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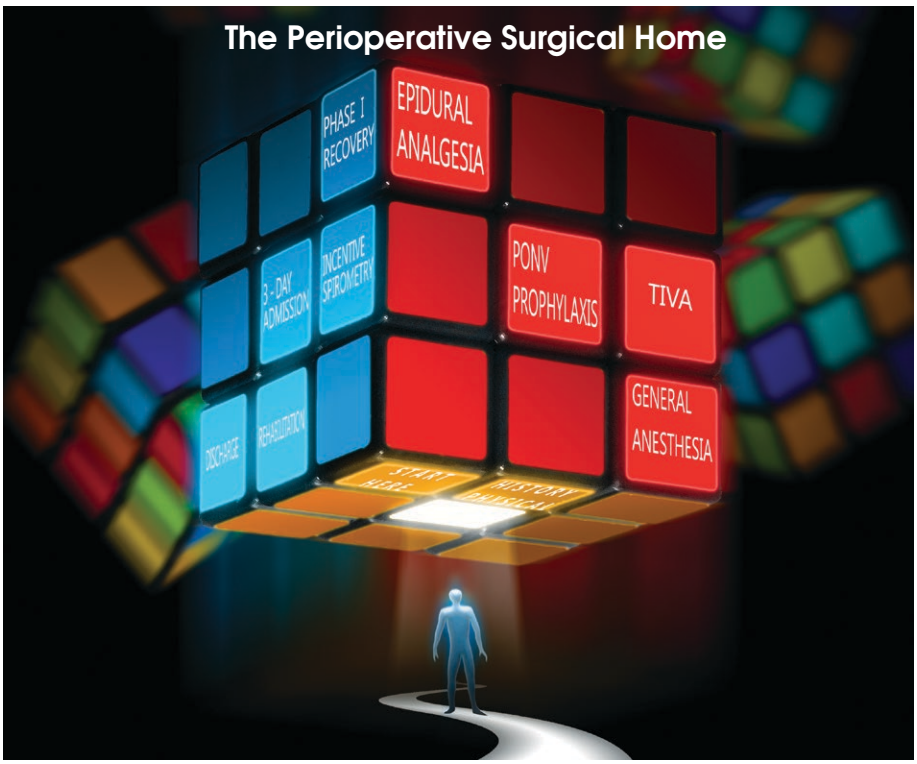

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Airway Management

S-1.

EMERGENCY INTUBATION WITH VIDEOLARYNGOSCOPY: PRELIMINARY DATA OF A PROSPECTIVE, RANDOMIZED, MULTICENTER OUT-OF-HOSPITAL TRIAL

AUTHORS: S. Janssen[1], F. Reifferscheid[1], V. Doerges[1], P. Knacke[2], A. Callies[3], E. Cavus[1]

AFFILIATION:[1]Anaesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein Campus Kiel, Kiel, Germany, [2]Anaesthesiology and Intensive Care Medicine, Sana Clinics Ost-Holstein, Eutin, Germany, [3]Anaesthesiology and Intensive Care Medicine, Klinikum Links der Weser, Bremen, Germany

INTRODUCTION: Videolaryngoscopy may be a valuable technique for pre-hospital endotracheal intubation[1]. However, the performance of different videolaryngoscopic systems in this setting is unclear. The aim of the present study was to compare three new portable videolaryngoscopes, the A.P. Advance® (APA; VENNER Medical, Kiel, Germany), the C-MAC® PM (CM; Karl Storz, Tuttlingen, Germany), and the channeled-blade King Vision® (KV; King Systems, Noblesville, USA) for pre-hospital emergency endotracheal intubation (ClinicalTrials.gov NCT01635660).

METHODS: Approval of the institutional review board was obtained. We report of 45 matched patients (15 for each device; age, median [range]: 65 [18-87]; 24 female), that had the need for pre-hospital emergency intubation, and that were treated by a physician introduced in the use of the devices.

RESULTS: Most frequent indications for pre-hospital intubation were cardiopulmonary resuscitation in 9 cases, and trauma in 20 cases (including maxillo-facial trauma in 4 cases), respectively. Glottic visualization was comparable with all 3 devices (Best achievable Cormack-Lehane classes: I: APA 8, CM 7, KV 8; II: APA 5, CM 8, KV 4; III: APA 1, KV1; IV: APA 1). Median [range] time to successful intubation for the APA was 30 [10-135] seconds, for the CM 45 [20-90] seconds, and for the KV 70 [20-140] seconds. Intubation success on the first attempt with APA, CM, and KV was 73%, 67%, and 47%, respectively. Overall success for APA, CM, and KV was 100%, 100%, and 60%, respectively.

Direct laryngoscopy for successful intubation after failed videolaryngoscopic attempts was necessary with the APA in 2 patients, and with the CM in 1 patient. In the KV group, 6 patients were intubated with a conventional Macintosh laryngoscope.

CONCLUSION: A.P. Advance, C-MAC PM, and King Vision® showed comparable glottis visualization during pre-hospital emergency endotracheal intubation; however, intubation success rates in non-standardized, challenging conditions may vary between the different videolaryngoscopic devices.

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S-2.

"THE PATIENT ACTUALLY LIKES IT!!": A SIMPLE AND NO-EXTRA-COST TSE-ALLOTEH NASAL CPAP MASK/CIRCUIT FOR A MORBDLY OBESE PATIENT WITH OBSTRUCTIVE SLEEP APNEA UNDER MAC FOR IRRIGATION AND DEBRIDEMENT OF ANKLE ULCER

AUTHORS: H. Skiff, C. W. Hunter, E. Pantin, R. Alloteh, S. Barsoum, C. Kloepping, J. Tse

AFFILIATION: Anesthesiology, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ

INTRODUCTION: Patients under monitored anesthesia care (MAC) routinely receive intravenous (IV) sedation and O_2. Over-sedation or airway obstruction may cause severe desaturation, especially in obese patients with obstructive sleep apnea (OSA). These patients may use nocturnal continuous positive airway pressure (CPAP) or bi-level continuous positive airway pressure (BiPAP) machine. Under sedation, they may require frequent chin-lift, jaw-thrust or insertion of a nasal airway. To avoid the risk of epistaxis when inserting a nasal airway, the TSE-Alloteh nasal CPAP mask/circuit has recently been shown to improve oxygenation in sedated OSA patients using existing anesthesia equipment[1-4]. We report a challenging case using this simple technique to improve oxygenation and comfort in a morbidly obese OSA patient under MAC.

CASE REPORT: A 48 y/o morbidly obese man (5'10", 141 kgs, Body Mass Index: 45 kg/m2) presented for irrigation and debridement of left ankle ulcer. He had prior extremely difficult endotracheal intubation, status post tracheostomy several year prior, severe peripheral neuropathy, CAD, IDDM, spina bifida, that did not restricted his mobility until recently, and OSA. He used a home BiPAP mask/machine (16/7 cm H2O). Because of his multiple comorbidities and severe peripheral neuropathy that made his wound insensible to pain, it was decided to proceed without local anesthesia or IV sedation. He was on nasal cannula (NC) O_2 (2 L/min) and his O_2 saturation (Sat) was 95% while sitting upright. His oropharynx was pretreated with 5% lidocaine cream for possible awake fiber optic intubation if need arose. He complained of dyspnea while lying down with a foam wedge (30 degree incline). His O2 Sat decreased to 92% even with NC O_2 (5L/min). He requested a BiPAP mask and was fit with an adult facial mask to provide CPAP using an adult anesthesia breathing circuit, but felt more comfortable when an infant mask with fully inflated air cushion. It was placed over his nose and secured with head straps to obtain a tight seal (Photo 1-3)1-4. It was connected to an adult breathing circuit attached to the anesthesia machine. Pressure-relief valve was adjusted to deliver CPAP (5 cm H_2O) with a mixture (0.75 FiO_2) of fresh O_2 (5 L/min) and fresh air (2 L/min). The patient was happy with this nasal CPAP mask and gave consent for photography. He maintained spontaneous respiration and 100% O_2 saturation throughout the procedure. He tolerated the procedure well without complication.

CONCLUSION: This simple nasal CPAP mask/circuit takes 2-3 min to assemble using existing anesthesia equipment and machine. This patient actually liked this nasal CPAP mask much better than a facial CPAP mask. It improves oxygenation and proactively prevents desaturation in sedated obese patients with OSA[1-4]. It can also be used to deliver assisted nasal mask ventilation without interrupting the procedure[1-4]. This simple technique may improve patient safety at no extra cost.

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S-3.

DIVERSITY OF OUT-OF-OPERATING-ROOM INTUBATIONS AMONG RESIDENCY PROGRAMS IN THE UNITED STATES

AUTHORS: P. Upadya, M. Conopio, J. Spaliaras, A. Padover, A. Krottapalli, S. Shodhan

AFFILIATION: Anesthesiology, St. Joseph's Regional Medical Center, Paterson, NJ

INTRODUCTION: Preparation is vital for intubation. After anecdotal complaints of lack of adequate equipment and resident dissatisfaction with out-of-operating-room intubations, we sought to investigate resident concerns for patient safety. The unavailability of essential equipment and staff can lead to difficult and hazardous situations. This study was undertaken to investigate the standard of equipment, medications and monitors available during out-of-operating-room intubations.

To understand how other anesthesia programs handle these situations, a survey was created to compare protocols from other hospitals.

METHODS: An IRB approved survey was sent out to all ACGME anesthesia program coordinators with an email address on file. Program coordinators were requested to forward the survey link to each anesthesia resident. This survey was created using the software, Survey Monkey (SurveyMonkey Inc., Portland, OR). Confidentiality of the participants was ensured through this software. The questionnaire consisted of 19 questions designed to evaluate how emergency out-of-operating-room intubations were logistically handled in each hospitals' setting.

RESULTS: Over a span of four months, 414 responses were collected. The majority of respondents (79.95%) were from a level 1 trauma center. The anesthesia department was primarily responsible for out-of-operating-room intubations (93.24%). Variations were noted among residents in the following categories: 1) Equipment: 70% bring their own equipment to the bedside versus bedside equipment available; 2) Emergency and Intubation Medications: 43% bring their own medications versus 43% available at bedside; 3) Bedside Monitoring Availability: EKG - 65.74%, BP - 80.15%, SpO2 - 85.28%, ETCO2 - 21.02%; and 4) Maintenance of Intubation Equipment Responsibility: Floor RN - 10.53%, Anesthesia resident on call - 45.43%, Anesthesia attending - 2.22%, Central Supply - 16.34%, Other (anesthesia technician/CRNA/RT/pharmacy) - 31.86%. Most importantly, respondents noted that lack of supplies was the cause of preventable morbidity in 13.47% of out-of-operating-room intubations.

DISCUSSION: From this survey, it is evident that there is diversity among anesthesia programs in the United States, on how each handles out-of-operating-room intubations. This includes but is no limited to personnel responding to the intubation and bedside availability of equipment, medication and monitoring. Diversity is acceptable until patient safety is compromised. Therefore, it is feasible to consider establishing a universal airway management protocol to enhance patient safety and efficiency during out-of-operating-room intubations.

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S-4.

A PILOT STUDY TO EVALUATE A NOVEL TECHNIQUE FOR BAG MASK VENTILATION IN A PATIENT WITH ESTABLISHED CRITERIA FOR DIFFICULT MASK VENTILATION

AUTHORS: D. Grech, S. Patel, H. Israel, A. Bekker

AFFILIATION: Anesthesiology, Rutgers New Jersey Medical School, Newark, NJ

INTRODUCTION: Masked ventilation is an essential skill that is practiced by virtually all medical professionals. It is a skill that when used correctly can save many lives. Traditionally, there are two main styles of mask ventilation, the one handed (the "C and E" grip, Figure a) and the traditional two handed (THT, figure c) grip. With the one handed grip, there is a risk of air leak on the side opposite to the stabilizing hand. The two handed grip provides better protection against an air leak but requires another provider to actually deliver the tidal volumes. We are proposing a novel sub-mandibular (NS, figures b & c) one handed grip that allows us to put adequate pressure on both sides of the mask and deliver adequate tidal volume using the other hand. The anesthesia provider (AP) will stand perpendicular to the long axis of the patient's body, aligning the AP's umbilicus to the patient's mentum. Next, the AP will place their fifth digit along the body of the left mandible. The fourth digit will be placed along the body of the right mandible. The AP will rotate clockwise at the hip while keeping their elbow against their body to lift the patient's chin to 45 degrees. This rotational force adds strength to the chin lift maneuver. The AP will avoid pressing the soft tissue in the submental triangle. The first digit will be used to apply pressure to the left border of the facemask while the second and third digits will be used to apply pressure to the right border of the facemask.

METHODS: We enrolled 28 patients undergoing elective surgery who were classified into various groups: edentulous, bearded, Obstructive sleep apnea (OSA), mallampati 3 or 4, and mallampati 1 or 2 serving as controls. After the induction of general anesthesia but before intubation, the provider would ventilate the patient using an adult sized facemask. A preset tidal volume of 8cc/kg was delivered for 8 breaths for each technique. TV, peak airway pressures, HR and O_2 saturation were recorded after each breath. The anesthesia providers were demonstrated the NS grip prior to induction.

RESULTS: All the groups, except OSA, showed improvement, although statistically insignificant, in tidal volumes delivered with the novel technique when compared to the traditional C&E one-handed grip. The two handed technique, as expected, provided the largest tidal volumes when compared to the other two techniques.

CONCLUSION: Our results show that the novel submandibular technique can prove to be a useful complement or alternative to the traditional one and two-handed techniques. Future studies can be undertaken to stratify the effectiveness of these techniques based on provider's hand size, grip strength, gender, and training level.

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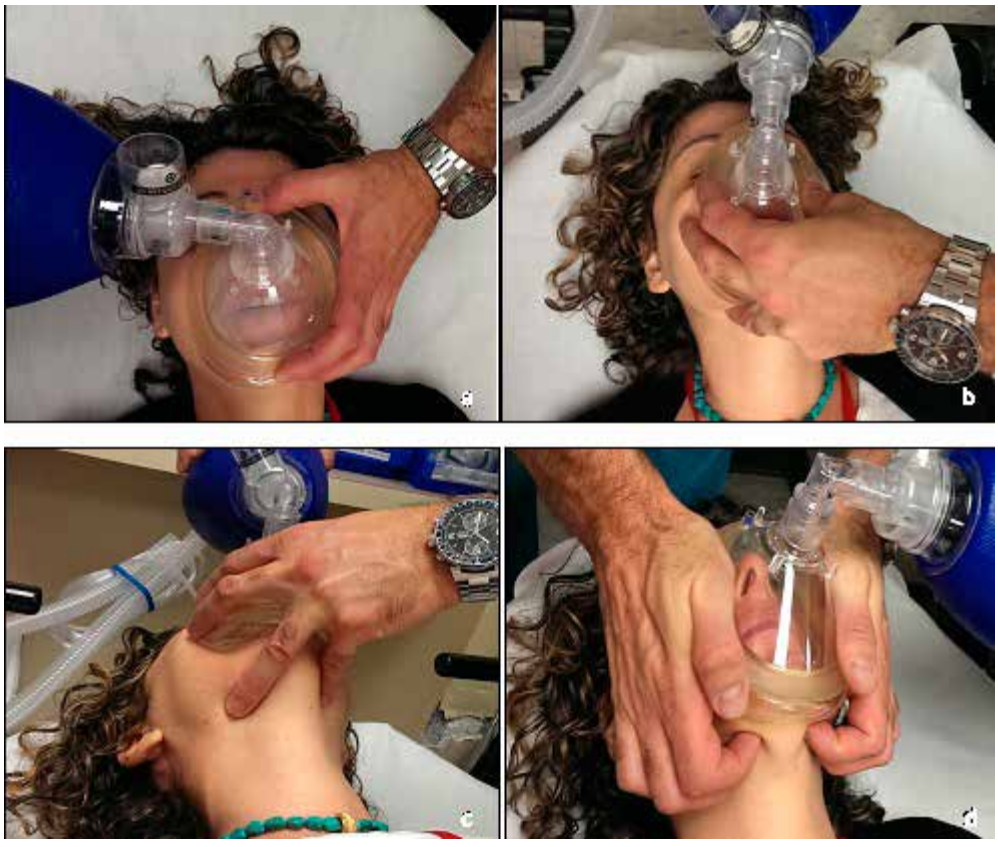

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S-5.

WITHDRAWN.

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S-6.

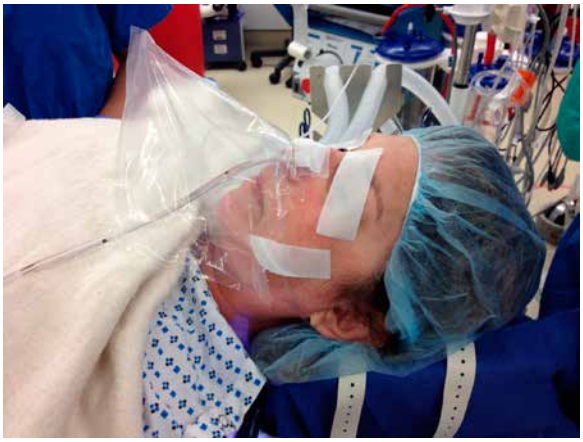
NO-COST TSE "MASK" FOR PRE-OXYGENATION PRIOR TO RAPID SEQUENCE INDUCTION OF GENERAL ANESTHESIA IN A PATIENT WITH LARGE BOWEL OBSTRUCTION, PAINFUL NASOGASTRIC TUBE, ANXIETY AND CLAUSTROPHOBIA

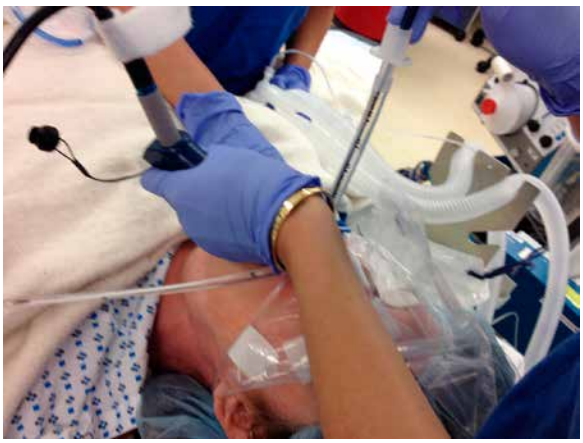
AUTHORS: J. Kim, S. Barsoum, N. Kumar, T. Mehta, S. Shah, C. W. Hunter, J. Tse

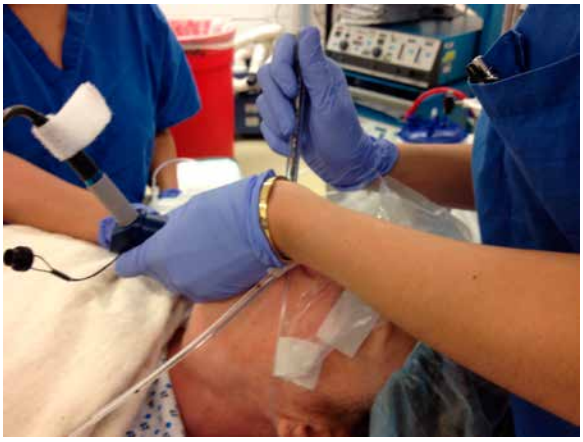
AFFILIATION: Anesthesiology, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ

INTRODUCTION: Rapid sequence induction (RSI) of general anesthesia (GA) is routinely performed after preoxygenation in patients with full stomach. It is difficult to adequately preoxygenate a patient who is claustrophobic and irritated by a nasogastric tube (NGT) with a face mask. A simple plastic bag was shown to improve oxygenation by transforming a nasal cannula (NC) to a face tent (TSE "Mask") in sedated patients during various procedures[1-3] and to improve oxygenation prior to perform RSI of GA for endotracheal intubation (ETI) in a combative trauma patient[4]. We report its use in improving preoxygenation in a patient with large bowel obstruction and claustrophobia.

CASE REPORT: A 65 y/o, 5'2", 128 lb, woman presented with large bowel obstruction for colonoscopy and subsequently for exploratory laparotomy 2 days later. She had diverticulosis, HTN, depression, anxiety and claustrophobia. GA with ETI was planned for colonoscopy due to distended abdomen with large bowel obstruction. She had pain and was very uncomfortable even with gentle manipulation of NGT during NGT suctioning. She anxiously requested not to use a face mask for preoxygenation because of extreme claustrophobia. After discussing the risks of inadequate preoxygenation, she agreed to preoxygenation with a NC and a clear plastic bag (TSE "Mask") as described1-3. Her O_2 saturation (Sat) increased from 98% to 100% after 4-5 min with TSE "Mask" and NC O_2 4 L/min (Photo 1). RSI (with cricoid pressure) of GA was performed with 100 mg lidocaine, 150 mg propofol and 100 mg succinylcholine. ETI was quickly and easily accomplished with a video-laryngoscope (Photo 2-3). Her O_2 Sat was 100% throughout. Anesthesia was maintained with sevoflurane and propofol. She was extubated fully awake and recovered without problem. Two days later, she was brought to OR for urgent exploratory laparotomy and Hartmann's procedure. She was pleased to see the same attending anesthesiologist and requested to have a TSE "Mask" for preoxygenation and gave consent for photography. Her O_2 Sat increased from 95% to 100% after 4-5 min preoxygenation with NC O_2 flow of 4 L/min and a TSE "Mask" (Photo 1). Modified RSI (with cricoid pressure) of GA was induced with 100 mcg fentanyl, 80 mg lidocaine, 150 mg propofol and 60 mg recuronium. ETI was again quickly and easily accomplished with a video-laryngoscope (Photo 2-3). Her O_2 Sat was 100% throughout. GA was maintained with desflurane and the surgical procedure was completed without complication. She was extubated awake in PACU without problem. She was discharged home after an uncomplicated postoperative course.







CONCLUSIONS: This patient might not gain adequate preoxygenation with a face mask prior to RSI of GA due to extreme claustrophobia and an irritating NGT. She was very pleased and comfortable with a TSE "Mask" for preoxygenation. After preoxygenation with this technique for a few minutes, GA with RSI and ETI can be accomplished without desaturation. This simple face tent can be prepared in a few sec without additional cost and may improve patient comfort and safety.

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S-7.

RANDOMIZED CONTROLLED TRIAL OF THE RIGID AND FLEXING LARYNGOSCOPE VERSUS THE FIBEROPTIC BRONCHOSCOPE FOR DIFFICULT AIRWAY MANAGEMENT

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INTRODUCTION: The fiberoptic bronchoscope is viewed as the gold standard device for difficult intubation. The rigid flexible laryngoscope is a newer device used for expected difficult endotracheal intubation. A comparative trial of these devices has not been performed.Methods: Adult surgical patients requiring endotracheal intubation with predicted difficult airways based on airway examination, body mass index and/or known difficult airway with previous intubation were randomized to undergo endotracheal intubation with either the Rigid and Flexing Laryngoscope (RIFL) or the Flexible Fiberoptic Bronchoscope (FOB). Induction was performed in usual manner by anesthesiologists, and intubation was performed by providers proficient with both airway devices. The primary outcomes measured were successful intubation, time to successful intubation, and number of attempts requiring additional airway assist maneuvers. The lowest observed oxygen saturation and airway trauma were also recorded. Results: A total of 41 patients were enrolled, with 20 randomized to each group and 1 withdrawal. Intubation was successful in all patients with both devices. The median time for successful intubation was significantly shorter in the RIFL group compared to the FOB group (49 vs. 64 seconds; $p=0.048$). Airway assist maneuvers were required in 2 (10%) intubations with the RIFL compared to 16 (80%) intubations with the FOB ($p<0.001$) There were no significant differences in lowest oxygen saturation or airway trauma.

CONCLUSION: The RIFL required significantly less time and airway assist maneuvers for successful endotracheal intubation compared to FOB when utilized by experienced providers in patients with anticipated difficult airways.

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S-8.

A NOVEL AIRWAY RESCUE TECHNIQUE: CAMERA IN TUBE INTUBATION THROUGH A SUPRAGLOTTIC AIRWAY

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INTRODUCTION: Airway rescue techniques are of vital importance in cases of unanticipated difficult airways and cannot intubate- cannot oxygenate scenario[1]. Tracheal intubation with a camera in tube intubation (CITI) technique through a supraglottic device may offer easier and faster intubation[2,3]. Aim of the current study was to compare this novel technique with direct laryngoscopy in a simulated position of difficult intubation- the lateral decubitus.

METHODS: Review Board approval was obtained for this study in the simulation lab. A Laerdal SimMan™ manikin was placed in the lateral decubitus on a bean bag mattress - left- and subsequently in right lateral tilt to simulate a difficult intubation position. Five participants- two 4th year registrars, two experienced consultants and one experienced nurse anesthetist were divided into sequential pairs. The first operator attempted conventionally tracheal intubation with a laryngoscope Macintosh blade 3 and this was followed by the second operator's attempt with CITI- Igel [a VivaSight™ (ET View) 7.0 through an I-gel 5.0]. Times were recorded until visual confirmation of correct tracheal tube placement. For both techniques the same VivaSight™ tube was used. Maximal time for intubation was set at 40 seconds. If the intubation took longer the intubation was scored as failed attempt. The intubation times were compared with a Mann-Whitney test (IBM SPSS 20.0).

RESULTS: A total of 120 intubations (60 with a laryngoscope and 60 with the CITI I-gel technique) were performed. With laryngoscopy 56 attempts (93%) were successful within 40 s with the CITI I-gel technique we observed the same overall success rate (93%). The mean (SD) time to intubation with a laryngoscope was 10.1 (4.2) s and with the CITI I-gel combination 10.6 (4.1) s (p=0.243). In contrast to the consultants and nurse anesthetist, the registrars had a higher success rate using the CITI I-gel technique (100%) than with the conventional method (83%). Their intubation times were also significantly faster using this technique, 10.3 (3.9) s vs 12.8 (4.9) s (p=0.041).

DISCUSSION: The use of a supraglottic airway is recommended as an adjunct to bag mask ventilation and it may be used to facilitate tracheal intubation[4]. This concept has not been previously formally evaluated or compared to laryngoscopy. Our study suggests that the I-gel may be a suitable conduit for intubation in the lateral position. Further the use of the tracheal tube with the embedded camera may increase the success of this technique. The difference between the trainees and the experienced with regards to success with the intubation through the I-gel both in time and attempts is also noteworthy. In conclusion, camera in tube intubation through a supraglottic airway is a fast technique for tracheal intubation of a manikin placed in a difficult intubation position.

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S-9.

WITHDRAWN.

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S-10.

A NOVEL LARYNGOSCOPE MODIFICATION FOR FASCILITATING DIRECT LARNYGOSCOPY IN THE SMALL LAB RODENT

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Introduction: Endotracheal intubation of the laboratory rat is a difficult task. There is a lack of specific equipment engineered for the small rodents' airway. The standard Miller blade 0 is wider than maximum mouth opening for the rat. We have developed a custom made laryngoscope modeled from a Miller 0 blade. This instrument is more suitable for direct visualization of the cords in small animals. Moreover it causes minimal trauma to the airway. All animals intubated using this technique have recovered and were extubated uneventfully with no complications of airway trauma.

METHODS: We used a standard pediatric Miller blade 0 with attached light source as a basis for this design. We then utilized a metal cutting saw to cut out one half of the width of the blade extending from the distal tip for approximately 2/3 of the entire length of the blade (Figure 1). The light source and the attachment site for the handle remained intact. The sides were sanded with sandpaper until no sharp fragments were felt and a smooth uniformed surface was present.

Prior to intubation a peripheral IV was placed in the lateral tail vein. A bolus of IV medication was then given for anesthesia induction. The animal was then placed on a custom made adjustable intubating stand fashioned from a metal book holder. The rat was secured with clear tape wrapped around the extremities and the mouth was secured open with rubber bands that maintained gentle pressure on the incisors. Once the animal was secured and connected to BP and pulse ox the rat was positioned in a 45 angle. The tongue was gently retracted using forceps. The operator then performed direct laryngoscopy from behind head looking directly into the oropharynx. The modified laryngoscope was able to slide smoothly into the oropharynx and lift the epiglottis to allow for direct visualization of the vocal cords. Once intubation was complete, the blade was easily removed from the mouth.

RESULTS: We successfully intubated 20 of 20 rats on the first attempt utilizing the modified laryngoscope. All rats were successfully extubated and recovered uneventfully with no evidence of significant airway trauma.

