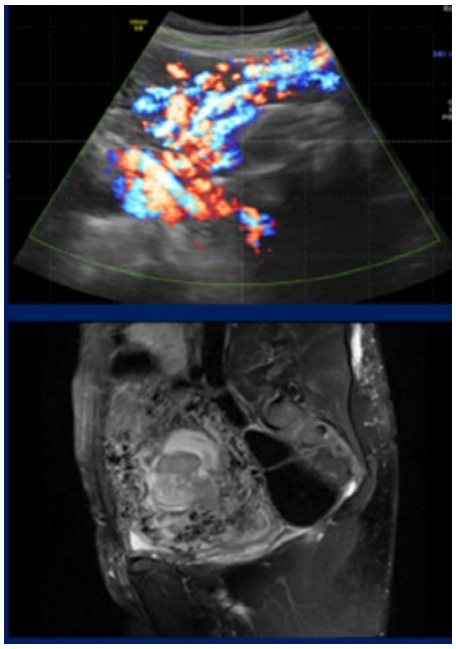

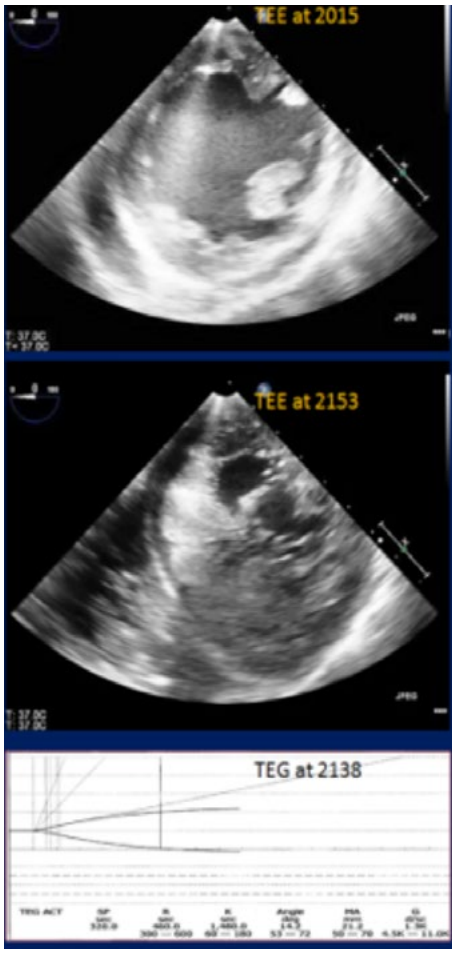

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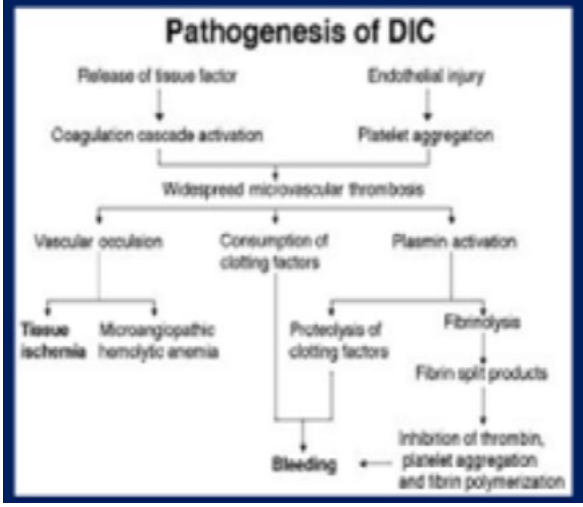
S-478 • continued

Laboratory Test	Result	Score
Platelet count (cells/uL)	>100,000	0
	50,000 – 100,000	1
	<50,000	2
Increase in fibrinogen and fibrin-related markers (eg, FDP's)	None	0
	Moderately increased	2
	Strongly increased	3
Prolonged prothrombin time	<3	0
	3-5.9	1
	>6	2
Fibrinogen	>1 g/dL	0
	<1 g/dL	1

ISTH Scoring System: >5 – Clear Diagnosis

Parameters	Modified ISTH score
Platelet count, 10^9/L	< 50 = 1
	50-100 = 2
	100-185 = 2
	> 185 = 0
INR	< 0.5 = 0
	0.5-1 = 5
	1.0-1.5 = 12
	> 1.5 = 25
Fibrinogen, mg/dL	300 = 25
	300-400 = 6
	400-450 = 1
	> 450 = 0
Calculated score	> 26 high probability for DIC

Modified ISTH Scoring System for Use In Pregnancy



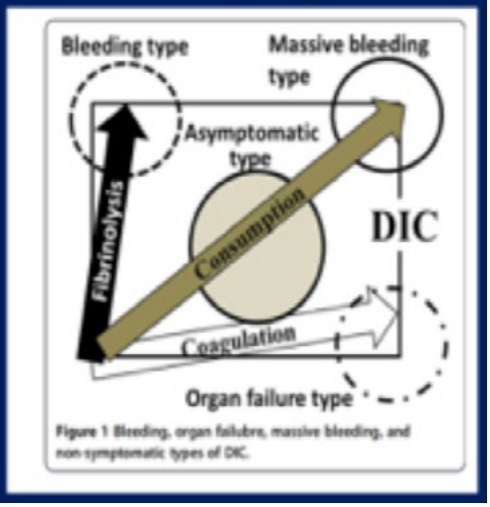


Figure 1 Bleeding, organ failure, massive bleeding, and non-symptomatic types of DIC.

Scholars' Abstracts

Pain Mechanisms

S-439.

DIFFERENTIAL INHIBITION OF SENSORY NEURONS AND ACTIVATION OF SYMPATHETIC OUTFLOW FROM THE DORSAL PERIAQUEDUCTAL GRAY OF ANESTHETIZED RATS

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INTRODUCTION: Sympatho-sensory integration in the dorsal periaqueductal gray (dPAG) is fundamental to the response to acute stress. A differential increase in sympathetic nerve activity and blood pressure accompany decreased sensitivity to pain (antinociception) to allow escape from a stress or. The ability to disassociate the two components could provide therapeutic potential to decrease the response to pain without the unwanted side effects of increased sympathetic outflow and blood pressure. This study was undertaken to determine if there is anatomical separation of neurons in the dPAG that influence autonomic and sensory neurons.

METHODS: Blood pressure, whole renal sympathetic nerve activity (RSNA) and unit discharges of dorsal horn neurons (DHN) responding to high intensity mechanical stimulation of the hindpaw were recorded from anesthetized rats. The synaptic excitant D,L-homocysteic acid was microinjected into the dPAG, targeting coordinates from which a stress response was evoked in previous studies[1]. Microinjections were made at 0.5 mm depth intervals and blue dye microinjected at the deepest microinjection site for subsequent histological mapping. Electrophysiological data were analyzed using Spike2 software and Sigma Plot 11. The animal use for this study was approved and supervised by the Institutional Animal Care and Use Committee (IACUC).

RESULTS: Four patterns of neural responses have been identified: i) increased RSNA with decreased DHN discharge - suggesting no anatomical discrimination of dPAG neurons; ii) increased RSNA with no change DHN - suggesting sympathetic control without DHN change; iii) no change in RSNA and a decrease in DHN - suggesting anatomical separation of dPAG neurons that control analgesia, but not sympathetic outflow; and iv) no change in either RSNA or DHN - suggesting a microinjection site outside of the stress pathway. Correlations performed to date of microinjection site to response pattern show no clear anatomical location of discriminate neurons.

CONCLUSIONS: These data demonstrate selective inhibition of DHN activity by dPAG neurons that could evoke antinociception without autonomic activation (tachycardia or hypertension). These findings are promising that a potential central therapeutic target for pain relief could be identified.

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S-440.

VALIDATION OF INSULA CONNECTIVITY CHANGES DURING PAIN

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AFFILIATION: Department of Anesthesiology, University of Pittsburgh, Pittsburgh, PA

INTRODUCTION: Pain is a complex, multidimensional sensory and emotional experience. As such, attempts to objectively measure pain have been met with limited success[1]. Functional connectivity MRI (fcMRI) offers a promising new avenue toward a neuroimaging based method for differentiating between pain and non-pain states[2,3]. The insula is a key region for pain processing, with changes in both activity and functional connectivity shown for acute and chronic pain states[4].

PURPOSE: Prior work has demonstrated that functional connectivity between the posterior insula (pIns) and posterior cingulate cortex (PCC) is uniquely altered by pain perceptio[n5]. Further, using a carefully selected pIns-PCC connectivity threshold value, we were able to differentiate pain scans from non-pain scans with 92% accuracy. The current study sought to validate our previous findings with the use of an independent sample, as well including innocuous touch as a non-painful control condition.

METHODS: We present interim results from 3T BOLD functional imaging data from 5 healthy adults in each of 4 conditions: rest, innocuous touch, light pain, and moderate pain. Innocuous touch consisted of a researcher continuously moving a gauze pad around the left volar forearm of each subject. Velocity, direction, and pressure were varied randomly to ensure the salience of this stimulus. Pain was induced with topical application of capsaicin to the same region of the left volar forearm. This remained in place for 30 minutes. The light pain condition occurred at the beginning of this 30-minute period; the moderate pain condition occurred at the end. Functional connectivity maps were generated using the CONN toolbox for SPM. ROC curves were generated to assess the capacity of pIns to PCC connectivity to identify the presence of pain. Our previously determined pIns-PCC connectivity threshold was assessed for overall accuracy of classification, sensitivity, and specificity.

RESULTS: Group average functional connectivity maps revealed altered pIns to PCC connectivity in response to pain, consistent with our previous findings (Figure 1). The area under the ROC curve for pIns-PCC connectivity in predicting the presence of pain was 0.71 (95% CI = 0.46-0.95; Figure 2). Using our previously determined connectivity threshold value, we were able to differentiate non-pain scans (i.e., rest, innocuous touch) from pain scans (i.e., light pain, moderate pain) with 70% overall accuracy (sensitivity = 0.9, specificity = 0.5).

CONCLUSIONS: These preliminary results support our prior findings that pIns-PCC functional connectivity is altered by pain perception, and suggests that a pIns-PCC connectivity threshold is sensitive to pain state, although improvements are needed to increase the specificity. This supports a potential role for pIns-PCC connectivity in a neuroimaging based method for differentiating between pain and non-pain states.

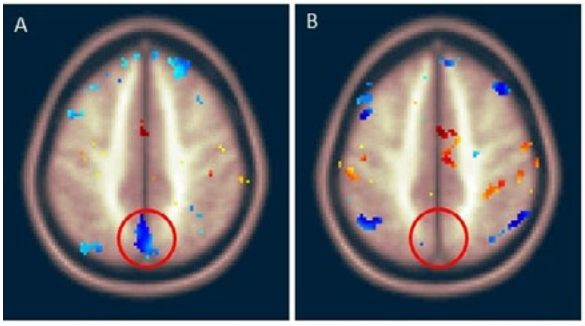

Figure 1. Group average connectivity maps showing the connectivity of the posterior insula at rest (panel A) and during moderate pain (panel B). The posterior cingulate cortex is outlined in red, highlighting the alteration in pIns-PCC connectivity in response to pain.

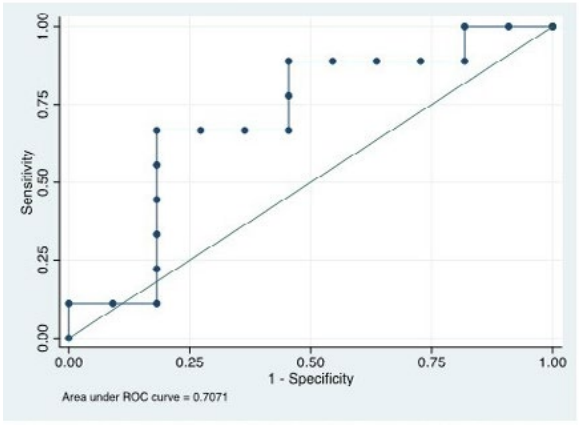

Figure 2. Receiver operating characteristic (ROC) curve for pIns-PCC connectivity in the detection of pain. Area under the curve is 0.71 (95% CI = 0.46 – 0.95).

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S-441.

CHARACTERIZATION OF NEURONS INVOLVED IN DESCENDING PAIN CONTROL REVEALS DELTA AND MU OPIOID RECEPTOR EXPRESSION IN MICE

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INTRODUCTION: The rostral ventromedial medulla (RVM) is a region in the brainstem that gates the descending control of pain. Subsets of projection neurons in the RVM modulate painful sensations by intercepting the incoming sensory information as it enters the spinal cord. Three populations of modulatory projecting neurons (ON, OFF, and Neutral cells) have been described in the RVM based on their firing pattern in response to a painful stimulus. At baseline, ON and OFF cells oscillate between periods of active firing and quiescence. In the event of a painful stimulus, ON cell activity increases and OFF cell activity decreases, while Neutral cell activity remains unchanged[1]. Studies in which pain thresholds are altered have shown that ON cells are more active in hypersensitive states (e.g. chronic injury) and OFF cells in hyposensitive pain states (e.g. systemic morphine)[2]. Thus, the bimodal coordination of ON and OFF cell activity in the RVM modulates pain thresholds by ON cell mediated facilitation or OFF cell mediated inhibition of pain signal transmission[1].

Mu and delta opioid receptors (MOR and DOR) are inhibitory G protein-coupled receptors that regulate neurotransmission. MOR distribution along descending RVM projections has been investigated using pharmacological and electrophysiological methods. These studies have suggested that MOR is expressed by ON cells and inhibits action potential firing in these neurons to depress descending pain facilitation. Unlike MOR, the role of DOR in the RVM remains unclear. In this study, we used knock-in reporter mice that express DOReGFP and MORmCherry fusion proteins to reveal the location of DOR expressing neurons in the RVM and examine possible DOR and MOR co-expression.

METHODS: Fluorogold, a retrograde tracer, was stereotaxically injected into the lumbar dorsal horn of reporter mice. Mice were transcardially perfused with a 4% formaldehyde solution and the hindbrain was sectioned on a cryostat. Tissues were processed using fluorescent immunohistochemistry.

RESULTS: Our immunohistochemical experiments revealed that 43% of spinally projecting neurons are DOR+. Further characterization showed that 60% of DOR+ cells are GABA+ while less than 1% of DOR+ cells express 5HT. Importantly, MOR and DOR expression in the RVM overlaps, with 57% of DOR+ cells co-expressing both receptors.

CONCLUSIONS: Altogether, our results suggest that DORs are predominately in inhibitory projection neurons, and, like MOR+ cells, DORs may be expressed by ON cells. Additionally, MORs and DORs are also expressed in separate populations which may be inhibitory interneurons, since the populations of MOR+ and DOR+ cells that independently express each receptor are predominately GABAergic. In combination with ongoing functional studies, these results will elucidate the function of DORs in projection and interneurons in the RVM and indicate how DORs and MORs cooperate to fine-tune descending pain control.

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Scholars' Abstracts

Pain Medicine

S-442.

THE ANALGESIC EFFECTS OF DOPAMINE IN MICE

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INTRODUCTION: Drugs which modulate neural dopamine (DA) produce significant analgesia, while also preventing the opioid-induced side effects of nausea, respiratory depression and sedation. Despite their potential, DA modulating agents have never become a clinical tool for the relief of pain, possibly due to a lack of understanding about their mechanism of action. We hypothesized that DA neurons in the periaqueductal gray (PAG) exert a powerful modulating effect on pain and are important participants in descending pain inhibition. To test this hypothesis, we used DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) to see if selective stimulation of DA neurons in the PAG could produce analgesia in an inflammatory pain model.

METHODS: This study was approved by the authors' IRB for animal research. DREADDs are G-protein coupled receptors engineered to be selectively activated by the ligand Clozapine N-Oxide (CNO). Male, adult DAT-cre mice received bilateral injections of adeno-associated virus carrying an excitatory DREADDs construct (hM3Dq) into the ventral lateral PAG. Control mice were similarly prepared, but received a construct lacking the hM3Dq receptor. After 4 weeks to allow stable viral transfection, thermal hyperalgesia was measured by injecting a carrageenan solution into a single hind paw and measuring the time latency for paw withdrawal upon thermal stimulation. Viral expression and localization were confirmed using immunohistochemistry upon completion of the study. D-amphetamine is a clinically available drug which modulates neural DA levels, and provides a translational approach to examine the clinical relevance of exciting DA neurons in the PAG. We subsequently treated carrageen-induced hind limb pain in adult male C57BL/6 mice with intraperitoneal (ip) D-amphetamine, and compared the analgesic effect with morphine treated mice. Results: We found that following ip CNO injection in control mice (n=8), paw withdrawal latency in the carrageenan injected paw was significantly decreased at 2.4±0.7s compared with 8.0±1.5s in the non-injected paw, indicating significant thermal hyperalgesia (FIG 1). Animals with DREADD activation of vlPAG DA neurons by CNO (n=9) showed no significant difference in paw withdrawal latencies between treated (8.2±1.7s) and untreated paws (9.3±1.6s), indicating that DA neuron activation in the PAG prevented inflammation-induced thermal hyperalgesia. Histologic examination of neural tissue following the experiments confirmed DREADD viral expression in PAG DA neurons. As shown in FIG 2, a dose dependent increase in paw withdrawal latencies was observed with ip. D-amphetamine treatment. 6mg/kg of D-amphetamine was as effective as 3mg/kg of morphine in eliminating hind paw pain in carrageenan induced inflammation, suggesting a powerful analgesic role for DA modulating drugs.

CONCLUSIONS: In summary, selective activation of DA neurons in the vlPAG as well as systemic administration of D-amphetamine produced profound analgesia in an inflammatory pain model. DA modulating agents may represent a novel new treatment for pain.

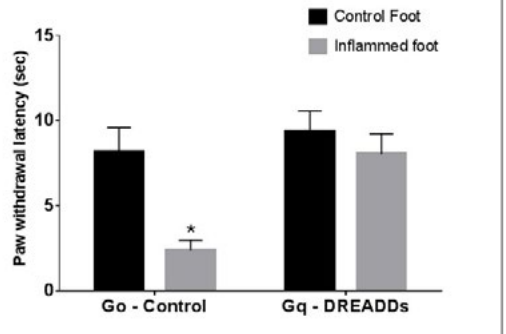

Figure 1. Effect of PAG dopamine neuron activation on thermal hyperalgesia. Control mice lacking the hM3Dq receptor (G_o – Control, n=8) exhibited significantly decreased paw withdrawal latency in the carrageenan injected paw, indicating significant thermal hyperalgesia. Activation of vlPAG DA neurons in mice prepared with Gq DREADDs (n=9) completely eliminated thermal hyperalgesia, as demonstrated by a lack of significant difference in paw withdrawal latencies between treated and untreated paws.

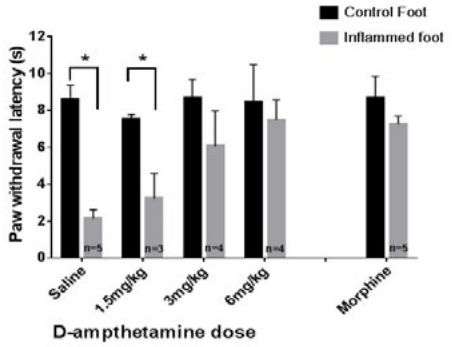

Figure 2. Analgesic effect of D-amphetamine. Mice experiencing thermal hyperalgesia due to carageenan induced inflammation exhibited a dose dependent increase in paw withdrawal latencies with D-amphetamine treatment, indicating an abolishment of the thermal hyperalgesia perceived by the mouse. 6mg/kg of D-amphetamine was found to be as effective as 3mg/kg of morphine in eliminating thermal hyperalgesia. (* indicates significance p<0.05.)

S-443.

LOW-DOSE KETAMINE INFUSIONS FOR ACUTE PAIN MANAGEMENT OF BURN PATIENTS

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INTRODUCTION: Ketamine is frequently used as an adjuvant non-opioid for pain management. A low-dose ketamine infusion, however, has been shown to limit opioid related side effects. The Cochrane Review in 2006 published "Perioperative ketamine for acute postoperative pain" and demonstrated that "ketamine in subanesthetic dose (that is a dose which is below that required to produce anesthesia) is effective in reducing morphine requirements in the first 24 hours after surgery. Adverse effects are mild or absent."[1] In the light of these results, we investigated the efficacy of pain management action of ketamine in burn patients and found lower Numeric Rating Scale (NRS) pain scores during and after ketamine infusion on average.

METHODS: Two matched cohorts consisting of 16 burn patients each were analyzed to determine the effect of ketamine infusion on numeric rating scale (NRS) pain scores. The patient groups were equally matched with respect to sex, percentage body surface area burned, and age. Patients received 48 to 96 hours of continuous low dose ketamine infusions, ranging between 0.1 to 0.25 mg/kg/hour based on actual body weight. All of the patients were followed by the Acute Pain Medicine service and placed on a scheduled multimodal analgesic regimen with a minimum of two non-opioid agents, in addition to low-dose ketamine.

RESULTS & DISCUSSION: For the cohort that received ketamine, the average reduction in Numeric Rating Scale (NRS) pain scores across 16 patients during the low-dose ketamine infusion was 1.6 points ± 2.3. Similarly, post completion of the ketamine infusion pain scores were also better than those recorded on the pre-ketamine day on average, with a reduction in average pain scores by 2.4 points ± 2.4. This represents a noticeable change in patient perception of pain after burns, leading to the conclusion that ketamine improves reported NRS pain scores and subjective pain control. It also represents the lasting benefit of a ketamine infusion on pain control post-infusion therapy.