CONCLUSIONS: We have created a modified laryngoscope that is an effective tool for performing direct laryngoscopy and intubation in the small laboratory rat. This blade allows direct visualization of the vocal cords in small rodents. We were able to achieve 100% success rate using this blade. We feel that our modification of the Miller 0 blade can help improve success of intubation for the lab rat and decrease the overall trauma associated with this procedure.

Figure 1: Modified Miller 0 Laryngoscope

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S-11.

LARYNGEAL MASK AIRWAY USE IN PATIENTS WITH ELEVATED BODY MASS INDEX, A RETROSPECTIVE REVIEW

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Introduction: The laryngeal mask airway (LMA) was introduced in the early 1980's, and has since become a mainstay in ambulatory anesthesia care. The LMA Unique™ is sized by weight with a maximum suggested limit of 100kg (size 5 LMA Unique™ package instructions). However, with additional provider experience and rising patient weights, the device has been pressed into use among an increasingly heavier group of individuals. Recent studies have also documented this trend.[1,2,3]

Given that weight alone does not necessarily determine difficulty, our retrospective study set out to analyze the success of LMA use among patients with elevated body mass index (BMI). We compared individuals with elevated BMI (>30kg/m2, >40kg/m2) with those of lower mass who were cared for in our ambulatory surgery center.

METHODS: Following Institutional Review Board approval, electronic medical records of patients having LMAs (LMA Unique™) placed in our ASC between 7/07 and 11/12 were analyzed. The total number of LMAs placed over the study period, the weight (kg) and height (m) of each patient, whether the device required intra-operative exchange to EI, and rates of elevated end tidal CO2 (ETCO2), inspiratory airway pressure (PIP), decreased SpO2, aspiration and bronchospasm were measured. When assessing event marker differences between patient populations ($\leq$30kg/m^2 vs >30kg/m^2, $\leq$40kg/m^2 vs >40kg/m^2), $p<0.05$ was considered statistically significant.

RESULTS: A total of 12395 patients had LMAs placed over the study period (8538 ($\leq$30kg/m^2); 4440 (>30kg/m^2); 12395 ($\leq$40kg/m^2); 583 (>40kg/m^2)). (Tables 1, 2) Rates of exchange of LMA to EI were higher in the >30kg/m^2 and >40kg/m^2 cohorts (1.4% vs 0.6%; 2.2% vs 0.8% respectively $p<0.001$). The incidence of increased end tidal CO_2, PIP and decreased SpO_2 were also greater among the >30kg/m^2 and >40kg/m^2 patient cohorts. (Tables 1, 2) Very few episodes of aspiration (n=3) and no episodes of bronchospasm were reported in any group.

CONCLUSIONS: The results of our study confirm the popular and effective use of the LMA in outpatient settings. Nearly 13,000 LMAs were placed in a 5 year period with less than a 1% requiring exchange to EI. Our results suggest that oxygenation and ventilation can be more difficult with LMA use in patients with BMI's >30 kg/m^2. Our study has the limitation of utilizing surrogate markers to define difficulties with LMA use. A more extensive chart analysis would be required to establish whether these surrogate markers are clinically significant. These results do show that the LMA is an effective airway tool in the outpatient setting and that it may be used safely in larger patients when vigilantly monitored.

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Table 1

	≤30 kg/m^2	>30 kg/m^2		
Total patients	8538 (65.8%)	4440 (34.2%)		
Complications			Chi-squared	P value
LMA to ETT	54 (0.6%)	60 (1.4%)	16.522	<0.0001
High $ETCO_2$[a]	1811 (21.2%)	1092 (24.6%)	19.063	<0.0001
High PIP[b]	96 (1.1%)	165 (3.7%)	98.261	<0.0001
Low SpO_2[c]	67 (0.8%)	166 (3.7%)	142.889	<0.0001
Aspiration	1	2	0.332	0.5643
Bronchospasm	0	0		

Table 2

	≤40 kg/m^2	>40 kg/m^2		
Total patients	12395 (95.5%)	583 (4.5%)		
Complications			Chi squared	P value
LMA to ETT	101 (0.8%)	13 (2.2%)	11.231	0.0008
High $ETCO_2$[a]	2738 (22.1%)	165 (28.3%)	12.020	0.0005
High PIP[b]	213 (1.7%)	48 (8.2%)	116.641	<0.0001
Low SpO_2[c]	182 (1.5%)	51 (8.7%)	163.249	<0.0001
Aspiration	3	0	0.141	0.7072
Bronchospasm	0	0		

[a] High end tidal CO_2 as defined by > 50 mmHg for 3 episodes or more per 10 minute period
[b] High peak inspiratory pressure as defined by > 25 cm H2O for 3 episodes or more per 10 minute period
[c] Low SpO_2 as defined by SpO2 < 90% for 3 episodes or more per 10 minute period

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S-12.

3-DIMENSIONAL DIRECT LARYNGOSCOPY – A FEASIBILITY STUDY

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INTRODUCTION: Conventional direct or video laryngoscopy affords a monoccular field of view, with little perception of depth. The normal inter-occular stereoscopic base is too wide for binoccular 3-dimensional vison in direct laryngoscopy. A modified commercially available camera allows still and video stereoscopic laryngoscopy, giving realistic images with true depth perception to aid instrumentation and diagnosis in the upper airway.

METHODS: A Fuji W3 camera was fitted with a macro prism (Cyclopital3D Inc), and a +2D close-up meniscus (Neewer). The camera zoom was adjusted for minimal vignetting, and the camera stereo image offset was centered for subjectively easy viewing. The flash was disabled. A Macintosh 3 blade was inserted into a rescuscitation training manikin, to view the vocal cords. The camera was then moved in place of the laryngoscopist's eye, the 3-dimensional viewfinder guiding exact placement.

Stereoscopic still or video images are captured easily.

The camera ".mpo"-format (Multi Picture Object) images are

displayed by the camera or a 3-D capable TV. The .mpo images are also split into left and right images of stereo pairs by software such as mposplit, or the author's splitmpo.sh (International Stereoscopic Union). These split and generate stereo pairs from a single or batched files. Right-left pairs are printed or computer-displayed for Holmes-type, cross-eyed, over-under, or red-cyan anaglyph viewing. The stereo optical base of the modified camera is 25mm.

RESULTS: Example images are a red-cyan anaglyph to be viewed with red-cyan glasses, and the same image presented as a "croos-eye" stereo pair, best viewed without special equipment using a cross-eyed gaze to the opposite images until they perceptually fuse into a single central 3D image. The modified camera is shown.

Proprotionate example geometry for a laryngoscope blade-mounted camera (see Conclusions):

stereo base 10mm, stereo angle of convergence 8 degrees:

Working distance - 0.5mm tan8 = 35mm or 1.4"

CONCLUSIONS: Direct laryngoscopy and intubation requires manipulation in 3 dimensions, usually with only one eye, or a single video-laryngoscope camera. Stereoscopy restores visual depth. The Cyclopital prism reduces the stereoscopic optical base from a normal interoccular distance of 70mm to 25mm, allowing binoccular stereoscopy at short working distances from outside the mouth. However, if the stereo camera were to be placed in a conventional video laryngoscope blade, proportionate calculations of the geometry indicate a suitable optical base of only 10mm or less for the decreased wortking distance. We suggest this should make the construction of a practical stereo video laryngoscope enterely feasible, with commercially available 3D displays as found on current cell phones and game devices.

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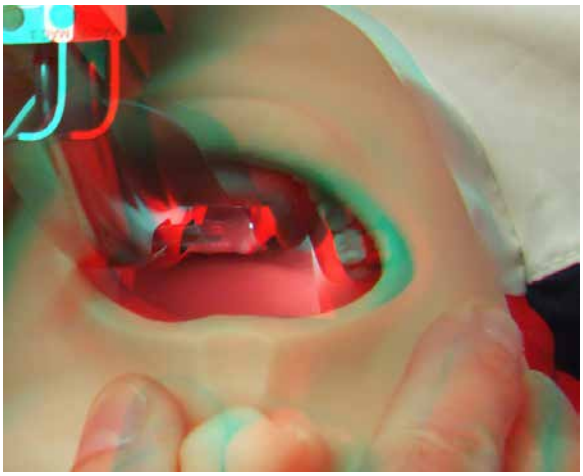

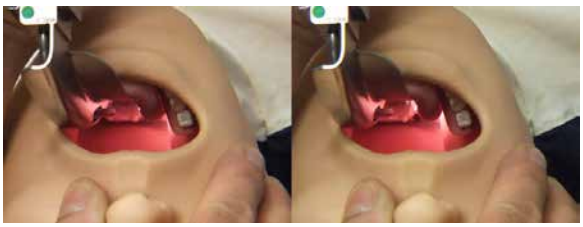

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S-13.

SIMULATION AS A SET-UP FOR TECHNICAL MASTERY: CAN A HIGH-FIDELITY VIRTUAL WARM-UP IMPROVE RESIDENT PERFORMANCE OF FIBEROPTIC INTUBATION?

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BACKGROUND: Fiberoptic intubation (FOI) is an essential procedure for anesthesiology residents to master during training. However, FOI is an advanced technical skill with a steep learning curve, and traditional training may not enable novice practitioners to safely perform this procedure under pressure. Recently in the surgical literature, a virtual "warm-up" has been described to prime a practitioner's skillset immediately before performing challenging procedures.[1,2] This study examines whether a similar warm-up can improve resident performance of FOI in the operating room using speed and graded technical performance as benchmarks.

METHODS: CA1 and CA2 anesthesiology residents were recruited to perform elective asleep oral FOI in the operating room. Residents in a warm-up cohort underwent a 5-minute guided exercise immediately prior to live FOI using a virtual bronchoscopy simulator, while those in the control cohort performed FOI without the warm-up. All subjects were timed achieving FOI and were graded on a 45-point validated skills scale by blinded observers. Previous resident FOI experience was determined by total number of FOI completed prior to sampling and time elapsed since the most recent attempt. To control for factors intrinsic to individuals (e.g. hand-eye coordination), all subjects completed a second FOI after a two-week washout period as a member of the opposite cohort. Mean scaled scores and times were calculated and multivariate analysis was performed to determine the effect of warm-up on time to achieve FOI and cumulative global skills score.

RESULTS: 33 anesthesiology residents were recruited, of which 22 were CA1 residents and 11 were CA2s. On univariate analysis, warmup was associated with a 43% decrease in time to achieve FOI in CA1 residents (mean 60 vs. 34 sec) and a 17% decrease for CA2s (32 vs. 26 sec), and was associated with a 9-point increase in global skills score for CA1 residents (mean 31 vs. 40) and a 3-point increase for CA2s (mean 39 vs. 42). Controlling for experience and intrinsic factors, virtual warm-up conferred a 37% reduction in time to achieve FOI for CA1s (mean 35 vs. 57 sec, $p<0.0001$) while time savings for CA2s increased to 26% (mean 23 vs. 31 sec, $p=0.01$). Global skills score increased by 4.8 points for CA1s (mean 32.8 vs. 37.6, $p<0.0001$) and 5.1 points for CA2s (37.7 vs. 42.8, $p<0.0001$). Crossover sequence was not statistically significant.

CONCLUSIONS: Virtual warm-up significantly improved resident performance of FOI as measured both by speed and by scaled skills evaluation. Warm-up conveyed a significant benefit even when controlling for prior experience level and intrinsic hand-eye coordination. For residents as well as more experienced practitioners, greater speed and efficiency gained by virtual warm-up prior to live FOI may confer clinical benefit, as time saved during intubation could be an important consideration in sicker patients.

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S-14.

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S-15.

THE INTRA-CUFF PRESSURE DOES NOT REFLECT THE PRESSURE EXERTED ON THE TRACHEAL WALL: AN IN VITRO STUDY USING ORIGINAL TRACHEAL MODEL

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INTRODUCTION: The cuff pressure of the endotracheal tube must be high enough to seal the trachea, preventing aspiration of the oropharyngeal secretions and avoiding air leaks. It must also be low enough to allow adequate perfusion of the tracheal mucosa. Clinically, the intra-cuff pressure (CP) is adjusted to within an acceptable range. However, it is not the CP but the tracheal wall pressure (WP) exerted on the tracheal wall by an inflated cuff that determines the risk of complications associated with mechanical ventilation. We assumed that the pressure on the tracheal wall would be influenced by the shape of the endotracheal tube cuff. Therefore, elucidating the tracheal wall pressure is useful for evaluating these complications. Measuring the WP itself is technologically difficult, and few reports have measured the WP at a few points.[1,2,3] The purpose of this study is to set up an original in vitro tracheal model to measure the WP and compare the WP exerted by various shapes of inflated cuffs under the same CP.

MATERIALS AND METHODS: The cylindrical rigid tracheal model with an inner diameter of 18 mm was made using a 3D printer. To measure the WP exerted by an intubated tracheal tube cuff, a thin pressure sensor sheet was installed inside the tracheal model. The pressure sensor sheet had a 0.1 mm thickness and a 1.91 mm spatial resolution. The sensor sheet was calibrated by pressing an equally expanded balloon with a known pressure into the tracheal model before the tests. Endotracheal tubes with three cuff shapes (spindle shape, high volume shape, and tapered shape) were intubated into the tracheal model. (Figure 1) The inner diameter of each tube was 8 mm, and the outer diameter of the tube was 10.9 mm for the spindle and high volume shapes and 10.8 mm for the tapered shape. The CP was controlled using a digital automated cuff pressure manometer. The WP was measured as the tracheal tube cuff was inflated from 0 to 90 cmH_2O at increments of 5 cmH_2O. Experiments were performed six times with the three types of tubes in a randomized order.

RESULTS: Figure 2 shows the averaged WP calculated from the overall sensing points. The slopes of the regression lines are 0.0341, 0.0457, and 0.0357 for the spindle, high volume, and tapered shapes, respectively. The WP increased almost linearly as the CP increased. The extent of the changes in WP showed differences among these three cuff shapes. Figure 3 shows the proportion of the sensing points, which output more than 3 kPa to all of the sensing points at each CP. These proportions at 10, 30, 90 cmH_2O of CP are also shown in Figure 4 and were different among the three kinds of cuff shapes. Near 30 cmH_2O of CP, more than 3 kPa points increased steeply at any shape of cuff. These findings suggest that the shape of the cuff influences the pressure on the tracheal wall, and the CP does not directly reflect the WP.

CONCLUSIONS: Our in vitro tracheal model revealed that the shape of the endotracheal tube cuff affects the tracheal wall pressure exerted by the inflated cuffs.

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Figure 1

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S-15 • continued

Figure 2

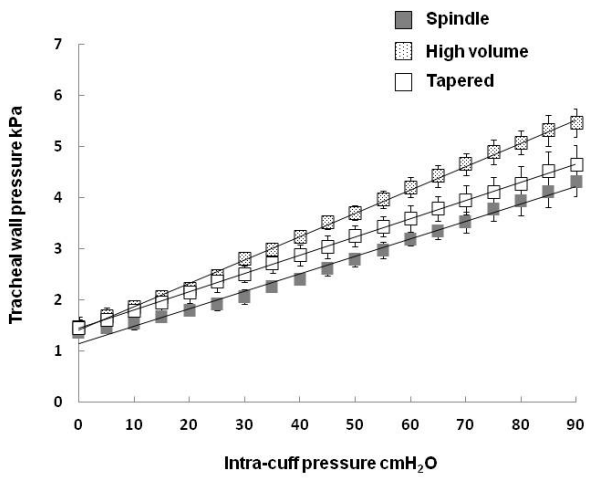


Figure 3

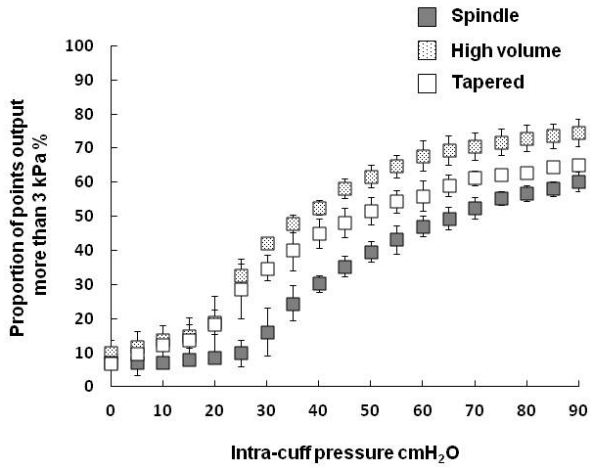
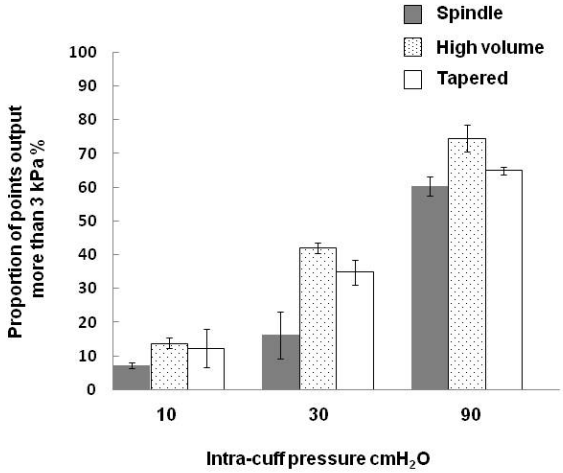


Figure 4



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S-16.

INCIDENCE AND MORTALITY OF ANESTHESIA-RELATED PULMONARY ASPIRATION: A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Since the official hour of birth of general anesthesia in 1846, the first public demonstration of ether anaesthesia at Massachusetts General Hospital in Boston, pulmonary aspiration is a relatively rare event associated with anesthesia. In 1848 J.Y. Simpson reported the first aspiration-related death in a young girl receiving a chloroform-based general anesthesia. However, despite tremendous innovations during the last decades, aspiration is an important cause of anesthesia-related relevant morbidity and mortality[1,2]. The aim of the present investigation was to provide single-centre based data from a german university hospital regarding incidence, morbidity, mortality and associated risk factors of anesthesia-related pulmonary aspiration.

MATERIALS AND METHODS: At the University Hospital of Schleswig-Holstein, Campus Kiel, Department of Anaesthesiology and Intensive Care Medicine, archived data base of bronchoscopic reports of the last 20 years were reviewed (n=3000) regarding the diagnosis "pulmonary aspiration". In case of suspected anesthesia-related pulmonary aspiration a bronchoscopy was performed to ensure or to rule out the aspiration (n=150). We considered pulmonary aspirations per definition, if the incidence took place between induction of general anesthesia and 24 hours after completion of anesthesia. Primarily we included all patients in whom the bronchoscopic diagnosis of aspiration was considered to be certain, likely or feasible. After analysing the individual medical notes of each patient, we excluded all the patients in whom the diagnosis "pulmonary aspiration" was the reason transferring them to our hospital for further therapy (n=6), in whom the medical history report was incomplete (n=10). At the end of the analysis 53 patients out of 150 with suspected aspiration ended up with anesthesia-related pulmonary aspiration.

RESULTS: In total 342.317 anaesthesia's were performed during the period of observation. We verified 53 cases of anesthesia-related pulmonary aspiration, which equals an incidence of 1.6/10.000 or 1 aspiration per 6452 anaesthesia's. All incidences took place during general anesthesia; 33 were associated with induction of anesthesia; 12 occurred within the first 24h after general anesthesia (Figure 1, 2). 17 patients died (32%; 1/20.118) during hospital stay. In consideration of the complexity of the underlying illness in principle, in 6 patients the pulmonary aspiration was identified to be the primary cause of death (11%; 1/57.000). As co-factors associated with a higher incidence and mortality of aspiration we identified advanced age, ASA classification ≥III and anesthesia tob e performed between 8 pm and 6 am.

CONCLUSION: Anesthesia-related pulmonary aspiration is still a rare but relevant complication, especially in patients showing a specific combination of associated risk factors such as age, higher ASA classification, emergency surgery between 8 pm and 6 am.

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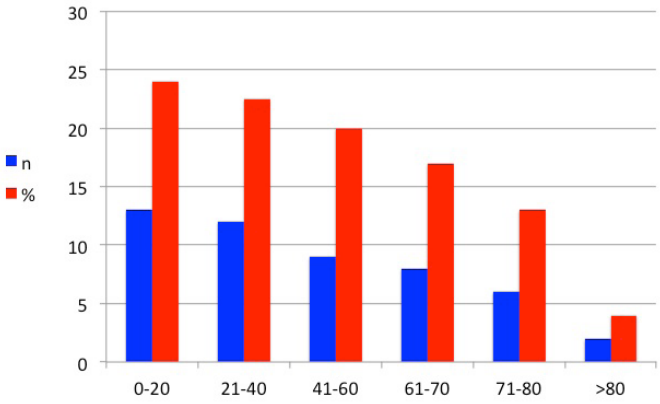

Figure 1: Age related incidence of pulmonary aspiration

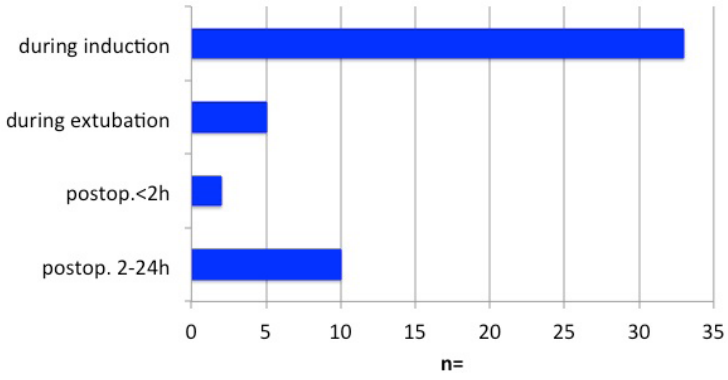

Figure 2: Number of pulmonary aspirations related to stage of anesthesia

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S-17.

INFLUENCE OF GLIDESCOPE ASSISTED ENDOTRACHEAL INTUBATION ON INTRAOCULAR PRESSURE

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INTRODUCTION: Direct laryngoscopy to facilitate tracheal intubation is traditionally performed by Macintoch laryngoscope. This manoeuvre is associated with increased intraocular pressure (IOP), tachycardia and hypertension . These changes are not suitable in ophthalmic patients like preexisting glaucoma and open globe injury. GlideScope video laryngoscope functions independent of the line of sight, reduces upward lifting forces to expose the glottis and requires less cervical neck movement for intubation making the Glidescope potentially less stimulating than Macintosh laryngoscope.[1,2,3] Aim of study was to assess the variations in IOP and hemodynamic changes after glidescope assisted intubation.

METHODS: After approval of the local IRB and informed patient consent, 50 adult ASA I & II patients with normal intraocular pressure were enrolled in prospective, randomized study for ophthalmic surgery requiring tracheal intubation. Anesthesia was achieved with fentanyl and propofol and rocuronium. Patients randomly selected by computer-generated number to use either Glidescope (group 1) or Macintoch laryngoscope (group 2) for intubation. IOP of non-operated eye, heart rate, blood pressure and duration of intubation were measured baseline,1 minute after induction, one minute and five minutes after tracheal intubation. Power analysis indicated that 25 patients were required in each arm to detect a difference of 30% in the intraocular pressure with 80% power and alpha error set to 0.050 two-sided. Statistical analysis was done using SPSS version 19. Differences between Glidescope and Macintosh in intubation time, intraocular pressure (IOP), heart rate and mean arterial pressure (MAP) were tested by Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

RESULTS: Demographic and clinical data was similar among both groups for age, sex, weight, height, Mallampati/ ASA classifications or duration of surgery. Intraocular pressure was not significantly different between groups before and after anesthetic induction and five minutes after tracheal intubation (P = 0.217, 0.726, 0.110 respectively). The only significant difference was for IOP for non operative eye at one minute after intubation (p=0.041) Fig 1. No significant difference noted between the two groups in Mean arterial pressure (P = 0.899, 0.62, 0.47, 0.82 respectively) and in the Heart rate (P= 0.21, 0.72, 0.07, 0.29 respectively) at all measurement levels. Duration of intubation was slightly longer in Glidescope compare to Macintoch group (20.12 ± 8.05 and 16.12 ± 5.67 seconds respectively) but this difference was not significant statistically (p= 0.079).

CONCLUSION: Glidescope may be preferable for use in patients in whom a rise in IOP is undesirable. However, further clinical trials are needed in a larger population to evaluate the benefit of Glidescope.

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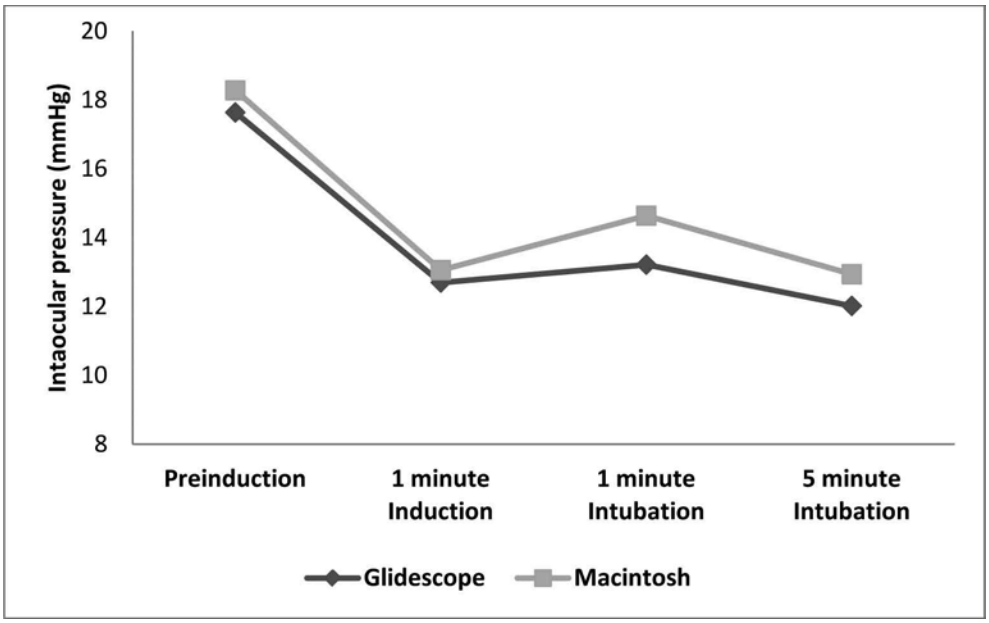

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S-18.

WITHDRAWN.

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S-19.

INCIDENCE OF DIFFICULT INTUBATION AND ASSOCIATED RISK FACTORS IN A PRIVATE HOSPITAL IN SÃO LUIS

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INTRODUCTION: The principal cause of death in anesthesia is relative to the difficult airway management[1]. Thus, we decided to investigate the incidence of difficult intubation and to identify independent clinical predictors to preview difficult airway during the preoperative period.

METHODS: After approval by the local Research Ethics Committee and written consent, the sample consisted of outpatients, aged over 16 years undergoing general anesthesia for elective surgical procedures from March to May 2012. In the preoperative period, all patients were evaluated about age, sex, height, weight, BMI, and ASA physical status. The anatomical parameters assessment was based on the Mallampati index, thyromental and sternomental distances, mouth opening, cervical spine extension and mandibular morphology. Difficult intubation was considered as grade IV, according to Cormack-Lehane classification system. For statistical analysis, we used Excel software for descriptive statistics. For correlation analysis of the potential risk factors for difficult airway was used the chi-square test. Relative risk of the risk factors was calculated. A value of $p<0.05$ was considered significant. Results

The sample consisted of 324 patients, that the major part was between 16 and 39 years old, non-obese (<30kg/m^2) and ASA I-II (Table 1).

Table 1. Demographic data

Sex	Frequency (n)	%
Male	191	59.0
Female	133	41.0
Age (years)		
16-39	157	48.5
40-59	114	35.5
≥60	52	16.0
BMI		
<30kg/m^2	202	62.5
≥30kg/m^2	122	37.5
ASA		
I-II	305	94.0
III-IV	19	6.0

Sixteen per cent of the patients presented difficult intubation during the anesthesia (Figure 1). Inside this group of patients, 52% presented obesity (BMI ≥30kg/m^2) (Figure 2). In relation to relative risk, it was demonstrated greater risk with mandibular morphology than either clinical signs (about 6.5).

CONCLUSIONS: In our study, it was found 16% of patients with difficult intubation, that is an unusual result[2]. This is probably because of the anatomical characteristics of the population attended in the hospital. Obesity was the most frequent risk factor present in the patients with difficult intubation (52%). However, when we observed the table of relative risk of each risk factor, patients with micrognathia or macrognathia presented greater risk than the others (about 6.5).

Several studies have examined a combination of factors, trying to improve on the prediction of a difficult airway. One study[3] on the combination of neck circumference (>43cm) and Mallampati score (>3) found that the combination was better than either factor alone with a PPV of 44%. Another article4 on the combination of the Mallampati score (>3) and thyromental distance (<6cm) demonstrated improved prediction of difficult intubation. Rao and colleagues[5] reported that positioning obese patients so that the ear is aligned with the sternal notch (the ramp position) seemed to facilitate tracheal intubation. Our study was responsible for organizing our anesthesia service. Moreover, we draw the attention of the teams of surgery and nursing for the risk of difficult intubation.

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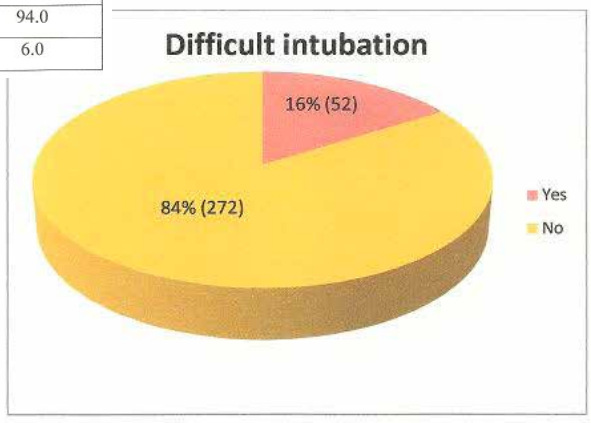

Figure 1. Incidence of difficult intubation

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S-19 • continued

Table 2. Risk factors and its relative risk to difficult intubation

Risk factor	Relative risk	Interval of confidence of 95%	P-value
Mallampati score 4	5.56	3.66-8.44	< 0.001
Sternomental distance < 12.5 cm	2.93	1.81-4.73	< 0.001
Thyromental distance < 6 cm	3.04	1.89-4.90	< 0.001
Interincisors distance < 3 cm	2.56	1.49-4.39	0.001
Cervical spine extension < 80°	1.72	0.89-3.32	0.106
Micrognathia	6.33	4.92-8.15	< 0.001
Macrognathia	6.33	4.92-8.15	< 0.001
BMI≥30kg/m²	1.79	1.09-2.94	0.022

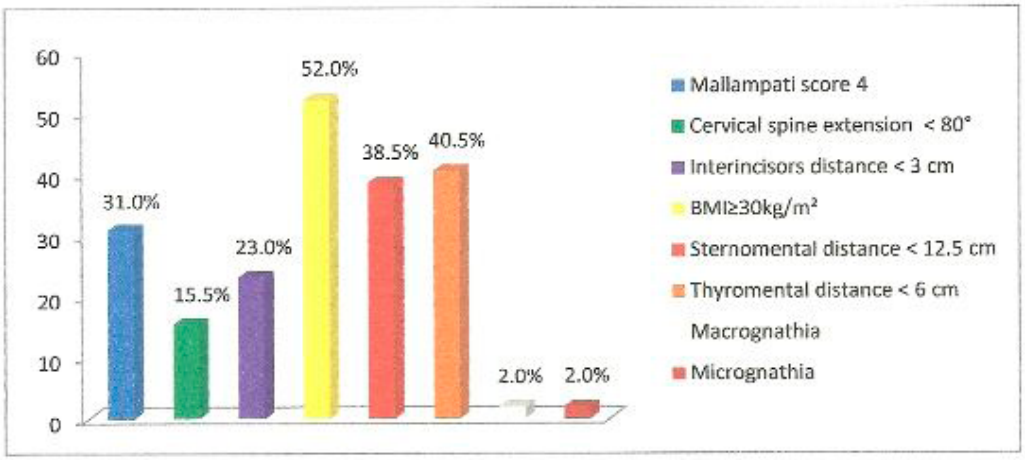

Figure 2. Incidence of each risk factor in patients with difficult intubation.

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S-20.

ANESTHESIA AND INCREASED HYPERCARBIC DRIVE IMPAIR THE COORDINATION BETWEEN BREATHING AND SWALLOWING

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INTRODUCTION: During procedural sedation, protective airway reflexes and the ability to swallow normally can be impaired. Swallowing can occur normally prior to or during expiration or pathologically during inspiration. The aspiration risk is more likely to be increased if swallowing occurs just prior to or during inspiration[1]. Currently, it is unclear if the incidence and timing of swallowing are modulated by anesthetics or changes in ventilatory drive. We hypothesize that propofol and sevoflurane affect the incidence and timing of swallowing, and increasing ventilatory drive with CO_2 can modulate these effects.

METHODS: Following IRB approval, we studied 11 ASA I, volunteers aged 18-45 as part of a protocol that has been described previously[2]. Briefly, hypopharyngeal pressure was measured with a Millar catheter threaded nasally and secured by a nasal mask, connected to a high flow circuit. Pneumotachometry and capnometry were used to measure airflow and PETCO2. Intramuscular genioglossus (GG) electrodes were used to measure phasic GG EMG. Equianesthetic doses (titrated to pain stimulus) of propofol (TCI) and sevoflurane were applied in a randomized cross over fashion. During wakefulness and anesthesia, the presence of spontaneous swallows was measured during inspiration and expiration. Measurements were also made during CO_2 insufflation in order to obtain stable PETCO2 levels of 4 or 8 mmHg (all CO_2 driven swallows are combined for analysis). The presence of a swallow was defined as a 200% increase in GG activity, deglutition apnea, and an increase in hypopharyngeal pressure by 15 cmH20. Swallows were categorized as expiratory (physiological) or inspiratory (pathological) (Fig.1)[3]. We analyzed the data with a mixed linear model to identify the effects of anesthesia and/or the CO2-induced increase in ventilatory drive on swallows/hour and the percentage of expiratory vs. inspiratory swallows.

RESULTS: 202 episodes met the criteria for swallows. There was a significantly lower number of swallows/hr during anesthesia (1.45 ± 3.08) vs. wakefulness (25.13 ± 18.516) (p<.001), but no significant difference between propofol (2.01 ± 3.76) and sevoflurane (.90 ± 2.31) (p = .421). The incidence of inspiratory swallows was higher during anesthesia vs. wakefulness (26.7% vs.3.1%, p <.001) (Fig. 2). The incidence of inspiratory swallows was higher when ventilatory drive was increased by hypercapnia during anesthesia (38.5% vs. 12.1%, p=0.047) (hypercapnia led to an average increase in minute ventilation of 0.54 L/min).

CONCLUSIONS: Sevoflurane and propofol decrease the frequency of swallowing and increase the likelihood that a swallow will occur during or just prior to inspiration. This is likely to increase the risk for pulmonary aspiration. An increase in ventilatory drive – which may occur during procedural sedation in response to increased $EtCO_2$ or a strong pain stimulus, further increases the likelihood of a inspiratory swallow and increases the risk for aspiration.

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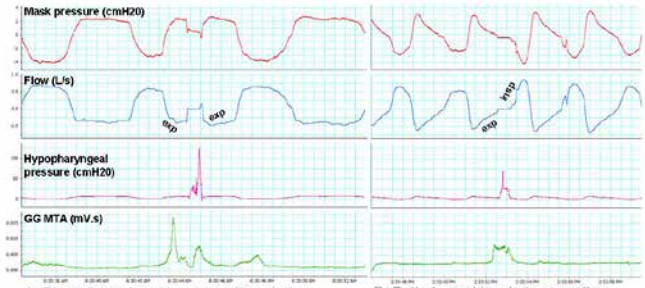

Figure 1: Original tracings of swallows during wakefulness (A) and propofol anesthesia (B)

MTA= moving time average, exp= expiratory flow, insp= inspiratory flow

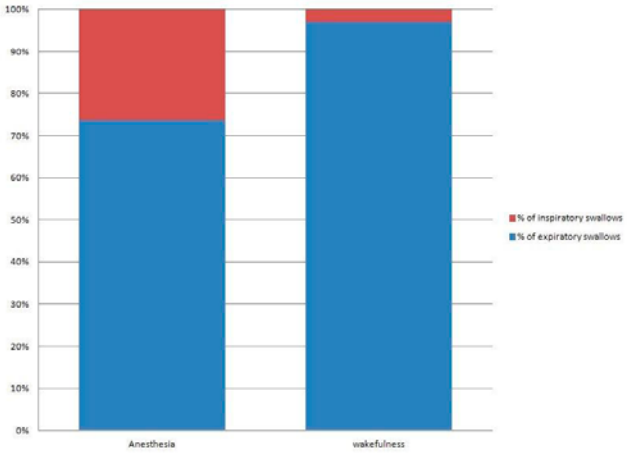

Figure 2: Percentage of inspiratory (pathological) and expiratory (physiological) swallows during anesthesia and wakefulness

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S-21.

CAN ULTRASOUND SCAN OF THE AIRWAY BE USED TO PREDICT DIFFICULTY OF AIRWAY MANAGEMENT? A COMPUTERIZED TOMOGRAPHY VALIDATION STUDY

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INTRODUCTION: Difficult airway management is the most common cause of major anesthesia-related morbidity and mortality.[1] Assessment of the airway to predict difficult airway management relies on several measurements including visual assessment of the Mallampati score, an estimate of tongue volume relative to oral cavity volume;[2] but the sensitivity and specificity of this measurement is limited and do not exceed 65%.[3] Consequently, difficult airway may not be discovered until laryngoscopy is attempted, a situation that carries potential risks. Additional bedside tests that increase the capacity to predict difficult airway management would improve safety. Ultrasound (US) airway scan is a simple non-invasive test that permits visualization and measurement of tongue and oral cavity dimensions that may be related to prediction of difficult airway management. However, the exploration of its utility as a diagnostic tool is precluded by the lack of proof of its validity and reliability. This observational study examines the validity of US measurement of tongue thickness relative to oral cavity height as an estimate of tongue volume relative to oral cavity volume by comparison to Computerized Tomography (CT). We also assess the inter- and intra-observer reliability.

METHODS: We recruited 42 adults undergoing high resolution CT scan of the head and neck for the management of lymphoma, breast, bladder, and cervical cancers. As part of the CT scan, the ratio of tongue volume to oral cavity volume was calculated; additionally, the ratio of tongue thickness to oral cavity height was also calculated. Furthermore, two sonographers separately performed US measurements of the ratio of tongue thickness to oral cavity height before and after CT scan. All patients had their CT and US scans performed in the same supine position with the mouths open, after depositing 5 mL of water in the mouth. The open mouth simulated airway dimensions in clinical scenarios, while water permitted replication of the tongue position and improved palate visualization by reducing air attenuation.

RESULTS: We analyzed data from 41 patients. The value of Cohen's kappa statistic for comparison of CT-measured values of the ratio of tongue thickness relative to oral cavity height, and the ratio of tongue volume to oral cavity volume was 0.94, suggesting that the first ratio is a highly accurate approximate of the second. The kappa value for the comparison of the US-measured values of the ratio of tongue thickness relative to oral cavity height, and the same ratio measured by CT-scan was 0.87, suggesting that the first ratio is an accurate approximation of the second. Furthermore, the kappa values for inter- and intra-operator US scans were 0.84 and 0.81, suggesting strong inter- and intra-operator reliability.

CONCLUSION: Our results indicate that US is a valid and reliable tool for measurement of airway dimensions predictive of airway difficulty. Further trials are needed to explore the utility of US scan in the assessment of difficulty of airway management.

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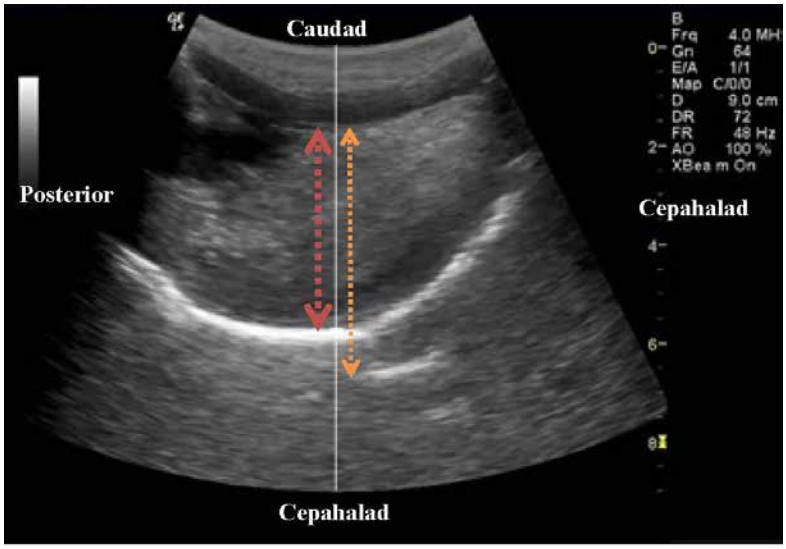

Figure 1: Sagittal ultrasound scan of the oral cavity. Red arrow designates tongue thickness; orange arrow designates oral cavity height.

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Ambulatory Anesthesia

S-22.

SUITABILITY OF THE FOREARM FOR AUTOMATED NON-INVASIVE BLOOD PRESSURE MEASUREMENT

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INTRODUCTION: To effectively evaluate treatment of hyper or hypotension anesthesiologists must reliably measure blood pressure (BP). Accurate BP measurement by an automated instrument is dependent on several factors including the use of an appropriate sized cuff. The most frequent error in measuring BP was use of an inappropriately sized cuff, with undercuffing large arms accounting for 84% of the 'miscuffings'[1]. Non-invasive blood pressure (NIBP), using an oscillometric technique, is traditionally measured by an inflatable cuff on the arm. In certain patients, either because the arm is too large, or is conical in shape, BP is measured on the forearm. However the suitability of the forearm, for reliable BP measurement, is not well studied especially in hypertensive or obese patients.

The aim of our study was to determine whether BP measured on the forearm displayed a good concordance with the arm BP measurement. We compared arm NIBP to forearm NIBP, in 400 same arm sequential paired BP measurements in 200 adult patients awaiting surgery at an ambulatory surgery center (ASC).

METHODS: All patients scheduled for a procedure at our ASC have their BP measured in the preoperative holding area. Verbal consent was obtained from adult patients (18-85 years) for their participation in this study. BP was measured on both the arm & forearm of the same limb by using an appropriate sized cuff. The appropriateness of the cuff size was ensured by first measuring the arm & forearm circumference using a measuring tape. A standard, small or large adult cuff was used when the circumference was 25-34 cm,&lt 25cm, or $gt 34 cm respectively. The study was conducted as a prospective randomized observational study. When the subject's study ID was odd BP was measured on the arm first & forearm second & vice versa if the study ID was even. The second BP was obtained within two minutes of the first measurement. The level of discomfort reported by patients at each site of measurement was documented using the visual analog score (VAS) with zero being no discomfort & 10 being unbearable discomfort.

RESULTS: The large adult cuff was used on the arm in about 32% of the patients. The forearm NIBP overestimated mean arterial, systolic & diastolic pressure. There was close agreement between the arm & forearm mean (r=0.71) & diastolic (r=0.78) BP & good agreement with respect to systolic BP, (r = 0.79). The mean BP measurement obtained on the forearm was on average 5.43 mmHg higher than the arm, the systolic BP was 10.66 mmHg higher & the diastolic BP was 4.71 mmHg higher in the forearm than the arm.

ANOVA demonstrated a statistically significant difference in the discomfort scores between the sites ($p < 0.001$). The arm demonstrated a higher discomfort score than the forearm.

CONCLUSIONS: Reliable NIBP measurements can be obtained when an appropriate size cuff is used on the forearm. The forearm may be a viable clinical alternative in situations where difficulty occurs with upper arm NIBP measurement. Patients may benefit from an accurate measurement of BP thereby avoiding unnecessary treatment from an erroneous measurement caused by "miscuffing".

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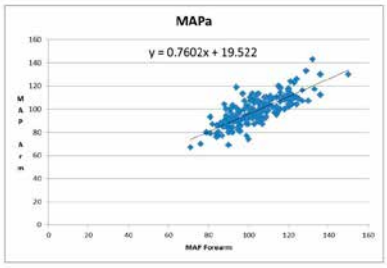
Predicting Arm BP (Y) from Forearm BP (X)



MAP Residual Plot Bland Altman Analysis

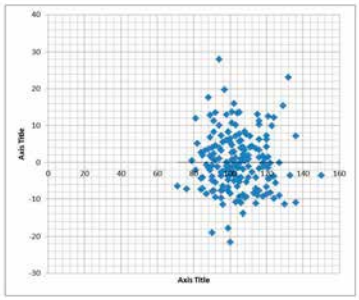


Table 1 Demographics, n=200

Gender	88 men	112 women
Systemic Hypertension	138 no	62 yes
Diabetes Mellitus	179 no	21 yes
BMI > 30	104 no	96 yes
Age in years (mean, SD)	50.55	15.44
BMI	29.77	6.06
Ponderal's Index	17.99	3.79

Table 2. Process Variables

BP Cuff size (no. of patients)	Arm (n=200)	Forearm (n=200)
Small	9	47
Standard	127	152
Large	64	1
	Mean (SD) cm	Mean (SD) cm
Upper circumference	32.69 (5.19)	25.60(3.50)
Lower circumference	27.19 (4.14)	18.69(6.58)

Table 3 Outcome Variables

	Arm	Forearm	Pearson Correlation Coefficient	Mean Difference	p-value
SAP mmHg	132 (19)	142 (21)	0.79	10.66	<0.001
MAP mmHg	99 (12)	104 (13)	0.78	5.43	<0.001
DAP mmHg	80 (10)	85 (12)	0.71	4.71	<0.001
Discomfort VAS (0-10)	1.13 (2.10)	0.88 (1.95)			0.004

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S-23.

THE CUT-OFF VALUE OF D-DIMER IN FRACTURE PATIENTS: SCREENING FOR PREOPERATIVE DEEP VEIN THROMBOSIS

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INTRODUCTION: Perioperative deep vein thrombosis (DVT) is common complications in femoral fracture patients. Several studies have evaluated the role of D-dimer assay in detecting DVT. However, the diagnostic reliability of D-dimer assay in detecting DVT in fracture patients remains unclear. In this study, we aimed to determine the preoperative cut-off value of D-dimer for detecting DVT in patients with femoral fracture.

METHODS: After IRB approval, we retrospectively collected data on all patients who underwent surgery for femoral fractures between April 2011 and March 2013. Preoperative D-dimer values and diagnostic results from the imaging tests, including color Doppler ultrasonography of lower limb deep vein or contrast enhanced computed tomography or both were obtained among the patients. We compared the D-dimer levels between patients with and without DVT. The results were compared using the Mann-Whitney U-test. Receiver operating characteristic (ROC) curve analysis was performed to determine the preoperative cut-off value of D-dimer.

RESULTS AND MAJOR FINDINGS: During the observation period, 200 patients with mean age of 74.5 years (range, 19-98 years) underwent scheduled femoral fracture surgeries. Of those, 125 patients were tested for D-dimer before surgery. Eleven patients (8.8%) were preoperatively diagnosed as DVT. The median value of D-dimer was higher ($p = 0.0018$) in patients with DVT (25.6μg/ml; range, 6.0-54.5) than those without DVT (7.95μg/ml; range, 0.1-189.3). The optimal cut-off point on the ROC curve was 20.7μg/ml. The area under the curve (AUC) was 0.79, and the sensitivity and specificity were 81.8% and 78.1%, respectively. In general, D-dimer levels are known to represent a wide range of elevation in trauma patients regardless of the presence of DVT. In our study, exactly, preoperative D-dimer levels of femoral fracture patients were quite variable. The large AUC value of 0.79, however, indicates good discriminatory ability of the predictive model. Our study suggests an optimal D-dimer cut-off value of more than 20.7μg/ml to detect DVT preoperatively.

CONCLUSIONS: The D-dimer assay was useful for screening preoperative DVT in femoral fracture patients. In our study, the best preoperative cut-off value of D-dimer for predicting preoperative DVT patients will be approximately 20μg/ml in such cases.

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S-24.

EFFECT OF DEXAMETHASONE ON BLOOD GLUCOSE IN AMBULATORY SURGERY

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INTRODUCTION: Dexamethasone (Dxm) is widely used during (ambulatory) surgery as a potent antiemetic and potential analgesic agent. Currently, the effects of low-dose Dxm on blood glucose are unclear. We investigated if blood glucose increases after single low-dose Dxm and to determine if potential hyperglycemia predisposes for complications after ambulatory surgery.

METHODS: In an observational cohort study, patients scheduled for ambulatory surgery, aged 18-85 years, were included. Patients received Dxm on discretion of the anesthesiologist. Capillary blood glucose was measured one hour before- and after surgery. Patients were called 3 months later to establish whether there were any complications, e.g. death, re-admission, infection, re-bleeding, delirium, thrombo-embolic events or other adverse events, after discharge. The Wilcoxon signed ranks, the Mann Whitney-U test, Pearson Chi Square test and multivariate binary logistic regression were used to analyze data.

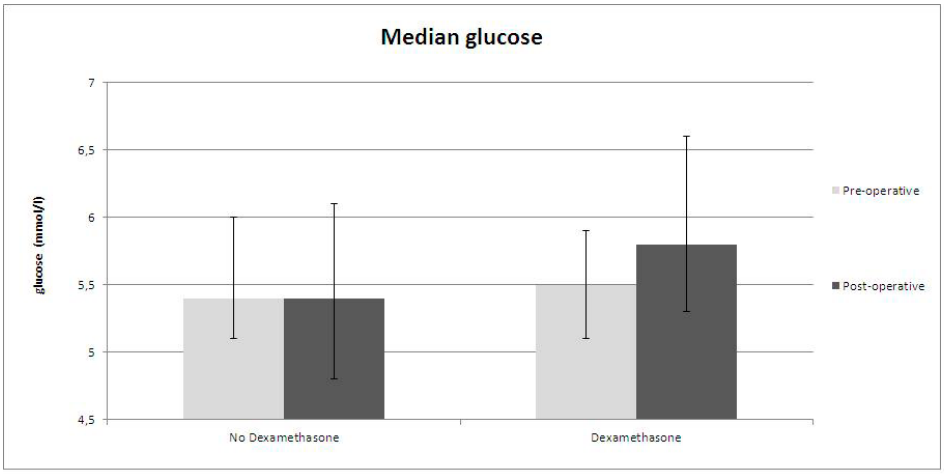
RESULTS: We included 951 patients in this study, 21 patients were excluded due to missing data (Table 1).

CONCLUSION: Blood glucose increases significantly after a single low dose of Dxm. However, the use of Dxm was not associated with postoperative complications.

Table 1: Patient characteristics

	No Dexamethasone	Dexamethasone	p value
Total (%)	514 (55.2)	416 (44.8)	
Male (%)	260 (50.7)	218 (52.4)	0.602
Mean age (SD)	47.2 (15.9)	46.8 (15.6)	0.714
Mean BMI (SD)	26.0 (4.9)	25.6 (4.2)	0.169
Diabetes mellitus (%)	42 (8.3)	7 (1.7)	<0.001
Complications (%)	58 (16.1)	35 (11.5)	0.086
ASA 1 (%)	291 (56.7)	251 (60.3)	0.171
ASA 2 (%)	207 (40.4)	157 (37.7)	0.171

In total, 416 (44.8%) patients received Dxm (mean 4.2 mg, SD 2.0) during surgery. In patients receiving Dxm, median glucose changed significantly from from 5.5 mmol/l to 5.8 mmol/l ($p < 0.001$, figure 1). In patients not receiving Dxm, glucose did not change (p=0.1). The median change in glucose in patients with diabetes mellitus (DM) who received Dxm was 1.4 mmol/l (IQR 1.7). This was significantly different from the patients with DM who did not receive Dxm, (p=0.007).



Follow up was completed for 665 (71.6%) patients. A complication occurred in 35 (11.5%) patients receiving Dxm, and in 58 (16.1%) patients not receiving Dxm. In the logistic regression analyses Dxm was not associated with development of relevant hyperglycemia (> 7.8 mmol/l), when adjusted for gender, age, BMI, ASA classification and operating time. Hyperglycemia or Dxm were not associated with postoperative complications.

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S-25.

DEEP SEDATION FOR OMFS USING DEXMEDETOMIDINE WITHOUT PROPOFOL

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INTRODUCTION: Propofol (PROP) is often used as part of an office based deep sedation technique. Although it is considered an anesthesia induction agent, as an adjunct to fentanyl (FEN) and midazolam (MID) in small doses it can provide deep sedation. This combination is often used in the office setting by an Oral Maxillo Facial Surgeon (OMFS). Our department routinely provides the deep sedation for an OMFS in a dental office. Over the past year we have experienced severe shortages of most of the sedation agents we use in this clinic. As such we have had to make changes to our sedation protocols to accommodate these serious shortages. For a period of time we had a severe shortage of PROP and rather than using higher doses of fentanyl and midazolam (both also in short supply) to provide the deep sedation we decided to use dexmedetomidine (DEX) as an adjunct. The lower risk for respiratory depression and the synergistic sedative effect that DEX demonstrates would allow us to provide deep sedation with a lower risk of respiratory depression and avoiding the use of PROP.

METHODS: A QA review of new sedation techniques was used to evaluate their efficacy, complications and surgeon satisfaction. This QA data was collected during the period of drug shortage for future consideration of this sedation technique. Data collected included patient demographics, depth of sedation, capnography cardiovascular parameters and procedure times. IRB approval was obtained to review the QA database and medical records.

The sedation method included a single loading dose of DEX (0.7 mcg/kg) diluted into 4 ml NS. The sedation protocol was: DEX 1ml, MID 2mg, DEX 1ml, FENT 100, DEX 1ml, MID 2mg, DEX 1ml at 1 minute intervals. The DEX load was thus given over 6 minutes as the other sedatives were titrated in. If the patient required additional sedation for the local anesthetic placement or during the procedure, then we used 10mg boluses of propofol as clinically indicated.

Results: During the period of PROP shortage we sedated 53 patients using this DEX based sedation technique. The mean age was 17.8 years,mean weight of 71.9 kg. The mean DEX, MID and FENT doses were 50.8 mcg, 4 mg, 99.5 mcg respectively. The DEX load was given over a mean time of 6 minutes. PROP was not required in 45% of these patients, a further 8 % only required 1 dose (10mg) of PROP. The median dose of PROP used was 0.3 mg/kg. The mean procedure time including local anesthesia was 20 minutes. The mean discharge time was 53 minutes. All patients received dexamethasone and 80% received ketorolac. Complications included 5 episodes of desaturation (< 90%), 17 episodes of obstruction requiring intervention and 3 episodes of bradycardia (HR <45). No treatment was required for the bradycardia episodes. Routinely monitored parameters are shown in table 1. The heart rate fell during sedation but returned to baseline values during the procedure. Patients were deeply sedated as per BIS and RASS assessments.

CONCLUSION: Deep sedation without PROP was possible in about 50% of the patients, there was some bradycardia noted during the DEX load. Respiratory events did occur occurred even with the perceived lower risk of using DEX.

	HR0	HR5	HR10	HR15	HR20	HR25	HR30	HR35	HR40
Mean	70.3	64.0	64.2	71.0	76.6	78.9	79.0	78.1	76.2
SD	11.3	10.4	10.6	15.3	14.6	12.1	11.3	11.6	11.8
	SYS0	SYS5	SYS10	SYS15	SYS20	SYS25	SYS30	SYS35	SYS40
Mean	11.3	10.4	10.6	15.3	14.6	12.1	11.3	11.6	11.8
SD	14.6	13.6	13.7	17.4	18.1	16.4	15.9	16.2	15.9
	ETCO2_0	ETCO2_5	ETCO2_10	ETCO2_15	ETCO2_20	ETCO2_25	ETCO2_30	ETCO2_35	ETCO2_40
Mean	39.0	40.6	45.7	46.6	47.1	47.4	45.7	45.6	44.9
SD	6.2	8.1	7.6	6.7	5.3	6.4	5.3	5.0	6.6
	BIS0	BIS5	BIS10	BIS15	BIS20	BIS25	BIS30	BIS35	BIS40
Mean	97.0	82.4	73.0	69.6	66.6	68.5	73.4	73.7	72.4
SD	1.3	7.1	7.4	10.2	8.4	9.0	9.0	10.4	11.6
	RASS0	RASS5	RASS10	RASS15	RASS20	RASS25	RASS30	RASS35	RASS40
Median	0	-2	-4	-4	-5	-5	-5	-4	-4
	BASE	SED1	SED2	LA	PROC_START	PROC2	PROC3	PROC_END	PACU5

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S-26.