CONCLUSION: Ketamine appears to be a safe and effective way to noticeably alleviate patients' suffering and improve pain control in the wake of significant burn injuries.[2,3] Additionally, at a cost of less than ten US dollars for a course of therapy, ketamine is a very cost effective medication in an era of value based care. In this study, patients reported lower NRS scores at rest and with dynamic activity, such as physical therapy. Thus, there now appears to be a clinical signal indicating a low-dose continuous ketamine infusion is safe and efficacious in improving acute pain control in the burn population without increased monitoring requirements, adverse effects, or respiratory depression.

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S-444.

WITHDRAWN.

S-445.

EXPLORING THE ROLE OF AYURVEDA IN ENHANCING CLINICAL PRACTICE AND PHARMACOTHERAPY IN PAIN MEDICINE

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INTRODUCTION: Complementary approaches for pain management are widespread.[1] Literature and clinical practice has focused on integration of Traditional Chinese Medicine techniques. This study aimed to explore Ayurveda, India's oldest medical system, as a potential source of clinical strategies in pain medicine.

METHODS: A review of the seminal Ayurvedic texts was conducted to determine core interventions used historically for pain management. This was followed by a PubMed literature review of existing data (2003-2015) on Ayurvedic pain management strategies, with an emphasis on identifying avenues for integration of Ayurvedic pain practices.

RESULTS: 8 Ayurvedic clinical strategies (table 1) and 13 herbal formulations (table 2), were identified for painful conditions. Several studies revealed statistically significant ($p<.05$) results in the reduction of pain in patients with arthritic conditions, degenerative disk disease, and low back pain.[2-17] Most promising include the use of Agnikarma for low back pain/sciatica, Basti for arthritic pain, Nasya for spondylosis pain, and Snehan for sciatic pain. Limitations included a small number of randomized studies, limited sample size, and predominance of open label studies. Among the Ayurvedic herbal formulations, several demonstrated statistically significant analgesia in animal models, along with reductions in joint pain and migraines in clinical trials.[18-30] Though human studies are limited, the finding of equivalence of Shunthi Guduchi to celexcoxib/glucosamine in joint pain reduction, and the effectiveness of AyTp in migraines are of particular note.

CONCLUSIONS: Ayurveda serves as a promising body of knowledge from which to further develop novel clinical interventions and pharmacotherapies in pain medicine. Ayurvedic herbomineral formulations demonstrate a valuable role in developing non-opioid analgesics and anti-inflammatories. In order to further generate a substantial body of scientific evidence to support and adopt Ayurvedic strategies into pain management, more robust clinical trial designs with a larger sample size, with an emphasis on safety and efficacy, may be important steps towards active integration by pain physicians.

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Table 1: Primary Interventional and Non-Interventional Modalities for Pain Therapy in Ayurveda

Name	Description	Targeted Pain in Ayurvedic Practice	Targeted Painful Conditions in Research Literature	Study Designs	Pain Scoring Methodologies	Major Study Conclusions
Katibasti	Localized topical oil therapy using circumferential ring of paste to define borders	Sciatic pain, low back pain	Sciatic pain	Randomized control open label	Numerical pain analogue scale	1. Total relief of pain in 50% of subjects using Katibasti 2. Significant (p<.01) reduction in pain with Agnikarma vs. Katibasti
Basti	Per rectal administration of oil and herbomineral formulations	Sciatic pain, low back pain, degenerative disk disease	Sciatic pain, avascular necrosis (AVN), osteoarthritis (OA), rheumatoid arthritis (RA), lumbar spondylosis (LS)	Case report, uncontrolled open label	Oswestry low back pain scale, Pain-VAS*, sciatic nerve tenderness	**AVN:** Reduction in pain score from 9 to 3 **OA:** Significant (P<.05) reduction in pain **RA:** Significant (P<.001) reduction in joint pain **LS:** Improvement in pain scores **Spondylosis:** Reduction in pain intensity **Sciatica:** Reduction in sciatic nerve tenderness
Nasya	Nasal insufflation of herbal formulations	Headaches, back pain, disk disease	Cervical spondylosis	Randomized control open label	Pain-VAS	Statistically significant (p<.001) improvement in pain individually and when compared to conservative management with herbal massage
Agnikarma	Cauterization therapy using heat transmitted through metallic point	Sciatic pain, joint pain, low back pain, soft tissue pain	Sciatic pain, tendonitis	Case report, randomized control open label	Numerical analogue pain scale, Pain-VAS	**Sciatica:** 1. Significant (p<.01) reduction in pain with Agnikarma vs. Katibasti 2. Significant reduction in pain with Agnikarma vs. Siravedha (puncture) 3. Significant reduction (p<.05) in pain using copper, iron, and mixed metal instrumentation
Marmapuncture/ Siravedhana	Use of needles to puncture vital "energy" points/ vessels in the body, similar to acupuncture	Headache, sciatic pain	Sciatic pain	Randomized control open label	Pain-VAS	Moderate to marked improvement in pain, though inferior to Katibasti
Suchika Voron	Local infiltration of venom into tissue	Joint pain	Arthritic pain	Rat model	Tail flick	Reduction in pain perception parameters
Snehan/ Swedan/ Abhyanga	Full body massage with heated and herbally-medicated oil	Low back pain	Sciatic pain	Randomized open label	4-point pain scale	Significant (P<.001) reduction in pain post administration of Snehan
Panchkarma	Combination of body massage, herbal oil on forehead, enema, and nasal insufflation	General bodyache	Fibromyalgia	Nonrandomized open label	Numerical pain analogue scale	Mild reduction in pain in the Panchkarma vs. conventional therapy approach, and reduction in FIQ** scores in both groups

*VAS: Visual analogue scale
**Fibromyalgia Impact Questionnaire

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S-445 • continued

Table 2: Existing Data on Ayurvedic Herbal Formulations for Pain Management

Herbal Entity/Formulation	Targeted Pain in Ayurvedic Practice	Targeted Painful Condition in Literature	Study Design	Pain Assessment Method	Conclusions
Conolodine from T. divaricate	Generalized pain	Generalized nociception	IV Conolodine vs. control in mouse model	Acetic acid, formalin	Significant (p<.01) reduction in pain parameters in induced model of acute and chronic nociceptive pain
Draksharishta (DRK)	Back pain, joint pain	Peripheral and central analgesia	Feasibility study in mouse model vs. control	Acetic acid, formalin test, hot plate	Significant (p<.05) reduction in acetic acid and writhing reaction, indicating potential peripheral analgesia
Gambhari (G. arborea Roxb)	Joint pain, headaches	Central and peripheral analgesia	Feasibility study in rat model vs. control	Acetic acid, hot plate	Significant (p<.01) reduction in hot plate and acetic writhing reaction, indicating potential peripheral analgesia
Laghupanchamula (five herb combination)	Joint pain, generalized pain	Central and peripheral analgesia	Feasibility study in rat model	Acetic acid, hot plate	Dose-dependent elevation in pain threshold and peak analgesic effect
C. ternatea	Generalized body ache, joint pain	Central and peripheral analgesia	Feasibility study in rat model	Acetic acid, hot plate, formalin	Significant (p<.05) reduction in pain parameters with evidence of central and peripheral effects
Shunthi Guduchi (4 herb formulation)	Joint pain	Joint pain	Randomized, double-blind, parallel-efficacy, four-arm, multicenter equivalence drug trial	Pain-VAS*	Significant (p<.05) reduction in joint pain and equivalence to celecoxib and glucosamine sulfate. Elevation in liver enzymes
Nerunjil (T. terristris)	Generalized pain	Neuropathic pain	Rat model with control	Hot plate, tail immersion, cold plate, formalin	Significant (p<.05) increase in pain threshold response and attenuation of hyperalgesia
A. calamus	Headache, joint pain, generalized body pain	Neuropathic pain	Rat model	Hot plate, Randall Selitto test apparatus	Significant (P<.05) amelioration of neuropathic pain threshold
AmrutBhallatak (S. anacardium)	Joint pain	Osteoarthritic pain	Randomized open comparative	Pain-VAS	Reduction in pain scores. Elevation in liver enzymes
W. somnifera	Joint pain	Arthritic pain	Randomized open comparative	Toe-spread and total print length	Significant (P<.05) decrease in pain parameters
B. monnieri	Mental health disorders, anxiety	Nociceptive pain	Feasibility study in rat models	Acetic acid, formalin, tail flick	Inhibition of observed nociceptive effects by formulation via adrenergic, opioid, and serotonin antagonists
Maharasnadhi Quathar (polyherbal formulation)	Joint pain	Arthritic pain	Rat model and feasibility study in humans	Hot plate, tail flick	Significant (p<.05) increase in pain threshold in rats and subjective improvement in pain in RA patients
AyTP (Narikel Lavan, Sootshekhar Rasa, Sitopaladi Churna, Rason Vati and Godanti Mishran)	Generalized pain	Migraine	Uncontrolled open label	Pain-VAS	Significant (p<.001) reduction in VAS score after beginning of AyTP

*VAS: Visual analogue scale
**RA: Rheumatoid Arthritis

S-479.

OPTIMIZING INTRAOPERATIVE ANALGESIC DRUG INJECTIONS AT THE SURGICAL WOUND SITE TO REDUCE POSTOPERATIVE PAIN AFTER KNEE SURGERY IN RATS

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AFFILATION: Department of Anesthesiology, Rush University Medical Center, Chicago, IL

INTRODUCTION: Many surgeons now use injections of drugs into the wound during total knee arthroplasty (TKA) surgery to reduce postoperative pain.1,2 However, despite widespread use of local infiltration analgesia, there is relatively limited evidence as to which drug and dose is adequate from clinical trials.2 To test the efficacy of this local route of administration under a controlled situation we tested rats with a knee surgery model that simulated some aspects of TKA.3

METHODS: With IACUC approval, rats were anesthetized with 1.5% isoflurane in oxygen and a 1-cm long skin incision made over the patella tendon. The tendon was freed from underlying fascia and moved laterally to expose the joint. Using a diamond bur, a 1.4-mm diameter, 0.5-mm deep hole was drilled in both the femur and the tibia, 2 mm above and below the knee joint respectively.3 Then, 10 μL of drug was injected into each hole (IH), and there was a 2-min delay for drug to be absorbed. The holes were then filled with cold-curing dental cement. The skin margins were elevated and 30 μL of drug was injected (PA) into the wound. The skin was closed with 4-0 nylon sutures. For systemic control injections, 50 μL of drug was injected subcutaneously beneath the abdominal skin. Drug combinations consisted of local anesthetic, NSAID, and steroid (0.75% bupivacaine, 6 mg/mL ketorolac, 2 mg/mL dexamethasone). After surgery, spontaneous rearing behavior was measured as a method to assess postoperative pain, with increased rearing indicating less pain.3

RESULTS: When the 3-drug combination was injected in the bone holes (IH, 10 μL per hole), and after cementing, injected periarticular (PA, 30 μL), rearing was increased at 2 h postsurgery compared to saline (fig. 1). The same 3-drug combination injected systemically (50 μL) did not have a significant effect on rearing (fig. 2). When bupivacaine alone was injected (IH +PA), there was not a significant effect on rearing. However, when ketorolac plus dexamethasone was injected (IH +PA), rearing was increased at 2 h postsurgery.

DISCUSSION: Local drug infiltration using a local anesthetic plus anti-inflammatory drugs reduces pain-related activity after knee surgery, while systemic injection of the same drugs was without effect. Preliminary results suggest that local infiltration of anti-inflammatory drugs are more important than the local anesthetic drug in reducing knee postoperative pain.

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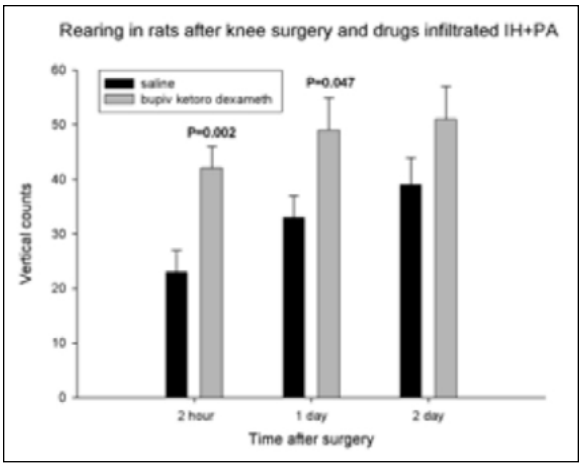

Figure 1.

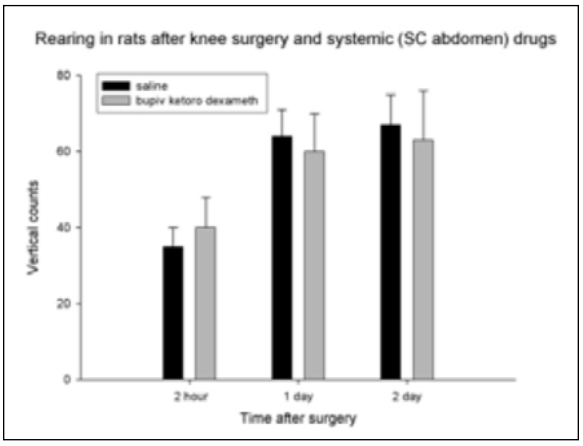

Figure 2.

Scholars' Abstracts

Patient Safety

S-446.

SIGNIFICANT REDUCTION IN PREOPERATIVE TESTING AT A PREOPERATIVE EVALUATION CLINIC IS NOT ASSOCIATED WITH INCREASE IN DAY OF SURGERY TESTING OR CASE CANCELLATIONS

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INTRODUCTION: Unnecessary preoperative testing has been scrutinized for rising healthcare costs in the United States[1,2] Our Preoperative Evaluation Clinic (PEC) and similar centers around the country evaluate risk for surgical patients and coordinate preoperative testing. Protocol changes at Vanderbilt have been adopted with the intention of reducing unnecessary preoperative testing, and we sought to evaluate their impact on downstream care.

METHODS: Our group reviewed clinical workup revisions made in Vanderbilt's PEC from 2010 to 2015 and identified a key interval of change leading to a significant reduction in preoperative testing. We then queried the Perioperative Data Warehouse for preoperative chemistry tests, complete blood counts, electrocardiograms, and chest x-rays before and after the key interval. Chi-square tests were then used to determine the effect of the reduction in preoperative testing on tests performed on the day of surgery and case cancellations.

RESULTS: We analyzed 100,496 anesthetic cases with PEC evaluations performed between January 2010 and October 2015. There was an overall downward trend in all preoperative tests and labs performed: electrocardiograms (62.9% to 32.7%, $p<0.01$), coagulation blood draws (71.4% to 51.4%, $p<0.01$), blood cell counts (71.38% to 51.42%, $p<0.01$) and basic metabolic panels (70.6% to 51.3%, $p<0.01$) after the protocol change without a change in tests ordered on the day of surgery. This was not associated with a significant increase in case cancellation.

CONCLUSION: A reduction in preoperative testing was seen at our PEC from 2012-2015 due to clinical protocol changes. This was not associated with a respective increase in day of surgery laboratory tests and imaging ordered or an increase in case cancellation rates.

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S-447.

COMPARISON OF THE EASE OF NASOGASTRIC TUBE INSERTION IN STANDARD SNIFFING POSITION AND IN ADDITIONAL FLEXION OF THE NECK

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INTRODUCTION: Nasogastric tube insertion is a common/ mandatory procedure for all major surgical procedures, sometimes it is technically challenging particularly in anesthetised, paralyzed, intubated or unconscious patients with reported failure rates of nearly 50% on the first attempt with the head in neutral position. There are recommendations for techniques to facilitate the nasogastric (NG) tube insertion but there are no trials that have studied the ideal neck position to improve the success of placement. We hypothesized that slight modifications in neck position while inserting NG tube would improve the overall success rate of insertion. The aim of this prospective, randomised, observational study was to compare the ease of insertion of NG Tube between the standard sniffing position and the modified technique of inserting it in additional neck flexion. We determined the success rate and average time for insertion, the number of manoeuvres used and the adverse events.

METHODS: This study has ethics committee approval. Two hundred patients of ASA physical status I and II were enrolled and a detailed preoperative assessment with respect to history, patients demographic data and the following airway measurements.(Thyro mental distance, Sterno mental distance, neck circumference, body mass index and modified Mallampatti grading).were taken. After induction of general anesthesia they were randomized into two groups with computer generated numbers. The success rate of the technique, duration of insertion procedure, and the occurrence of complications (bleeding, coiling,) were noted. The starting point of the procedure is the time when NG tube insertion was begun and the end point was the time when there was successful insertion of the NG tube. The following manoeuvres were used if NG tube insertion was failed in first attempt First Jaw lift, laryngeal lift, change in the direction of the ryles tube use of ureteral guide wire, or Magill's forceps and change of nostril. The following criteria was used to define failure 1. Not able to insert the tube in 2 attempts, 2. Using more than one alternative technique such as jaw lift, laryngeal lift, use of laryngoscope, magills, 3. Time more than 90 sec. Failure was If 2 or >2 criteria were used.

RESULTS: Demographic data was comparable between the groups. Results shown in Table 1.

Success of insertion of NG tube in both the groups

Parameter	Sniffing position	Additional Flexion	p value
Attempts 2or less	68	92	0.000
Change in direction of the Ryles tube	30	14	0.005
Jaw lift	57	31	0.000
Laryngeal lift	38	14	0.000
Manoeuvres >2	41	15	0.000
Failure(Criteria >2)	32	8	0.000
Time of insertion >90 sec	14	2	0.001

CONCLUSION: We conclude further flexion of neck over standard sniffing position seems better alternative to the conventional method for successful, quick and reliable NGT insertion without increase in the adverse events in anaesthetised patients.

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S-448.

GI ENDOSCOPY INSUFFLATING GAS PRESSURE: HOW REGULATED IS THE REGULATOR?

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INTRODUCTION: To achieve visualization during an endoscopic procedure, the inspected lumen must be distended. Distension of a viscus risks migration of the distending medium, usually air or carbon dioxide (CO_2), into the circulation. A prior in vitro study demonstrated that endoscopic gas insufflation using a hospital wall source CO_2 set up to bypass the Olympus Evis Exera III CLV-190 (Olympus America, Inc., Central Valley, PA) produced distending pressures capable of exceeding 300 mmHg[1]. This pressure obviously exceeds venous pressure and therefore risks potential intravascular gas embolism. A review by Mathew et al. notes that ERCP-associated air embolisms, although rare, have been reported in the literature at an increasing rate, and that they are associated with a mortality rate >40%[2].

This in vitro study was undertaken to determine the gas pressures that can be generated by the Olympus UCR CO2 Insufflator (Olympus America, Inc.) using two standard Olympus endoscopes. The UCR CO2 device was developed for controlled CO2 endoscopic insufflation.

METHODS: We examined two Olympus endoscopes: GIF-Q180 (EGD) and TJF-Q180 (ERCP) under simulated conditions of use and measured peak distending pressure generated at their distal exit ports. A plastic US Endoscopy Guardus Overtube (Ref 00711146, Lot #1314227) sealed at its distal end and a sideport connection to an electronic pressure transducer (Edwards Lifesciences Corp., Irvine, CA) was used as an airtight sleeve for each of the examined endoscopes. The distal end of each endoscope was placed within the overtube sleeve and the gas flush button was occluded for six total measurements of the maximum pressure generated for each endoscope. Two insufflating gas source connections and flows were compared: the Olympus UCR CO_2 Insufflator and the Olympus Evis Exera III CLV-190 (wall source CO_2).

RESULTS: (See table.)

CONCLUSIONS: The regulation of insufflating gas pressure using the UCR or Evis Exera III CLV-190 Olympus gas insufflator does not appear to be clinically pressure limited. It remains a clinical concern that even via the UCR CO2 unit, the in vitro measured luminal distending pressure can vastly exceed local venous pressures. Great care and vigilance still needs to be taken regarding signs and symptoms of a gas embolism during GI endoscopies. The strong recommendation for using CO2 in preference to air as the endoscopic insufflating medium seems prudent due to the favorable blood solubility properties of carbon dioxide over air should the distending gas gain entrance to the vascular system.

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Scope	UCR Low Flow (mean mmHg + SD)	UCR High Flow (mean mmHg + SD)	Exera Low Flow (mean mmHg + SD)	Exera High Flow (mean mmHg + SD)
EGD-GIF-Q180	165.8 ± 7.63	207.8 ± 11.3	126.2 ± 12.99	144.2 ± 5.15
ERCP-TJF-Q180	175.5 ± 5.32	192.7 ± .52	161.3 ± 4.18	198.5 ± 7.79

S-449.

OBSERVATIONAL PILOT STUDY INVESTIGATING SAFE ANESTHESIA PRACTICES DURING CAESARIAN SECTION IN KENYA

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BACKGROUND: Maternal mortality is 100 times greater in East Africa than in the developed world, with the availability of safe anesthesia for cesarean section being poor. We have previously described the creation of a Safe Anesthesia for Cesarean Section Checklist (Figure 1). While this was created through a modified Delphi technique with input from over 60 East African anaesthetists, the adherence to such principles in the clinical setting prior to checklist implementation remains unknown in Kenya.