A NOVEL SEDATION REGIMEN: ADMINISTRATION OF INTRANASAL REMIFENTANIL FOR PEDIATRIC DENTAL SEDATION FOR ADJUNCT SEDATION

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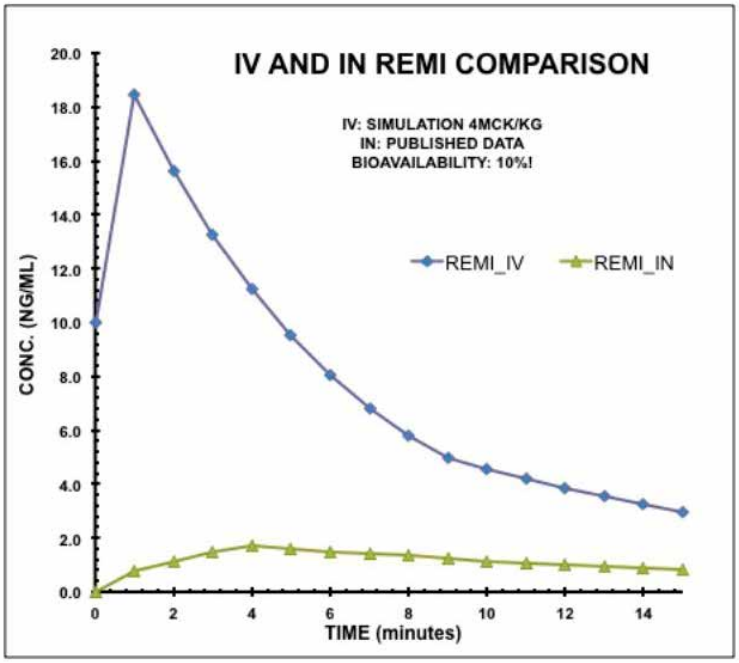
PURPOSE: Oral midazolam (MID) sedation is often used for pediatric dental procedures, however the quality of procedural sedation is variable and maybe inadequate for successful procedure completion. Intranasal (IN) sedative administration can be a useful sedation adjunct, it has a more rapid onset and can be repeated as needed. MID can also be given IN, however it burns and often results in irritation. Routinely, we have used IN sufentanil, however, due to a prolonged drug shortage / unavailability (> 1 year), we decided to evaluate the efficacy and safety of IN remifentanil (REMI), an ultra short acting synthetic opiate. There is little published literature on this topic. A report of 150 children, given IN REMI as an adjunct to intubation, did not find any problems. The kinetics demonstrated a fast onset of IN REMI and a rapid elimination as expected.

METHODS: Children scheduled for elective moderate dental sedation procedures were given 0.7 mg/kg oral midazolam. Two to four doses (2mcg/kg) of IN REMI (Maximum REMI dose used was 40 mcg) was administered. The first dose was given 25 minutes after the MID dose. The next dose was given when the child was in the dental chair. Any subsequent doses were given at a minimum of 5 minute intervals at the request of the dentist performing the procedure. All patients were monitored with pulse oximetry, HR and NIBP. Our QA evaluation process assessed: quality of sedation, airway complications and discharge times. The REMI was prepared each day at a 100 mcg/ml concentration and administered using a MAD atomizer device. The volume for each spray was about 0.3-0.4 ml. The right nares was used first and then the alternate nares was used for any repeat dosing. After obtaining IRB approval and informed consent, we completed a retrospective chart and QA database review of this novel sedation technique.

RESULTS: Data was collected on 53 children. The mean age was 5.5 years (Range 2 - 13), mean weight was 22.6kg (Range 12 - 68). The mean MID dose was 12.6. mg, 51% were female. The median number of dental procedures performed on each child was 3 (range 1-9). The mean total dose of REMI given was 111 ± 37 mcg (5.1 mcg/kg). The median number of REMI doses given was 3 (range 2-4). The depth of sedation was assessed using the RASS score. The median RASS score at: MID dosing, entry into the room, procedure, and arrival in PACU were: 0, -1, -1, -1, respectively. The mean discharge time was 46 minutes. All procedures were completed successfully. There were 2 airway complications noted. Two patients had a desaturation to 90, this was treated with supplemental oxygen in 1 child (2 REMI doses) and no treatment was required in the other (3 REMI doses). There were no episodes of apnea, airway obstruction, or bradycardia.

CONCLUSION: The REMI appeared to be an effective adjunct to oral MID. Due to its short half-life, repeat dosing of the REMI appears necessary to obtain an useful duration of effect. Although we had minimal respiratory side effects, as there is a risk of apnea and rigidity from this potent opiate we decided to titrate the dosing of REMI to the desired effect. The optimal dosage strategy still needs to be determined. Please see Figure 1.



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S-27.

ASSESSING A MULTIMODAL CURRICULUM TO DEVELOP RESIDENT PROFESSIONALISM AND COMMUNICATION SKILLS – A PILOT STUDY

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INTRODUCTION: Though critical for patient satisfaction and experience of care, professionalism and communication skills are often not taught explicitly in residency training.[1] The goal in this study was to enhance anesthesia residents' professionalism and communication skills. We hypothesized that a targeted simulation and web-based curriculum in professionalism and communication for anesthesia residents would improve patient satisfaction with these aspects of resident performance as measured by a survey tool based on the Four Habits Model.[2]

METHODS: This study was a cohort study of anesthesia residents from September 2012 to June 2013 (Figure 1). We adapted a previously validated patient survey tool based on the Four Habits Model into a 10-question survey for ambulatory surgical patients to assess anesthesia residents' professionalism and communication skills.[2] After four months of survey data collection, we designed and implemented a curricular intervention consisting of three simulated scenarios (Table 1). Residents were expected to discuss the scenarios during live sessions, view the scenarios and answer reflective questions through an online module, or both. After three months of post-intervention data collection, we compared the pre- and post-intervention responses with a chi-squared test for each survey question as the primary analysis. To control for resident variation, we performed Student's t-tests on the residents' average ratings for questions showing statistical significance in the primary analysis. To control for resident variation, we performed Student's t-tests on the residents' average ratings for questions showing statistical significance in the primary analysis.

RESULTS: The response rates for the pre-intervention and post-intervention surveys were 233/920 (25.3%) and 236/689 (34.3%), respectively. 38 residents participated. In the primary analysis, pre- and post-intervention responses to the three questions corresponding to the curricular focus were significantly different ($p = 0.01$, $p = 0.048$, and $p = 0.02$; Table 2, Figure 2). When controlling for resident variation, differences in the responses to these questions were not statistically significant (Table 3).

CONCLUSIONS: We designed a survey to assess residents' professionalism and communication skills from the patients' perspectives. After the curricular intervention, responses to the survey questions corresponding to the curricular focus improved, but further research is necessary to assess the curriculum's efficacy.

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Figure 1: Study timeline. After about four months of pre-intervention survey data collection, we designed and implemented a targeted curriculum for about three months. Then we collected post-intervention survey data for three months.

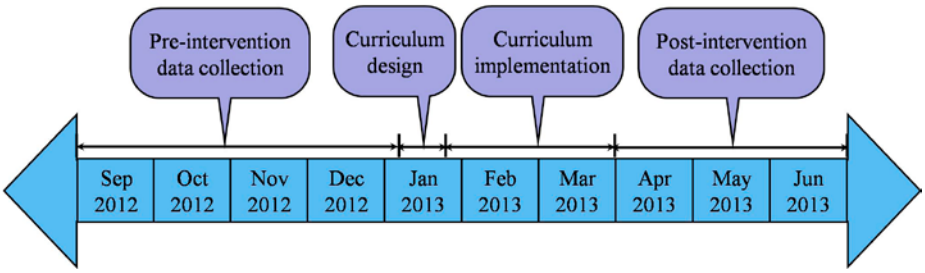

Table 1: Simulated Scenarios for Curriculum

Scenario	Target Area	Patient/Scenario Description	Reflective Questions on Online Module
1	Patient's expectations	• Passive aggressive, defensive attorney concerned about cognitive issues • Did a lot of online research and has a physician friend as a consultant	1. How would you engage a distracted patient? 2. How do you address expectations of a patient regarding recovery from anesthesia? 3. How should you respond when asked how long you've been "doing this"? 4. Cite at least one positive behavior or action in this scenario.
2	Patient's feelings/emotions	• High anxiety female patient about to have breast surgery • Significant Postoperative nausea and vomiting (PONV) • Has a family member that experienced a bad anesthetic outcome	1. How do you approach concerns about PONV? 2. How do you tackle concerns based on family member or friend experiences? 3. When patients become emotional, how do you acknowledge their feelings and concerns? 4. Cite at least one positive behavior or action in this scenario.
3	Shared decision making	• Orthopedic case with a nerve block • If pre-anesthetic consultation goes well, then the post-anesthetic encounter would be fairly low-key. If pre-anesthetic consultation is not thorough, the patient would have pain control issues and a concerned family member at his bedside creating a small situation for the resident to handle.	1. How do you tackle the discussion of a nerve block when the patient says, "I don't want to remember anything"? 2. What techniques do you use to verify patient understanding and agreement to the plan? 3. How do you address concerns of recall or awareness under anesthesia? 4. Cite at least one positive behavior or action in this scenario.

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Table 2: Proportion of "Definitely yes" responses for each question

Question	Pre-intervention n	Pre-intervention "Definitely yes"	Post-intervention n	Post-intervention "Definitely yes"	Chi-square p-value
1) Did the anesthesia resident introduce him/herself and explain his/her role in your care?	202	95%	189	95%	0.879
2) Did the anesthesia resident seem to know the important information about your medical history?	197	77%	188	84%	0.088
3) Did the anesthesia resident seem interested in finding out how you thought about the health concerns?	199	71%	187	78%	0.134
4) Did the anesthesia resident ask about your expectations for the anesthetic?	195	63%	187	70%	0.183
5) Did the anesthesia resident provide ample opportunity for you to express your emotions?	194	75%	184	82%	0.112
6) Did the anesthesia resident do anything to help you feel okay about whatever emotions you were feeling?	187	69%	177	80%	0.014
7) Did the anesthesia resident give you information that directly addressed the concerns you had expressed?	180	78%	176	81%	0.417
8) After the anesthesia resident gave you information, did s/he make sure to find out how well you understood the information?	188	72%	184	80%	0.088
9) Did the anesthesia resident encourage you to be as much involved as you would like in the decisions about your anesthetic plan?	188	64%	184	73%	0.048
10) Prior to your procedure, did the anesthesia resident help set expectations regarding your stay in the recovery room?	195	62%	186	73%	0.022

Figure 2: Proportion of "Definitely yes" responses. The proportion of "Definitely yes" responses either remained about the same or increased for all questions from pre-intervention to post-intervention. The difference was statistically significant for questions 6, 9, and 10.

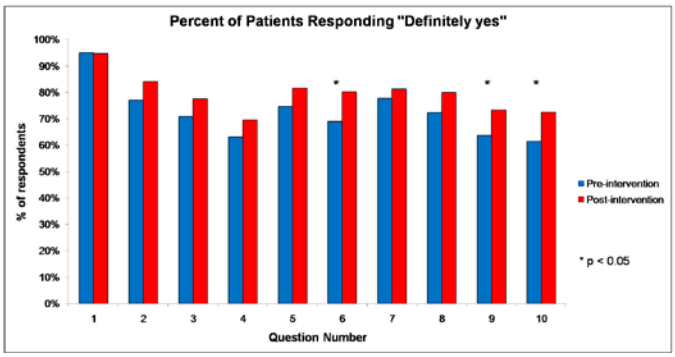

Table 3: Averages of the 38 residents' average ratings for questions 6, 9, and 10 (1 = "Definitely no", 2 = "Somewhat no", 3 = "Somewhat yes", 4 = "Definitely yes")

Question	Pre-intervention Average (n = 38)	Post-intervention Average (n = 38)	t-test (paired) p-value	t-test (unpaired) p-value
6) Did the anesthesia resident do anything to help you feel okay about whatever emotions you were feeling?	3.51	3.69	0.06	0.07
9) Did the anesthesia resident encourage you to be as much involved as you would like in the decisions about your anesthetic plan?	3.33	3.49	0.18	0.24
10) Prior to your procedure, did the anesthesia resident help set expectations regarding your stay in the recovery room?	3.32	3.51	0.14	0.19

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S-28.

COMPARISON OF PROPOFOL VS. PROPOFOL/FENTANYL ANESTHESIA FOR UPPER GASTROINTENSTINAL ENDOSCOPY

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PURPOSE: Propofol is widely used for anesthesia during esophagogastroduodenoscopy (EGD). Its rapid onset and short therapeutic effect provides optimal conditions for the endoscopist, comfort to the patient, and rapid recovery. Because it has no analgesic properties, large doses of propofol are often required to reach the adequate anesthesia depth required for the initiation of EGD and the attenuation of the gag reflex.[1,2] This can result in the undesirable side effects of airway obstruction and hypotension.[3] Opiates have anti-gag and anti-cough properties. Fentanyl is therefore frequently used in combination with propofol to provide sedation during EGD. The synergy that results from combining the 2 drugs, however, can increase the potential for apnea and hypotension. This pilot study was designed to test the hypothesis that propofol/fentanyl combination provides better anesthesia conditions than propofol alone during EGD.

METHODS: With IRB approval, 100 consented patients undergoing EGD were enrolled in this double blinded, prospective, placebo controlled study. Patients were randomly assigned into two groups. In a blinded manner, patients in group A (F/P Group) received fentanyl 1 mcg/kg followed by propofol 0.75 mg/kg bolus, while patients in group B (P Group) received propofol 1.5 mg/kg bolus. In both groups, additional 20 mg propofol boluses were given at 1-2 min intervals until adequate depth of anesthesia was reached as judged by insertion of a soft rubber nasal airway deep into the oro-pharynx. Propofol 150 mcg/kg/min infusion was started. The propofol infusion rate was adjusted as needed to maintain adequate depth of anesthesia for the procedure. The quality of anesthesia was rated by the blinded endoscopist using a 10-point scale (10=perfect). Cardiovascular and respiratory variables were monitored noninvasively. Hypotension was defined as systolic blood pressure <90 mmHg, and hypoxia as arterial O2 saturation <85%. The time patients spent in PACU was recorded in an uncontrolled way. The patients were contacted the following day to inquire about nausea, vomiting or drowsiness. They were asked to rate their overall anesthesia experience on a 10-point scale (10=perfect). Data from the 2 groups were compared by the Wilcoxon rank test for the primary endpoint, by t-test for continuous measures, and by chi-square for proportions including hypoxia and hypotension.

RESULTS: There was no difference between the 2 groups in patient demographics or the duration of the procedures. (Table 1) Table 2 summarizes the endoscopists evaluation scores. As illustrated in Table 3, the endoscopists evaluation scores were statistically significantly higher in the F/P Group. Fentanyl had a statistically significant sparing effect on propofol induction dose. No statistically significant difference between the 2 groups was found in the other study parameters.

CONCLUSIONS:

The combination of propofol and fentanyl provides better quality of anesthesia than propofol alone during EGD.

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Table 1: Patient Demographics and Procedure Times

	Fentanyl/Propofol (N=49)	Propofol (N=49)
Age (years)	44.1 ± 14.7	46.9 ± 12.1
Gender (M/F)	27/22 (55.1%/44.9%)	22/27 (44.0%/55.1%)
Height (cm)	170.2 ± 11.4	172.2 ± 11.2
Weight (kg)	75.9 ± (12.7)	74.7 ± 13.8
BMI (Kg/m²)	26.3 ± 4.5	25.2 ± 4.3
Procedure time (min)	9 ± 6	8 ± 5

Data Presented as n(%) or mean ± standard deviation

Table 2: Endoscopist's Evaluation Score

Sedation Condition Score (1-10, 10 = perfect)	Number of Patients in the Fentanyl/Propofol Group	Number of Patients in the propofol Group
9-10	44	31
7-8	2	9
5-6	3	7
3-4	0	2
1-2	0	1

Table 3: Study outcomes

	Fentanyl/Propofol	Propofol	P-value
Endoscopist's Evaluation Score (1-10, 10=perfect)	9.6 ± 0.1	8.3 ± 0.3	<0.001
Fentanyl Dose (mcg)	75.7 ±1.8	0	
Propofol Induction Dose (mg/kg)	1.6 ± 0.1	2.5 ± 0.1	<0.001
Hypoxia (N)	2 (4.1%)	7 (14.3%)	0.08
Hypotension (N)	7 (14.3%)	2 (4.1%)	0.08
PACU time (min)	37.5 ± 1.8	36.1 ± 1.7	
Postop Drowsiness (N)	27 (55.1%)	29 (59.2%)	
Postop Nausea (N)	5 (10.2%)	3 (6.1%)	
Patient's Evaluation Score (1-10, 10 = perfect)	9.3 ± 0.2	9.5 ±0.1	

Data presented as score, n(%), or mean ± standard deviation

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S-29.

EFFECT OF SINGLE DOSE IV ACETAMINOPHEN ON POSTOPERATIVE/POSTDISCHARGE NAUSEA AND VOMITING, PAIN, AND PATIENT SATISFACTION IN OUTPATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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INTRODUCTION: Outpatient laparoscopic cholecystectomy (OLC) is a well established, safe and cost effective option for surgical treatment of non-emergent, symptomatic cholelithiasis. However, complications such as postoperative pain, postoperative and postdischarge nausea and vomiting (PONV/PDNV) can result in delayed discharge and unanticipated admissions[1,2]. Parenteral opioids are causative of some of these side effects and thus opioid sparing techniques are gaining favor in this population. Intravenous acetaminophen (OFIRMEV) has been shown to reduce PONV yet not always reduce opioid use[3,4]. The objective of this study is to evaluate the effect of a single intraoperative dose of IV acetaminophen (IVA) on pain and PONV in the PACU, and PDNV and patient satisfaction, compared to standard practice in OLC patients.

METHODS: Following IRB approval and informed consent, patients scheduled for non emergent OLC were randomized into 2 groups, stratified by risk for PONV (5). All subjects received opioid and inhalational anesthesia based regimen with preemptive antiemetics. One group received 1000mg of IVA after removal of the gallbladder but prior to emergence whereas the second group received analgesics, including ketorolac, per usual practice. Pain was scored with an eleven point NRS before surgery and at 10 minute intervals in the PACU. The incidence of PONV and rescue narcotic doses was documented. PDNV and patient satisfaction was assessed within 7 days of surgery.

RESULTS:

Three sites enrolled 65, ASA I-III adult patients over six months. There were no significant differences in PACU pain scores (Table 1) at 10min (control group: n=33, mean [SD], 2.3 [3], IVA group (n=32, 1.4 [3.1]; p=.12) nor at 1hr (control group, 2.1[2.3], vs IVA group, 2.6 [2.5]; p=0.77). Total opioid dose (intraoperative plus PACU), as measured by morphine equivalents, were not significantly different between groups (control group, 72 mg [36], vs IVA group, 69 mg [36]; p=0.9.)

During PACU stay, 36% of subjects in the control group experienced PONV as compared with 21% of the IVA group (p=0.3). Following discharge, the overall incidence PDNV was 38% in the control group and 14% in IVA group (p =0.08). PDNV was more prolonged in the control group, with 24% of control group subjects reporting PDNV on day of surgery (DOS) and 7% and 7% on days 2 and 3 respectively. In the IVA group, patients reported PDNV on DOS only, (p <0.05). Patient satisfaction with pain, PONV management and overall experience trended in favor of IVA, at 67%, 71% and 84% respectively in the control group and 84%, 93% and 96% respectively in the IVA group (p=0.5; 0.1; 0.4).

Conclusions: Preliminary data indicates a trend of reduced PONV, PDNV, and improved patient satisfaction following a single pre-emergent dose of IVA, when compared with the standard opioid based analgesic regimens. Further enrollment will confirm whether these trends become significant benefits to the use of IV acetaminophen before emergence in OLC.

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Anesthetic Pharmacology

S-30.

DEXMEDETOMIDINE INFUSION AS AN ANESTHETIC ADJUNCT REDUCES THE UTILIZATION OF SEVOFLURANE DURING GENERAL ANESTHESIA

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ABSTRACT: The intravenous anesthetic adjunct dexmedetomidine (Dex) has been shown to be neuroprotective[1,2]. Dexmedetomidine HCl is an α2-agonist. It may decrease the amount of inhalation agent required thereby preventing or reducing possible neurotoxic effects of volatile agents, smooth emergence, alleviate post-operative pain, decrease post-operative nausea and vomiting. In this retrospective study, we compared the use of Dex with the concentrations of utilized inhaled anesthetics [1,2, 7].

METHODS: One hundred thirty patients were selected from the operating room cases at Virginia Commonwealth University in a retrospective review. The patients who underwent general anesthesia were divided into two matched groups: A) control group (n=80) and B) intravenous infusion dexmedetomidine during surgery (n=50). The age, gender, body weight and the end of expiratory sevoflurane, were recorded for each patient during the anesthetic, data collected from electronic charting (Innovian electronic record keeping-Draeger Inc). Age (years),gender, weight were demographics.. Amount of inhaled sevoflurane (Sevo), (minimum alveolar concentration-MAC), was defined as percentage of end expiratory inhaled anesthetics mathematically averaged by the record keeper.

RESULTS: The end of expiratory sevoflurane (%) in Dex group was significantly less than that in the control group (0.941±0.046 vs. 1.444±0.028, p< 0.001). There was no statistic significant difference in ages among groups (47.74±2.2 in Dex group vs. 42.95 ±1.7 in control group, p=0.09). Further, the reduction of Sevo in Dex infusion group was not significantly related with sex, gender, and weight when compared with control group.

CONCLUSION: An intraoperative infusion of Dex combined with inhalation Sevo can reduce the use of Sevo(inhalation anesthetics) during general anesthesia.

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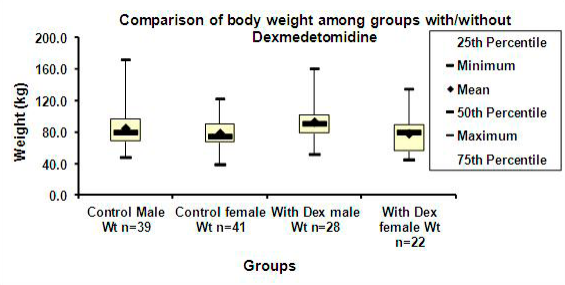

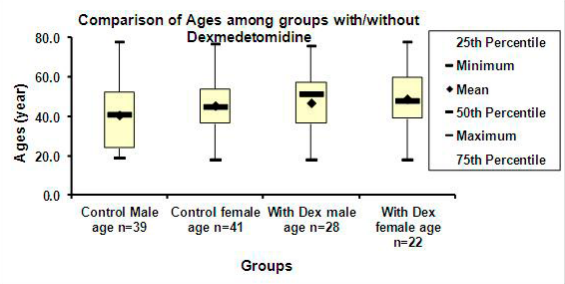

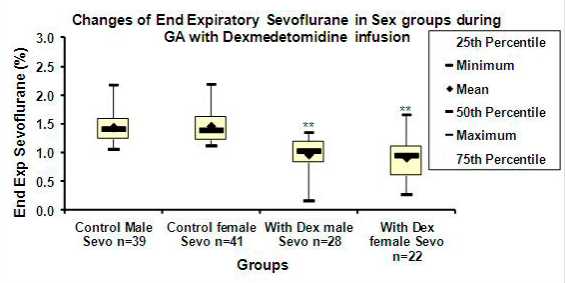

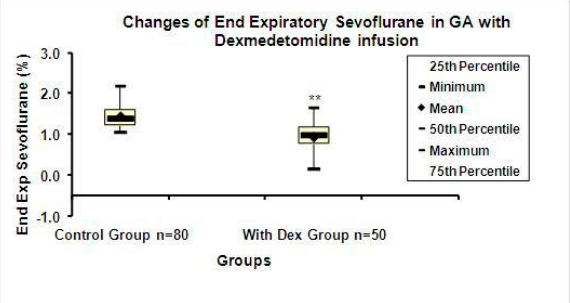

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S-31.

WITHDRAWN.

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S-32.

LIQUID SEVOFLURANE DOES NOT SUPPORT BACTERIAL GROWTH

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AFFILIATION:[1]Anesthesia and Intensive Care, University of Pecs, Pecs, Hungary, [2]Medical Microbiology, University of Pecs, Pecs, Hungary

INTRODUCTION: Bacterial growth in anesthetic vapors has been investigated for various reasons. The role of general anesthesia using anesthetic vapors in the development of postoperative pneumonia has been questioned for a long time. On the other hand it was feared that inhalational anaesthesia for bronchoalveolar lavage may influence the results if inhibits bacterial growth itself. The previous studies revealed controversial results[1,2]. In this study we examined bacterial growth in liquid sevoflurane for another reason. Medications used in anesthesia and intensive care may be responsible for serious infections if contaminated and supports bacterial growth[3].

METHODS: The growth of Staphylococcus aureus (American Type Culture Collection [ATCC] 25923), Escherichia coli (ATCC 25922), and Pseudomonas aeruginosa (ATCC 27853) in sevoflurane was investigated. One mL sevoflurane was inoculated with the above strains and kept at room temperature. The initial bacterial inoculums were 1,5 x 104 colony forming units (cfu) mL-1. At 0, 1, 2, 3, 6, 12, and 24 hours 10µL was plated on Mueller - Hinton (MH) agar. At 48 hours the remaining contaminated sevoflurane (930 µL) was spread on MH agar. Having incubated for 24 hours at 37oC the cfu was counted. Three parallels were performed. Saline 0.9%, MH broth controls and sevoflurane sterility check was also applied. Two-way analysis of variance served as the statistical method.

RESULTS: The cfu of all examined strains decreased significantly following 1 hour exposure. We could detect viable cells of all strains after 12 hours exposure. At the end of the experiment (48 h) only a few staphylococci survived.

CONCLUSIONS: Our results suggest that bacterial count decreases fast in liquid sevoflurane. However, the facts that viable cells can be detected even after 48 hours exposure sterile conditions are recommended during sevoflurane handling and vaporizer filling.

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S-33.

REFINED METHODS FOR TAIL VENOUS CATHETERIZATION AND INTUBATION FOR TOTAL INTRAVENOUS ANESTHESIA IN RATS

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INTRODUCTION: Small animal models, specifically the rat, are commonly used in lab research to study various intravenous general anesthetics. However, it is technically challenge to place IV cannulation and intubation in small animal for total intravenous general anesthesia (TIVA) by a single anesthetic agent because of the small subject size and the lack of equipment specially designed for these tasks. In this study, we describe a methodology refined in our lab that encompasses IV placement in the awake rat, rapid intravenous induction, and intubation with refined laryngoscope, maintenance of general anesthesia with target infusion, and an easy recovery with minimal residual effects.

METHODS: Female SD rats were used in this experiment with the approval by Rutgers Institutional Animal Care and Use Committee (IACUC).The first step in this study was to place an IV cannulation in the tail vein in the awake rat. Rats were gently restrained to a rat chamber and a 24 gauge IV catheter was inserted to the lateral tail vein after placing the tail in warm water for 10 minutes. The catheter was fixed in place using tape and was attached to a T-connector for drug administration. A depth of anesthesia was achieved by giving a bolus of propofol, ketamine or etomidate. The next step was to perform intubation with the aid of a modified laryngoscope. It was important to cut off one half of the width of the Miller blade 0 extending from the distal tip for approximately 2/3 of the entire length to match the airway of rat. To improve airway visualization, the animal was fixed to a 45°-inclined metal book holder in a dorsal position by means of a ribbon hooked around the upper incisors. A18-gauge intravenous catheter as an endotracheal tube was easily to put in rats under the direct vision of the vocal cords. After intubation, the animal was connected to a ventilator (tidal volume 10 ml/kg with rate of 80/minutes) with FiO2 60-70% and TIVA was maintained by continuous infusion of the same intravenous agent for one hour. The arterial oxygen saturation, pulse strength, heart rate were continuously monitored using tail pulse oximetry. Temperature was monitored and maintained in the range of 37 ± 0.5 °C. In propofol group, arterial blood was collected for blood gas analysis.

RESULTS: 20 rats were tested using this system. 10 out of 20 received propofol anesthesia, 7 for ketamine and 3 for etomidate. IV placement, intubation and ventilation were successfully performed in all rats without major technical problems. All rats rapidly recovered to baseline activity within 10-15 minutes after discontinued infusion. The vital signs of all rats throughout TIVA were stable. Blood gas measurement did not detect any metabolic acidosis, hypoxia, hypercarbia or glucose abnormalities in the rats who received propofol infusion for one hour.

CONCLUSION: These results indicate that TIVA can be performed effectively and safely in the small animal using the methods refined in this study. These techniques are easily reproducible and learned.

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S-34.

WITHDRAWN.

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S-35.

DO DELTA SUBUNITS INTRODUCE ASYMMETRY IN GABA-A RECEPTOR ETOMIDATE SITES?

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INTRODUCTION: Etomidate (ETO) induces general anesthesia by enhancing the activity of inhibitory GABAA receptors in the CNS. Prior studies in α1β2γ2 synaptic receptors demonstrated two ETO sites per receptor, formed between α-M1 and β-M3 domains[1]. Using concatenated subunit assemblies, we showed that the two ETO sites contribute equally to receptor modulation[2]. GABAA receptors with extrasynaptic α1β3δ subunits show ETO sensitivity similar to α1β3γ2[3], but it is not known if ETO sites remain equivalent in α1β3δ receptors.

METHODS: Xenopus frogs were used with IACUC approval. We mutated DNA encoding concatenated β3-α1 dimer (D) and β3-α1-δ trimer (T) constructs to incorporate β3N265M mutations (D* and T*), which eliminate ETO sensitivity in α1β2γ2[4]. Mixtures of mRNA transcripts were injected into Xenopus oocytes. ETO (3.2 μM) effects on GABA concentration-responses were quantified using two microelectrode voltage-clamp electrophysiology. Concentration-response curves were analyzed by fitting with Hill equations in Graphpad Prism.

RESULTS: Wild-type α1β3δ (DT) receptor currents were modulated by ETO, which increased maximal currents about 15-fold and reduced GABA EC50 3-fold. Double mutant (D*T*) receptor currents were unaffected by ETO. Dimer mutant (D*T) and trimer mutant (DT*) receptor currents showed distinct modulation by ETO. Maximal D*T responses increased 4-fold and GABA EC50 shift was insignificant. Maximal DT* responses increased 14-fold and GABA EC50 shift was insignificant.

CONCLUSIONS: Unlike prior results in concatemeric α1β2γ2 GABAA receptors with αM236W mutations (2), α1β3δ concatemer studies with β3N265M mutations suggest asymmetrical ETO site effects. Preliminary studies with β3N265M mutations in α1β3γ2 concatemeric receptors (β3-α1-γ2/β3-α1) show similar asymmetrical effects. Thus, these apparently unequal ETO site effects may be due to another variable in our experimental system, such as the location of the mutation itself.

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S-36.

A PROSPECTIVE RANDOMIZED DOUBLE BLIND TRIAL COMPARING THE EFFICACITY OF A BOLUS OF IV LIDOCAINE AND REMIFENTANYL ON THE INCIDENCE OF COUGHING AT EMERGENCE

AUTHORS: L. Poulin[1], F. Gaulin[2], G. Arcand[3], A. Lallo[3], F. Girard[3]

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INTRODUCTION: Several strategies have been evaluated to reduce the incidence of cough at emergence of general anesthesia. There are studies supporting the administration of intravenous opioids before emergence to reduce cough, agitation and hemodynamic stimulation. The goal of this randomized prospective trial was to compare a bolus of remifentanil with lidocaine before extubation regarding the incidence of cough.

METHOD: 62 patients aged 18-80 years undergoing surgery excluding the area of the head and neck and requiring tracheal intubation were randomized to receive a bolus of lidocaine 1 mg.kg-1 (LIDO) or a bolus of remifentanil 0.25 mcg.kg-1 (REMI) prior to emergence. The incidence of cough, sedation, variation in mean arterial pressure (MAP), time to extubation and the presence and severity of sore throat were then evaluated.

RESULTS: LIDO and REMI demographics were comparable. There was no statistically significant difference in the incidence of cough (58% without cough for both devices, P = 1), time to extubation , post- extubation sedation and sore throat between the two groups. Post extubation MAP variation was less important in the group REMI (ΔMAP = 11 ± 14 mmHg) than the LIDO group (ΔMAP = 18 ± 13 mmHg , P = 0.03)

CONCLUSION: This study shows that the use of a remifentanil bolus at emergence of general anesthesia is equivalent to a bolus of lidocaine in terms of prevention of episodes of coughing. However, the hemodynamic response to extubation has been less important in the remifentanil group. Consequently, the use of remifentanil 0.25 mcg.kg-1 has the advantage of further reducing the hemodynamic response to extubation compare with the use of lidocaine 1 mg.kg-1

REGISTERED CLINICAL TRIAL: Clinicaltrials.gov reference number NCT01026129

Anesth Analg 2009 108(4): 1157-60

Anaesthesia, 2010, 65, 930-935

Anaesthesia 2012, 67, 765-770

BJA, 2009, 102 (6): 775-8

BJA, 2011, 106 (3): 410-15

Journal of International Medical Research, 2012, 40: 174

Table 1: Demographic Data

	LIDO 1 mg/kg (n=31)	REMI 0,25 mcg/kg (n=31)
Age (y)*	52 ± 14	52 ± 16
Height (m)*	1,64 ± 0,09	1,66 ± 0,10
Weight real (kg)*	70 ± 20	75 ± 17
ideal (kg)*	57 ± 7	59 ± 9
Body Mass Index (kg.m-2)*	26 ± 7	27 ± 7
Sex (male/female)	5 / 26	11 / 20
Smoking (yes/no)	7 / 24	10 / 21
Lenght of surgery (min)*	154 ± 65	135 ± 54

*Mean ± SD

Table 2: Type of surgery

Type of surgery	LIDO 1 mg/kg (n=31)	REMI 0,25 mcg/kg (n=31)
Generale	7	10
Gynecology	7	7
Orthopedic	4	4
Ophtalmology	4	4
Plastic surgery	7	6
Radiology	2	0

Table 3: Emergence data

	LIDO 1 mg/kg (n=31)	REMI 0,25 mcg/kg (n=31)	
Cough Scale*			
No cough (0) (%)	18 (58%)	18 (58%)	P = 1
Cough (1-2-3) (%)	8 / 2 / 3 (42%)	8 / 3 / 2 (42%)	
Extubation time (s)**	488 (± 166)	444 (± 128)	P = 0,25
MAP variation (mmHg)**	18 (± 13)	11 (± 14)	**P = 0,0316**
Sore throat***			
0 to 3	22	23	P = 0,51
4 to 7	6	4	
>7	1	0	
(OAA/S) Scale****			
Without physical contact (5-4-3) (%)	16 / 4 / 6 (84%)	14 / 9 / 2 (81%)	P = 0,74
With physical contact (2-1-0) (%)	1 / 0 / 4 (16%)	3 / 0 / 3 (19%)	

* Cough Scale (adapted from Minogue and colleagues)
0 = no cough; 1 = single cough (1-2 episodes); 2= more than one episode of non sustained cough (3-4 episodes); 3 = sustain and repetitive cough (5-6 episodes)

** Mean + SD

*** 0-10 Numeric Rating Scale (0 = no pain, 10 = worst pain possible)

**** The Observer's Assessment of Alertness/Sedation
5 (alert) Responds readily to voice with normal tone; 4 : Responds slowly to voice with normal tone; 3: Responds after calling loudly or repeatedly; 2: Responds after mild prodding or shaking; 1: Does not respond to mild prodding or shaking; 0:Does not respond to pain

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S-37.

ESTIMATING THE POTENCY OF MUSCLE RELAXANTS. COMPARING NON-LINEAR REGRESSION WITH INDIVIDUAL ESTIMATES OF POTENCY USING THE HILL EQUATION.

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INTRODUCTION: Estimates of potency of nondepolarizing muscle relaxants (MR) can be made using a nonlinear regression (NLR) analysis after obtaining numerous dose-response data points from multiple patients. Alternatively, Kopman[1] has suggested that because the slopes of the dose-response relationship of all muscle relaxants are identical, the assumed value of the slope (γ) can be placed in the Hill equation. If a dose of a MR is administered to a patient and the twitch depression caused by this dose is measured, then the Hill equation can be solved with the assumed value of γ. Solving the Hill equation will yield estimates of potency -ED50 or ED95 for that patient. We have conducted the following investigation to compare the two methods (NLR and Hill equation) for estimating ED50 for vecuronium, rocuronium, pancuronium and cis-atracurium

METHOD: Following IRB approval, and obtaining informed consent, ASA I or II adults free from neuromuscular disease were included. Following premedication with midazolam, anesthesia was induced with fentanyl and propofol, and tracheal intubation was accomplished without the aid of muscle relaxants. Mechanical ventilation was commenced and adjusted to obtain normocapnia. Anesthesia was maintained with fentanyl, propofol and N2O. The patient's ulnar nerve was stimulated at the wrist (single twitch 0.1 Hz) and force of contraction of the adductor pollicis brevis was measured using a force transducer (Gould FT-10). After a period of stabilization, we injected a single dose of a MR intravenously. The doses were chosen to produce varying degrees of neuromuscular blockade, from 5%-95%. The doses for the four muscle relaxants were Vecuronium 0.013-0.04 mg/Kg (18 patients), rocuronium 0.1-0.25 mg/kg (20 patients), pancuronium 0.015 - 0.025 mg/kg (12 patients) and cis-atracurium 0.02 to 0.045 mg/Kg (13 patients). Potency was estimated as ED50 using the Hill equation for each individual subject according to the method of Kopman(1). γ in the Hill equation was assigned a value of 4.5. NLR regression was performed on the pooled data from all subjects for each individual MR. NLR was performed using GraphPad Prism V6 for Windows (GraphPad Software Inc., La Jolla, CA). We used the log-dose vs response -variable slope (four parameters) function of the GraphPad Prism computer program for the NLR.

RESULTS: Potency (ED50) for all four MR's obtained by NLR and the Hill equation are presented in Table 1. The NLR analysis for all four MR's is presented in Figure 1. The percentage differences in the estimates of ED50 obtained by the two methods (NLR or the Hill equation) were 4% for pancuronium and cis-atracurium, 6% for vecuronium and 10% for rocuronium. Estimates of ED50 by either method are within the range reported by other investigators[2].

CONCLUSION: Individual estimates of ED50 obtained using the Hill equation can reasonably substitute for non-linear regression analysis of pooled data from many subject s.

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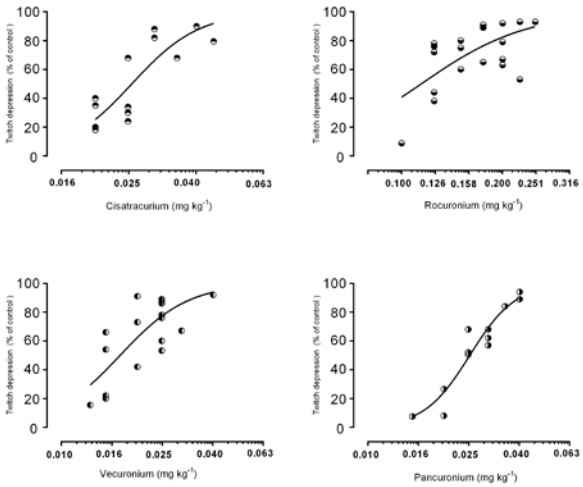

Fig 1 The best-fit lines of non-linear regression log dose *vs* percent twitch depression.

Table 1: ED 50 values as determined by non-linear regression analysis (NLR) or by the Hill equation.

	ED50 mg/kg (95% confidence interval)	
	Non-Linear regression	Hill equation
Rocuronium (n=20)	0.114 (0.09 - 0.14)	0.133 (0.147 - 0.118)
Vecuronium (n=18)	0.017 (0.015 - 0.02)	0.018 (0.020 - 0.017)
Cisatracurium (n=13)	0.024 (0.023 - 0.029)	0.026 (0.029 - 0.024)
Pancuronium (n=12)	0.025 (0.024 - 0.027)	0.026 (0.028 - 0.24)

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S-38.

GAS MAN DERIVED COMPARTMENTAL AND LEROU PHYSIOLOGICAL MODEL VS LU ET AL CLINICAL DATA FOR DESFLURANE.

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INTRODUCTION : The end tidal desflurane concentrations are available clinically but it is a delay of equilibration with the brain, which is the effect site.

The usefulness of the pharmacokinetic models depends on their accuracy.

We evaluated the prediction of both the end tidal and effect site brain concentrations of desflurane of the Gas Man derived compartmental model and the Lerou physiological model vs the Lu et al clinical data.

METHOD : Lu et al measured the end tidal (Ce) and the jugular-bulb (Cj), surrogate for effect site, brain (Fb), concentrations of desflurane in 13 patients undergoing elective coronary artery bypass grafting. The patients were volume controlled ventilated for 1 hour, fresh gas flow (FGF) 5l/min, vaporizer settings (FD) 5%.[1]

We simulated the end tidal (Fet) and brain (Fb) concentrations for a patient weight Wt=68kg, tidal volume Vt=600cc, respiratory rate RR=10breath/min for both the Gas Man derived compartmental[2] with an added effect site compartment with a ke0=0.61min-1 (Rehberg et al) and Lerou physiological model used by AnestAssist program (Palma Healthcare Systems LLC). The cardiac output (CO), a covariate of the compartmental model, that is not routinely available clinically, was 5l/min, with the caveat that in this patient population it is low and under anesthesia it would decrease even further.

RESULTS : We calculated the median prediction error (MPE) and median absolute prediction error (MAPE), as a measure for bias and accuracy, respectively, for the end tidal and brain concentrations, of the compartmental model and the Lerou physiological model vs the data of Lu et al for desflurane.[3] (Table 1).Conclusion:There was no significant difference between the compartmental and physiological models, both estimated the end tidal desflurane concentrations (Fet) with good accuracy <16% with a negative bias, but the accuracy for brain concentrations (Fb) was <38% with a positive bias. The high predicted effect site brain concentrations predicted by both the compartmental and physiologic models compared with the clinical data could be due to the use of a normal cardiac output for the simulation. Under anesthesia the cardiac output and the cerebral perfusion are low in the cardiac patients for CABG surgery.

The Gas Man derived compartmental model has to be used with caution when predicting effect site concentrations of desflurane.

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Table 1

Desflurane Gas Man Derived Compartmental Model vs Lu Data			
MDPE Fet-Ce [%]	MDAPE Fet-Ce [%]	MDPE Fb-Cj [%]	MDAPE Fb-Cj [%]
-13	13	38	38
Desflurane Lerou Physiological Model vs Lu Data			
MDPE Fet-Ce [%]	MDAPE Fet-Ce [%]	MDPE Fb-Cj [%]	MDAPE Fb-Cj [%]
-16	16	22	34

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S-39.

GAS MAN DERIVED COMPARTMENTAL VS LEROU PHYSIOLOGICAL MODEL FOR DESFLURANE

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INTRODUCTION : The parsimonious compartmental models of volatile agents are important because they can be fitted to clinically data available in the operating room and can be used to describe the course of their partial pressure over time.

Hendrickx et al derived a classical three compartmental model with two covariate, cardiac output and body weight, from the physiological uptake model used by Gas Man program (Med Man Simulations, Inc.,Chestnut Hill, MA)[1].

We tested the predictive performance of the derived compartmental model vs the Lerou physiological model used by AnestAssist program (Palma Healthcare Systems LLC) for desflurane.

METHOD: For the simulations we used model covariates weight (Wt), fixed cardiac output (CO) at 5 l/min (not usually clinically available), ventilation in volume controlled mod with tidal volume (Vt), respiratory rate (RR), fresh gas flow (FGF), as ventilator settings, and vaporizer desflurane concentration (FD) as model inputs. Outputs of the model simulations are desflurane inspiratory (Fi), end-tidal (Fet) and effect site, brain, concentration (Fb). For the compartmental model we calculated the inspiratory concentration Fi : Fi=Fet+(FD-Fet)*FGF/(Vt*RR) and the uptake Ut : Ut=(Fi-Fet)*(Vt*RR). For calculation of the brain desflurane concentrations we added an effect site compartment with a ke0=0.61min-1 to the compartmental model (Rehberg et al). We run 1 hour simulations for a virtual 70kg patient, Vt=600cc, RR=10breath/min. Washin, maintenance and washout Fet and Fb concentrations resulted for 3 different scenarios (S). S1 : FGF=6l/min, FD=6% time=0 to 45min than FD=0% ;S2 : FGF=2l/min, FD=6% time=0 to 45min than FD=0%; S3 : FGF=6l/min FD=6% time=0 to 15 and FD=0% time=45 to 60 and FGF=2l/min FD=6% time=16 to 44min.Results : We calculated the median prediction error (MPE) and median absolute prediction error (MAPE), as a measure for bias and accuracy, respectively, for the end tidal and brain concentrations, of the compartmental model vs the Lerou physiological model as reference.[2] (Table 1).

Table 1

	Fet MDPE [%]	Fet MDAPE [%]	Fb MDPE [%]	Fb MDAPE [%]
Simulation 1				
Overall	-2	3	5	3
Washin	8	8	18	18
Maintenance	-2	2	-1	2
Washout	-87	87	-87	87
Simulation 2				
Overall	-13	15	4	15
Washin	13	13	31	31
Maintenance	-13	13	-13	13
Washout	-88	87	-87	87
Simulation 3				
Overall	-16	16	5	16
Washin	8	8	18	18
Maintenance	-16	16	-16	16
Washout	-89	88	-88	88

CONCLUSION : It appeared that it was a good estimation of the end tidal and brain desflurane concentrations of the compartmental vs the physiological model overall with an accuracy of <16%, negative bias for Fet and positive for Fb. However during washin it reached 13% for Fet and 31% for Fb with a positive bias and during washout 88% for Fet and Fb with a negative bias. The accuracy decreased with decreased FGF and more FD changes. The acceptable approximation of the end tidal concentrations by the Gas Man derived compartmental model compared to the Lerou physiological model, that was previously clinically validated, is promising to its use in the study of volatile anesthetic agents.

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S-41.

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S-42.

CANNABINOID 2 RECEPTOR MODULATION IN MURINE SEPSIS

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INTRODUCTION: Sepsis results from a dysregulated immune response to an infection. Current medical treatments are of limited efficacy with regard to improvement of survival. The endocannabinoid system (ECS) opens a novel avenue in sepsis therapy due to its unique characteristics. Cannabinoid 2 (CB2) receptors are expressed on the surface of all immune cells, providing a direct approach to the modulation of the immune system. The present study explored the effects of CB2 receptor modulation in a mouse model of acute sepsis (endotoxemia).

METHODS: Endotoxemia was induced by intravenous administration of lipopolysaccharide (LPS, 5 mg/kg; from E. coli, serotype: O26:B6). Six groups of mice were used to assess leukocyte activation within the intestinal microcirculation as well as functional capillary density (FCD) by intravital microscopy. The treatment compounds tested were: a specific CB2 receptor agonist, HU308, a CB2 receptor antagonist/inverse agonist, AM630, and the cannabinoid degradation enzyme inhibitors URB597 (fatty acid amide hydrolase inhibitor), and JZL184 (monoacylglycerol lipase inhibitor).

RESULTS: Administration of the CB2 receptor agonist, HU308, reduced significantly the number of adhering leukocytes in submucosal venules, but did not restore muscular and mucosal villi FCD in endotoxemic mice. The CB2 receptor antagonist, AM630, did not exacerbate leukocyte activation within the intestinal microcirculation, but further reduced muscular and mucosal FCD oft he intestinal wall. The cannabinoid degradation enzyme inhibitors URB597 and JZL184 both significantly reduced the number of adhering leukocytes in submucosal venules. Furthermore, JZL184 administration completely restored muscular FCD.

CONCLUSIONS: CB2 receptor activation by a specific agonist or cannabinoid degradation enzyme inhibition was effective in reduction of leukocyte activation within the intestinal microcirculation. The CB2 receptor pathway seems to be involved in the inflammatory cascade elicited early during sepsis. Therefore, modulation of the CB2 receptor pathway might offer new therapeutic options for the manipulation of the immune system in sepsis.

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S-43.

RAPID AND IMMEDIATE ANTAGONISM BY L-CYSTEINE OF THE NEW ULTRA-SHORT ACTING NONDEPOLARIZER CW 1759-50: PAIRED STUDIES IN RHESUS MONKEYS GIVEN CONTINUOUS INFUSIONS AT 2 X ED99 DOSAGE TO MAINTAIN 100% BLOCK OF TWITCH

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BACKGROUND: CW 1759-50 shows ultra-short duration (6-8 mins from injection at ED99 bolus dosage to return of twitch and TOF to 95% of control values) in the Rhesus Monkey. The block is rapidly antagonized by L-cysteine. The following study was performed to document rapid antagonism of CW 1759-50 blockade by L-cysteine at the end of continuous infusions of varying length where CW 1759-50 block was maintained at very deep levels (100% twitch block) by administering 2x ED99 dosage throughout the infusion. These experiments were meant to simulate clinical scenarios where a continuous overdose of CW 1759-50 may have been administered over a lengthy period of time, yet rapid recovery may nevertheless be desired.

METHODS: Adult male Rhesus monkeys weighing 10-20 kg were studied under isoflurane (1.5 - 2.0%) and N2O/O2 (70/30 mixture) anesthesia. The study was approved by the IACUC of Albany Medical Center, where the experiments were performed. Arterial pressure, twitch at 0.15 Hz, and TOF were measured continuously. Temperature and SpO2 were monitored continuously. Ventilation was controlled at 20 BPM, 15 mL/kg.

EXPERIMENTAL PROCEDURE: Infusions varied in length from as short as 20 mins to as long as 75 min. Infusions were done in pairs. First dosage for maintenance of continuous block at 99% block of twitch (mcg/kg/min) was established. Then this rate was doubled (2x ED99) and maintained for the rest of the infusion. Spontaneous recovery after this infusion was observed (Infusion C). Then a new baseline was established, and the same dose (2x ED99) was administered for the same length of time (Infusion D). Infusion D was then terminated, and one minute later, L-cysteine (30 mg/kg) was administered. Recovery times following Infusion C (spontaneous recovery) and Infusion D (L-cysteine antagonism) were compared by paired t-test.

RESULTS: Data are shown in Table 1. All comparisons are highly significant ($p < 0.01$). There was no significant difference between the durations of infusions C and D.

DISCUSSION: The data show that a standard dose of L-cysteine (30 mg/kg) given 1 min after discontinuation of infusion rapidly antagonizes deep CW 1759-50 block where infusions have been given at high dosage (2x ED99) to maintain 100% twitch block. Reversal is nearly as rapid (3.7 ± 0.6 min vs. 2.1 ± 0.5 min) as following infusions where 99% block (ED99) has been maintained.[1] Rapid antagonism of CW 1759-50 immediately following deep block may be clinically advantageous.

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Table 1 **

Infusion	Recovery	Infusion Rate (mcg/kg/min)		Duration of Infusion at 2 X ED99 (min)
		ED99	2 X ED99	
Infusion C (control)	Spontaneous	20.7 ± 7.2	41.3 ± 14.5	39.2 ± 21.8 (20-75)
Infusion D (reversal)	L-cysteine reversal	18.9 ± 6.4	37.8 ± 12.7	39.2 ± 21.8 (20-75)

Table 1 ** (cont)

Infusion	Recovery	5-95% twitch recovery (min)	5% twitch – 95% TOF recovery (min)
Infusion C (control)	Spontaneous	7.3 ± 1.4	11.2 ± 3.2
Infusion D (reversal)	L-cysteine reversal	3.7 ± 0.6 *	4.9 ± 0.8 *

* P < 0.01, ** n=6 for all data points

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S-44.

LIDOCAINE PROTECTED PC12 CELLS AND CULTURED CORTICAL NEURONS FROM BETA AMYLOID TOXICITY

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INTRODUCTION: Amyloid-beta is neurotoxic and plays an important role in the etiology of Alzheimer's disease. It has been shown that the inhalation anesthetic isoflurane enhanced the effect of amyloid-beta[1]. Lidocaine is a common local anesthetic, which has been shown to be neuroproctective at antiarrhythmic dose in animal and in patients undergoing cardiopulmonary bypass[2]. The effect of lidocaine in amyloid-beta toxicity is unknown. At the present study, we investigated the effect of lidocaine against beta-amyloid neurotoxicity on neuron cell line PC12 cells and mouse cultured neurons.

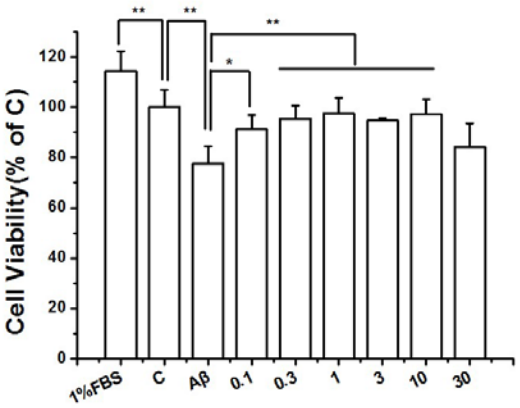
METHODS: PC12 cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM, Gibco, USA) supplemented with 10% fetal bovine serum (FBS, Gibco, USA), 1% penicillin/ streptomycin solution (Gibco, USA) in a humidified incubator at 37°C and 5% CO2. Cortical primary culture neurons were prepared and maintained as described as before[3], from embryonic day 14 pregnant Kunming mice.

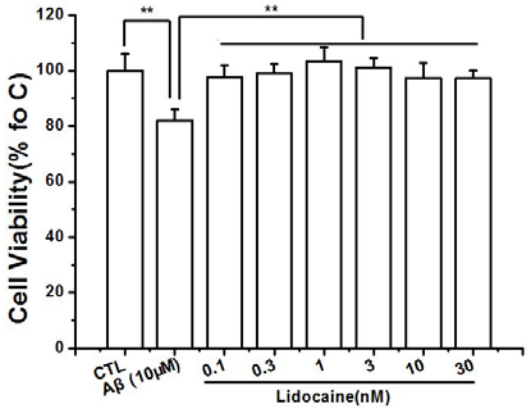
The viability of PC12 cells and cortical cultured primary neurons were determined by the MTT assay (Sigma, USA). Cells grew in 96-well plates at a density of 2×105 cells/well and were serum starvated for 24 h, then incubated with 0.5 mg/ml of MTT for an additional 4 h. The medium was removed and the formazan crystals were dissolved by 100μl DMSO added to the well. The absorbance of each well was obtained with a Multiskan ascent Revelation plate reader (Thermo, USA) at wavelength of 570 nm.

To study the protective effect of lidocaine on neuronal cells from amyloid-beta toxicity, PC12 cells were treated with different concentration of lidocaine (0-10 nM) and 10 μM Aβ25-35 for 24 hours and the viability of these cells was determined.

The results were expressed as mean ± the standard error of the mean (SEM). Results are expressed as the percentage of the corresponding control value. Data are shown as the mean ± SEM. *p<0.05, ** p<0.01 (n = 4). The data was evaluated by unpaired two-tailed Student t-test. A p-value < 0.05 was considered statistically significant.

RESULTS: 10 μM Aβ25-35 caused 20-40 percent of cell death. Lidocaine reversed the effect of 10 μM Aβ25-35 dose dependently. The effect of lidocaine was significant at 0.1 nM and plateaued at 3-10 nM. The protection was decreased when concentration was 30 nM (Figure 1). Consistent with above results, lidocaine also increased the survival of primary cultured mouse cortical neurons from 10 μM Aβ25-35 induced toxicity. The maximal effect on primary cortical neuron was observed at about 1 nM (Figure 2).





CONCLUSION: Our results have shown that lidocane protected neurons cells from amyloid-beta induced neurotoxicity in a concentration-dependent manner.

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S-45.

MIDAZOLAM INHIBITS PROLIFERATION OF HUMAN GLIOBLASTOMA MGR2 CELLS

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INTRODUCTION: Glioblastoma (GBM) is the most common primary brain tumor. It is the most aggressive malignancy in humans with rapid proliferation. Surgical resection is often the treatment of choice but the prognosis is poor[1]. Midiazolam is routinely used as an anxiolytic and sedative perioperatively.