METHODS: In June 2015, twenty-five consecutive cesarean sections were observed by trained personnel. Performance of steps on the checklist was recorded without interference or input from the personnel. Results: On average, 80% of the steps applicable to any give case were performed. However, for urgent and emergent cases, there was a sharp decline in completion of indicated steps (see Figure 2). Of note, in urgent and emergent cases, almost no providers a) checked to see if blood or additional intravenous fluid was available, b) performed general anesthesia with rapid sequence induction (instead of spinal), c) ensured presence of antihypertensive medications in presence of severe pre-eclampsia, or d) checked for latest coagulation studies in pre-eclamptic patients.

CONCLUSIONS: We report on the baseline observational performance of anesthesia practices during elective and urgent/emergent cesarean cases in a tertiary referral center in Kenya. While overall performance was adequate, further room for improvement remains, particularly in the setting of urgent and emergent cases. Further studies are needed to investigate the effects of implementing the safe anesthesia checklist in low resource settings, as this simple tool may be able to save maternal and newborn lives. Funding: General Electric Foundation

C-SECTION: Safe Anesthesia Checklist

For ALL Cesarean Section Cases
*****If Urgent/Emergent, CALL FOR HELP now!*****

Step 1: Operating Theatre Preparation (prior to patient in room)

- ❑ Perform anesthesia machine check
- ❑ Confirm working monitors: ○BP ○Pulse Oximeter ○ ECG
- ❑ Confirm suction is available and working
- ❑ Confirm oxygen is available in OR
- ❑ Confirm spinal kit and drugs ready
- ❑ Prepare airway equipment: ○LMA ○ETT/stylet ○Ambu
- ❑ Prepare anesthesia drugs: ○STP, Prop, or Ketamine ○Succ
- ❑ Confirm oxytocin ≥40u available in OR
- ❑ Prepare resuscitation drugs: ○adrenaline ○ephedrine ○atropine

Step 2: Patient Preparation (prior to incision)

- ❑ Confirm Recent Hgb value
- ❑ Confirm PIV is working (size ≥18G)
- ❑ Place monitors and check BP
- ❑ Confirm ≥2L NS/LR in room
- ❑ Give Pre/Co-load (≥500mL) with spinal
- ❑ Give antibiotics prior to incision
- ❑ Left uterine displacement when supine
- ❑ Confirm postoperative monitoring plan

Step 3: Neonatal Team and Equipment (prior to incision)

- ❑ Confirm that Midwife/Neonatal Resuscitation **Team** is present
- ❑ Confirm that Neonatal Resuscitation **Equipment** is present: ○oxygen ○ambu bag ○mask ○warm environment

Step 4: If an URGENT/EMERGENT C-SECTION: CALL FOR HELP, place O_2 on patient, and follow steps below based on condition

Peripartum Hemorrhage	Pre-Eclampsia/Eclampsia	Obstructed Labor/ Fetal Distress
❑ Confirm Type & Cross sent **STAT**	❑ Confirm PLT/Coag values	❑ Confirm left uterine displacement
❑ Confirm ≥2 large bore IV (>18G) in place	❑ Confirm anti-HTN drugs available in OR	❑ Discontinue oxytocin immediately
❑ Confirm ≥2 units blood T&C and available in OR	❑ Confirm $MgSO_4$ infusion	❑ If FHR<100, perform GA
❑ Confirm ≥5L of NS/LR available in OR	❑ Succ for RSI (avoid non-depolarizers if on $MgSO_4$)	❑ If FHR>100 perform spinal
❑ Induce GA via RSI	❑ No spinal if PLT<100,000	❑ Consider vasopressor and IVF to improve circulation, goal = MAP>70mmHg
❑ Consider vasopressor and IVF to improve circulation, goal = MAP>70mmHg	**ECLAMPSIA**	
	❑ GA via RSI* (STP or prop **preferred**; add benzo if only ketamine available)	
	❑ Avoid fluid overload – consider pulm edema	

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Figure 1: This figure depicts a safe anesthesia checklist for cesarean section in Kenya. The checklist was created through a modified Delphi technique over two days at an annual CME conference for anesthesia providers in East Africa. Over 60 anesthesia providers participated in creating this best practice checklist that is also context-relevant for low and middle income countries.

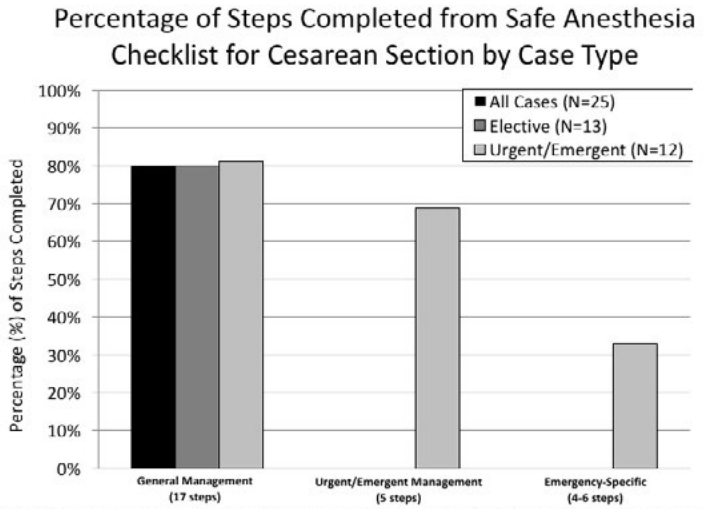

Figure 2: This figure illustrates the percentage of steps that were completed during clinical observations of cesarean sections (elective and urgent/emergent) at a tertiary referral center in Kenya. There was no difference in the performance of general case management steps, but a noticeable reduction in the completion of general urgent and emergent case management steps and a further reduction in emergency-specific steps for managing peripartum hemorrhage, fetal distress, or severe pre-eclampsia/eclampsia. See Figure 1 for listing of specific steps.

S-450.

PSYCHOMETRIC VALIDATION OF THE NURSING CONFIDENCE IN MANAGING SEDATION COMPLICATIONS SCALE

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INTRODUCTION: Prompt detection and initiation of appropriate treatment for sedation-related complications is vital to ensure patient safety during nurse-administered procedural sedation and analgesia (PSA). People will exert maximal effort and persist despite failure if they believe they are capable in completing a given task.1 It is possible that nurses may not take necessary actions to manage sedation-related complications if they lack confidence in their abilities to complete the task. The aim of this study was to develop and validate the nursing confidence in managing sedation complications scale (NCMSCS).

METHODS: A draft version of the NCMSCS was developed from clinical practice guidelines. An expert panel of nurses and medical practitioners who have expertise in anaesthesia or PSA were asked to rate the relevance of each item. Items with a content validity index of less than 0.78 were revised and those with very low index values were deleted. To evaluate the psychometric properties of the revised scale, an online survey was distributed to nurses who were members of operating theatre, endoscopy, cardiac cath lab, radiology and critical care specialty nursing associations. Exploratory factor analysis was undertaken to provide evidence of the structural validity of the scale. A matrix of polychoric correlations was generated for the exploratory factor analysis due to the use of ordinal response variables. Parallel analysis was used to determine the optimal number of factors for extraction and principal axis factoring with promax rotation was used for factor extraction. Multivariable linear regression was used to identify associations between scale scores and nurses' experience and education regarding sedation. Internal consistency was calculated to examine reliability.

RESULTS: Pre-specified criteria for content validity was met with the item-content validity index being higher than 0.78 for 34 items and the scale content validity index was 0.91. Usable data for psychometric assessment was obtained from 214 nurses. Demographic characteristics are presented in Table 1. The original 34 item scale was reduced to 27 items. Factor analysis resulted in a four-factor solution (Table 2). Cronbach's alpha was .96. Construct validity was established with significant differences ($p<0.001$) in NCMSCS scores relative to years of nursing experience and specialty area of practice (critical care/anaesthesia nurses reported higher NCMSCS scores than procedural/operating theatre nurses).

CONCLUSIONS: The psychometric properties of the NCMSCS are encouraging. Further testing of the instrument is required in different samples to provide evidence of cross-cultural validity and to determine responsiveness. A particularly important further test of the validity of the NCMSCS will be to determine if higher levels of confidence (as assessed by the scale) are associated with safer patient care. Once validated, this scale could be used to guide and inform education and training of nurses as well as complement formal competency assessment.

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Table 1. Demographic characteristics (n=214)

Characteristic	n	%	Mean(SD)
Years of nursing experience			25.5(11)
Years of sedation experience			14.2(9)
Critical care nurse	36	17	
Emergency nurse	8	4	
Anaesthetics nurse	27	13	
Cardiac cath lab nurse	27	13	
Endoscopy nurse	65	30	
Radiology nurse	23	11	
Operating theatre nurse	24	12	
Received formal education in sedation	80	37	
Certified in Advanced life support	133	63	
Required to undergo sedation competency assessment	42	20	
Unit has a policy for sedation	132	62	

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S-450 • continued

Table 2. Rotated factor matrix for 27-item NCMSCS (n=214)

Item[a]	Factor loadings			
	1	2	3	4
Identify when a patient is under-ventilating (lower than normal breath volumes) during or following an episode of sedation	**.59**	.20	.09	.03
Identify abnormal respiratory rate during or following an episode of sedation	**.63**	-.11	.17	.19
Identify allergic reactions or anaphylaxis	**.69**	.20	-.08	.02
Identify when level of sedation is deeper than intended	**.42**	.24	.02	.19
Identify bradycardia during or following an episode of sedation	**.85**	-.11	.03	.03
Identify hypotension during or following an episode of sedation	**.69**	-.07	.16	.15
Respond appropriately when underventilation (lower than normal breath volumes) is detected during or following an episode of sedation	**.73**	.16	.01	.01
Respond appropriately when hypoxia is detected during or following an episode of sedation	**.39**	.13	.16	.22
Respond appropriately when bradycardia is detected during or following an episode of sedation	**.79**	.19	-.05	-.02
Respond appropriately when hypotension is detected during or following an episode of sedation	**.81**	-.01	.05	.03
Use information about a patient's previous anaesthesia and sedation history to assess risk for sedation-related complications	.14	**.63**	-.12	.26
interpret results from a screening tool for Obstructive Sleep Apnoea to assess risk of sedation-related complications	-.07	**.70**	.10	.04
identify in advance which patients might be more difficult to intubate	-.04	**.72**	.16	.04
identify in advance patients which patients might be difficult to bag-mask ventilate	.09	**.77**	-.04	.04
use ASA physical classification status to assess risk of sedation-related complications	-.06	**.80**	.02	-.05
use information about comorbidities to assess risk of sedation-related complications	.30	**.53**	-.06	.06
body mass index to assess risk of sedation-related complications	-.05	**.80**	.07	.04
information about cardiorespiratory reserve to assess risk for sedation-related complications	.37	**.57**	.03	-.16
Insert an oropharyngeal airway correctly	.36	.00	**.52**	-.12
Insert an nasopharyngeal airway correctly	.29	.22	**.46**	-.16
Apply jaw support correctly	-.06	.02	**.87**	.06
Apply chin lift correctly	.07	.03	**.84**	.04
Deliver effective breaths using bag-mask ventilation	.26	.10	**.46**	.21
Request that the proceduralist cease the procedure if I think it is required to safely assess the patient	.15	.13	-.02	**.62**
Request that the proceduralist cease the procedure if I think it is required to safely assess the patient	.14	.08	-.08	**.74**
Identify when extra assistance may be required to respond appropriately to a sedation-related complication	.31	-.15	.13	**.53**
Access extra assistance when I deem it is required to respond appropriately to a sedation-related complication	-.11	.07	.20	**.68**
Eigenvalue	14.4	1.65	.97	.80
Percentage of explained variance, after rotation (total 40%)	12.5	10.2	9.1	8.2

[a]Item prefix is: I am confident I am able to...

S-451.

HANDOFF STANDARDIZATION IN TWO MIXED SURGICAL INTENSIVE CARE UNITS IMPROVES TEAMWORK AND INFORMATION EXCHANGE: PRELIMINARY FINDINGS FROM THE HANDOFFS AND TRANSITIONS IN CRITICAL CARE (HATRICC) STUDY

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BACKGROUND: Operating room (OR) to intensive care unit (ICU) handoffs have been shown to place patients at increased risk of preventable harm. Previous studies showed improvements in handoff quality with standardization, but this has been primarily reported in the context of pediatric cardiac surgery. The present study aims to explore these findings in adult mixed surgical populations, developing a standardized OR-to-ICU handoff process to improve postoperative communication and care quality.

METHODS: This ongoing study is a prospective interventional cohort study based in two mixed surgical ICUs in the same urban academic health system (Table 1). The study employs qualitative and quantitative research techniques and has 3 phases: Evaluation of the current handoff process, including observations and clinician interviews, focus groups, and surveys (Phase 1, 7/2014-4/2015); development, in-situ simulation, and implementation of a new handoff process (Phase 2, 4/2015-6/2015); and evaluation of the new process (Phase 3, 7/2015-present). The primary outcome is number of information omissions, but qualitative and patient outcomes will also be analyzed (Table 2). The study utilizes a pre-post design, but patient data from a similar non-study ICU within the same health system will be analyzed to test whether secular changes explain any observed differences in patient outcomes before and after the intervention. For bivariate analyses by phase, Fisher's exact test (categorical variables) and the Mann-Whitney U test (continuous variables) were used to compare differences in study outcomes.

RESULTS: Phase 1: 61 OR-to-ICU transfers were observed, but bedside handoff did not occur for 8 of these transfers. For the 53 observed handoffs, out of 13 possible key information elements, a mean 6.5±2.8 elements were observed. In 24 (45%) handoffs, teamwork was deemed unsatisfactory due to lack of coordination/cooperation or unclear provider responsibility. In interviews and focus groups, clinicians reported that time pressure and role ambiguity were barriers to achieving satisfactory handoffs. Phase 2: a choreographed handoff process and information template were developed, tested, adapted, and implemented. Phase 3: 86 handoffs have been observed. Information elements transmitted increased to 8.1±2.5 (25% increase, $p<0.0001$). 14 of 86 (16.3%) handoffs had unsatisfactory communication, a decrease of 28.7% ($p<0.001$). Handoff duration increased from a mean 3.4 minutes to 8.3 minutes ($p<0.001$). In interviews, focus groups, and surveys, clinicians report improved reliability of the process, improved satisfaction, and, for ICU clinicians, less time spent gathering patient information after the handoff.

CONCLUSIONS: Preliminary data suggest that standardizing OR-to-ICU handoffs in two mixed surgical ICUs improved information exchange, teamwork, and provider satisfaction with the handoff process. More study is needed to determine whether learned improvements in process outcomes are retained for extended time frames and translate to better patient outcomes.

Table 1. Study ICU characteristics

Characteristic	Study unit 1	Study unit 2
Surgical specialties represented	Endocrine oncologic surgery, general surgery, orthopedic surgery, otorhinolaryngology, plastic surgery, transplant surgery, urology, vascular surgery	General surgery, orthopedic surgery, thoracic surgery, trauma surgery, urology, vascular surgery
Beds	24	20
ICU model	Semi-closed*	
Clinicians	• Registered nurses • Attending physicians: ICU**, surgery • Fellows: ICU, surgery • Residents: anesthesia, ICU, surgery • Advanced practitioners: CRNAs, NPs, PAs	• Registered nurses • Attending physicians: ICU, surgery • Fellows: ICU, surgery • Residents: anesthesia, ICU, surgery
Patient demographics	50% white, 40% black, 1% Asian, 9% other	

*All patient orders are written by the intensive care unit team in close coordination with the primary surgical service. **Designation of clinicians as "ICU" indicates that their primary role is caring for the patient in the intensive care unit, not the operating room. ICU physicians are anesthesiologists, emergency medicine physicians, or surgeons. CRNA: certified registered nurse anesthetist; ICU: intensive care unit; NP: nurse practitioner; PA: physician assistant.

Table 2. Study measures.

		Measure Type	
		Effectiveness	*Implementation*
Data type	*Quantitative*	Number of information omissions Composite adverse event measure* Patient ICU length of stay Patient ICU mortality Patient hospital mortality Handoff accuracy Handoff duration	Intervention fidelity
	Qualitative	Handoff quality Teamwork quality Professionalism	Intervention acceptability Intervention fidelity Intervention sustainability

*Cardiopulmonary resuscitation, operative re-exploration, or death within 24 hours. ICU: intensive care unit.

Scholars' Abstracts

Pediatric Anesthesiology

S-452.

FREQUENCY AND PREDICTORS OF PERIOPERATIVE PULMONARY ASPIRATION IN CHILDREN

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INTRODUCTION: Pulmonary aspiration is one of the most feared complications during the perioperative period. It may precipitate a variety of disorders such as bronchitis, asthma exacerbation, chemical pneumonitis, pneumonia, and acute respiratory distress syndrome (ARDS)[1] and contributes to significant perioperative morbidity[2]. Reports in the literature suggest that perioperative aspiration is rare (varying from 1-10 events per 10,000 patients) and may be more common[3,4,5] in pediatric populations. Younger age, emergency surgery, and higher ASA status have been reported to increase risk[3,6]. Given its infrequency, aspiration is difficult to study, with few recent studies addressing this event in children. The purpose of this study was to utilize the MS-CHONY Pediatric Anesthesia census quality assurance (QA) database to identify the frequency and risk factors for aspiration in a tertiary care children's hospital.

METHODS: We reviewed the QA records for all pediatric patients with a procedure requiring an anesthetic in our children's hospital between 2008 and 2015. QA entries include demographic information such as age, gender, ASA status, admission type, as well as a wide array of risk factors and adverse events, which are entered by the anesthesia provider at the time the anesthetic record is completed. All QA records were matched with their corresponding operating room record, in order to obtain additional information such as height, weight, admission status, and location (OR v. offsite).

RESULTS: A total of 54,250 anesthetic cases were evaluated. Aspiration reportedly occurred in 24 (0.044% or a rate of 4.4 out of 10,000) of the cases. Children with reported aspirations were similar in age, height, weight, gender, location of anesthesia care (OR vs offsite), and admission status compared to those without reported aspiration.(Table 1) Children with reported aspirations also were not found to differ significantly in ASA status compared to those who did not aspirate (43% ASA 3 or greater in non-aspirators vs. 58% in aspirators).

CONCLUSIONS: Overall, anesthesia-related pulmonary aspiration was found to be a rare event in this tertiary pediatric center. Our rate of 4.4 aspirations in 10,000 cases is consistent with the average rate reported in the published literature, and is no higher than that commonly reported in adults. While others have identified specific risk factors for aspiration, we were unable to confirm those risk factors with our data despite having similar sample sizes as other studies. Perioperative aspiration may vary based on the patient populations/ institutions studied as well as experience level of providers, and therefore its occurrence may be difficult to predict.

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TABLE 1: Demographic comparison of patients who aspirated with those who did not aspirate

	No Aspiration	Aspiration	Overall
Age in years (mean ±SD)	7.65 ± 6.1	8.40 ± 6.4	7.65 ± 6.1
Height in cm (mean ±SD)	117.46 ± 44.9	119.72 ± 38.9	117.46 ± 44.9
Weight in kg (mean ±SD)	29.61 ± 24.3	33.82 ± 26.2	29.61 ± 24.3

	No Aspiration	Aspiration	Overall	Aspiration Rate
Gender				
Male	30964(57%)	14(58%)	30978(57%)	0.05%
Female	23241(43%)	10(42%)	23251(43%)	0.04%
Missing	21(0.04%)	0(0%)	21(0.04%)	0%
Location				
OR	31332(58%)	13(54%)	31345(58%)	0.04%
Offsite	19225(35%)	10(42%)	19235(35%)	0.05%
Missing	3669(7%)	1(4%)	3670(7%)	0.03%
Admission Status				
Inpatient	12948(24%)	5(21%)	12953(24%)	0.04%
Outpatient	33102(61%)	14(58%)	33116(61%)	0.04%
ER	131(0.2%)	0(0%)	131(0.2%)	0%
Same Day	7141(13%)	5(21%)	7146(13%)	0.07%
Missing	904(2%)	0(0%)	904(2%)	0%
ASA Status				
1	11279(21%)	2(8%)	11281(21%)	0.02%
2	19636(36%)	8(33%)	19644(36%)	0.04%
3	19608(36%)	14(58%)	19622(36%)	0.07%
4	3476(6%)	0(0%)	3476(6%)	0%
5	164(0.3%)	0(0%)	164(0.3%)	0%
6	8(0.01%)	0(0%)	8(0.01%)	0%
Missing	55(0.1%)	0(0%)	55(0.1%)	0%
Total	**54226**	**24**	**54250**	**0.04%**

S-453.

INCREASED USE OF INHALED NITRIC OXIDE IN SINGLE VENTRICLE PATIENTS WITH LOW NASAL NITRIC OXIDE UNDERGOING CONGENITAL HEART SURGERY

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INTRODUCTION: Cardiopulmonary bypass impairs endogenous production of nitric oxide (NO) leading to increased pulmonary vascular resistance (PVR) and associated increased stress on an already vulnerable ventricle1. Supplemental inhaled NO (iNO) decreases PVR and has improved post-bypass mortality[1]. We hypothesized nasal NO (nNO), which can be sampled in a quick, easy, non-invasive bedside test, may be a biomarker for endogenous NO homeostasis, thus patients with low nNO undergoing cardiac surgery may be predicted to have increased perioperative iNO use.

METHODS: With institutional review board approval, 132 congenital heart disease patients undergoing cardiac surgery were consented into the study. Nasal NO was obtained using an Eco Physics CLD 88sp NO analyzer. Patients were categorized as having normal or low nNO based on established cutoff values[2,3]. Charts were reviewed for perioperative iNO administration. All health care providers were blinded to the study.

RESULTS: Sixty-four patients had low nNO (48.5%). Of these, 35 patients (54.7%) received perioperative iNO compared to 21/68 (30.9%) patients with normal nNO (p=0.006, OR 2.7 [1.3-5.5]) (Table 1). There were significantly more single ventricle physiology (SV) patients in the low nNO group (29/64 vs. 16/68, p=0.008). Subgroup analysis showed the incidence of receiving perioperative iNO was significantly higher in SV patients with low nNO than in SV patients with normal nNO (21/29 [72.4%] vs. 5/16 [31.2%], p=0.007, OR 5.8 [1.5-21.9]). There was no significant difference in iNO use between SV and two-ventricle (2V) patients with normal nNO (5/16 vs. 16/52, p=1), but there was a difference in the low nNO groups (21/29 vs. 14/35, p=0.01).

CONCLUSIONS: SV patients with low nNO undergoing cardiac surgeries are more likely to receive perioperative supplemental iNO. Patients with normal nNO and 2V patients with low nNO are less likely to receive perioperative iNO. These findings suggest that nNO sampling obtained at the bedside can help identify patients who can benefit from supplemental iNO for their cardiac procedure. By mitigating delays in treatment with iNO, this may help improve postsurgical outcome by preventing severe hemodynamic derangements due to NO deficiency.

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Table 1.

	Did not receive iNO	Received iNO	p	OR
All pts, low nNO (%)	29 (45.3)	35 (54.7)	0.006	2.7 (1.3-5.5)
All pts, normal nNO (%)	47 (69.1)	21 (30.9)		
SV, low nNO (%)	8 (27.6)	21 (72.4)	0.007	5.8 (1.5-21.9)
SV, normal nNO (%)	11 (68.8)	5 (31.2)		
Low nNO, SV (%)	8 (27.6)	21 (72.4)	0.01	3.9 (1.4-11.3)
Low nNO, 2V (%)	21 (60)	14 (40)		
Normal nNO, SV (%)	11 (68.8)	5 (31.2)	1	1 (0.3-3.4)
Normal nNO, 2V (%)	36 (69.2)	16 (30.8)		

Table showing increased odds of receiving iNO perioperatively for patients with low nNO.
Key: pts - patients, iNO - inhaled nitric oxide, nNO - nasal nitric oxide, SV - single ventricle physiology, 2V - two-ventricle physiology

S-454.

PEDIATRIC EXTERNAL BEAM RADIATION THERAPY TREATMENT INTERRUPTIONS ASSOCIATED WITH CHANGE IN AIRWAY MANAGEMENT IN PEDIATRIC RADIATION ONCOLOGY - A 3-YEAR RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Children undergoing radiation therapy receive treatments on a daily basis over days to weeks, and often require general anesthesia to achieve immobilization and optimal positioning during treatment[1].

Failure to achieve the prescribed position is an absolute contraindication to treatment[2] and may result in a treatment interruption[3-6]. Treatment interruptions have been associated with suboptimal therapeutic results[7-10]. The objective was to determine whether airway management device changes during radiation treatments contribute to treatment interruptions.

METHODS: With IRB approval, we performed a retrospective cohort study of children less than 18 years of age who underwent GA (minimum 4 sessions) for radiation therapy between 7/1/2011 and 6/30/2014. Airway devices included natural airway, laryngeal mask airway, oral endotracheal tube, or tracheostomy. Patients were classified in 3 groups: Group A) supine without immobilization mask; Group B) supine with immobilization mask; or Group C) prone with immobilization mask. Interruptions of 5 or more days were defined as prolonged and evaluated for co-occurrence with airway device changes. We designed a visual analytics application to identify and evaluate the relationship between interruptions and airway device changes over the entire course of treatment for each patient.

RESULTS: 182 courses (Group A: 57, Group B: 106, Group C: 19) of radiation therapy for children receiving general anesthesia were included. Only 3 patients in Group B required unplanned CT simulation to reconfigure the treatment protocol. Five patients in Group B experienced interruptions, the longest of which was 8 days. Two of these patients required a new airway device. There was an association between unplanned CT simulation and airway device change in Group B (2-sided Fisher's exact p=0.045, odds ratio 9.4, confidence interval 0.407-501.190). All patients with prolonged interruptions were scheduled to receive more than 20 treatment sessions. The interruptions associated with airway device changes occurred within the first 10 sessions.

CONCLUSIONS: Our findings suggest that patients at risk for failure to achieve the prescribed position require different airway devices while receiving radiation therapy in the supine position with a thermoplastic mask. Patients who require different airway devices may have prolonged treatment interruptions due to failure to achieve the prescribed position with a mask. Anesthesiologists should carefully consider positioning, mask fit, and duration of treatment when designing the anesthetic plan. It is important to realize how the anesthetic plan can impact adherence to the radiation course protocol, particularly if the patient's position cannot be reproduced.

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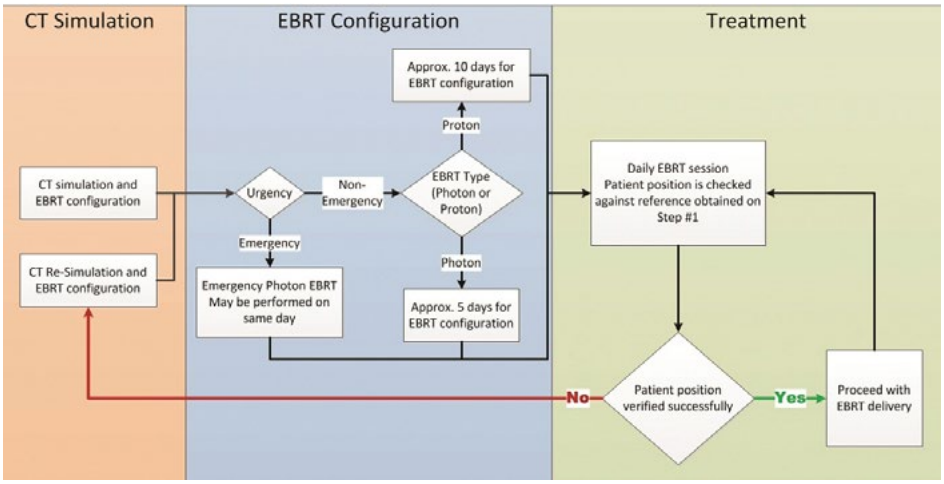

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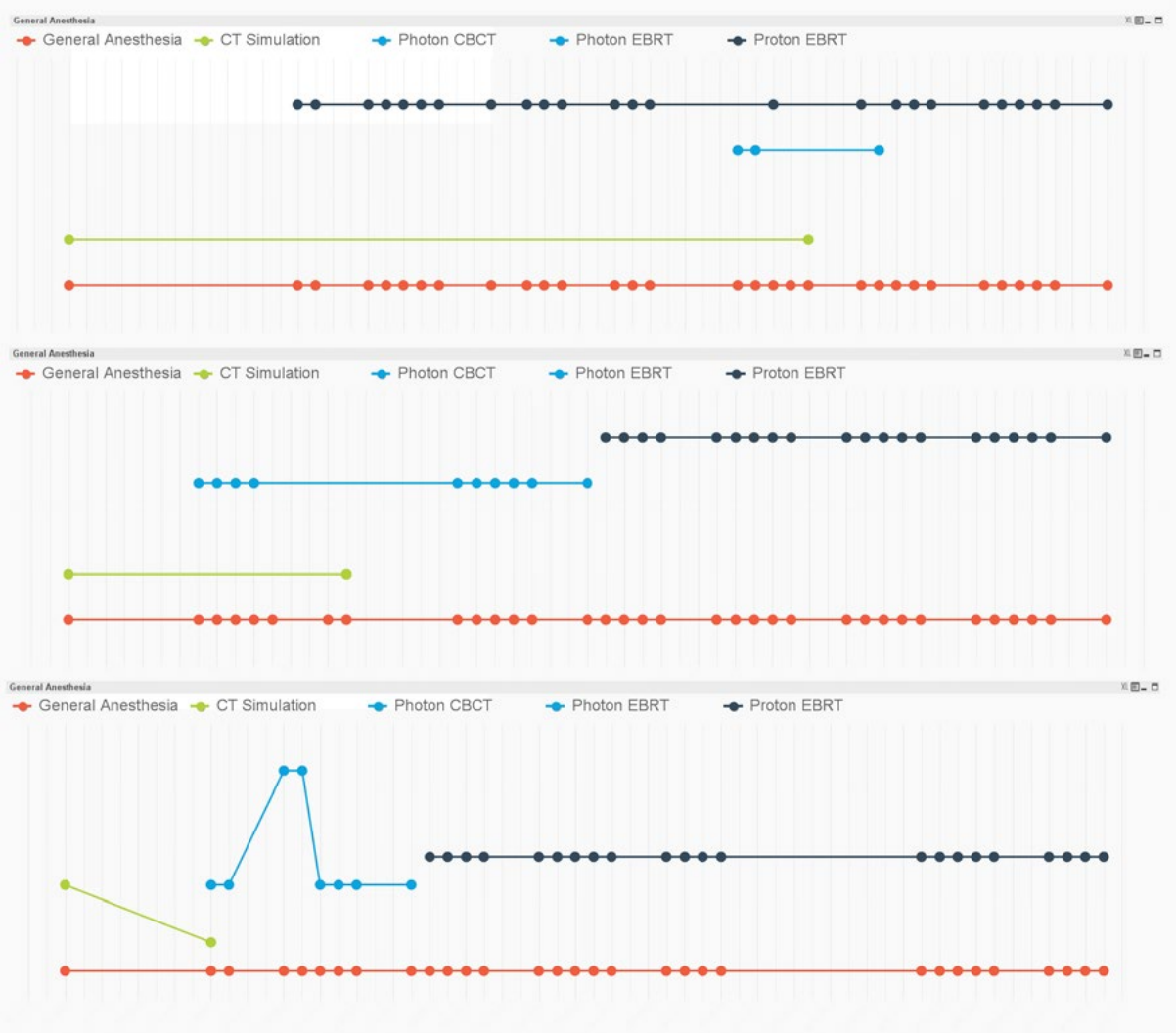

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Table 1 – Patient Characteristics

	Group A - Without thermoplastic mask		Group B - Supine with Thermoplastic Mask		Group C - Prone with Thermoplastic Mask		Total (Groups A,B,C)	
	(n)	%	(n)	%	(n)	%	(n)	%
Total number of EBRT courses	57		106		19		182	
Age								
30 days - 1 year	2	3.5%	3	2.8%	0	0.0%	5	2.7%
1 year - 5 years	40	70.2%	70	66.0%	2	10.5%	112	61.5%
5 years - 13 years	13	22.8%	26	24.5%	17	89.5%	56	30.8%
13 years - 18 years	2	3.5%	7	6.6%	0	0.0%	9	4.9%
All Ages (Total)	**57**		**106**		**19**		**182**	
Gender								
Male	28	49.1%	57	53.77%	7	36.8%	92	50.5%
Female	29	50.9%	49	46.23%	12	63.2%	90	49.5%
Total	**57**		**106**		**19**		**182**	
Radiation Type								
Photon	35	61.4%	24	22.6%	0	0.0%	59	32.4%
Proton	22	38.6%	82	77.4%	19	100.0%	123	67.6%
Total	**57**		**106**		**19**		**182**	
Number of EBRT sessions								
Less than 20	45	78.9%	26	24.5%	3	15.8%	74	40.7%
20 or more	12	21.1%	80	75.5%	16	84.2%	108	59.3%
Total	**57**		**106**		**19**		**182**	
Primary tumor diagnosis								
CNS tumor	0	0.0%	60	56.6%	19	100.0%	79	43.4%
Leukemia	13	22.8%	9	8.5%	0	0.0%	22	12.1%
Lymphoma	0	0.0%	2	1.9%	0	0.0%	2	1.1%
Neuroblastoma	20	35.1%	12	11.3%	0	0.0%	32	17.6%
Rhabdomyosarcoma	7	12.3%	13	12.3%	0	0.0%	20	11.0%
Sarcoma	1	1.8%	1	0.9%	0	0.0%	2	1.1%
Ewing's Sarcoma	2	3.5%	5	4.7%	0	0.0%	7	3.8%
Wilms tumor	14	24.6%	0	0.0%	0	0.0%	14	7.7%
Malignant rhabdoid tumor	0	0.0%	1	0.9%	0	0.0%	1	0.5%
Head/Neck	0	0.0%	1	0.9%	0	0.0%	1	0.5%
Other	0	0.0%	2	1.9%	0	0.0%	2	1.1%

Table 2 – EBRT interruptions

	Group A - Supine without thermoplastic mask		Group B - Supine with thermoplastic mask		Group C - Prone with thermoplastic mask	
	(n)	(%)	(n)	(%)	(n)	(%)
Number of EBRT courses	**64**		**107**		**19**	
EBRT without interruptions	46	71.9%	48	44.9%	8	42.1%
EBRT courses with interruptions	11	17.2%	58	54.2%	11	57.9%
EBRT interruption less than 5 days	11	100.0%	50	90.9%	11	100.0%
EBRT interruption 5 days or more	0	0.0%	5	9.1%	0	0.0%
Average number of days without EBRT (Standard Deviation)	2.36 (+/- 1.03)		2.29(+/- 1.62)		1.73 (+/- 0.79)	
Patients with airway device change, no unplanned CT simulation	20		20		10	
Patients without airway device change, no unplanned CT simulation	44		84		9	
Unplanned CT simulation and EBRT impact concurrent with airway device change	0		2		0	
Unplanned CT simulation and EBRT impact without airway device change	0		1		0	
Association of airway device change and unplanned CT simulation						
Fisher's Exact Test	n/a		p = 0.045		n/a	
OR (CI)	n/a		8.4 (0.407-501.190)		n/a	

OR = odds ratio; CI = confidence interval.

S-480.

SUDDEN SENSORINEURAL HEARING LOSS AFTER GENERAL ANESTHESIA FOLLOWING NON-CARDIOPULMONARY AND NON-OTOLOGIC GENERAL SURGERY: TWO CASE REPORTS AND A REVIEW OF THE LITERATURE

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BACKGROUND: Sudden sensorineural hearing loss (SSNHL) is a rare phenomenon that has been demonstrated with every anesthetic technique with a reported incidence of five to twenty per 100K persons annually. Several etiologies for this loss have been proposed, but no proven pathogenesis has been confirmed. Suggested etiologies include infection, vascular compromise, trauma, neoplasm, inner ear anomaly and autoimmune cochlear malfunction.

CASE DESCRIPTION: We report two cases of unilateral sudden sensorineural hearing loss after non-cardiopulmonary and non-otologic general surgeries, both within a year span at out facility. Specifically, the procedures included a cardiac catherization in an adolescent female without any intervention performed as well as an excision of a pancreatic ampullary mass, common bile duct and pancreatic duct exploration, and reconstruction and pancreatic and biliary stent placement in a middle-aged female patient. The literature is reviewed and potential etiologies, treatment and prognosis are discussed.

CONCLUSION: Multiple etiologies have been proposed for SSNHL following non-cardiopulmonary, non-otologic surgery. Implicated implosive forces include excessive positive pressure airway pressure and nitrous oxide administration during GA with resulting cochlear or middle ear membrane breaks. Explosive forces include increases in CSF pressure seen with straining, Valsalva maneuvers and emesis with subsequent labyrinthine membrane rupture as a potential etiology. Also CSF leak leading to inner ear hydromechanical imbalance is also a proposed etiology. Multiple sources cite that disruption of inner ear microcirculation from damage to vascular endothelium produces damage to stereocilia. There is no definitive treatment of postoperative SSNHL and the decision to treat is dependent upon etiology with recovery noted to be independent of treatment. Fifty percent of cases of SSNHL after GA for non-CPB and non-otologic surgery achieve at least partial recovery. The scarcity of reported cases makes definite conclusions difficult. The encouragement of reporting of cases will promote understanding of this rare complication.

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Scholars' Abstracts

Perioperative Anesthesia

S-455.

A NOVEL ASSOCIATION BETWEEN HIGH DENSITY LIPOPROTEIN LEVELS AND THE RISK OF ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY

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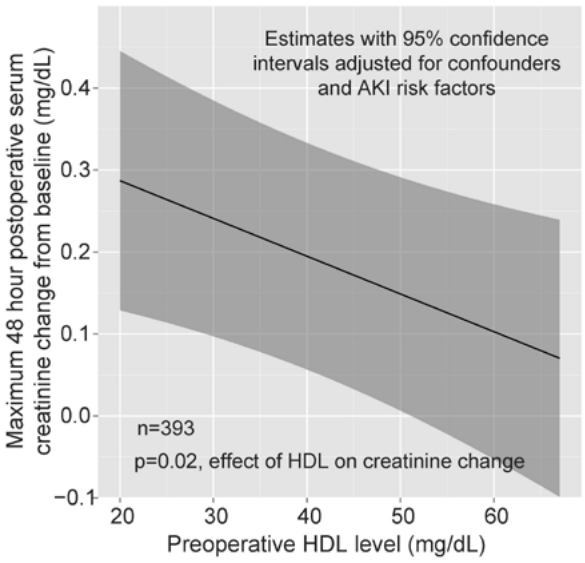
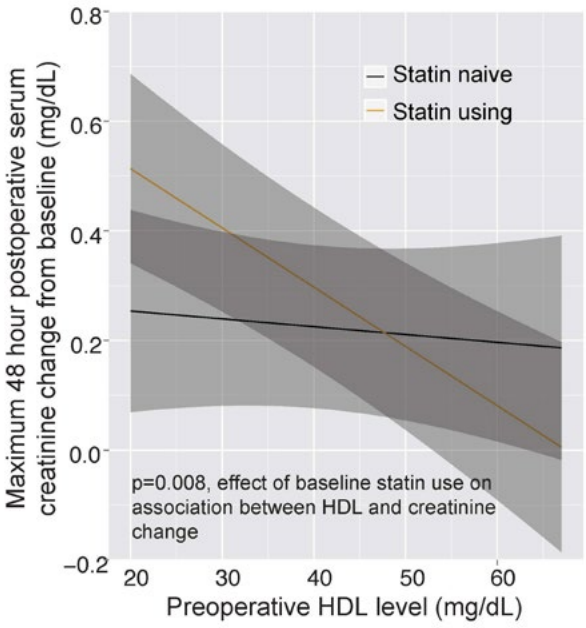
INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Acute kidney injury (AKI) after cardiac surgery occurs in up to 30% of patients and is an independent predictor of death.[1] HDL has known anti-oxidant and anti-inflammatory properties[2] and may attenuate mechanisms of AKI. We hypothesized that a high preoperative HDL cholesterol concentration is protective against postoperative AKI.

METHODS: After IRB approval, data were obtained from a prospective, 393-subject trial of perioperative atorvastatin to prevent post-cardiac surgery AKI. Statin-using patients were randomized to placebo or 80mg atorvastatin the morning of surgery and 40mg on postoperative day 1. Stain-naïve patients were randomized to placebo or 80mg the day prior to surgery and 40mg daily thereafter during hospitalization. The association between HDL level and maximum serum creatinine change from baseline in the first 48 postoperative hours was assessed using a two-component latent variable mixture model with potential confounders and AKI risk factors. Regression analyses assessed interactions of chronic statin use, perioperative atorvastatin treatment, and HDL level on AKI risk.

RESULTS AND MAJOR FINDINGS: Postoperative AKI occurred in 99 patients (25.2%). Median (10th, 90th percentile) preoperative HDL was 37.6 (25.0, 54.0) mg/dl and postoperative creatinine change 0.09 (-0.11, 0.59) mg/dl. Lower HDL levels were independently associated with increased creatinine rise (p=0.02) (Figure 1). Regression analysis showed this association was present in statin-using but not statin-naïve patients (p=0.008) (Figure 2). The protective effect of high HDL in chronic statin users was enhanced with perioperative atorvastatin treatment (p=0.004) (Figure 3) and with increasing chronic statin dose (p=0.003) (Figure 4). Similar analyses using LDL found no association with postoperative AKI risk (p=0.51).

CONCLUSIONS: Higher preoperative HDL was associated with less risk of AKI. Statin exposure modified this association. Specifically, subjects with higher HDL levels on chronic statin therapy had less creatinine rise and appeared to further benefit from higher chronic statin dose and perioperative atorvastatin therapy. These findings support a possible pleotropic effect of statins on HDL in the context of AKI and a potential new role for HDL during the perioperative period. Future work involves identifying the biological mechanism underlying these associations.