It has been evidenced that anesthesia techniques affect the outcome of surgical patients[2]. The direct effect of anesthetics may have more impact when the approach of regional anesthesia is not practical. We have shown that midazolam inhibited the proliferation of hypopharyngeal squamous cancer cells[3]. In this study we tested the effect of midazolam on the proliferation of GBM cell line MGR2.

METHODS: MGR2 glioma cells were maintained in DMEM supplemented with 10% fetal bovine serum, 100 U/mL penicillin, and 100 mg/mL streptomycin in a humidified atmosphere of 5% CO2 at 37 C. Cell Viability Assay was tested by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT; Sigma) assay. MGR2 cells were planted in 96-well plates and treated with midazolam at various concentrations for various times. Cell proliferation assays were performed using a 5-bromo-2'-deoxyuridine (BrdU) cell proliferation ELISA kit. Cytotoxicity was evaluated by lactate dehydrogenase (LDH) release assay which was quantified with a CytoTox 96 nonradioactive cytotoxicity assay kit.

RESULTS: Midazolam decreased MGR2 viability (Figure 2) by inhibiting proliferation (Figure 2) but does not cause cell death (Figure 3) in MGR2 cells. MGR2 cells were exposed with 0, 6.25, 12.5, 25, 50, and 100 mM midazolam for 24 or 48 hours. Cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide absorbance . Effect on the cell proliferation was measured by BrdU incorporation assay. Cytotoxicity was determined by lactate dehydrogenase (LDH) absorbance after 48 hours treatment with midazolam at the concentrations above. C

CONCLUSIONS: Midazolam significantly reduced the cell viability of MGR2 cells by inhibiting their proliferation. The effect was both dose-dependent and time-dependent. This may be beneficial in the regiment for surgical patients with GBM.

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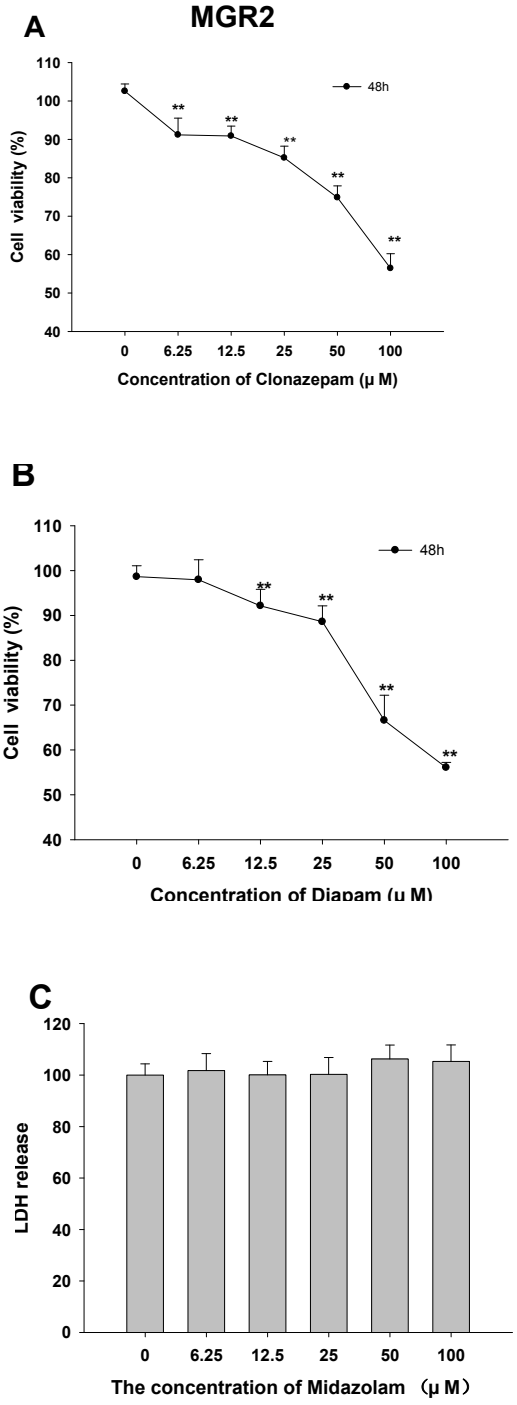

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S-46.

THE EFFECT OF VOLATILE ANESTHETICS ON ADHESION MOLECULE αMβ2

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Previously we demonstrated that volatile anesthetics isoflurane and sevoflurane bound and inhibited adhesion molecule αLβ2. Both inhibited αLβ2 allosterically by binding to "lovastatin site," the cavity within the ligand binding domain of αL subunit away from the actual ligand binding site. αMβ2 is another adhesion molecule, which is homologous to αLβ2, has a similar pocket within αM subunit and share the same ligand with αLβ2. Due to their structural and functional similarities, we postulated that both isoflurane and sevoflurane would inhibit αMβ2.

METHODS: Ligand binding assay αMβ2 ligand ICAM-1 was coated on V-bottom 96 wells, blocked with 2% BSA. αMβ2 transfectants were stained with BCECF-AM and incubated in 96 wells with or without isoflurane or sevoflurane for 30 minutes at 370C. Then plates were centrifuged at 200 x g for 5 minutes and read using the fluorescence reader with excitation 485 nm/ emission 535 nm. Binding % was defined as [(fluorescence of control) - (fluorescence at various concentrations of sevoflurane (or isoflurane))]/[fluorescence of control] x 100%.

RIGID DOCKING USING GLIDE: Computer docking simulation of isoflurane or sevoflurane was performed on αM ligand binding domain.

RESULTS AND MAJOR FINDINGS: Different from our finding of αLβ2 experiments, isoflurane inhibited αMβ2, but sevoflurane did not. Docking simulation demonstrated only isoflurane bound to the cavity, supporting the result of ligand binding.

CONCLUSIONS: We demonstrated that αMβ2 was inhibited by isoflurane, not sevoflurane. This may indicate that there may be difference in immunomodulatory effect between isoflurane and sevoflurane.

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S-47.

COMPARISON BETWEEN PROPOFOL-REMIFENTANIL ANESTHESIA AND DESFLURANE-REMIFENTANIL WITH REGARD TO POST-ANESTHETIC FUNCTIONAL RECOVERY MEASURED WITH QOR-40

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BACKGROUND: Total intravenous anesthesia (TIVA) and anesthesia with volatile agents are both widely and safely used. There have been many previous studies that compared TIVA and anesthesia with volatile anesthetics on various aspects. However, studies comparing the quality of recovery from the different methods of general anesthesia have not been conducted. Functional recovery is an important perspective when choosing an anesthetic method because it is related with early discharge and fast return to daily life. Our main objective in this study was to compare the functional recovery after general anesthesia with TIVA and volatile anesthetic.

METHODS: This study was a prospective, randomized, controlled and double blind study. With informed consent, eighty healthy females undergoing thyroid surgery were recruited and randomized to TIVA with propofol-remifentanil (TIVA group) or desflurane-remifentanil anesthesia (desflurane group). The quality of recovery-40 questionnaire (QoR-40) score, which was qualified in validity and reliability, was used for assessment of functional recovery, and the score was evaluated three times - before surgery, and at 24hours and 48 hours after the surgery. The primary outcome was the comparison of QoR-40 score at 24 hours after surgery. Other data collected included the duration of hospital stay, duration and type of surgery, blood pressure, pulse rate, nausea or vomiting, consumption of antiemetic and analgesic agents in ward and PACU. Data were analyzed using the T-test, Fisher's exact test, and Pearson chi-square test. A P value < 0.05 was considered statistically significant.

RESULTS: TIVA group had higher quality of recovery scores in physical comfort at 24 hours and 48 hours after the surgery while physical independence, psychological support and total QoR-40 were higher only at 24 hour. The demographic characteristics, blood pressure, duration of hospital stay, duration and type of surgery did not differ between two groups.

CONCLUSION: This study demonstrates that TIVA provides better quality of recovery than does desflurane anesthesia at 24 hours after the surgery. TIVA seems to be a good choice of anesthetic plan for earlier functional recovery especially for ambulatory surgeries requiring faster functional recovery.

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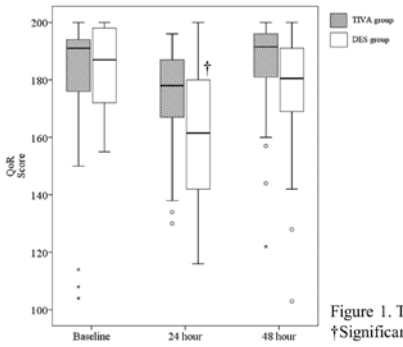

Figure 1. Total QoR-40 score, †Significant difference, P=0.05

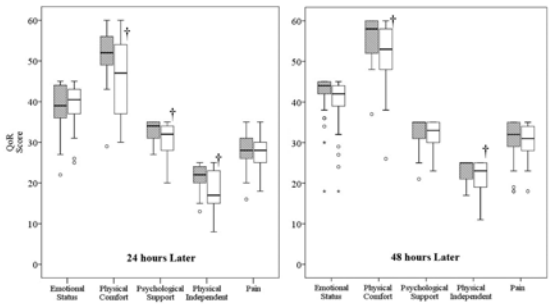

Figure 2. QoR-40 score completed 24 hours and 48 hours after thyroidectomy. Median values shown as solid line within box of 25th and 75th percentile values. Whiskers represent 5th and 95th percentile values. †Significant difference, p=0.05

Table 1. QoR-40 score after the surgery

		TIVA group	Des group	P-value
24 hours	Emotional Status	40.18±4.83	38.26±5.43	0.107
	Physical Comfort*	51.89±5.89	46.50±8.58	0.002*
	Psychological Support*	32.89±2.76	30.63±3.83	0.004*
	Physical Independence*	21.11±3.38	18.08±4.65	0.002*
	Pain	28.05±4.34	27.05±4.54	0.330
	Total QoR-40*	174.13±17.33	160.53±22.23	0.004*
48 hours	Emotional Status	42.00±5.29	40.03±6.32	0.144
	Physical Comfort†	55.92±4.98	51.89±7.53	0.008†
	Psychological Support	32.79±3.49	31.97±3.58	0.317
	Physical Independence†	23.16±2.51	21.50±3.43	0.019†
	Pain	30.68±4.74	30.45±4.00	0.814
	Total QoR-40	184.55±17.61	175.84±21.25	0.056

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S-48.

A NEW METHOD FOR MEASURING DEPTH OF SEDATION IN BEAGLE DOGS; COMPARISON OF A NOVEL SEDATIVE TO PROPOFOL

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INTRODUCTION: A current challenge in developing novel drugs targeting specific levels of sedation (e.g., moderate sedation) is the lack of sensitive preclinical assays. Loss of righting reflex in rodents and the induction of lateral recumbency in dogs are useful as gross measures of sedation, but not for measuring the depth of sedation.

METHODS: Here we report a novel behavioral method for measuring multiple levels of sedation in beagle dogs. This method uses auditory and somatosensory stimuli of increasing intensity to define four levels of alertness/sedation: 1) Awake, 2) Moderate Sedation, 3) Deep Sedation and 4) General Anesthesia.

RESULTS: Validation studies were performed with propofol and involved the rapid induction of general anesthesia (6 mg/kg IV over 1 minute) followed by sequential decrementing constant rate infusion steps (400 – 105 µg/kg/min), each lasting 50 minutes. Behavioral testing occurred after the bolus administration and at the 45 minute time point of each constant rate infusion step. Test article plasma concentration was measured 3 minutes after the bolus and at 15 minute intervals throughout the study. When plasma concentrations of propofol were normalized to the highest value observed during normal alertness (awake), small increases were required to achieve moderate sedation (MS, 1.6-fold), deep sedation (DS, 1.8-fold), and general anesthesia (GA, 2.5-fold). In contrast, the novel synthetic neuroactive steroid (NAS) sedative, SGE-746, exhibited a wider exposure-response relationship than propofol. When normalized to the test article plasma concentration upon recovery from sedation (while awake), much larger increases were required to achieve moderate sedation, deep sedation, and general anesthesia with SGE-746 (MS: 4.2-fold, DS: 5.3-fold, GA: 7.3-fold) relative to propofol (Figure 1).

CONCLUSIONS: Results of these studies recapitulate in dogs the clinical observation that small increases in propofol exposure result in a rapid transition through multiple depths of sedation. In addition, the method presented here is useful for developing sedatives that target specific depths of sedation.

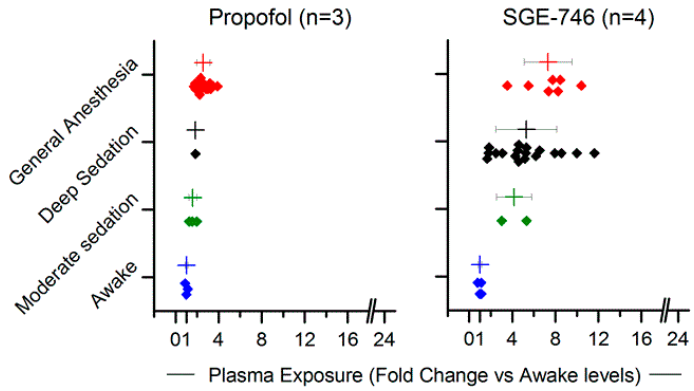

Figure 1. Plasma concentrations at each level of sedation were normalized to the plasma exposure measured at recovery from sedation (awake). Note that the fold increase in exposure required to move from moderate sedation to general anesthesia is larger (with shallower exposure-response) for the synthetic neuroactive steroid SGE-746 relative to propofol. Diamonds represent individual measurements. Crosshairs and whiskers are mean±stdev.

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S-49.

PROPOFOL CONFERS CARDIOPROTECTION VIA HO-1 DEPENDENT STAT3 ACTIVATION IN NORMAL RATS BUT VIA ADIPONECTIN DEPENDENT STAT3 ACTIVATION IN TYPE 1 DIABETIC RATS

AUTHORS: H. Li[1], X. Mao[1], M. G. Irwin1,[2], G. T. Wong[1,2], A. S. Clanachan[3], P. M. Vanhoutte[2,4], Z. Xia[1,2,5]

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INTRODUCTION: Ischemic heart disease leads to an exceedingly high mortality, especially in patients with diabetes. Propofol, an anesthetic with antioxidant and peroxynitrite scavenging properties, when given during early reperfusion (propofol postconditioning, PPC) attenuates myocardial ischemia/reperfusion injury (IRI)[1]. However, the underlying mechanism of PPC cardioprotection is unclear. Moreover, diabetic heart is more vulnerable to IRI and not sensitive to postconditioning (IPost) cardioprotection with unclear mechanism[2]. The aims of this study were to examine whether PPC cardioprotection is mainly achieved via scavenging peroxynitirite, and whether PPC is effective in diabetes. Further, we aimed to study the role of heme oxygenase-1 (HO-1) and signal transducer and activator of transcription 3 (STAT3), key proteins in IPost cardioprotection in PPC, and their association with adiponectin (APN), a molecule with anti-diabetic property.

METHODS: Control (C) and streptozotocin induced diabetic (D) adult Sprague-Dawley rats were subjected myocardial IRI induced by 30min coronary occlusion followed by 2 hours of reperfusion, without or with PPC [perfused with propofol, 2mg/kg body weight], FeTPPS (peroxynitrite scavenger, 10mg/kg), or SIN-1 (peroxynitrite generator, 1.5 mg/kg) for 15min at the onset of reperfusion. Some of the D rats were injected with APN adenovirus (1X109 pfu) 7 days before inducing IRI. Cultured rat cardiac H9C2 cells exposed to normal glucose (NG, 5mM) or high glucose (HG, 30 mM) were subjected to 45min hypoxia and 90min reoxygenation (H/R) without or with HO-1, STAT3, or APN gene knock-down achieved by siRNA infection.

RESULTS: PPC significantly reduce post-ischemic myocardial infarct size and plasma creatine kinase-MB release, accompanied with improved cardiac functions manifested as increased end systolic pressure and dP/dtmax, decreased end diastolic pressure and dP/dtmin in C rats (all $P<0.05$ PPC vs. C), concomitant with decreased peroxynitrite production and increased cardiac HO-1 and STAT3 phosphorylation (p-STAT3) at site Tyr705. All these changes were enhanced by the FeTPPS but abolished by SIN-1 (all $P<0.05$ PPC vs. C). Similarly, PPC significantly reduced post-hypoxic lactate dehydrogenase release and apoptotic cells in cultured H9C2 cells exposed to NG, where these cellular protection of PPC were cancelled by either HO-1 or STAT3 gene knock-down. However, cardioprotective effects of PPC were abolished in D rats and HG treated H9C2 cells, which was associated with decreased APN. APN supplementation restored PPC cardioprotection in D rats or HG treated cells, accompanied with increased p-STAT3 but not HO-1 expression, while STAT3 or APN gene knockdown but not HO-1 gene knockdown abolished APN-mediated restoration of PPC cardioprotection.

CONCLUSIONS: Under normal condition, PPC confers cardioprotection by HO-1-dependent STAT3 activation subsequent to reducing peroxynitrite, while under hyperglycemic condition, PPC confers cardioprotection via APN-dependent STAT3 activation.

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S-50.

CALABADION II REVERSES STEROIDAL NEUROMUSCULAR BLOCKING AGENTS FASTER THAN SUGAMMADEX AND REVERSES THE EFFECTS OF BENZYLISOQUINOLINES, WITHOUT ALTERING THE EFFECTS OF SUCCINYLCHOLINE IN RATS

AUTHORS: I. Moreno Duarte[1], F. Haerter[1], J. Simons[1], D. Diaz Gil1, K. Eikermann-Haerter[2], L. Isaacs[3], E. Matthias[1]

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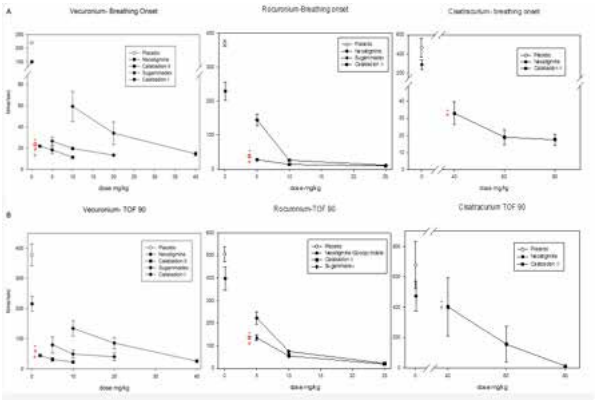
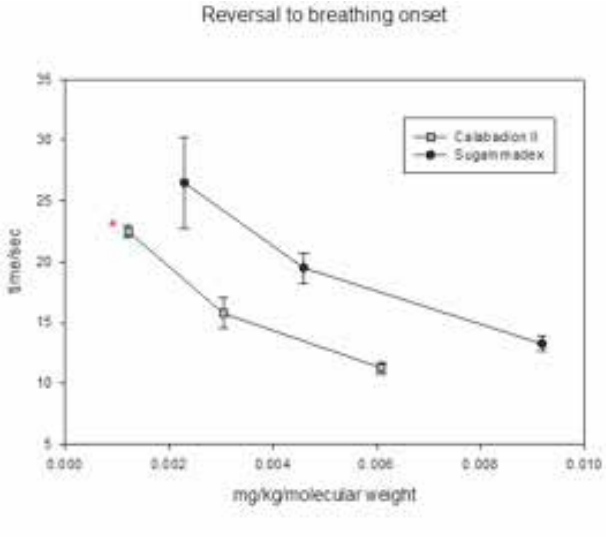
BACKGROUND: Neuromuscular blocking agents (NMBA) are used in more than 400 million patients each year. The NMBA-associated increase in vulnerability for respiratory complications[1] is not ameliorated by the use of Neostigmine, a non-selective reversal agent[2]. Recently, the acyclic Cucurbit[n]uril-type molecular container Calabadion I was reported to reverse Rocuronium and Cisatracurium with a modest binding affinity[3]. Here we present a new reversal agent (Calabadion II) with higher binding affinity to non-depolarizing NMBA. The main aim of this study is to evaluate the dose-response relationship of Calabadion II in reversing non-depolarizing NMBA compared to the effects of other available reversal agents. We also evaluated the effects of previous Calabadion reversal of non-depolarizing NMBA on the effects of subsequent succinylcholine injection.

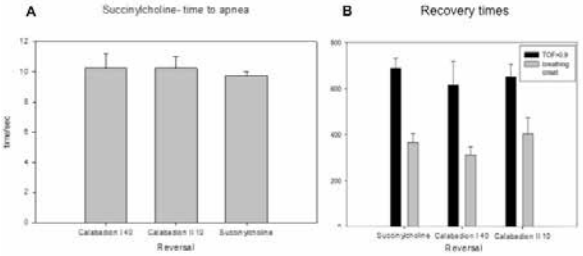
METHODS: In a translational pharmacophysiological interaction trial, 105 tracheotomized rats were instrumented and neuromuscular transmission was quantified by acceleromyography. We administered the 2-fold ED90 of three NMBAs (Vecuronium, Cisatracurium, and Rocuronium) and tested the effects of different doses of four reversal agents (Neostigmine/Glycopyrrolate, Sugammadex, Calabadion I, Calabadion II) or saline as a placebo administered 30 seconds after onset of apnea. Blood pressure and arterial blood gases were measured. Succinylcholine was administered after high-dose Calabadion reversal in a subgroup of 13 rats 30 seconds after recovery from Vecuronium-induced neuromuscular blockade.

RESULTS: 1). Effectiveness on steroid-induced NMBA reversal: Following the administration of Rocuronium and Vecuronium, dose-response curves of Calabadion II reversal (Figure 1) were significantly shifted to the left compared with placebo, Neostigmine/Glycopyrrolate, Sugammadex and Calabadion I ($p<0.05$). Adjusting by molecular weight, the dose-response curve of Calabadion II reversal of Vecuronium was significantly shifted to the left compared to Sugammadex ($p<0.05$; Figure 2). 2). Effectiveness on benzylisoquinoline-induced neuromuscular blockade reversal: Calabadion II reversed Cisatracurium faster than Calabadion I, Placebo and Neostigmine, and its dose-response relationship was shifted to the right compared to their effectiveness to reverse steroidal NMBA (Figure 1) 3). Onset of apnea and recovery times following Succinylcholine injection were not statistically different among the rats pre-treated with Calabadion I or II (Figure 3).

CONCLUSION: Calabadion II is a selective broad spectrum reversal agent for non-depolarizing NMBA including both, steroids (with an improved pharmacokinetic profile compared with Sugammadex) and benzylisoquinolines. Previous Calabadion I and II administration does not affect Succinylcholine-induced NMBA, indicating that Succinylcholine can be safely and effectively administered following Calabadion reversal.







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Cardiovascular Anesthesiology

S-51.

PERIOPERATIVE ADULT CARDIAC SURGERY BLOOD UTILIZATION IN THE POST APROTININ ERA: A SINGLE CENTER, 4 YEAR, 634 PATIENT RETROSPECTIVE REVIEW.

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INTRODUCTION: Cardiac surgery consumes 20% of the nations blood supply. After FDA withdrawal of Aprotinin in 2007, lysine analogues are the only prophylactic anti fibrinolytics available to reduce bleeding. To evaluate and manage post Aprotinin blood transfusion needs better, we investigated our blood utilization [up to 72 hours postoperatively] from 2009 to 2012.

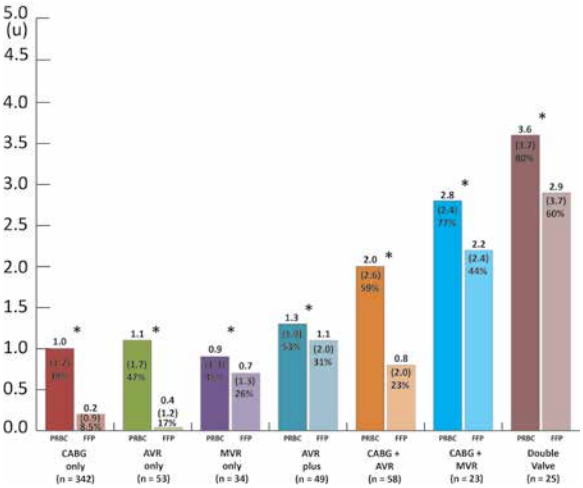
STUDY DESIGN: A retrospective, single center, observational study.

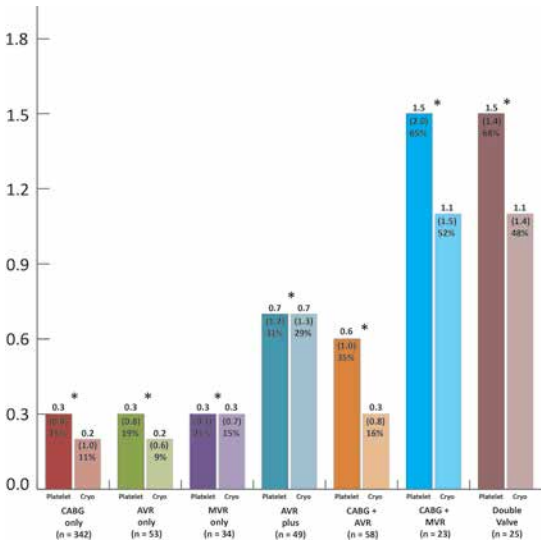
METHODS: After IRB approval, data were collected for 634 patients. Patients who underwent cardiac surgery with CPB were included. Patients received Ɛ -aminocaproic acid with 10 g as the initial dose, followed by 2 g/hour by infusion. CPB management included a normothermic systemic temperature maintained at 37 C, α-stat pH management, targeted mean perfusion pressure between 50-70 mm Hg and pump flow rates of 2.0-2.5 L/min/m2. Heparin anticoagulation dosage was determined utilizing Hepcon HMS Plus (Medtronic Inc). During CPB, pericardial shed blood was salvaged into the cardiotomy suction reservoir and re-infused via the CPB circuit as long as the patient was anticoagulated. Post-CPB blood salvage and reinfusion was achieved by utilizing a continuous auto- transfusion system (C.A.T.STM). Data was reported as mean ± standard deviation. For continuous variables we employed an Analysis of Variance test for comparing groups with respect to their mean values. Tukey HSD test was used as a post-hoc test for comparing groups pairwise while maintaining the error rate at 5%. For categorical variables we analyzed the data using a Chi-square method for independent group comparisons. P value of less than 0.05 was considered statistically significant.

RESULTS: Figures 1-5 patient demographics/blood/colloid utilization, 8 hour CTO, and CSB administered. **A)** Intraoperative. **PRBC** administration for all groups was 20.0%. CABG or MVR only groups had the lowest usage at 15.0%, (P<.0001). Highest utilization was for CABG+MVR group at 50.0%, (P<.0001). **FFP** administration for all groups was 11.0%. Lowest utilization was for CABG group at 3.0%, (P<.0001). Highest utilization was for double valve replacement group at 52.0%, (P<.0001). **Platelet** administration for all groups was 14.0%. Lowest utilization was for CABG only group at 8.0%, (P<.0001). Highest utilization was for CABG+MVR, and double valve replacement groups at 48.0%, (P<.0001). **Cryoprecipitate** administration for all groups was 8.0%. Lowest utilization was for the CABG only or MVR groups at 4.0 and 3.0% respectively, (P<.0001). Highest utilization was for double valve replacement group at 52%, (P<.0001). **B)** Intraoperative hextastarch and 5% albumin utilization was 8% and 73% respectively. **C)** For all patients, mean cell saved blood administered, and 8 hour CTO cc (SD) was 716,(386)cc and 455,(338)cc. **D)** Mean length of stay was 8.0,(5.9),5-8 days, highest for double valve replacement patients 14,(11),8-16 days (P<.05).

CONCLUSIONS: In the post Aprotinin era, despite efforts to reduce blood transfusions, administration of PRBC, FFP, platelet, and cryoprecipitate for all patient groups up-to 72 hours postoperatively was 47%, 18%, 24%, and 16%.