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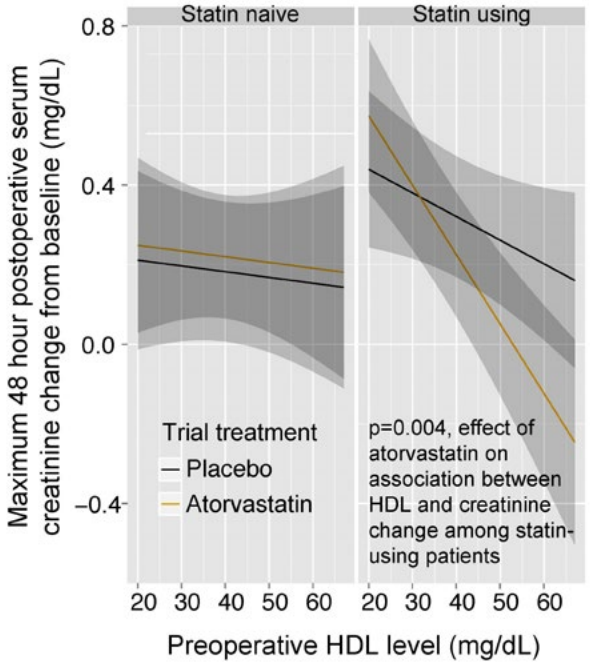

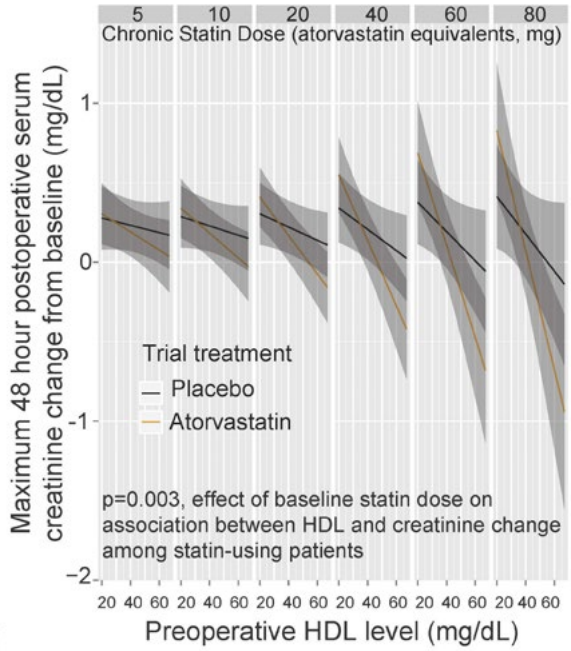

S-456.

PERIOPERATIVE TLR4 MODULATION IN A MOUSE MODEL OF SURGICAL TRAUMA: A SYSTEMS-WIDE ANALYSIS BY SINGLE-CELL MASS CYTOMETRY

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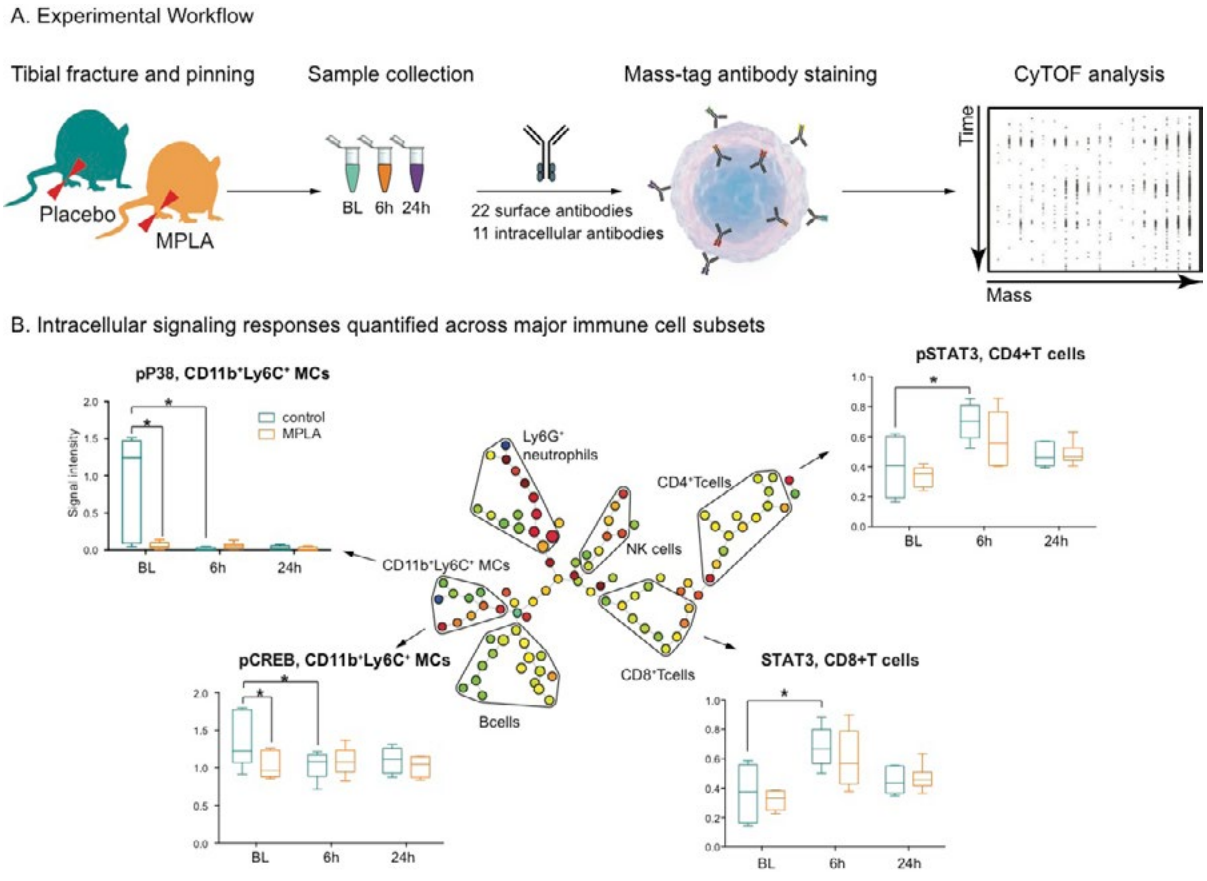
INTRODUCTION: Impaired recovery characterized by chronic post-surgical pain and difficulty with daily functioning affects 30% of patients and bears substantial economic costs. Recent advances in Enhanced Recovery After Surgery (ERAS) pathways highlight the significance of protracted surgical recovery. However the elements of these protocols that may improve recovery are uncertain. To identify patient-specific modifiers that may be targeted pre-operatively to improve surgical recovery, a precise understanding of the biological mechanisms that drive surgical recovery is critically needed.

Accumulating evidence from mouse and human models implicate the Toll-Like Receptor 4 (TLR4) signaling in essential aspects of the innate immune response to surgery. In a recent mass cytometry analysis of patients' immune system *before* surgery, activation of the MyD88 branch of the TLR4 signaling pathway in monocytes accounted for ~ 50% of inter-patient variability in recovery from pain and functional impairment. Here, we propose a novel high dimensional mass cytometry assay in a murine model of surgery to 1) establish a pre-clinical paradigm that recapitulates important components of the human immune response to surgery, 2) enable the systems-wide analysis of pharmacological manipulation of TLR4 signaling *in vivo*, and 3) demonstrate a causative link between TLR4 signaling in monocytes and functional recovery from surgery.

METHODS: In order to positively modulate the immune response, we performed TLR4 priming of innate immune cells using the TLR4 agonist monophosphoryl lipid A (MPLA), a bacterial cell wall component that is used in several human vaccines. C57Bl6/J mice received intraperitoneal injections of MPLA 20 µg or saline once daily for two consecutive days. Following MPLA injection, mice were subjected to tibial fracture and intramedullary pinning. Whole blood samples were collected before, then 6h or 24h after surgery. A panel containing 22 cell surface and 11 intracellular antibodies was utilized to quantify surgery-induced changes in cell frequency and associated intracellular signaling across all major immune cell subsets using mass cytometry (Figure 1).

RESULTS: The systems-wide analysis of the murine immune response to surgery revealed cell-type specific immune features that remarkably mimicked human immune signatures of surgical recovery. Within the innate compartment, we found robust activation of STAT3 in *lin*-CD11b^{+}LyC^{+} monocytes and the concomitant dephosphorylation of P38/CREB and NFkB, six hours after surgery. Interestingly, TLR4 priming with MPLA dramatically suppressed baseline P38, MAPKAPK2 and CREB phosphorylation in *lin*-CD11b^{+}LyC^{+}, while NFkB phosphorylation remained unchanged.

CONCLUSIONS: This study provides the foundation for a promising animal model to comprehensively study the effect of pre-operative TLR4-modulation on cellular mechanisms relevant to the human immune response to surgery. Further dissection of the individual cellular contributions will allow the development of interventions that can be translated back to humans to enhance recovery after surgery.



S-457.

THE VAPE STUDY: VETERAN ATTITUDES TOWARDS PERIOPERATIVE SMOKING CESSATION AND E-CIGARETTE USE

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INTRODUCTION: Cigarette smoking is known to increase the risk of complications in patients undergoing surgery[1]. Veterans smoke more than the general population and face unique challenges in quitting[2]. Electronic cigarettes (e-cigarettes) have been proposed as an alternative smoking cessation technology[3]. It is unclear whether veterans are interested in quitting smoking perioperatively, or in using e-cigarettes for cessation. Therefore we explored veterans' attitudes and behaviors towards smoking cessation and e-cigarette use in a perioperative cohort.

METHODS: After IRB approval, veterans seen in the Anesthesia Preoperative Clinic at a large Veterans Affairs Medical Center were screened and identified as current cigarette smokers. After informed consent, the patients responded to two surveys, one at their preoperative visit, and one postoperative within one day of surgery.

RESULTS: Of the 639 Anesthesia Preoperative Clinic patients seen during the study period, 18.3% (117) were smokers and 71 were invited to participate. Forty-three patients consented (response rate 60.6%) and only 1 was lost to follow-up. The average participant was 59±11.1 years old, with a median 16 pack-year smoking history (interquartile range 10-35), and a mean Fagerström score of 3.5±2.0. Preoperatively, 18 (41.9%) participants indicated that they were seriously thinking of quitting smoking within the next 30 days, indicating preparation stage of change. Most (95.3%, n=41) participants had heard of e-cigarettes and around half (48.8%, n=21) had tried them. Around half (48.8%, n=21) would have been willing to use e-cigarettes as a means of cutting down or staying off regular cigarettes. However, 20 (46.6%) participants were concerned that e-cigarettes are not safe. Eighteen (42.9%) participants reported at least a 50% reduction in cigarettes smoked in the two days before surgery. Twenty-one (50.0%) were advised to quit smoking in preparation for surgery, with the top three sources of advice coming from anesthesia (n=19, 45.2%), primary care provider (n=7, 16.7%), and surgery (n=6, 14.3%). Only 4 (9.5%) participants received smoking cessation pharmacotherapy and 4 (9.5%) received counseling.

CONCLUSIONS: Veterans preparing for surgery have a strong interest in quitting smoking. However, despite the recommendation that patients be advised to quit smoking at every healthcare encounter, half of the patients did not recall any advice to quit and only a few received any pharmacotherapy or counseling. There is some interest in e-cigarettes as a potential aid to quit smoking in the perioperative period, but further studies are needed to determine the safety and efficacy of this practice.

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S-458.

PRACTICE PATTERNS AND OUTCOMES OF OLDER ANESTHESIOLOGISTS

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INTRODUCTION: Anesthesiology is a demanding medical specialty, but there are no data that provide a comprehensive picture of whether older anesthesiologists' practice patterns and reported adverse outcome rates differ from younger anesthesiologists'. We hypothesize that anesthesiologists 65 and older will have systematically different patterns of clinical practice, but no significantly different rate of adverse outcomes compared with younger anesthesiologists.

METHODS: Cases performed between 1/1/2010 and 6/30/2015 and reported to the National Anesthesia Clinical Outcomes Registry (NACOR) were included. We excluded organ donors, pain procedures, nonprocedural billing codes, cases without a listed physician (MD or DO) anesthesiologist or where the anesthesiologist had an unknown year of birth, and cases with >1 listed physician anesthesiologist. Practice measures included work shifts (day/night, weekend, and holiday shifts), anesthetic technique, types of procedures, and patient characteristics. Prespecified outcome measures were death or cardiac arrest, severe respiratory events (respiratory failure, arrest, or reintubation), postoperative nausea/vomiting (PONV), and process measures (case cancellation, unplanned admission, and unplanned ICU admission). The primary predictor for practice patterns was anesthesiologist age at the time of the case (<65 and 65+). For the association with outcomes we used a more granular measure of provider age: <40, 40-50, 51-64, and 65+ years old.

RESULTS: We analyzed 18,903,360 cases (3,012,428 with outcome collection) from 21,076 providers, 575 (2.7%) of whom were >65. After adjustment with logistic regression clustered by provider, older anesthesiologists were significantly more likely to be university-affiliated, less likely to perform cases overnight or during the weekend, less likely to perform anesthesia on patients under 18 years, and less likely to perform emergency cases. Older providers were significantly more likely to provide care for patients undergoing endoscopy, eye surgery, and non-OR anesthesia care, compared with younger anesthesiologists (Table 1). Four separate clustered logistic regression models were developed to evaluate adjusted associations between provider age and perioperative adverse outcomes. After adjustment, there was no association between provider age and report of death/cardiac arrest, severe respiratory events, severe PONV, or case cancellation or unplanned hospital/ICU admission (Table 2).

CONCLUSIONS: There are systematic differences in the cases older providers report to NACOR, including fewer cases performed on weekends and overnight, fewer emergency cases, and more non-operating room anesthetic cases. We found no evidence for increased rates of adverse outcomes in older providers. This may reflect differential reporting practices, preference for a more predictable or flexible schedule and reduced case complexity near retirement, and/or effective self-compensation for the physiologic changes of aging.

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Table 1. Comparison of temporal, patient, and case characteristics of cases reported to NACOR that were attributed to exactly one physician anesthesiologist with a known year of birth. Complete case analysis for the logistic regression included 14,313,499 patients.

			Provider-level analysis[1]		
			Provider <65	Provider 65+	Univariate p value
Number of providers			20,501 (97.3%)	575 (2.7%)	
Cases contributed to NACOR, per provider			292 [40-1068]	524 [36-1753]	0.001
			Per-case analysis[2]		
			Provider <65	Provider 65+	Univariate p value	Adjusted OR
Number of cases			17,929,907 (94.8%)	973,953 (5.2%)		
When cases were performed		4:00PM-6:29AM	1,792,493 (10.3%)	66,061 (6.9%)	<0.001	**0.71 [0.66-0.77]**
		Holiday	300,252 (1.7%)	16,002 (1.6%)	0.018	0.99 [0.94-1.04]
		Weekend	867,824 (4.8%)	29,182 (3.0%)	<0.001	**0.70 [0.62-0.79]**
Facility type		University	1,560,715 (8.9%)	105,023 (10.9%)	<0.001	**1.40 [1.03-1.91]**
		Large community	2,907,404 (16.5%)	162,354 (16.9%)		1.16 [0.87-1.55]
		Medium community	6,287,775 (35.7%)	320,477 (33.4%)		[ref]
		Small community	624,055 (3.5%)	28,547 (3.0%)		0.75 [0.50-1.12]
		Specialty hospital or surgical center	3,443,205 (19.6%)	197,631 (20.6%)		0.95 [0.75-1.21]
		Surgeon's office or dentist	119,804 (0.68%)	3,912 (0.41%)		1.00 [0.53-1.89]
		Not reported	2,673,126 (15.2%)	142,743 (14.9%)		0.93 [0.72-1.19]
Patient demographics						
Age		<1	285,328 (1.6%)	7,236 (0.75%)	<0.001	**0.49 [0.37-0.63]**
		1-18	1,627,833 (9.2%)	56,024 (5.8%)		**0.67 [0.58-0.78]**
		19-49	6,122,139 (34.5%)	318,623 (33.0%)		[ref]
		50-64	4,658,374 (26.3%)	277,423 (28.7%)		1.01 [0.98-1.04]
		65-79	3,815,673 (21.5%)	232,661 (24.1%)		0.998 [0.95-1.05]
		80+	1,214,429 (6.9%)	74,441 (7.7%)		1.03 [0.96-1.10]
Female gender			10,338,005 (59.5%)	570,011 (59.8%)	<0.001	1.02 [0.99-1.04]
ASA physical status		1 or 2	10,069,384 (67.5%)	539,557 (64.6%)	<0.001	[ref]
		3	4,045,137 (27.1%)	250,726 (30.0%)		1.02 [0.92-1.12]
		4	782,689 (5.3%)	44,139 (5.3%)		0.97 [0.83-1.13]
		5	19,829 (0.13%)	854 (0.10%)		0.93 [0.71-1.22]
Emergency case			830,368 (5.6%)	30,707 (3.7%)	<0.001	**0.68 [0.49-0.94]**
Case characteristics						
Top 5 procedural CPT codes, by number of procedures	1		Screening colonoscopy	Screening colonoscopy		
	2		Cataract removal	Cataract removal		
	3		Esophagogastroduodenoscopy	Esophagogastroduodenoscopy		
	4		Laparoscopic cholecystectomy	Electroconvulsive therapy		
	5		Total knee arthroplasty	Laparoscopic cholecystectomy		
Top 5 procedural CPT codes, by total time billed	1		Vaginal delivery	Vaginal delivery		
	2		Total knee arthroplasty	Screening colonoscopy		
	3		Laparoscopic cholecystectomy	Cataract removal		
	4		Total hip arthroplasty	Total knee arthroplasty		
	5		Screening colonoscopy	Laparoscopic cholecystectomy		
Duration, minutes, median [interquartile range]			70 [40-124]	65 [36-119]	<0.001	[ns[3]]
Anesthetic technique		General anesthesia	9,473,190 (68.6%)	509,313 (65.9%)	<0.001	[ref]
		MAC, sedation or local	2,735,957 (19.8%)	194,625 (25.2%)		1.08 [0.88-1.32]
		Regional or neuraxial	1,499,635 (10.9%)	64,581 (8.4%)		0.97 [0.83-1.14]
		Other	101,767 (0.74%)	4,102 (0.5%)		0.84 [0.42-1.69]
		Not stated	4,119,358 (23.0%)	201,332 (20.7%)		1.02 [0.79-1.33]
Type of case		Extremity	3,648,168 (20.4%)	165,169 (17.0%)	<0.001	[ref]
		Head/spine	1,937,189 (10.8%)	84,036 (8.6%)		1.03 [0.92-1.16]
		Neck/thorax	1,747,123 (9.8%)	88,222 (9.1%)		1.09 [0.99-1.20]
		Abdomen/pelvis	4,145,644 (23.1%)	229,258 (23.6%)		**1.19 [1.07-1.32]**
		Eye	1,042,734 (5.8%)	83,580 (8.6%)		**1.47 [1.08-2.01]**
		Obstetric	1,583,448 (8.8%)	65,154 (6.7%)		1.03 [0.84-1.26]
		Radiology	166,003 (0.93%)	7,296 (0.75%)		0.93 [0.78-1.11]
		GI endoscopy	2,016,557 (11.3%)	148,613 (15.3%)		**1.76 [1.43-2.16]**
		Other non-operating room	1,395,276 (7.8%)	80,889 (8.3%)		**1.35 [1.16-1.56]**
		Electroconvulsive therapy	230,054 (1.3%)	20,760 (2.1%)		1.59 [0.82-3.10]

Totals may not sum to 18,903,860 because of missing data. Adjusted OR is derived from a logistic regression adjusting for all variables in the table (day vs overnight shift, holiday, weekend; facility type; patient age, gender, ASA physical status, emergency case status, case duration [in categories], anesthesia technique, and type of case), with variance adjusted for clustering by individual provider. Statistically significant odds ratios are highlighted in bold text. [1]To be in the 65+ group, the mean age of the provider, averaged across all cases from that provider, during the 5.5-year study period had to be 65+. [2]In the per-case analysis, cases were considered to have a provider 65+ if the provider was 65+ in the year during which the case occurred. [3]Categories were 1-30m, 31-60m, 61-120m [ref], 121-240m, and >240m; none of the adjusted comparisons were significant, nor was the overall f-test for significance of the variable.

Table 2. Adjusted reported rates of major outcomes, stratified by provider age. Provider age was not statistically significant in any of the adjusted models.

Provider age	Death or cardiac arrest		Respiratory events		Severe PONV		Process measures*	
	Raw rate	Adjusted OR**	Raw rate	Adjusted OR	Raw rate	Adjusted OR**	Raw rate	Adjusted OR
<40	286/475,952 (0.060%)	1.11 [0.87-1.42]	288/557,225 (0.052%)	0.98 [0.82-1.16]	8,872/456,804 (1.94%)	1.22 [0.98-1.53]	979/393,727 (0.25%)	1.11 [0.91-1.34]
40-50	326/689,490 (0.047%)	1.01 [0.81-1.25]	389/803,809 (0.048%)	1.04 [0.89-1.21]	10,773/679,222 (1.56%)	1.04 [0.88-1.22]	1,441/590,985 (0.24%)	1.09 [0.93-1.28]
51-64	414/799,250 (0.052%)	[ref]	441/933,668 (0.047%)	[ref]	14,834/838,169 (1.77%)	[ref]	1,614/703,742 (0.23%)	[ref]
65+	50/146,852 (0.034%)	1.21 [0.84-1.76]	57/173,157 (0.033%)	0.87 [0.65-1.17]	966/111,434 (0.87%)	0.97 [0.69-1.35]	210/114,129 (0.18%)	0.83 [0.58-1.21]
Total	1,076/2,111,544 (0.051%)		1,175/2,467,859 (0.048%)		35,445/2,096,402 (1.69%)		4,244/1,802,583 (0.24%)	

*"Process measures" includes case cancellation, unplanned admission, and unplanned ICU admission. All regression models were adjusted by day/night and holiday/weekend status, facility type, patient age, ASA physical status, emergency case status, duration, anesthetic technique, and type of case, with variance adjusted for clustering by provider. **Death/cardiac arrest rates and PONV were additionally adjusted by patient sex.

S-459.

IMPLEMENTATION OF CLINICAL CARE PATHWAYS IS ASSOCIATED WITH A GENERALIZED INCREASE IN THE USE OF NON-OPIOID MULTIMODAL ANALGESIA

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INTRODUCTION: Enhanced recovery after surgery (ERAS) pathways provide the opportunity to reduce surgical costs and complications, yet they have not been widely adopted in the United States.[1,2,3] Our institution established a Perioperative Consult Service (PCS) to implement ERAS pathways. This study examines the adoption of multimodal analgesia both inside and outside of ERAS pathways and factors influencing the utilization of multimodal analgesia.

METHODS: Surgical cases between January 2013 and October 2015 were retrieved using our Perioperative Data Warehouse. We compared surgical cases before and after ERAS education and implementation (April-June 2014), and examined cases outside of ERAS pathways. Outcomes included provider, patient, and procedural factors associated with utilization of multimodal analgesia.

RESULTS: We studied 62,595 surgical cases, including 59,300 cases outside of ERAS pathways. Cases utilizing any element of non-opioid multimodal analgesia increased from 25.38% to 38.32% ($p<0.001$) before and after the initial ERAS pathway implementation. Factors influencing this adoption included patient-specific factors such as lower American Society of Anesthesiologists Physical Status Class, younger age, and Caucasian race. Provider-specific factors included greater number of prior ERAS pathway cases for attending anesthesiologists and resident and trainees as in-room providers (vs. certified registered nurse anesthetists). Procedure-specific factors included laparoscopy and specific surgical services (gynecology, neurosurgery, orthopedics).

DISCUSSION: An increase in multimodal analgesia usage was seen at our institution from 2013 to 2015 outside of the ERAS pathway implementations. This approach tended to be used more by trainees, providers with more ERAS pathway experience, with patients who were younger, heathier, female, Caucasian race and specific surgical services.

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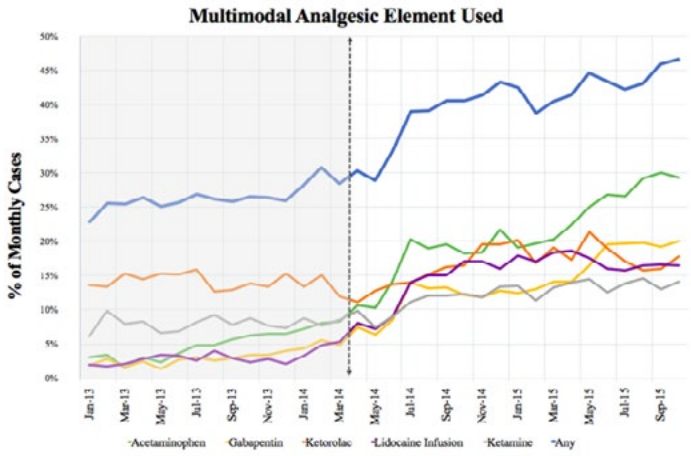
Chi Square Analysis for non-ERAS pathway Cases (n=59,300), using formal PCS implementation in CRS date of June 30, 2014 as delineation for before and after intervention

	Any	Acetaminophen	Gabapentin	Ketorolac	Lidocaine	Ketamine
Before	26.11%	6.30%	3.90%	12.20%	3.97%	8.09%
After	39.77%	20.43%	12.60%	16.67%	13.25%	9.64%
P value	<.001*	<.001*	<.001*	<.001*	<.001*	<.001*

*Statistically significant ($p<0.05$)
CRS: Colorectal Surgery Service
ERAS: Enhanced Recovery After Surgery
PCS: Perioperative Consult Service



Percent of all cases (n=62,595) with multimodal analgesic element used by month from January 2013 to October 2015. Black dashed line represents implementation of PCS (Perioperative Consult Service) in CRS on April 2014, delineating before-implementation and after-implementation.

S-460.

POSTOPERATIVE COMPLICATIONS ARE ASSOCIATED WITH PERSISTENT PAIN

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INTRODUCTION: Despite improvements in surgical morbidity and mortality over the past few decades, our understanding of patients' postoperative trajectories, including functionality, burden of pain, and quality of life remains limited.[1] Few studies have examined the impact of perioperative complications on patient-centered outcomes after hospital discharge. An important determinant of quality of life and patient satisfaction after surgery is pain, but mechanisms driving persistent postoperative pain are poorly understood[2] The primary purpose of this study was to describe the burden of persistent (lasting >30 days) postoperative pain in patients across a range of surgical subspecialties, and to explore whether there was an association between postoperative complications and persistent pain.

METHODS: This is a retrospective, descriptive study of 12,983 patients enrolled in the Systematic Assessment and Targeted Improvement of Services Following Yearlong Surgical Outcomes Surveys (SATISFY-SOS, NCT 02032030) study. All patients underwent elective surgery at Washington University in St. Louis, and responded to a postoperative survey (>1 month after surgery) that contained the Veterans RAND 12-Item Health Survey (VR-12), structured questions about persistent pain, and specific questions about cardiac, pulmonary, wound, thrombotic, and renal complications. Patients were stratified by surgical subspecialty, and by whether or not they experienced a complication. Within each subgroup, we described the prevalence of postoperative pain that significantly interfered with patients' ability to work inside or outside the home. Unadjusted odds ratios were calculated. Statistical analysis was performed using SAS® version 9.4 and JMP® version 11.0.0 (SAS Institute Inc., Cary, NC).

RESULTS: Postoperative complications were reported by 14.3% of all patients, and 20.5% reported significant pain. Patients who reported any complication were over twice as likely to report persistent postoperative pain (odds ratio [OR], 2.29; CI 95%, 2.06-2.54) compared with patients who did not report complications (Figure 1). This result was consistent across various surgical subspecialties. Odds ratios ranged from 2.28 for urological and gynecological surgery to 3.19 for minimally-invasive surgery (Figure 2).

CONCLUSIONS: Postoperative complications might be linked to increased risk for persistent postoperative pain after diverse elective surgeries. Further analyses accounting for candidate confounding variables are needed.

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Figure 2. Odds ratios for persistent pain across surgical specialties between patients reporting and not reporting postoperative complications

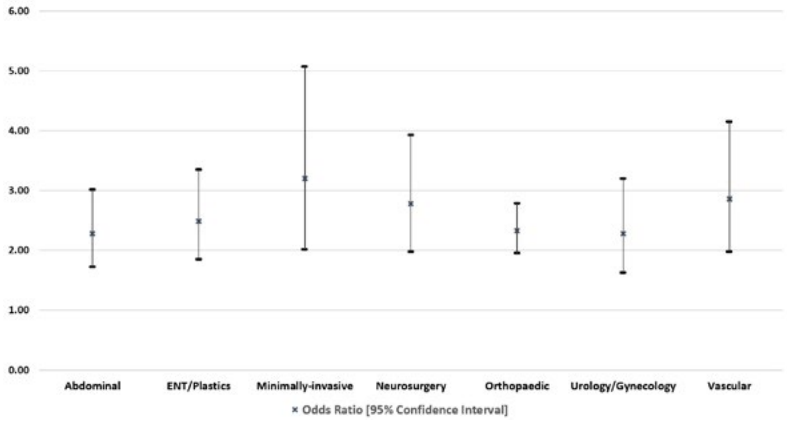
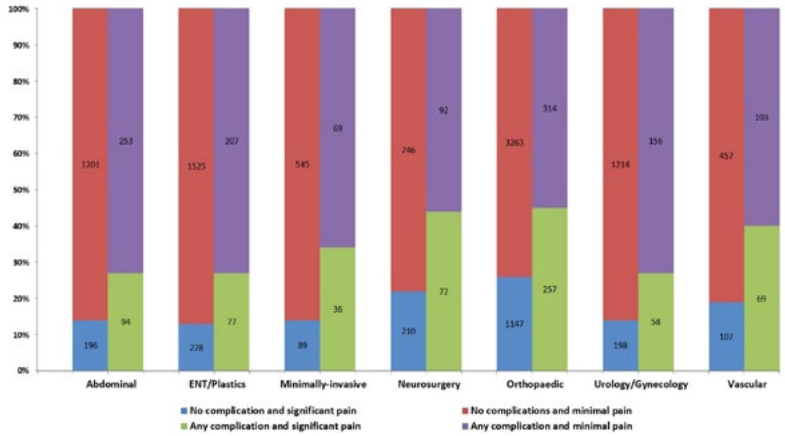


Figure 1. Patient reported postoperative complications and persistent postoperative pain (N=12,983)



S-461.

EFFECTS OF PERIOPERATIVE HEMORRHAGE AND BETA-BLOCKER THERAPY ON CARDIOVASCULAR OUTCOMES AFTER NONCARDIAC SURGERY

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INTRODUCTION: Perioperative beta-blocker use continues to be controversial. While beta-blockers may reduce the risk of adverse cardiac events in the perioperative setting, they may increase the risk of death, stroke, bradycardia and hypotension.[1] We aimed to determine if patients receiving chronic beta-blockers are at higher risk for adverse outcomes after major non-cardiac surgery when they experience significant perioperative hemorrhage.[2]

METHODS: This study retrospectively analyzed prospectively collected data from the Vitamins in Nitrous Oxide Trial. Patients on chronic beta-blocker therapy were compared with patients who were not by an interaction term for estimated blood loss (EBL). Propensity scores were used to create strata of similar baseline characteristics between beta-blocker users (BB) and non-users (non-BB) based on the following potential confounders: sex, race age, BMI, CARDS (composite of cardiovascular comorbidities), diabetes, congestive heart failure, chronic kidney disease, stroke/ TIA or atrial fibrillation.

The primary outcomes were postoperative myocardial injury (MINS) defined by cardiac troponin I elevation, and myocardial infarction (MI) defined by the Universal Definition. Secondary outcomes were acute kidney injury (AKI), multi-organ dysfunction syndrome (MODS), and death at 30 days and 1 year. AKI was defined by the Kidney Disease Improving Global Outcomes guidelines[3], and MODS was defined by the Sequential Organ Failure Assessment Score (SOFA).[4]

RESULTS: A total of 602 patients were used in the propensity match. Patients on BB had more comorbidities, but after propensity matching, both groups were well balanced. There were 316 BB users, of which 291(92%) had less than 1L of bleeding, compared to 308 non-BB users, of which 278(90%) had less than 1L of bleeding.

The rate of MINS was higher in patients on BB who experienced greater than 1L of bleeding. After propensity matching on potentially confounding comorbidities, the interaction of BB use with increased bleeding was associated with greater MINS, and trended towards significance (Table 1). The rate of MI was also higher in patients on BB who experienced greater than 1L of bleeding, but the propensity matched interaction was not significant. After propensity matching, the interaction of BB use with increased blood loss had negligible effect on outcomes of AKI, MODS, and death. (Table 1)

CONCLUSIONS: In patients undergoing non-cardiac surgery, chronic beta-blocker use may not be associated with worse postoperative outcomes even if patients experience concurrent perioperative hemorrhage, except for myocardial injury.

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TABLE 1: Outcomes by Subgroups of Beta-Blocker Use and Bleeding

	Chronic Beta-Blocker Use					Propensity matched interaction p-value[1]
OUTCOMES	Yes (n= 316)		No (n=308)		TOTALS (N=624)	
Estimated Blood Loss	0-1000mL (n=292)	>1000mL (n=23)	0-1000mL (n= 278)	>1000mL (n=29)		
Myocardial Injury	37/292 (13%)	8/23 (35%)	35/278 (13%)	2/29 (7%)	82/622 (13%)	0.088
Myocardial Infarctions (3d)	11/290 (4%)	4/23 (17%)	14/277 (5.1%)	2/28 (7.1%)	31/620 (5.0%)	0.530
Myocardial Infarction (30d)	13/285 (5%)	4/23 (17%)	14/272 (5%)	2/28 (7%)	34/609 (6%)	0.501
Death at 30d	2/265 (0.8%)	1/20 (5%)	1/262 (0%)	0/28 (0%)	4/578 (0.7%)	0.524
Death at 1yr	23/265 (9%)	2/20 (10%)	24/262 (9%)	1/28 (3.6%)	50/578 (9%)	0.640
Acute Kidney Injury	19/264 (7%)	2/23 (9%)	12/255 (4.7%)	0/26 (0%)	34/568 (6%)	0.291
AKI with CKD	4/38 (11%)	2/7 (29%)	4/15 (27%)	0/2 (0%)	10/62 (16%)	
End of Surgery (SOFA >=2)[2]	18/195 (9%)	4/21 (19%)	14/193 (7%)	4/25 (16%)	40/434 (9%)	0.777
Multi-Organ Dysfunction Syndrome (SOFA >=Δ2)	13/218 (6%)	4/21 (19%)	7/213 (3.3%)	4/17 (24%)	28/469 (6%)	0.493

1- Propensity matched interaction of BB use with EBL as a continuous variable on outcomes
2- SOFA (Sequential Organ Failure Assessment Score)[3]

S-462.

SATISFACTION OF ANESTHESIA PROVIDERS WITH CURRENT PRACTICES OF TRANSITIONS OF CARE

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INTRODUCTION: Effective communication is essential for safe patient care. Hand-offs between providers are known to be critical times when errors in patient information transmission can occur[1]. These deficits in communication can be detrimental to patient safety and can lead to morbidity and mortality. The importance of handovers is especially important in the perioperative setting during transfers of care between anesthesia providers. This is a sensitive time during which errors in communication can negatively affect patient outcomes. The Accreditation Council for Graduate Medical Education (ACGME) requires that residency programs teach residents about hand-offs and there is a strong emphasis on resident curriculum development[2]. The purpose of this study was to examine satisfaction with the current hand-off practices between anesthesia providers intraoperatively.

METHODS: A survey (Surveymonkey.com) was developed and distributed to the anesthesia department. This eighteen-question survey assessed aspects of the hand-off process and current level of adherence to these practices. A ten point percentage scale was utilized to express how often elements of the hand-off process were communicated. Also included was a tool for providers to rank twelve elements, in order of importance, that were necessary to communicate during hand-offs.

RESULTS: Of the 42 responses, only 3 participants were satisfied with current hand-off practices 100% of time (7.14%) and more than half (56.7%) were satisfied with current practices less than 70% of time. Majority of the time, 33.3% of respondents felt they received an incomplete hand-off. The lack of adequate hand-offs could result in morbidity and mortality, thought over 90% of respondents. Time constraints were not believed to be the cause of inadequate hand-offs as reported by more than 50% of participants. The predominance of respondents (16.67%) perceived that postoperative analgesic plan was conveyed only 50% of the time.

CONCLUSION: The ACGME has emphasized and mandated the importance of hand-off communication. Intraoperative hand-offs are a sensitive time during which errors in communication can negatively affect patient outcomes. Although satisfaction with current hand-off practices are adequate as perceived by the providers, there is an overwhelming interest in improving perioperative transitions of care thereby warranting the implementation of a formal hand-off tool. Utilization of such tools in the perioperative period, entailing multiple transitions of care, plausibly correlates to an increase in provider satisfaction and positive patient outcomes.

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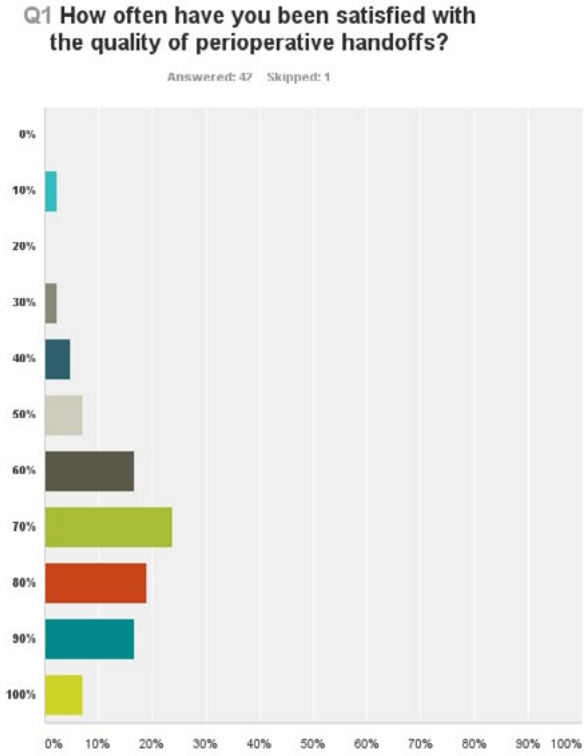

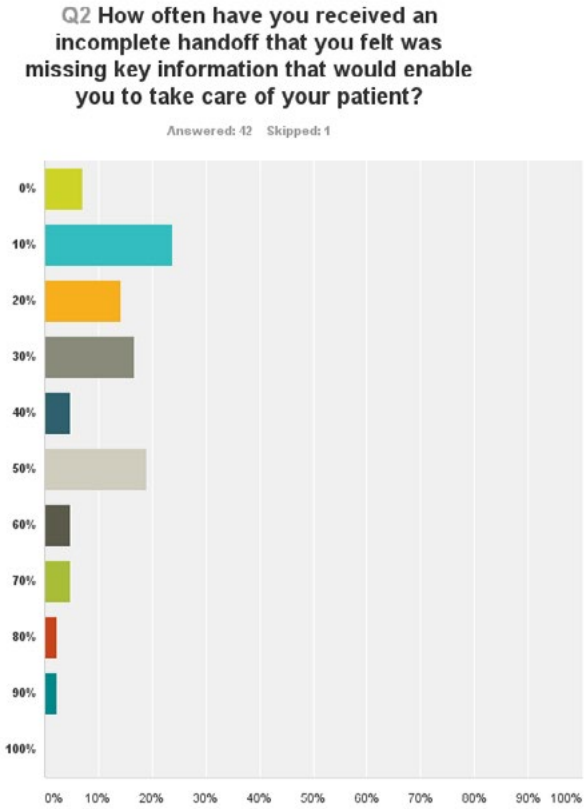

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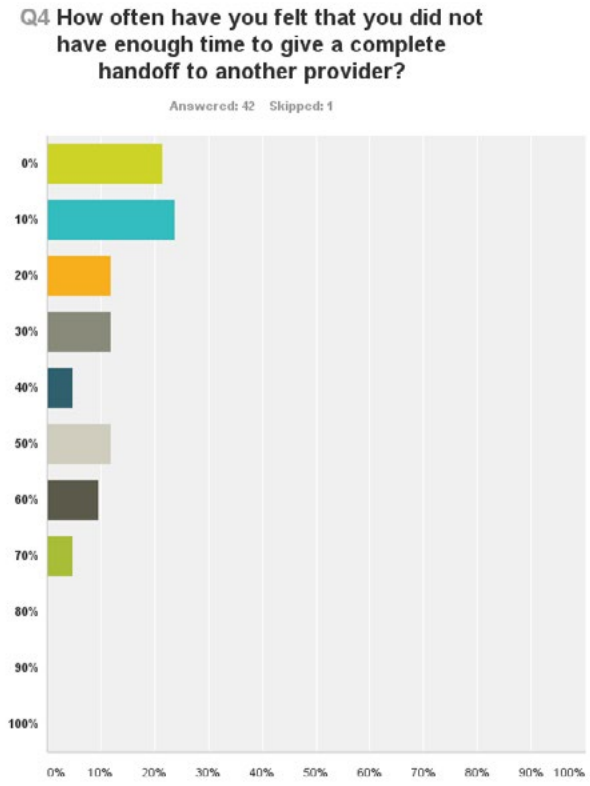

S-463.

A RANDOMIZED CONTROLLED TRIAL OF NABILONE FOR THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN ELECTIVE SURGERY

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INTRODUCTION: Nabilone (Cesamet®) is a synthetic cannabinoid with properties that make it an appealing candidate as a postoperative nausea and vomiting (PONV) prophylactic adjunct[1]. Nabilone has proven clinical utility in chemo-therapy related nausea and vomiting[2] and has not been adequately tested as a PONV prophylactic.

METHODS: Single centre randomized blinded trial assessing prophylactic oral nabilone versus placebo for the prevention of PONV. Eligible patients scheduled for elective surgery under general anaesthesia who had a pre-operative risk of PONV greater than 60%[3,4] received either nabilone 0.5 mg or placebo orally within 3 hours prior to surgery. The primary outcome was incidence of PONV. Secondary outcomes included the effect on pain, speed of recovery and drug side effects.

RESULTS: 340 patients were randomized, 172 received nabilone and 168 received placebo. There was no difference in the incidence of PONV, which occurred in 20.9% in the nabilone group and 21.4% in the placebo group (95%CI= 0.89 to 1.11, RR = 0.98, p=1.00). Subjective sensation of PONV and/or treatment with antiemetic in the PACU occurred in of 41.7% and 41.8% of the nabilone and placebo groups respectively (95%CI= 0.77 to 1.28, RR = 0.995, p=1.00). There were no differences in pain scores or opioid consumption. Patients who received nabilone achieved a rest and recovery score (RRS) >8 (meeting PACU discharge criteria) 4 minutes earlier (nabilone: median time = 31 minutes; Q1=30; Q3=40), Placebo: median time = 35 minutes; Q1=30; Q3=65; p=0.025)

CONCLUSION: Nabilone 0.5 mg given orally as a single dose prior to surgery was not effective in preventing PONV. Patients receiving nabilone did not have any changes in pain scores; they did however achieve PACU discharge criteria 4 minutes faster. Future studies may help to further establish proper role of cannabinoids in prevention and treatment of PONV.