Characteristics	*Median (IQR) or %*
A) Patient Demographic	
Age (years)	68 (59-75)
Gender (M/F)	67%/33%
BSA (meters)^2	2.01 (1.84-2.15)
Diabetic	30%
Pre-operative EF%	60% (50%-65%)
B) Medications	
ASA	78%
ACE Inhibitors	43%
Beta Blockers	81%
Amiodarone	16%
Statins	81%
Clopidogrel	10%
C) Intraoperative data	
CPB (minutes)	116.4 (88.3-157.2)
Cross clamp time (minutes)	88.2 (65.3-126.3)
IABP use	4%
D) Postoperative data	
Time to extubation (hours)	5.1 (3.9-9.2)
Total length of stay (days)	8 (5-8)
% patients alive 30 days post surgery	97%





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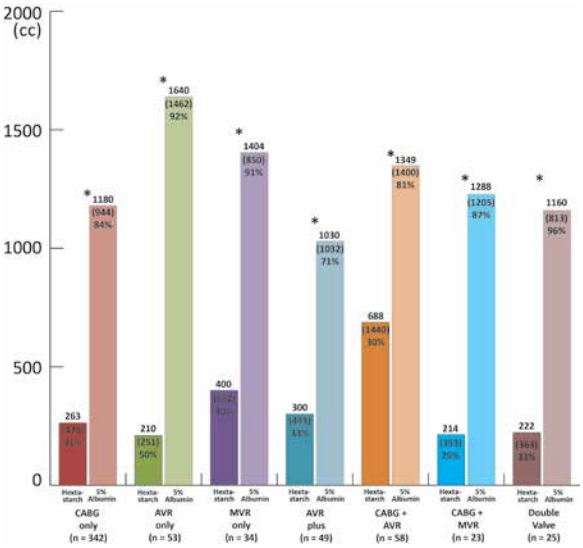

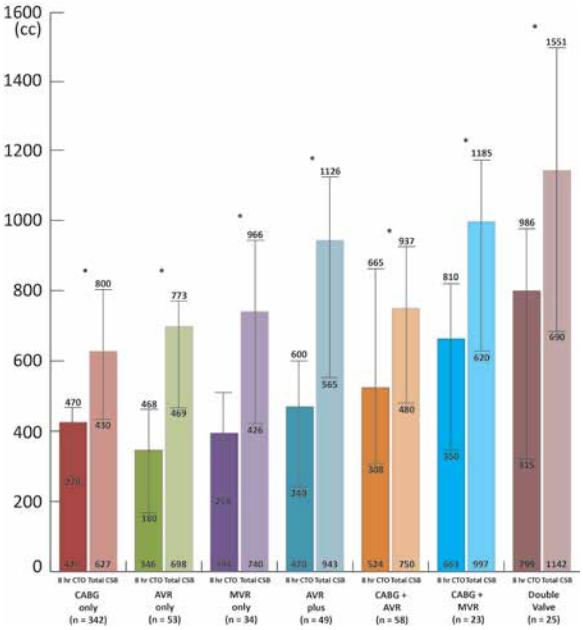

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S-52.

DEXMEDETOMIDINE DOES NOT PREVENT POSTOPERATIVE ATRIAL FIBRILLATION AFTER LUNG CANCER SURGERY

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INTRODUCTION: Postoperative atrial fibrillation (AF) is a common complication after thoracic surgery[1]. Although the physiopathogenesis of this arrhythmia is poorly understood in the context of non-cardiac surgery; catecholamines, as part of the so called surgical stress response, have been speculated to be of the main factors.[1] Dexmedetomidine (DEX), a selective alpha2-agonist, strongly modulates the activity of the sympathetic system which is significantly increased during surgery; hence our hypothesis is that the use of intraoperative catecholamines during lung cancer surgery reduces the incidence of postoperative AF.

METHODS: After obtaining Institutional Review Board approval from our institution, we reviewed electronic medical records from patients who underwent lung cancer resection within 2004 and 2008. We obtained medical information regarding age, gender, body mass index, ASA status, co-morbodities, preoperative medications and the use of DEX intraoperatively. We excluded patients younger than 18 years-old and with history of chronic AF. Descriptive statistics including mean, standard deviation, median, and range for continuous variables are provided. Frequency counts and percentages for categorical variables are provided. Fisher's exact test or Chi-square test was used to evaluate the association between two categorical variables. Wilcoxon rank sum test was used to evaluate the difference in a continuous variable between patient groups. Logistic regression models were used for multivariate analysis to include important and significant covariates. Statistical software SAS 9.1.3 (SAS, Cary, NC) and S-Plus 8.0 (TIBCO Software Inc, Palo Alto, CA) were used for all the analyses.

RESULTS: We collected data from 703 patients with the mean age of 64.69 +/- 10.53 years (Table 1). The overall rate of postoperative AF was 19.35% (n= 136) with a mean onset 3.01 +/- 2.03 days. The rate of conversion to normal sinus rhythm after treatment was 97.79% and recurrence of AF was 94.0%. All patients had general balanced anesthesia. Two-hundred and four (29.02%) patients received DEX intraoperatively, the reminder did not. Our analysis demonstrated that there were more male (60.8%) in the DEX group than in the control group (50.7%, p=0.015). The incidence of postoperative AF was comparable and not statistically significant (p=0.46) between DEX (21.1%) and non-DEX (18.6%) treated patients. The mean onset time of the arrhythmia was similar in both group of patients (DEX: 2.93 +/- 2.49 days versus non-DEX: 3.05 +/- 1.79 days, p=0.1465). The multivariate analysis showed that male gender, age and preoperative use of non-dyhydroperidine was associated with postoperative AF (table 2)

CONCLUSION: The use of dexmedetomidine intraoperatively was not associated with a lower incidence of postoperative AF after lung cancer surgery. Our study has several limitations. First, this a retrospective study; hence, there are unknown factors that may have affected our results. Second, data on betablockers administration was not available.

[1] Semin Thorac Cardiovasc Surg. (22) 310-20, 2010.

[2] Curr Pharm Des. (18) 6257-65, 2012.

Table 1: Demographic and outcome variables (unvariate analysis).

Covariate		No DEX (n=499)	DEX (n=204)	p-value
Age, mean (SD)	Years	64.95(10.42)	64.03(10.79)	0.27
Gender	F	246 (49.3%)	80 (39.2%)	0.015
	M	253 (50.7%)	124 (60.8%)	.
BMI, mean (SD)		26.73 (5.18)	27.29 (5.32)	0.133
ASA	2	50 (10%)	24 (11.8%)	0.3274
	3	416 (83.4%)	172 (84.3%)	.
	4	33 (6.6%)	8 (3.9%)	.
Diabetes mellitus	N	456 (91.4%)	180 (88.2%)	0.1971
	Y	43 (8.6%)	24 (11.8%)	.
Systemic hypertension	N	275 (55.1%)	112 (54.9%)	0.9598
	Y	224 (44.9%)	92 (45.1%)	.
Coronary artery disease	N	416 (83.4%)	167 (81.9%)	0.6305
	Y	83 (16.6%)	37 (18.1%)	.
Creatinine > 2 mg/dL	N	493 (98.8%)	203 (99.5%)	0.6798
	Y	6 (1.2%)	1 (0.5%)	.
Chronic obstructive	N	422 (84.6%)	169 (82.8%)	0.5704
pulmonary disease	Y	77 (15.4%)	35 (17.2%)	.
Stroke	N	483 (96.8%)	197 (96.6%)	0.8791
	Y	16 (3.2%)	7 (3.4%)	.
Preoperative statins	0	348 (69.7%)	134 (65.7%)	0.2935
	1	151 (30.3%)	70 (34.3%)	.
Preoperative	0	477 (95.6%)	200 (98%)	0.1842
Nondihydropyridines	1	22 (4.4%)	4 (2%)	.
Postoperative atrial	0	406 (81.4%)	161 (78.9%)	0.4571
fibrillation	1	93 (18.6%)	43 (21.1%)	.
Atrial fibrillation onset, mean (SD)	Days	3.05(1.79)	2.93(2.49)	0.146
Hospital length of stay, mean (SD)	Days	7.61(6.16)	8.26(7.04)	0.585

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S-53.

PROSPECTIVE RANDOMIZED CLINICAL TRIAL COMPARING ROUTINE INTRAOPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAPHY TO STANDARD CARE DURING RADICAL CYSTECTOMY

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AFFILIATION: Department of Anesthesia and Critical Care, The University of Chicago Medicine, Chicago, IL

INTRODUCTION: Radical cystectomy is an invasive surgery often performed on patients who have multiple co-morbidities, and can result in significant morbidity and mortality rates (45% and 3%, respectively), making the maintenance of intraoperative hemodynamic stability more important/challenging.[1,2] We hypothesized that transesophageal echocardiography (TEE) might be helpful in monitoring patient's volume status and contractility to guide management. Thus, a prospective randomized clinical trial was developed to compare the use of intraoperative TEE to standard care.

METHODS: A clinical trial was performed after IRB approval/ informed consent was obtained. Patients undergoing elective radical cystectomy were prospectively randomized into two groups, the first assigned to a TEE board-certified cardiac anesthesiologist who utilized TEE for monitoring throughout the intraoperative period. The second group was assigned to a general anesthesiologist who did not use TEE. Both groups received standardized perioperative care, with the same anesthetic technique, medications, and mechanical ventilation parameters given to each, with the goal of extubation at the end of the procedure.

RESULTS: A total of sixty patients were studied. Each group had comparable preoperative characteristics (i.e. age, height, weight, gender, and ASA classification). Intra-operatively, they received similar resuscitation using crystalloid (TEE 3528 vs. 4090 cc), colloid (TEE 688 vs. 697), and pRBCs (TEE 0.8 vs. 1.8 units). They also had comparable wound closure arterial oxygenation (TEE 275 mmHg vs. 295 mmHg). All 28 TEE patients were extubated in the operating room, but 3 of the 32 patients in the control group required postoperative mechanical ventilation. The TEE group had 11 morbidities/ 0 mortalities while the control group had 13 morbidities/ 1 mortality. While differences were not statistically significant, TEE patients had a lower mean ICU Length of Stay (LOS) (0.8 days vs. 1.1 days) and Hospital LOS (9.0 days vs. 10.6 days) when compared to non-TEE monitored patients. These results seem to indicate that the patients who received TEE monitoring required less postoperative mechanical ventilation and were discharged from the ICU/Hospital sooner than their counterparts.

CONCLUSIONS: Radical cystectomy is a surgery associated with major blood loss in high-risk patients. Although the use of a cardiac anesthesiologist utilizing TEE might be assumed to be advantageous for these patients when compared to monitoring by a general anesthesiologist without TEE, our study found that there were no significant differences between groups in terms of intraoperative fluid management. However, the trends toward less intraoperative pRBC use, fewer patients requiring postoperative mechanical ventilation, and earlier ICU/Hospital discharge in patients managed by a cardiac anesthesiologist with intraoperative TEE are intriguing and require further study.

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2. Eur Urol 51:397-402, 2007

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S-54.

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S-55.

PREOPERATIVE PLATELET COUNT IMPROVES TEG-BASED PREDICTION OF THROMBOCYTOPENIA AFTER CARDIOPULMONARY BYPASS

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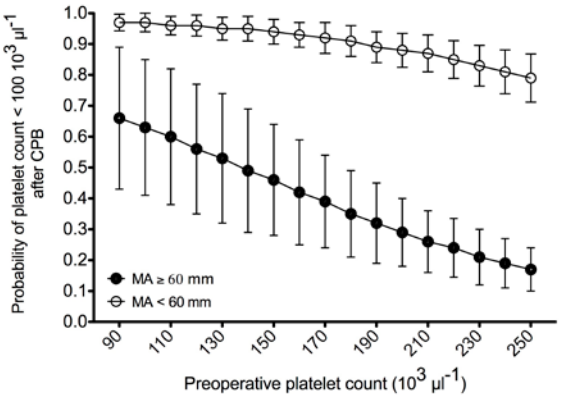
INTRODUCTION: Coagulation is frequently deranged after on-pump cardiac surgery. Early goal-directed therapy in bleeding patients is thought to reduce overall exposure to blood products and to improve outcome. Thromboelastography (TEG) has the advantage of being readily available and to assess whole blood clotting. However its sensitivity for detecting a low platelet count and a low fibrinogen level might be low in the perioperative setting[1]. We tested the hypothesis that taking into account the preoperative platelet count in addition to TEG parameters obtained after cardiopulmonary bypass (CPB) would improve the sensitivity to detect a low platelet count after CPB.

METHODS: After IRB approval, data were retrospectively collected on 67 consecutive adult patients considered at risk of bleeding after cardiac surgery involving CPB. Preoperatively, a platelet count and usual clotting tests were available for all patients. Heparinase TEG (TEG® 5000, Haemoscope Corp®, IL, USA), platelet count and usual clotting tests were obtained after CPB, 10 minutes after protamine administration. TEG parameters associated with a postoperative platelet count < 100 103 µl-1 were identified in a stepwise backward multiple logistic regression model with a P value threshold of 0.05 for leaving the model. The nested model including TEG parameters only was then compared with a full model comprising both the preoperative platelet count and the TEG parameters using the likelihood ratio test.

RESULTS: The maximal amplitude (MA) was the only TEG parameter significantly associated with a platelet count lower than 100 103 µl-1 after CPB ($P < 0.001$). In this TEG-based model, best sensitivity (88.6 %) and specificity (81.2 %) for detecting patients with platelets ≤ 100 103 µl-1 were obtained using MA < 60mm as a threshold value. Adding the preoperative platelet count to the TEG-based model resulted in a significant improvement of the model ($P=0.018$). Figure 1 shows how the preoperative platelet count affects the probability of having a platelet count < 100 103 µl-1 after CPB according to whether MA is superior to 60 mm or not.



CONCLUSIONS: Taking into account the preoperative platelet count refines the TEG-based diagnostic probability of thrombocytopenia after CPB. The impact of the preoperative platelet count on the probability of thrombocytopenia after CPB seems particularly important when MA is above 60 mm. The impact of the fibrinogen level on the relationship between MA and platelet count deserves further investigations.

REFERENCE:

1. Thromboelastography (TEG(R)) compared to conventional coagulation tests in surgical patients--a

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S-56.

IS TRANSFUSION ASSOCIATED WITH DECREASED GRAFT PATENCY AFTER CARDIAC SURGERY?

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AFFILIATION: [1]Anesthesiology, University of Michigan, Ann Arbor, MI, [2]Cardiothoracic Surgery, University of Toledo, Toledo, OH, [3]Cardiac Surgery, University of Michigan, Ann Arbor, MI, [4]Internal Medicine, American University of Beirut, Beirut, Lebanon

INTRODUCTION: Blood transfusion has been repeatedly associated with increased long-term mortality after coronary artery bypass grafting (CABG),[1] but a mechanism has not been found. We hypothesized that transfusion of red blood cells (RBC) would be associated with earlier graft occlusion.

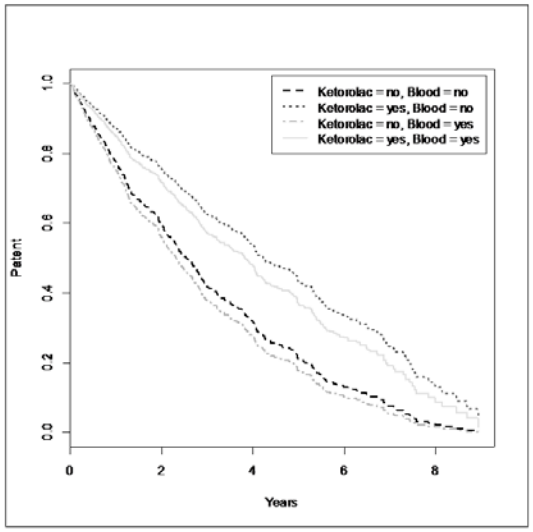
METHODS: After CABG, coronary angiograms were done by the patients' cardiologists based on the development of symptoms suggestive of recurrent coronary artery disease. Angiograms were performed and read by the patients' cardiologists, who were generally unaware of the patients' perioperative transfusion history. Cox modeling with adjustment for demographics, comorbidities, and medicine use and with stratification to control for the different number of grafts per patient was used to determine the hazard ratios. $P < .05$ and 95% confidence intervals that excluded 1 denoted statistical significance.

RESULTS: 940 patients with 3 + 1 (mean + standard deviation) grafts were studied 2.4 + 2.0 yr after CABG. 539 of 940 patients (57%) had 1 or more occluded grafts. In the initial model, there was a trend to earlier graft closure (hazard ratio = 1.22, 95% CI = 0.96 - 1.55, p = .11) from RBC with a small non-significant RBC-ketorolac interaction (1.05, 0.73 - 1.52, p = 0.80). With the interaction term removed, use of RBC was statistically associated with graft closure (1.24, 1.03 -1.50, p = .02). In the final model, RBC shortened time to graft occlusion (Table & Figure), while ketorolac delayed graft occlusion.

CONCLUSION: After adjustment, RBC had a small but statistically significant association with earlier graft occlusion, that was partially ameliorated by ketorolac.

REFERENCE: 1: Ann Thorac Surg 2002;74:1180-6

Median Time to Graft Occlusion		
3.822.964.88	Time (yr)	95% confidence interval (yr)
Ketorolac = no, RBC = no	2.55	2.223 - 2.90
Ketorolac = yes, RBC = no	4.24	3.86 - 4.97
Ketorolac = no, RBC = yes	2.32	1.98 - 2.81
Ketorolac = yes, RBC = yes	3.82	2.96 - 4.88



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S-57.

ESTIMATION OF CARDIAC OUTPUT BY NINE DIFFERENT PULSE CONTOUR ALGORITHMS IN CARDIAC SURGERY PATIENTS

AUTHORS: O. Broch[1], A. Carstens[2], M. Gruenewald[3], M. Albrecht[2], J. Renner[4]

AFFILIATION:[1]Department of Anesthesiology and Intensive Care Me, University Schleswig-Holstein, Campus Kiel, Kiel, Germany, [2]Department of Anesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein, Kiel, Germany, [3]Department of Anesthesiology and Intensive Care Medicine, University Hospital SH, Kiel, Kiel, Germany, [4]Depaertment of Anesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein, Campus Kie, Kiel, Germany

INTRODUCTION: Several studies could demonstrate that goal-directed perioperative optimization of cardiac output (CO) is associated with beneficial effects on both morbidity and the length of stay on the intensive care unit[1]. With respect to risk-benefit ratio, invasive procedures like right heart catheterization are not always justified or practicable. Therefore, less-invasive, simple to interpret and quickly available continuous monitoring of CO without the need for calibration has gained increasing interest. The aim of our study was to investigate the accuracy of CO generated by nine different pulse contour algorithms (CO_{X1-X9}) in patients undergoing coronary artery bypass grafting (CABG) with CO by transcardiopulmonary thermodilution (CO_{TPTD}).

METHODS: The study was conducted according to the Ethical Principles for Medical Research involving Human Subjects outlined in the Declaration of Helsinki.

15 patients scheduled for elective CABG operation were studied after induction of anesthesia and before starting operation. Each patient was monitored with the PiCCO system (Pulsion® Medical System, Munich, Germany), a central venous line and an esophageal doppler probe with integrated pulse contour algorithms (CardioQ™, Deltex Medical™, Chichester, UK). CO by esophageal doppler was used to calibrate the different pulse contour algorithms. Thereafter, a passive leg raising maneuver was performed. Hemodynamic variables included measurement of CO_{TPTD}, $CO_{Doppler}$ and CO_{X1-X9} before, during and after passive leg raising. Statistical analysis included correlations, Bland-Altman analysis and percentage changes in CO.

RESULTS: There was a significant correlation between $CO_{Doppler,}$ CO_{X1-X9} and $CO_{TPTD.}$ Bland-Altman analysis of $CO^{Doppler}$, CO_{X1-X9} and CO_{TPTD} was represented in Table 1. With respect to percentage changes in CO, all pulse contour algorithms were able to reflect hemodynamic changes with moderate fashion due to the passive leg raising maneuver. However, the oldest algorithm X4 seems to be one of the most accurate methods for measuring CO.

CONCLUSIONS: CO measurement by nine different semi-invasive pulse contour algorithms showed different accuracy providing CO compared with TPTD. Best performance was observed for the oldest algorithm. With respect to hemodynamic changes semi-invasive algorithms showed different ability for tracking trends in CO.

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1. Hamilton MA. Anesth Analg, 2011; 112:1392-402.

Table 1 - Bland-Altman analysis showing 95% limits of agreement, confidence interval and percentage error during passive leg raising (PLR) for cardiac output by esophageal doppler ($CO_{Doppler}$) and nine different pulse contour algorithms (CO_{X1-X9}) compared with CO by transcardiopulmonary thermodilution (CO_{TPTD}).

	PLR					PLR				
	CO Doppler	CO X1	CO X2	CO X3	CO X4	CO X5	CO X6	CO X7	CO X8	CO X9
	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)	(L/min)
Mean (L/min)	2.65	2.59	2.55	2.57	2.57	2.64	2.58	2.6	2.53	2.56
Bias (L/min)	0.09	0.15	0.19	0.17	0.17	0.1	0.16	0.14	0.21	0.18
SD of bias (L/min)	0.65	0.68	0.61	0.61	0.46	0.57	0.59	0.68	0.6	0.59
CI of LOA (L/min)	0.17	0.19	0.21	0.2	0.18	0.17	0.21	0.22	0.19	0.2
95% Limits of agreement (L/min)	-1.37 to + 1.19	-1.48 to +1.18	-1.39 to +1.01	-1.37 to +1.03	-1.07 to +0.73	-1.21 to +1.01	-1.33 to +1.01	-1.48 to +1.19	-1.37 to +0.95	-1.35 to +0.99

$CO_{Doppler}$: cardiac output by esophageal doppler probe; CO_{X1-X9}: cardiac output by different pulse contour algorithms; CO_{TPTD}: cardiac output by transcardiopulmonary thermodilution; CI of LOA: confidence interval of the limits of agreement; PLR: passive leg raising.

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S-58.

INCIDENCE OF POSTOPERATIVE ACUTE RENAL DYSFUNCTIONS DEPENDENT ON SURGICAL PROCEDURE USED IN RADICAL OPERATION FOR ABDOMINAL AORTIC ANEURYSM - OPEN ARTIFICIAL GRAFT REPAIR VS. ENDVASCULAR AORTIC REPAIR

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INTRODUCTION: Generally, renal function is deteriorated after surgery. Especially in patients with an abdominal aortic aneurysm (AAA), the risk of perioperative acute kidney injury (AKI) is high due to background factors and operative site. We compared AKI incidence between open surgical grafing repair (OR) and endovascular aortic repair (EVAR) in patients who underwent operation for an AAA.

METHODS: One hundred ninety-two patients underwent AAA surgery in the period from January 2007 to November 2013 in our institution. Reoperation, thoraco-abdominal aneurysm, simultaneous heart-abdominal surgery, fatal, and dialysis cases were excluded. General anesthesia was administered to all patients. For defining AKI, we used the AKIN criteria published Acute Kidney Injury Network and the severity was also staged using this criteria. Using preoperative serum creatinine (SCr) as a baseline, the maximum SCr level within postoperative day 5 was used for staging, as follows. Stage 1, elevation of more than or equal to1.5 times to 2.0 times or increase more than or equal to 0.3 mg/dL; Stage 2, elevation of 2 times to 3 times; stage 3, elevation of 3 times or more from baseline.

RESULTS: We analyzed 87 patients who underwent open repair surgery and 90 who underwent EVAR. There were no significant differences regarding patient background factors (age, sex, disease history, history of present illness) and anesthetic procedures. In the 87 who underwent open repair surgery (including 13 emergency operations for rupture), AKI developed in 17 (6 emergency cases). As for staging, 11 (3 emergency cases) were classified as Stage 1, 5 (2 emergency cases) as Stage 2, and 1 (emergency case) as Stage 3. Of the 90 EVAR patients (9 emergency cases), AKI developed in 5 (no emergency cases), while 4 and 1 cases were classified as Stage 1 and 2, respectively. There was a significant difference in AKI incidence between the operative procedures regardless of emergency cases or not.($p=0.042$)Hospital stay, ICU stay and the days until a meal start and a walk start after operation were all significant shoter in EVAR patients than in OR patients.(all $p<0.0001$)

DISCUSSION: It is known that deterioration of renal function after AAA surgery is an important complication. Reduced renal blood flow associated with aortic occlusion is considered to be the main cause in cases of OR surgery and contrast-induced nephropathy is the likely cause in EVAR cases. Our findings show that the choice of surgical procedure itself has an effect and highlights the importance of protecting renal function of patients with an AAA.

Conclusion: The postoperative incidence of AKI was significantly reduced in AAA patients who underwent an EVAR procedure.

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S-59.

A DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED TRIAL OF PERIOPERATIVE INTRAVENOUS ACETAMINOPHEN IN CARDIAC SURGERY

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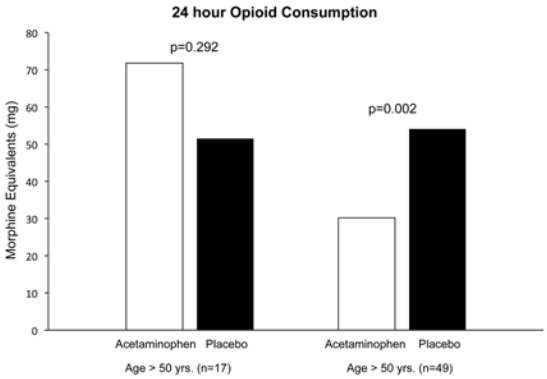
INTRODUCTION: Cardiac surgery patients experience significant pain during the first 24 hours after surgery[1], leading to increased sympathetic nervous system activation and a heightened hormonal stress response. Improved pain control after sternotomy has the potential to reduce adverse patient outcomes[2]. Intravenous (IV) acetaminophen was recently approved by the Food and Drug Administration for the management of moderate to severe pain as an adjunct to opioids and has the potential to improve acute postoperative analgesia after cardiac surgery.

METHODS: A total of 68 patients were enrolled in this single center, double-blind, randomized, placebo controlled trial. 2 of 68 patients were excluded due to duration of mechanical ventilation longer than 24 hours. 66 patients were randomized to receive either 1000 mg of IV acetaminophen or placebo immediately after induction (but prior to incision), at the end of surgery, and then every 6 hours for the first 24 hours in the intensive care unit (ICU). Postoperative pain management was administered per standard cardiac surgery protocol. Total opioid consumption for 24 and 48 hours post sternotomy was collected from the electronic medication administration record and converted into morphine equivalents. The incision pain scores using the numerical response scale and the extent of mechanical hyperalgesia was assessed at 24 and 48 hours post sternotomy by investigators (PR and SJ) per previously described methods[3]. Patient satisfaction survey was also administered by the investigators (PR and SJ) at 48 hours post sternotomy.

RESULTS: The baseline characteristics of the subjects in the acetaminophen and placebo groups were similar. The differences in postoperative 24-hour opioid consumption, extent of mechanical hyperalgesia and pain scores (at rest and with movement) were not statistically significant between the acetaminophen and placebo groups (p=0.061, p=0.473, p=0.724 and p=0.638, respectively). In addition, at 48 hours post sternotomy, there were no statistically significant differences in opioid consumption, extent of mechanical hyperalgesia and pain scores between the acetaminophen and placebo groups (table 1). However, in patients over the age of 50 years (n=49), there was a statistically significant decrease in postoperative 24-hour opioid consumption among those patients who received IV acetaminophen vs. placebo (p=0.002; figure 1). There was no statistically significant difference in 48-hour survey responses between the acetaminophen and placebo groups.

	Acetaminophen Group mean ±SD (n)	Placebo Group mean ±SD (n)	p-value
24-hour opioid consumption (as morphine equivalents in mg)	42.8 ±28.9 (33)	53.5 ±25.9 (33)	0.061
24-hour extent of mechanical hyperalgesia	3.2 ±2.7 (32)	3.8 ±3.7 (32)	0.473
24-hour incision pain scores at rest (NRS)	3.7 ±2.3 (33)	3.9 ±2.3 (31)	0.724
24-hour incision pain scores with movement (NRS)	6.0 ±2.5 (33)	6.3 ±2.5 (30)	0.638
48-hour opioid consumption (as morphine equivalents in mg)	32.0 ±16.6 (33)	34.6 ±17.1 (32)	0.532
48-hour extent of mechanical hyperalgesia	3.6 ±2.5 (33)	3.5 ±3.1 (33)	0.443
48-hour incision pain scores at rest (NRS)	2.0 ±1.8 (32)	2.4 ±2.2 (30)	0.397
48-hour incision pain scores with movement (NRS)	4.6 ±2.0 (32)	5.1 ±2.9 (30)	0.399
48-hour overall pain experience response (Likert scale)	2.8 ±0.9 (23)	2.3 ±1.2 (23)	0.105



CONCLUSION: The addition of IV acetaminophen in the acute pain management of cardiac surgery patients at our institution did not result in a statistically significant decrease in opioid consumption, the extent of mechanical hyperalgesia or pain scores. However, in patients older than 50 years of age, IV acetaminophen significantly reduced opioid consumption in the first 24 hours following sternotomy.