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Scholars' Abstracts

Regional Anesthesia

S-465.

WITHDRAWN.

S-466.

WITHDRAWN.

Scholars' Abstracts

Technology, Computing and Simulation, Equipment Monitoring

S-467.

PATTERNS OF USE OF A CLINICAL ANESTHESIA CALCULATOR AND DECISION SUPPORT TOOL IN AN INTERNATIONAL PROVIDER POPULATION

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INTRODUCTION: Understanding mobile medical app use allows creators of content the ability to iteratively improve that content while disseminating targeted information. Additionally, by studying this usage, we may be able to understand clusters and frequency of rare events, usage patterns indicating CME or other resource needs, and discover practice patterns. "Anesthesiologist," released in 2011, is a free Android app designed for anesthesia healthcare professionals providing age- and weight-based physiological information and drug dosing (Figure 1). It is installed on 97,098 devices globally. To quantify the user base, we collected basic demographic information via surveys as well as app use analytics. We are interested how use of this technology impacts clinical care and in characterizing practice patterns around the world.

METHODS: After IRB approval, the cloud-integrated Survalytics platform[1] was integrated into the app, allowing collection of in-app analytics and user demographics. Statistical analysis was performed in R[2].

RESULTS: 7,928 users have updated the app to the study version; 4,253 (54%) subjects consented to enrollment (Figure 2a). Users are from 168 countries (Table 1), including all levels of healthcare providers (Tables 2 and 3). 72% report having used the app in an emergency, supported by data indicating app activations during evenings and weekends (Figures 2b and 2c, dark blue bars). Free text responses indicate frequent use in pediatric emergencies and calculating RSI dosing. The app is primarily used for pediatrics, with 66% of uses involving patients less than 12 years old, and 24% under 12 months. Mining 33,500 app uses, we have detected rare events such as interest in intralipid (35 clicks, 2 web searches) and dantrolene (15 clicks, 3 web searches).

CONCLUSIONS: This study demonstrates the power of app analytics to understand population level behavior with study size and reach previously difficult to attain, and promises to achieve much more. Many users have used the app in emergency circumstances and rare events, possibly highlighting need for additional continuing education and availability of in-app checklists for emergency management. By asking additional targeted questions based on previous responses and/or location, we hope to achieve a nuanced understanding of practice patterns and rare events as well as deliver targeted educational content. With a large enough user base, we also hope to be able to see patterns in global access to anesthetic care by indirectly characterizing practitioner density.

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Figure 1: 'Anesthesiologist' screenshot

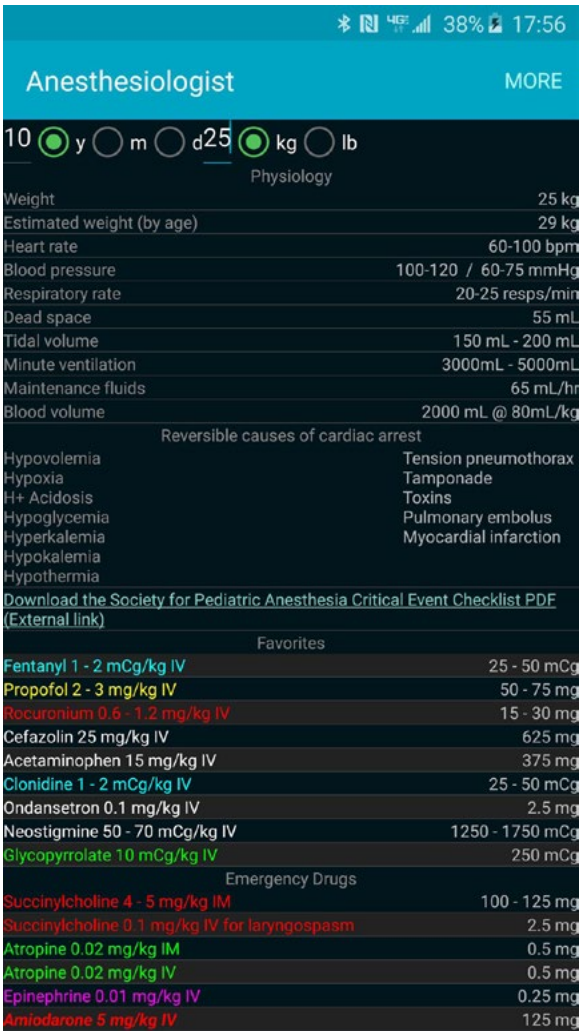

Figure 1. 'Anesthesiologist' screenshot

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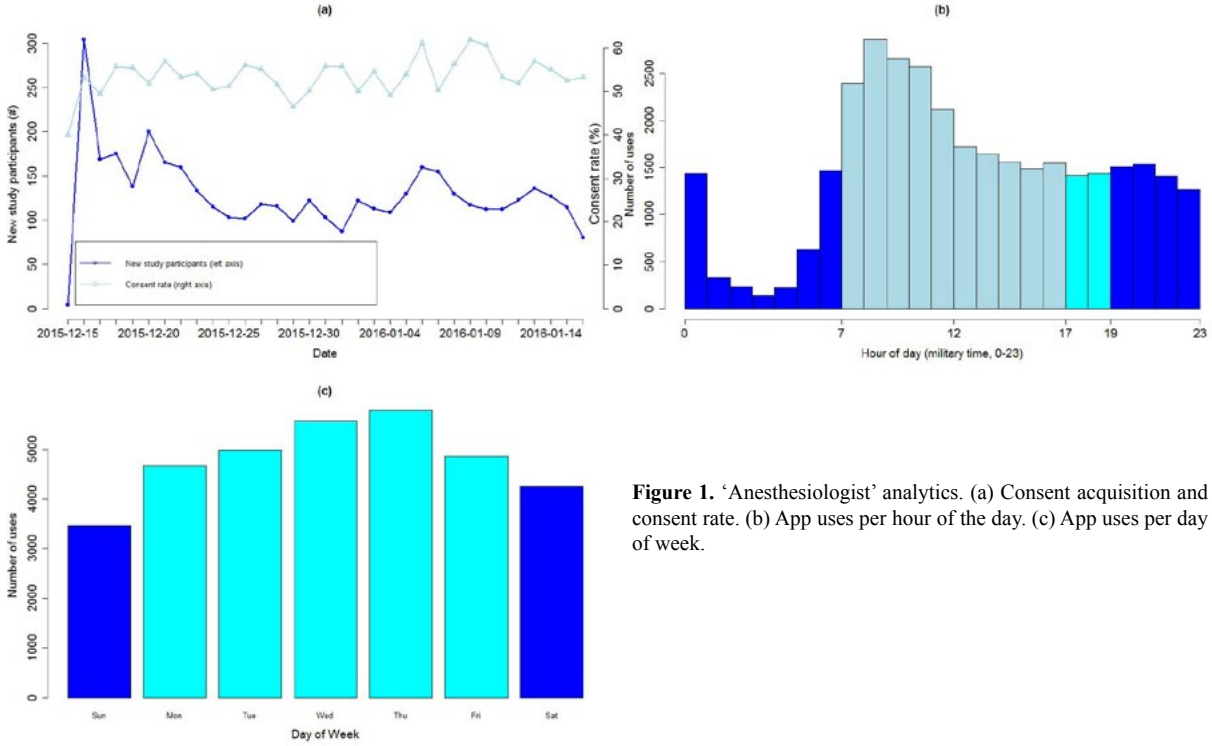

Figure 1. 'Anesthesiologist' analytics. (a) Consent acquisition and consent rate. (b) App uses per hour of the day. (c) App uses per day of week.

Table 1: Participating users of Anesthesiologist by country (below 1% excluded)

Country	Total	Percentage
India	379	8.9%
United States	283	6.7%
Germany	241	5.7%
Russian Federation	208	4.9%
Italy	184	4.3%
Mexico	165	3.9%
Indonesia	163	3.8%
Turkey	135	3.2%
Poland	131	3.1%
Brazil	124	2.9%
Egypt	118	2.8%
Spain	103	2.4%
Colombia	101	2.4%
Iran, Islamic Republic of	85	2.0%
Pakistan	83	2.0%
France	80	1.9%
Saudi Arabia	67	1.6%
Algeria	60	1.4%
Ukraine	55	1.3%
Netherlands	54	1.3%
Argentina	53	1.3%
Romania	53	1.3%
Portugal	49	1.2%
Peru	43	1.0%
Philippines	43	1.0%
Venezuela, Bolivarian Republic of	42	1.0%

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Table 2: Breakdown of healthcare practitioners using Anesthesiologist by role

Role	Total	Percentage
Physician: Attending/Consultant	844	32.9%
Physician: Fellow/Resident/Registrar	635	24.8%
Anesthesia Assistant (PA)	300	11.7%
Nurse Anesthetist (CRNA)	245	9.6%
Anesthesia Technician	112	4.4%
Paramedic/EMT	85	3.3%
Nurse (RN)	73	2.8%
Medical Student	70	2.7%
Student Nurse Anesthetist	51	2.0%
Technically Trained in Anesthesia	50	1.9%
Student AA	36	1.4%
Other type of medical provider	29	1.1%
I am not a medical practitioner	14	0.5%
Pharmacist	14	0.5%
Respiratory Therapist	7	0.3%

Table 3: Specialties of physician users of Anesthesiologist

Specialty	Total Attendings	Percent Attendings	Total Trainees	Percent Trainees
Anesthesiology	644	80.8%	506	83.9%
Adult Critical Care	208	26.1%	144	23.9%
Emergency Medicine	199	25.0%	134	22.2%
Pediatric Anesthesiology	132	16.6%	100	16.6%
Pain Medicine	128	16.1%	97	16.1%
Obstetric Anesthesiology	124	15.6%	99	16.4%
Cardiothoracic Anesthesiology	86	10.8%	79	13.1%
Pediatric Critical Care	85	10.7%	63	10.4%
Internal Medicine	67	8.4%	45	7.5%
Pediatrics	53	6.6%	28	4.6%
Other	54	6.8%	31	5.1%

S-468.

EFFECTIVENESS OF HYPOTENSION TREATMENT BETWEEN BOLUS AND CONTINUOUS INFUSION OF PHENYLEPHRINE: A RANDOMIZED COMPARISON USING AN IN SILICA SIMULATION

AUTHORS: S. S. Pfost[1], N. Ribeiro Marques[1], J. Wolf[1], G. Cao[2], T. Luspay[2], K. Grigoriadis[2], G. Kramer[1]

AFFILIATION: [1]Anesthesiology, University of Texas Medical Branch, Galveston, TX, [2]Mechanical Engineering, University of Houston, Houston, TX

INTRODUCTION: Effective treatment of hypotension continues to be a challenge in the operating room and correlates with poor outcome. We determined the effectiveness of trained Anesthesiology residents in preventing and treating hypotension using two regimens of boluses versus constant infusions of vasopressor using a computer modeled simulator.

METHODS: We mathematically modeled the blood pressure response to sodium nitroprusside (SNP) and phenylephrine (PHP) using experimental data from anesthetized swine. The model encompasses the sensitivity, first order dynamics and time delay of the blood pressure response to SNP and PHP infusions using adjustable parameters estimated to approximate the experimental response. Noise is included in the model to provide realistic variability. The model was implemented in silica as a vital sign monitor with a pressor delivery control panel, Figure 1. Our long-term goal is to use the simulator for training; the capture of clinical expertise; and comparison of closed-loop pressor delivery systems versus care providers. Eleven Anesthesiology residents were tasked to maintain mean arterial pressure (MAP) during a set 20 minute infusion of SNP. SNP infusion alone produced MAP drop over a range of 75 to 90 mmHg, Figure 2. A target mean arterial pressure (MAP) of 90 mmHg was assigned and optimal performance was defined as MAP within 85 to 95 mmHg. Using a randomized order crossover design hypotension was treated in two trials per anesthesiologist; one with boluses and the other with adjusting infusion rate. A touch screen and key board allowed the anesthesiologist to deliver a bolus, and start, adjust or stop a continuous infusion.

RESULTS: Four 1st year Clinical Anesthesiology residents (CA-1), three 2nd year Clinical Anesthesiology residents (CA-2), and four 3rd year Clinical Anesthesiology residents (CA-3) participated in our study. PHP bolus infusion had greatest MAP control compared to PHP continuous infusion for CA-1, CA-2, and CA-3. MAP was within 5 mmHg of target for 85%, 77%, and 84% of study time with bolus infusion versus 41%, 61%, and 50% of study time for continuous infusion. All three groups had a small negative bias during bolus infusion ranging from -1.9 to -0.3 mmHg, and a small positive bias with continuous infusion, from 1.9 to 3.2 mmHg. The median absolute performance, a measure of inaccuracy, was lower during the bolus infusion compared to continuous infusion: 2.4, 3.2, 2.4 vs. 8.1, 4.6, and 5.2 for CA-1, CA-2, and CA-3 respectively. On average the anesthesiologists' performance was not improved during the second test versus the first trial. Figure 3 graphically depicts the superiority of MAP control during bolus infusion.

CONCLUSION: Simulators may be an effective tool to assess trainee competences and help to develop skills. In this study we captured pressor infusion expertise. The three resident groups maintained MAP closest to target using bolus infusion. Further studies are planned to compare closed-loop control algorithms versus human performance.

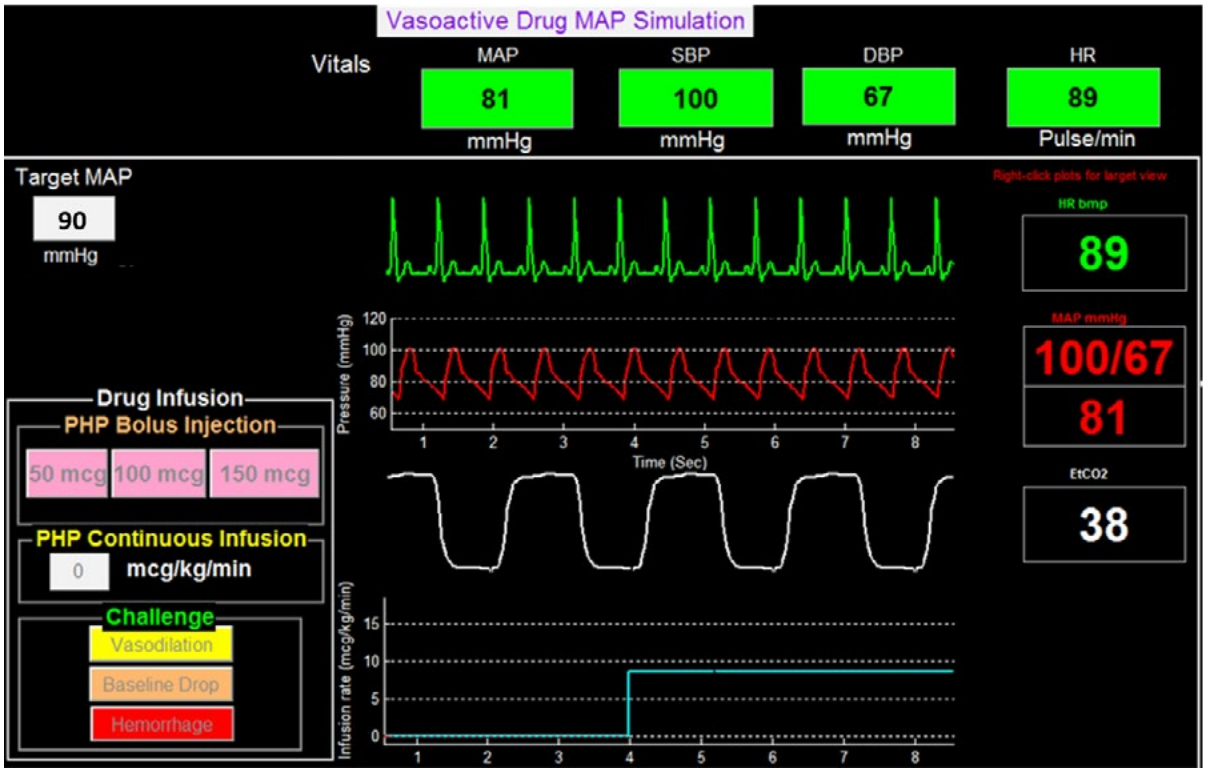

Figure 1.

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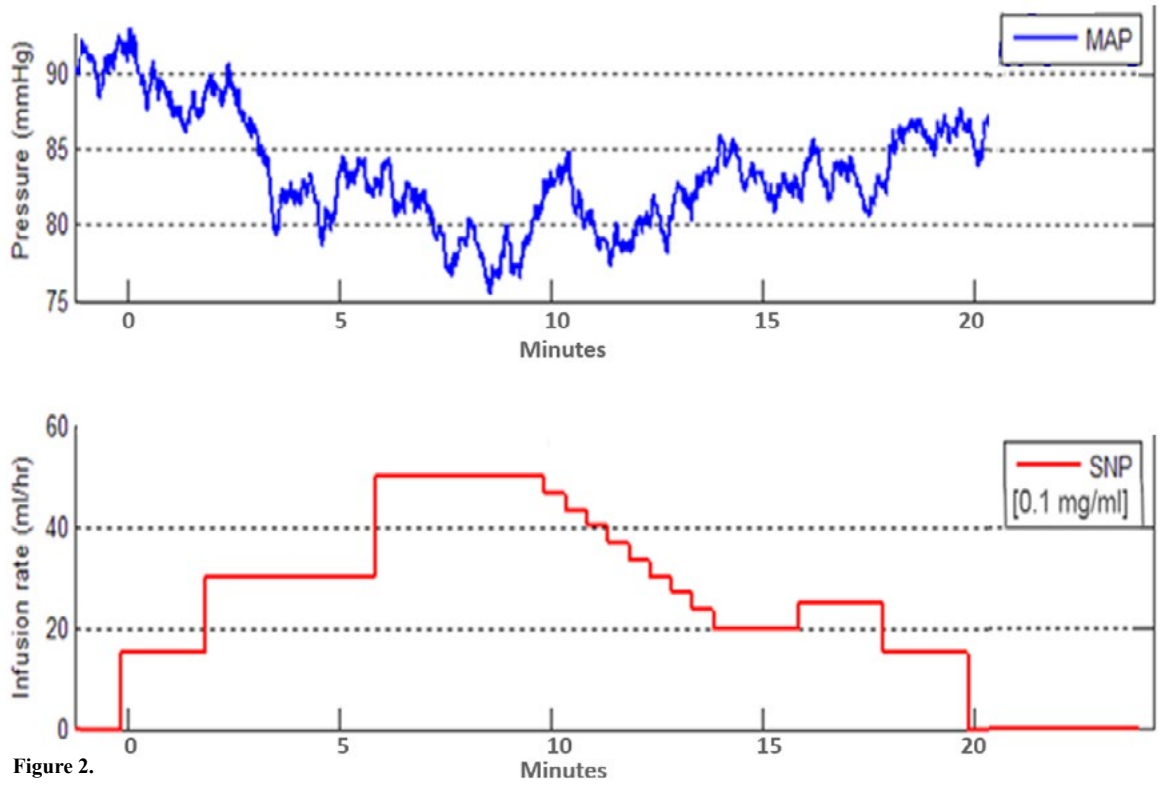

Figure 2.

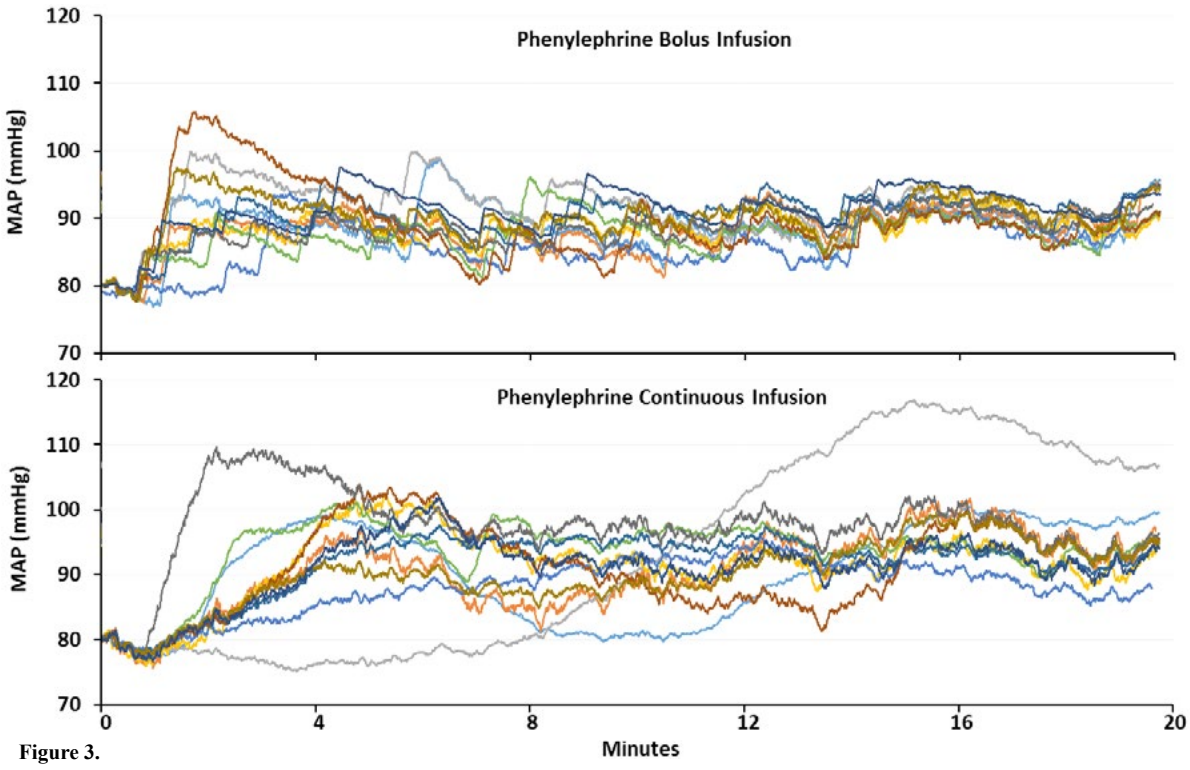

Figure 3.

S-469.

A SYSTEMATIC REVIEW AND META-ANALYSIS OF DEPTH OF ANAESTHESIA MONITORING DURING PROCEDURAL SEDATION AND ANALGESIA

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INTRODUCTION: Electroencephalogram-based depth of anaesthesia (DoA) monitoring devices provide an additional method to monitor level of consciousness during procedural sedation and analgesia (PSA). The objective of this systematic review was to determine whether using DoA monitoring during PSA improves sedation safety (hypoxia, hypotension, adverse events) and efficacy (doses required for sedation, duration of recovery, rates of abandoned procedures due to inadequate sedation).

METHODS: Electronic databases (CENTRAL; Medline; CINAHL) were searched to May 2015. Randomized controlled trials that compared DoA monitoring to a control group without DoA monitoring during PSA were included. Study selection, data extraction and risk of bias assessment (Cochrane risk of bias tool) were performed by two reviewers.

RESULTS: A total of 16 trials (2138 participants) were included. Evidence rating for outcomes was downgraded to either low or moderate quality due to study limitations and imprecision. Meta-analysis of 8 trials (766 participants) found no difference in hypoxaemia (RR 0.87; 95% CI=0.67 to 1.12). No statistically significant difference in hypotension was observed in meta-analysis of 8 trials (RR 0.96; 95% CI=0.54 to 1.7; 942 participants). Meta-analysis of 9 trials (1131 participants) that reported on the amount of propofol that was used during procedures revealed there was no statistically significant difference between DoA and standard monitoring (mean difference -2.49mg (95% CI=-9.43mg to 4.46mg). Mean dose of propofol was 51mg lower for participants randomised to DoA monitoring (95% CI=-88.7mg to -13.3mg) in subgroup meta-analysis of results from four trials conducted with 434 participants who underwent interventional endoscopy procedures with propofol infusions to maintain sedation. Recovery duration was defined differently in each trial so results were not pooled. The greatest mean difference in recovery time between DoA and standard monitoring groups reported in an individual trial was 4 minutes (95% CI -7.29 to -0.71). Meta-analysis of results from two trials that reported on the number of procedures that were not completed due to inadequate sedation revealed there was no statistically significant difference between the DoA and standard monitoring groups (RR 0.54; 95% CI=0.16-1.8).

CONCLUSIONS: DoA monitoring did impact decision-making regarding sedation titration during interventional procedures with propofol infusions. For this reason, it seems reasonable for clinicians who already have access to and are trained in its use, (i.e. anaesthetists who use DoA monitoring during general anaesthesia) to utilise DoA monitoring for select populations of patients if it is decided that limiting the amount of sedation would be beneficial for the individual patient. However, there is no need to invest in purchasing extra equipment or training staff who are not familiar with this technology (e.g. non-anaesthetists who don't routinely use DoA monitoring during general anaesthesia) to use it because there is no high quality evidence supporting the clinical benefits of using DoA monitoring during PSA.

S-470.

DESIGNING A NOVEL MANUAL COMMUNICATION SYSTEM FOR MECHANICALLY VENTILATED ICU PATIENTS

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INTRODUCTION: Current research shows that the existing methods for mechanically ventilated (MV) ICU patients to communicate are insufficient. While a number of basic communication methods are often tried with these patients (such as writing on whiteboards/ clipboards, use of letter boards, and mouthing words), patients and caregivers consistently report dissatisfaction with available methods and limited success in their use.[1] Furthermore, patients consider the lack of successful communication strategies to be extremely stressful.[2] The ICU setting is more complicated for assistive communication technology use than other settings due to patient population heterogeneity; variation in individuals' physical/ cognitive capabilities over time; robustness and hygiene concerns for communication tools; and a lack of available training time prior to patients' need for communication assistance.

METHODS: We are developing a communication system that is easily accessible by MV patients who lack sufficient dexterity to write clearly due to complications of critical illness. Using this novel system, a patient will manually operate a hand-held component that communicates in real time with a tablet computer, producing audiovisual content specific to ICU patient needs. Three sets of system requirements have guided the design of this technology: features required by the ICU setting, by the patient, and by the nurses/care team. Features required by the ICU setting include the presence of ICU-specific topics and cost-effective design that is appropriately hygienic. The patient-related system requirements involve a short learning curve; hardware and software that is adaptable to individual patients; and inclusion of non-medical topics of value to patients and their families. Synthesized speech output and some form of tactile feedback are also planned for the final system version to meet patient needs. In considering the requirements of the nurses and care team, the system should be accessible despite physical restraints and should demonstrate a patient's level of responsiveness, allowing for a clearer assessment of a patient's cognitive state.

RESULTS: This system has been demonstrated in its prototype form to physicians, nurses, researchers, and engineers. Based on their feedback, we have prepared more than a dozen improved versions of the device in preparation for deployment with MV ICU patients. Figure 1 shows the design of the communication device in its current version. The system will undergo proof-of-concept testing in a pilot trial in MV patients.

CONCLUSIONS: Existing communication methods for MV ICU patients do not meet the emotional and logistical needs of these patients. We are designing and testing a new communication system with the goal of allowing MV ICU patients to communicate despite a variety of physical impairments.

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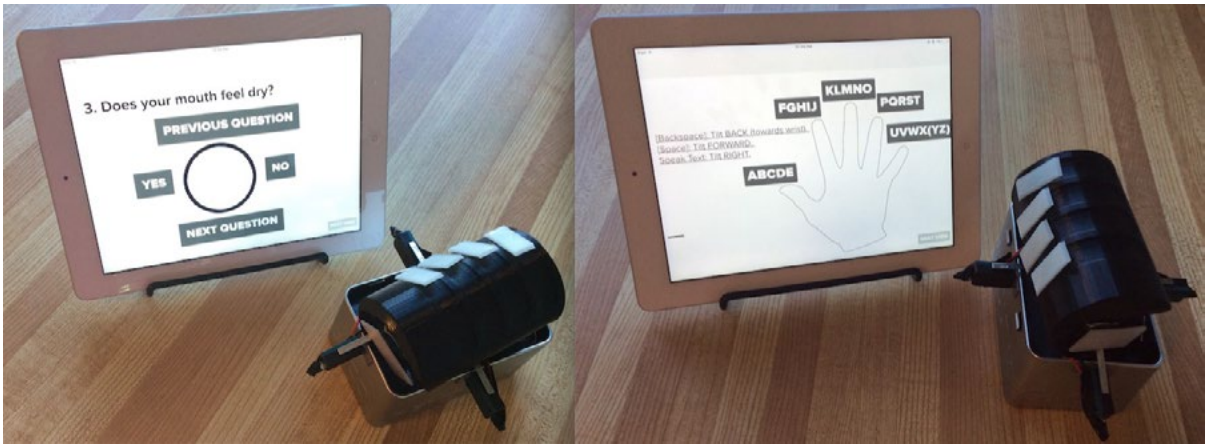

S-471.

EFFECT OF NON-INVASIVE BLOOD PRESSURE CUFF INFLATION ON INTRA-ARTERIAL BLOOD PRESSURE VALUES

AUTHORS: V. Sheshadri[1], A. Tiwari[1], M. Nagappa[2], L. Venkatraghavan[1]

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INTRODUCTION: Both noninvasive and invasive arterial blood pressure (NIBP and IABP) measurements are routinely used in the perioperative period and intensive care units. These two techniques often produce different values, and the relationship between them is not fully understood. Previous studies in the non-surgical patient population have shown that NIBP cuff inflation at the arm can cause transient rise in BP because of either pain, anxiety resulting from "alerting response" or discomfort and muscular activity.[1-3] Similar data in the perioperative setting is lacking. The aim of our study was to determine the effect of NIBP cuff inflation on the resting IABP measurements, recorded in the contralateral arm. We hypothesize that the mere act of cuff inflation will increase IABP in line with the alerting response.

METHODS: After Institutional review board approval and informed patient consent, 100 consecutive adult patients undergoing surgery that required IABP monitoring were recruited in this prospective observational study. The study was conducted in the post anesthesia care unit postoperatively. Arterial lines were inserted preoperatively and an appropriate sized cuff was used in the contralateral arm. Baseline IABP, NIBP and heart rate were recorded. NIBP cuff was then set to cycle every 5 minutes for 3 times and then a rest period of 30 minutes followed by another set of 3 measurements were obtained. During each cuff inflation cycle, changes in IABP values, heart rate and the duration of cuff inflation were recorded. After exclusion, a total of 582 measurements were included for data analysis. Statistical analysis was done using paired 't' test, Chi-square and two-way ANOVA.

RESULTS: The mean age of the study population was 54 years and history of hypertension was present in 48.5% and diabetes in 10.3% of patients. The mean duration of BP cuff inflation was 36±10 seconds. Majority (73.4%) of the patients had increase in the baseline systolic blood pressure (SBP) by 0-10mmHg with minimal variation in diastolic blood pressure. The change in

IABP was independent of the baseline SBP (Fig 1A). There were no substantial differences in the IABP values with cuff inflation between hypertensive and non-hypertensive patients (p=0.732) (Fig 1B). Similarly, successive cuff inflation had minimal effect on changes in IABP (Fig 1C). There was no statistical difference in the heart rate with cuff inflation. There was no correlation between duration of cuff inflation and change in the IABP.

CONCLUSIONS: Our study demonstrated that NIBP cuff inflation does cause a variable increase in IBP values. This is an important information in the perioperative and intensive care settings, where both these measurement techniques are routinely used. The exact mechanism for this effect is not known but may be explained on the basis of alerting response.

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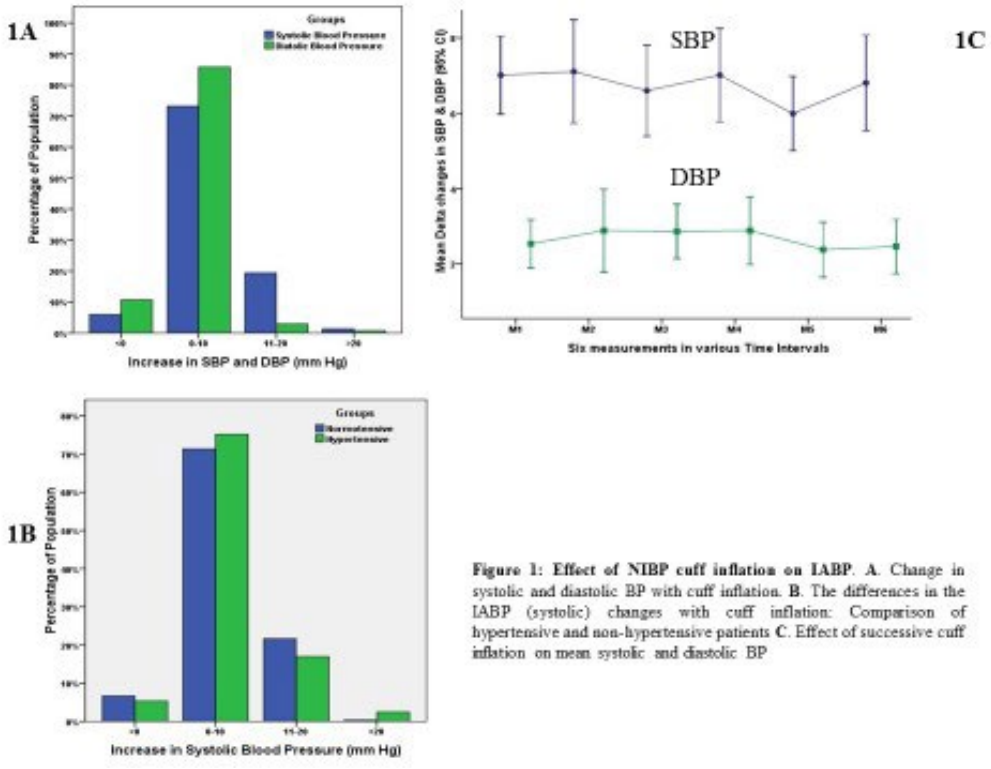

Figure 1: Effect of NIBP cuff inflation on IABP. A. Change in systolic and diastolic BP with cuff inflation. **B.** The differences in the IABP (systolic) changes with cuff inflation: Comparison of hypertensive and non-hypertensive patients **C.** Effect of successive cuff inflation on mean systolic and diastolic BP

S-472.

STATE OF THE ANESTHESIA BLOGOSPHERE IN 2016

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INTRODUCTION: The term "blogosphere" represents all the blogs on the internet and their interconnections. While various studies have examined the size, scope and reach of medical blogs in general, to date no studies have attempted to catalogue the anesthesia blogosphere. The purpose of this study is to review the current anesthesia blogosphere and evaluate the overall interactiveness, interconnectivity, and popularity of the anesthesia blogosphere as it stands in 2016.

METHODS: Google.com and blogsearchengine.com were used to catalogue anesthesia blogs. Once this list was compiled the "blogroll" (hyperlinks connecting to other blogs) was examined to find other related blogs. An anesthesia blog was defined as one in which a self-identified anesthesia provider was the primary author. Alexia.com and similarweb.com were used for analysis of traffic data, and blogs were excluded if no data were available. Blogs were further categorized by presence of a blogroll, RSS (real simple syndication) feed availability, US and global page ranking, commenting ability, and date of most recent update.

RESULTS: A total of n=32 blogs were identified after internet searches and literature review. Of these, n=11 were excluded due to lack of ability to obtain internet traffic data. 48% (n=10) had a blogroll with links to other anesthesia blogs, 95% (n=20) possessed the ability for visitor comments, 100% (n=21) had an RSS feed, and 42% (n=9) had not been updated since 2014. Traffic analysis revealed an average of 24.2 sites linking to each blog (95%CI[14.5-36.4]), with an average global page rank of 15.08 million (95%CI[8.31m-20.74m]). For blogs with United States page rank available (n=13), the average page rank was 3.49 million (95%CI[1.51m-5.09m]).

CONCLUSIONS: To our knowledge, this is the first formalized attempt to quantify the extent of the anesthesia blogosphere. In its current state the abilities exist for interaction with end users, as is evidenced by the large number of blogs that allow visitor comments and possess RSS feed capability. However, a significant number of these blogs have not been updated since 2014. This coincides with trends on the internet at large, where blogs have slowly been replaced by big company social media such as Facebook and Twitter. The blogs included in this study were also very well connected, with an average of 24.2 sites linking to them. In conclusion, the anesthesia blogosphere appears to be a loosely associated group of several dozen providers who were most active in the first 10 years of the 21st century. Future research could attempt to determine whether Twitter and Facebook have provided the same forum for literary anesthesia, or whether efforts would be worthwhile to formally organize and reinvigorate the anesthesia blogosphere.

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Scholars' Abstracts

Trauma

S-474.

EFFECTIVENESS AND EFFICIENCY OF HEMORRHAGIC HYPOVOLEMIA FLUID RESUSCITATION BETWEEN STANDARD OF CARE PRACTICE AND AUTOMATED STRATEGIES

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INTRODUCTION: The optimal fluid resuscitation strategy for hemorrhage has not been established. The primary goal after controlling bleeding is to restore circulating blood volume. Interaction between fluid volume, infusion rates, and dynamics of vascular volume retention will ultimately determine Effectiveness (the ability to maintain physiologic targets e.g. blood pressure [BP]) and Efficiency (the total volume required). Decision support (DS) and closed loop (CL) systems can guide infusion rate, while standard of care often replaces a blood loss with a fixed ratio of fluid to estimated blood loss e.g. 3:1. We compared the performance of three resuscitation strategies to determine hemodynamic control and fluid balance associated with each method. We hypothesize that perioperative hemodynamic support can be enhanced with fluid titration using a closed-loop and decision support system.

METHODS: Fourteen volunteers undergoing hemorrhage (10ml/kg over 20 min) were randomized to semi-automated (DS group) or fully automated (CL group) or standard of care (SC group) fluid therapy in a crossover study. Fluid therapy started at the beginning of hemorrhage. DS group algorithm included a BP matrix (look up table) algorithm giving fluid recommendations every 1-5 min. CL group algorithm infused fluid automated based on BP every 3-5 seconds. The SC group received 30ml/kg of lactated Ringer's over 20 min. We used the Office of Naval Research Tablet System that interfaced a vital sign monitor, an IV pump and a tablet computer hub.

RESULTS: The effectiveness of the groups were similar. The percentages of time that mean arterial pressure (MAP) was within 5 mmHg of target were 39%, 34% and 35% for the DS, CL, SC groups ($p=0.6$), respectively. The median absolute performance error (metric of inaccuracy) was 13 mmHg for all three groups ($p=0.8$), and the median performance error (bias) was 0.6, 1.8, and -4.8 mmHg for the DS, CL, SC groups ($p=0.5$), respectively. The total volumes of fluid infused averaged 10 ml/kg, 7ml/kg and 30ml/kg for the DS, CL, and SC groups ($p<0.0001$). The mean times to achieve target were 35, 25, and 55 min for the DS, CL, SC groups, respectively. The SC and CL groups showed significant difference ($p=0.02$) between time to reach target, while the differences between SC and DS groups ($p=0.12$), and DS and CL groups ($p=0.53$) were less prominent. The DS and CL groups were more efficient than the SC group as they maintained MAP at similar levels infusing less fluid. The SC group had higher urine output (8.6 ml/kg, $p<0.0001$) and greater extra vascular volume expansion (17.8 ml/kg, $p<0.0001$) compared to DS (3.5 ml/kg UO and 5.4 ml/kg EVV) and CL (4.1 ml/kg UO and 1.4 ml/kg EVV) groups. The effects of associated hemodilution were similar in all groups and led to increased cardiac output and decreased hemoglobin levels.

CONCLUSION: SC fluid therapy was associated with excess volume that could lead to edema. Both DS and CL groups behaved as a volume sparing system and were as effective as SC. The autonomous systems accomplished hemodynamic stability with negative fluid balance and may be able to reduce incidence and complications of fluid overload.

Best Medically Challenging Case

Critical Care

MC-45.

VICKS VAPORUB® INTOXICATION: AN UNUSUAL PRESENTATION OF MULTIORGAN FAILURE

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INTRODUCTION: Vicks VapoRub® is an over-the-counter cold remedy with cough suppressant and analgesic properties. This topically applied ointment contains synthetic camphor 4.8%[1]. Toxic camphor levels cause neurologic, gastrointestinal, hepatic, respiratory and cardiac compromise. Here we describe a patient with multiple comorbidities who presented with multiorgan failure after chronic Vicks VapoRub® ingestion.

CASE REPORT: A 54-year-old African American woman with a Heartmate II LVAD due to non-ischemic cardiomyopathy, atrial fibrillation, chronic kidney disease, hypothyroidism and asthma presented with acute onset of altered mental status (AMS), chest pain, shortness of breath and hypercapnic respiratory failure.

Upon ICU admission, the LVAD Pulse Index (PI) was low, and AICD interrogation revealed multiple episodes of ventricular tachycardia and fibrillation terminated by appropriately administered shocks. CXR showed mild pulmonary edema. Labs were significant for hypoxemia, metabolic acidosis (pH 7.12 Anion Gap 18), and elevated creatinine and liver enzymes. The clinical picture could not be explained by a single etiology and she was therefore treated symptomatically; fluid resuscitation and empiric antibiotics were started. Her low PI improved, but AMS, metabolic acidosis and acute-on-chronic kidney injury persisted.

Upon further investigation, we learned that the patient ingested three, 50g containers of Vicks VapoRub® weekly. Toxicology was consulted and a working diagnosis of camphor intoxication was made. It was speculated that her multiorgan failure could be best explained by acute on chronic camphor toxicity. Supportive measures continued, and over 2 weeks, mental status and laboratory abnormalities corrected to baseline. Lipid hemodialysis, while recommended for detoxification was not considered given the patient's gradual improvement[2].

CONCLUSIONS: Synthetic camphor is a primary, active ingredient of Vicks VapoRub® ointment. Acute camphor poisoning is predominantly seen in children; adults account for only ~10% of toxic exposures[3]. Consumption of 1g or 20mg/kg of camphor is considered highly toxic and our patient ingested roughly 5x this amount weekly[4]. Camphor toxicity affects all organ systems, causing seizures, altered mental status, dysrhythmias, myocarditis, mucosal irritation, nausea, vomiting, ventilatory failure and more. Treatment is largely supportive. Benzodiazepines are recommended for control of camphor related seizures. Ipecac induced emesis is discouraged. The utility of activated charcoal for detoxification is questionable[3,4].

This case demonstrates the misuse of over-the-counter remedies as a public health concern. Critical care physicians should be familiar with the presentation of camphor toxicity to enable early diagnosis and treatment. To our knowledge, this is the first report describing camphor toxicity in an adult secondary to Vicks VapoRub® ingestion.

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