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S-60.

WITHDRAWN.

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S-61.

EVALUATION OF DIASTOLIC DYSFUNCTION IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE REPLACEMENT.

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INTRODUCTION: Diastolic dysfunction in patients with aortic stenosis is associated with increased mortality[1, 2]. The validity of the American Society of Echocardiography (ASE) recommendations for evaluating diastolic function[3] in patients undergoing transcatheter aortic valve replacement (TAVR) has yet to be defined.

METHODS: The ASE recommendations were retrospectively assessed in 229 consecutive patients who underwent TAVR with the Edwards SAPIEN balloon-expandable prosthetic valve. Patients with mitral or aortic regurgitation >1+ were excluded. A decreased septal (<8 cm/s) and lateral (<10 cm/s) early diastolic myocardial velocity (e') and elevated left atrial volume index (LAVI ≥34 ml/m2) were used for the diagnosis of diastolic dysfunction. Grading was performed using at least two of the ASE diastolic parameters: the transmitral early (E) to late (A) filling velocity (E/A) ratio, E deceleration time (DT), E/e' ratio, pulmonary vein flow (PVF) atrial reversal - A duration (Ar-A), and PVF systolic / diastolic velocity (S/D) ratio.

RESULTS: 91 patients were included in the analysis. Of these, 64 patients (70%) were diagnosed with diastolic dysfunction (grades I to III), while 25 patients (27%) could not meet the three diagnostic parameters for diastolic dysfunction (see table 1). 27 (42%) patients with diastolic dysfunction had decreased ejection fraction (defined as <55%) and 10 (16%) had atrial fibrillation. Depending on the criteria used for classification, there was considerable variation in the number of patients within each diastolic dysfunction grade (see table 2). Analyzing the same criteria in combination failed to provide meaningful classification for the majority of patients.

CONCLUSIONS: The majority of the TAVR patients were diagnosed with grade I diastolic dysfunction (impaired relaxation). This may be due to their relatively preserved ejection fraction. However, the assessment of the severity of diastolic dysfunction varies depending on the criteria utilized. The ASE recommendations for diastolic function evaluation should be examined in larger TAVR cohorts to explore which criteria may be associated with perioperative risk and outcomes.

TABLE 1: Diastolic function assessment

	n (%)
Total patients reviewed	229
Patients meeting inclusion criteria	91 (40%)
• Diastolic dysfunction *[Septal e' <8 cm/s and Lateral e' <10 cm/s and LAVI ≥34 ml/m²]*	64 (70%)
• Normal diastolic function *[Septal e' ≥ 8 cm/s and Lateral e' ≥10 cm/s and LAVI < 34 ml/m²]*	0 (0%)
• Athlete's heart, constriction or normal *[Septal e' ≥ 8 cm/s and Lateral e' ≥10 cm/s and LAVI ≥ 34 ml/m²]*	2 (2%)
• Unclassifiable using the above criteria	25 (27%)

TABLE 2: Grading of diastolic dysfunction

	Criterion	n	Grade I Impaired Relaxation	Grade II Pseudonormal	Grade III Restriction	Classified patients, n (%)
A.	E/A Mean ± SD n (%)	53	E/A <0.8 0.62 ± 0.12 22 (42%)	E/A 0.8-1.5 1.1 ± 0.2 22 (42%)	E/A ≥2 2.3 ± 0.3 5 (9%)	49 (92%)
B.	DT Mean ± SD n (%)	57	DT >200ms 316 ± 95 ms 40 (70%)	DT 160-200ms 184 ± 14 ms 11 (19%)	DT <160ms 137 ± 15 ms 6 (11%)	57 (100%)
C.	E/e' Mean ± SD n (%)	61	E/e'≤8 6.7 1 (2%)	E/e' 9-12 11.3 ± 0.3 4 (7%)	E/e' ≥13 26.8 ± 11.2 56 (92%)	61 (100%)
D.	Ar-A Mean ± SD n (%)	34	Ar-A <0ms -35 ± 21 ms 24 (71%)	Ar-A ≥30ms 33 ms 1 (3%)		25 (74%)
E.	S/D Mean ± SD n (%)	47	S/D >1 1.65± 0.33 25(53%)	S/D<1 0.64 ± 0.18 22 (47%)		47 (100%)
	A, B and C	49	1 (2%)	0	3 (6%)	4 (8%)
	A, B, C, D and E	34	0	0	0	0 (0%)
	Any 2 of A, B and C	64	17 (27%)	8 (13%)	7 (10%)	32 (50%)
	Any 3 of A, B, C, D, E	64	20 (31%)	2 (3%)	7 (11%)	29 (45%)

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S-62.

PREDICTION OF ICU LENGTH OF STAY AFTER CARDIAC SURGERY FROM NEURAL NETWORK ANALYSIS OF PRE-OPERATIVE FACTORS

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INTRODUCTION: We previously presented our application of predictive analytical techniques to estimate ICU length of stay (LOS) after cardiac surgery; the possible prognosticators for this outcome included 36 **pre-incision** variables.[1] We present here our comparison of linear and artificial neural network (ANN) modeling of 28 **pre-operative** variables, in an attempt to identify even earlier factors that may contribute to ICU-LOS.

METHODS: New York Medical College IRB approval was obtained to collect data with complete confidentiality from the entire medical records of a total of 219 patients, to date, who underwent CABG or valve surgeries, or a combination of both. All of the patients underwent surgery with cardiopulmonary bypass. The "Automatic Linear Modeling" module of IBM SPSS Amos 21 statistical software was applied to the following set of a total of 28 pre-operative variables (data collection did not extend beyond the pre-anesthetic assessment):

NOMINAL FACTORS: Use of an ACE inhibitor, beta blocker, or a statin drug; presence/history of atrial fibrillation (Afib), acute coronary syndrome, serum creatinine >1.3, diabetes, heart failure (HF), hypercholesterolemia, hypertension; history of previous cardiac surgery, smoking during previous 5 years; existing pacemaker; pre-operative intra-aortic balloon pump (IABP), cardiac pacing, use of positive inotropic agents; gender; valve surgery included in current operation.

ORDINAL FACTOR: Number of anticipated coronary artery bypass grafts.

CONTINUOUS VARIABLES: Age; body mass index; ejection fraction (EF); hematocrit (Hct); heart rate, systolic pressure, diastolic pressure, pulse pressure, mean arterial pressure.

RESULTS: Linear modeling identified 9 factors of primary importance in relation to LOS; in order of importance, **IABP, gender, age, diabetes, EF, Hct, HF, Afib, inotrope use**. The association of these combined factors with ICU LOS had an r2 value of 0.315, p <0.0001 (Fig. 1). These same 9 factors were then analyzed with the IBM-SPSS ANN module. The r2 value for this analysis was 0.683, p <0.0001 (Fig. 2).

DISCUSSION: Both linear and ANN algorithms are capable of modeling combinations of nominal, ordinal and continuous variable data. However, ANN models appear to have an advantage in prediction accuracy due to the fact that they analyze the importance of all interactions among a set of variables. (Linear models only consider the independent contribution of each variable.) The ANN analysis appeared to predict, with some confidence, the length of stay that might be expected following cardiac surgery. Predictive information of this type may help to anticipate risks and the possible need for interventions in individual patients. Such information may also have value in anticipating the need for ICU resources. The present ANN model must be further evaluated for its prediction accuracy with data that are independent of the trained model.[2]

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FIGURE 1 Linear Model for Prediction of ICU LOS
(From 9 Pre-Operative Variables)

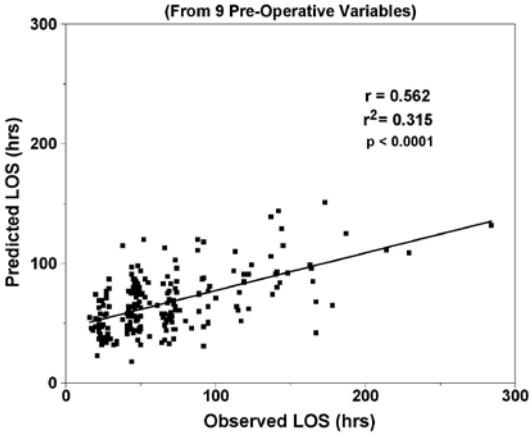
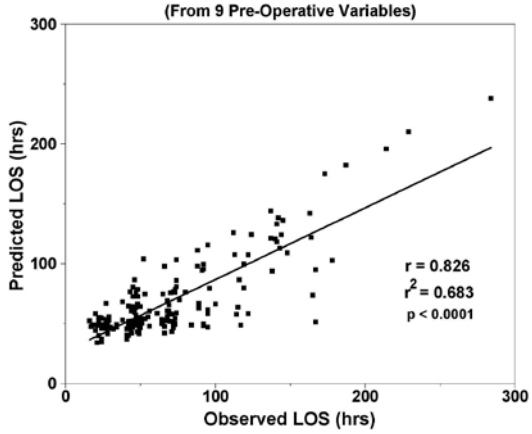


FIGURE 2
Artificial Neural Network Model for Prediction of ICU LOS
(From 9 Pre-Operative Variables)



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S-63.

ANESTHESIA INDUCTION TIME IS PROLONGED BY PROPOFOL INFUSION IN AORTIC REGURGITATION PATIENTS.

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INTRODUCTION: The regurgitant fraction of the stroke volume in severe aortic regurgitation (AR) is associated with a reduced forward bloodflow and increased the left ventricular end diastolic volume. We hypothesize that the intravenous induction of anesthesia might take longer than the competent aortic valve.

METHODS: Institutional Ethical Committee approval was obtained for the clinical study and after written informed consent, consecutive 24 adult male patients were included in two study groups. Group 1 (No AR) (n=12) patients were planned for coronary artery bypass graft with normal aortic valve (AV). Group 2 (AR) (n=12) patients were having aortic regurgitation of grades 3 or 4 and were due for aortic valve replacement. Induction of anesthesia was initiated with infusion of propofol (1%) @0.5ml. kg-1.hr-1and fentanyl (25 µg.ml-1) @200ml.hr-1. We monitored continuously for the heart rate, intra-arterial pressure and bispectral index (BIS). We observed for the clinical end points of induction of anesthesia (loss of verbal command and apnea) and the onset of BIS<60. We analyzed the induction doses of the propofol and fentanyl and hemodynamic changes.

RESULTS: There was a significant ($p<0.05$) difference between the two groups in terms of induction time of anesthesia (319.17±84.33 s in Group 1 vs. 563.33±112.76 s in Group 2). Patients of group 2 (AR) required significantly larger doses of propofol (0.91±0.40 mg.kg-1) than group 1 (0.49±0.17mg.kg-1) patients. Similarly, patients with AR required significantly larger dose of fentanyl (20.82±15.98 µg/kg) than group 1 (9.18±2.92 µg/kg) patients. Hemodynamic response was similar in patients of both groups.

CONCLUSIONS: Authors conclude that during propofol infusion the induction time of anesthesia is significantly prolonged in presence of AR than in patients with competent AV.

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S-64.

INDIVIDUALIZED BLOOD MANAGEMENT IN CARDIAC SURGERY USING POINT-OF-CARE BASED TRANSFUSION ALGORITHM

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INTRODUCTION: Coagulopathy leading to excessive blood loss, blood product transfusion, and adverse outcomes is a major complication of cardiac surgery with cardiopulmonary bypass.[1,2] Current management of coagulopathic bleeding relies on conventional coagulation testing that have long turnaround times[3] and are not able to detect important coagulation defects such as fibrinolysis, platelet dysfunction, or specific factor deficiencies.[4] These shortcomings hamper management, forcing clinicians to delay therapy until the results become available or resort to empiric therapy based on their clinical judgment. These strategies are inefficient and potentially harmful because they can lead to underuse of blood products in some patients, leading to excessive blood loss and possibly re-exploration, and to overuse of blood products in others.[2] Individualized blood management using a transfusion algorithm that employs point-of-care coagulation tests may alleviate these problems.

METHODS: An integrated transfusion algorithm (Figure) that employed viscoelastic (ROTEM) and aggregometric (Platelet Works) point-of-care tests, as well as an objective measure of blood loss, was incorporated into routine practice at our hospital on January 2013. Following REB approval, we retrospectively compared the transfusion and clinical outcomes of patients operated from January to July 2013 (post-algorithm) to those operated on during 2012 (pre-algorithm), using multivariable Poisson regression (with robust confidence limits) to adjust for baseline differences.

RESULT: Patients had similar characteristics pre- and post-algorithm, but transfusion and some adverse events were substantially reduced post-algorithm (Table). Nadir and discharge hemoglobin concentrations were similar, suggesting that reduced transfusions were not due to a more restrictive transfusion strategy.

CONCLUSIONS: Individualized blood management using transfusion algorithm that employs point-of-care coagulation tests can reduce transfusions and improve outcomes. Whether these results are generalizable to other centres, however, needs to be determined.

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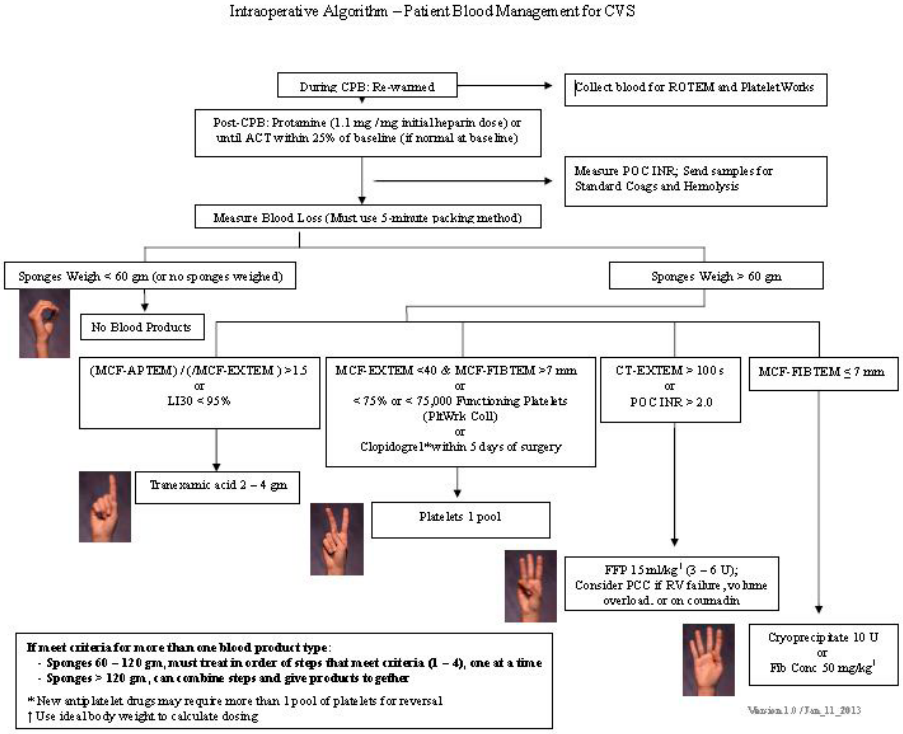

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Table 1: Data on the effectiveness of the POC-based transfusion algorithm

	Pre-algorithm 2012(n = 1303)	Post-algorithm 2013(n = 632)	P-value	RR (95% CI) risk-adjusted
Transfusions				
Received red blood cells	52%	40%	< 0.0001	0.79 (0.72 – 0.87)
Received platelets	34%	19%	< 0.0001	0.56 (0.48 – 0.66)
Received plasma	34%	13%	< 0.0001	0.37 (0.30 – 0.45)
Received cryoprecipitate	4.1%	2.5%	0.09	0.69 (0.39 – 1.22)
Process outcomes (median, 25th and 75th percentiles)				
Chest tube drainage at 24 hours (mL)	450 (340, 610)	420 (320, 580)	0.006	
Lowest hemoglobin during CPB	93 (81, 105)	93 (79, 106)	0.6	
Discharge hemoglobin	98 (91, 107)	98 (91, 106)	0.9	
Clinical Outcomes				
Re-exploration	6.5%	2.9%	0.001	0.48 (0.30 – 0.79)
Major blood loss (≥ 4 RBCs or re- exploration)	20%	11%	< 0.0001	0.51 (0.40 – 0.64)
Refractory coagulopathy	3.4%	1.1%	0.002	0.28 (0.12 – 0.6)
Kidney injury (Stage 2 AKIN)	6.1%	3.3%	0.008	0.48 (0.30 – 0.77)

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S-65.

THE FRACTAL DIMENSION OF SYSTEMIC VASCULAR RESISTANCE

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BACKGROUND: Heart rate variability (HRV) as a marker of cardiovascular function has been a topic of extensive research over the past twenty years. HRV exhibits fractal characteristics in healthy subjects but loses this complexity in critically ill patients. While the HRV has been well examined, there has been little research examining the complexity of other hemodynamic parameters. We hypothesize that systemic vascular resistance exhibits fractal behavior, and in this study analyze the fractal dimension of Systemic Vascular Resistance (SVR) using a non-invasive cardiac output monitor.

METHODS: After IRB approval, analysis of hemodynamic data was conducted using an existing database of hemodynamic data from an unrelated study on bariatric surgical patients. The data was acquired using a Nexfin© device (Edwards Lifesciences BMEYE, Amsterdam, Netherlands). Analysis of complexity in SVR was performed on 88 patients (25 male, 63 female; 21 - 72 years old). Fractal dimension was calculated for SVR by performing best linear fit to the data at multiple time scales. The root mean square error of these linear regressions exhibits a power law scaling. This power was taken to be the fractal dimension of variability[1]The patients were then grouped into quartiles for the dP/dt(max). High and low quartiles were compared using Wilcoxian Rank Sum analysis.

RESULTS : Analysis of complexity in SVR using fractal dimension from Nexfin© data was possible in each of the 88 patients. The fractal dimension of the SVR was significantly different in both the SV (bottom quartile mean 0.708, SD 0.064; top quartile mean 0.648, SD 0.137; p= 0.0044) and dP/dt(max). (bottom quartile mean 0.686, SD 0.078; top quartile mean 0.621, SD 0.068; p= 0.0121).

CONCLUSION: Our pilot study demonstrates a statistically significant difference between the fractal dimension of SVR in quartile analysis based on both SV and dP/dt(max). This is the first time that relationship between fractal complexity of systemic vascular resistance and left ventricle contractility as measured by dP/dt(max) has been documented. The etiology of this statistically significant relationship is unclear. Other authors have demonstrated the complexity of vascular resistance time series.[2] The use of non-invasive technology to assess fractal dimension of additional hemodynamic parameters other than HRV opens a novel arena of cardiovascular study and research.

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Figure 1a: Fractal dimension of SVR in low and high left ventricular contractility quartiles as measured by dP/dT(max)

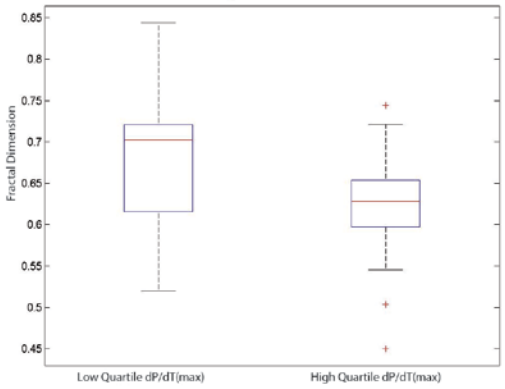

Figure 1b: Fractal dimension of SVR in low and high stroke volume quartiles

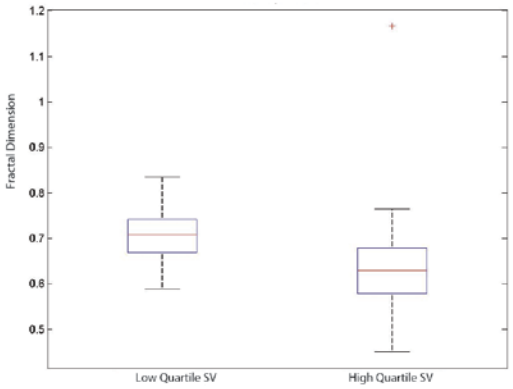

Figure 1: Fractal dimension of the systemic vascular resistance (SVR) was calculated for 88 patients undergoing bariatric surgery using detrended fluctuation analysis of hemodynamic data extracted from a Nexfin minimally invasive cardiac output monitor. The complexity of the SVR signal was significantly different in both the SV (bottom quartile mean 0.708, SD 0.064; top quartile mean 0.648, SD 0.137; p= 0.0044) and dP/dt(max) (bottom quartile mean 0.686, SD 0.078; top quartile mean 0.621, SD 0.068; p= 0.0121).

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S-66.

SAME DAY CANCELLATION OF CARDAC SURGERY: A RETROSPECTIVE REVIEW AT A LARGE ACADEMIC TERTIARY REFERRAL CENTER

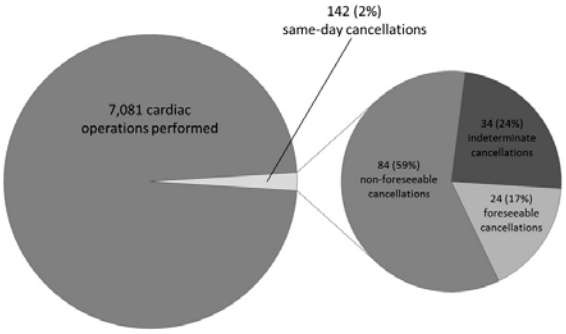
AUTHORS: M. M. Smith[1], W. J. Mauermann[1], D. J. Cook1, J. A. Hyder[2], D. W. Barbara[1]

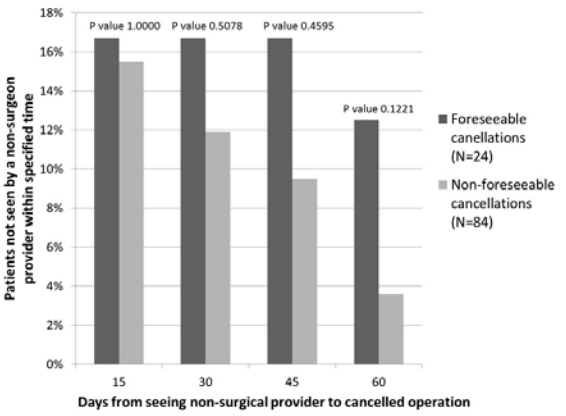
AFFILIATION:[1]Anesthesiology, Mayo Clinic, Rochester, MN, [2]Anesthesiology, Massachusetts General Hospital, Boston, MA

INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Same-day cancellations of cardiac surgery are unfortunate and costly occurrences that potentially place patients at risk for adverse events[1-3]. The purpose of this investigation was to retrospectively examine same day cancellation of cardiac operations at a large tertiary academic referral center, with particular interest towards: 1) identifying foreseeable causes of cancellation, 2) interval from a non-surgeon provider visit prior to planned operation, and 3) quantifying operative delay.

METHODS: We retrospectively reviewed all same-day cancellations of cardiac operations requiring cardiopulmonary bypass from 2010-2012 at a large academic tertiary referral center. Cancellations were classified as foreseeable, non-foreseeable, or indeterminate. Duration of time from seeing a non-surgeon provider to cancellation was noted and analyzed.

RESULTS: During the study period, 7,081 cardiac operations requiring cardiopulmonary bypass were performed. One hundred thirty-four patients experienced 142 (2%) same-day cancellations of cardiac surgery (Figure 1). Foreseeable cancellation causes comprised 17% of cancellations, non-foreseeable 59%, and indeterminate 24%. Reasons for cancellation were medical (51%), administrative/scheduling (17%), unknown (12%), procedure no longer required (11%), patient cancellation (6%), and preincisional complication (3%). Mean time interval from seeing a non-surgeon provider to cancellation was 8.6 ± 16.2 days. There were no statistically significant differences between foreseeable compared to non-foreseeable cancellations in seeing a non-surgeon provider 15, 30, 45, and 60 days prior to cancellation (Figure 2). Seven patients (5%) died within 30 days of cancellation. Twenty-eight (20%) of 142 cancelled surgical procedures were never subsequently performed.





CONCLUSIONS: Same-day cancellation of cardiac surgery occurred infrequently (2% of cardiac operations performed) at our institution, in contrast to previous published cardiac surgical cancellation rates of 15-24% [1-3]. Cancellations were due to foreseeable causes in the minority of cases (17%). Seeing a non-surgeon provider more recently before cancellation was not significantly associated with non-foreseeable compared to foreseeable cancellations. Same-day cancellations should viewed as an opportunity for practice improvement given the foreseeable nature of some cancelations, associated 30-day mortality, and portion of patients who did not subsequently undergo cardiac surgery.

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S-67.

HEPARIN DOSE-RESPONSE VARIABILITY IS AFFECTED BY GENETIC VARIANTS IN THE COAGULATION PATHWAY: KNG1 POLYMORPHISMS

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INTRODUCTION: Heparin is one of the most widely utilized anticoagulants. Variability in the heparin dose-response mandates monitoring of its effect. It has been estimated that up to 95% of inter-patient variability in drug response can be attributed to genetic factors.[1] We hypothesize that some of the heparin pharmacodynamic and kinetic variability is explained by genetic variation. Using a candidate gene approach in patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB), we examined single nucleotide polymorphisms (SNPs) in genes in the coagulation pathway that affect heparin dose-response variability as measured by post-heparin activated clotting time (ACT), total heparin dose, and baseline antithrombin III levels.

METHODS: After obtaining IRB approval and patient consent, clinical and demographic data were prospectively collected on 968 patients undergoing primary non-emergent CABG between 2001 and 2007 as part of the CABG Genomics Program. 122 SNPs in twelve coagulation pathway genes (coagulation factors *F2, F7, F9, F10, F11, F12*, kininogen 1 *(KNG1)*, phosphatidylinositol 4-kinase *(PI4KA)*, calcium-activated chloride channel *(TMEM16B),* transporter *(SLC34A1)*, and tissue factor pathway inhibitor *(TFPI)* were chosen using Tagger (HaploView v.4.2) and genotyped using Illumina Sequenom technology.

RESULTS: Three SNPs in kininogen 1 (KNG1) were significantly associated with higher post-heparin ACT (p-value <0.05) after adjusting for demographic and clinical variables and correction for multiple testing using false discovery rate.

CONCLUSIONS: KNG1 is an essential part of coagulation and the assembly of the kallikrein-kinin system.[2,3] We show a novel association between variants in KNG1 and heparin variability in cardiac surgical patients. *KNG1* uses alternative splicing to generate high molecular weight kininogen (HMWK) and low molecular weight kininogen (LMWK). HMWK is essential for blood coagulation, kallikrein-kinin system assembly, and the production of bradykinin. To date, these SNPs do not have any known effects on gene function; however, the location of the SNPs suggests that they may alter functionality of the gene product by altering gene splicing.

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SNP	Gene	Location	P-value (FDR)	Effect size (β)	MAF
rs6796803	KNG1	Intergenic region, downstream	0.0356	14.3	0.261
rs710449	KNG1	Intron	0.0356	14.3	0.221
rs9817038	KNG1	Promoter	0.0356	12.2	0.426

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S-68.

PLATELET TRANSFUSION IS NOT ASSOCIATED WITH INCREASED RISK OF POSTOPERATIVE THROMBOEMBOLIC EVENTS IN CARDIAC SURGERY

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Platelet dysfunction is common cause of bleeding in cardiac surgery. Platelet transfusion is the primary treatment, mostly administered prophylactically or when there is clinical suspicion of platelet dysfunction. However, there is no agreement among clinicians of transfusion indications and transfusion practices vary greatly among hospitals[1].

A group at particular risk of developing platelet dysfunction is coronary artery bypass grafting (CABG) patients treated with antiplatelet agents, notably aspirin and oral adenosine diphosphate-receptor antagonists. These drugs are effective in reducing ischaemic events, but also aggravate the bleeding tendency associated with cardiac surgery[2-3].

Despite their widespread use little is known about the overall risk of platelet transfusions in cardiac surgery. Platelets play an important role in thrombus formation, but whether they carry a risk of perioperative thromboembolic events has not been investigated. Randomized trials aiming on this relation are non-existent and the few observational studies are limited in size and yielded contradictory results [4-5]. The aim of this study was to analyze the association between platelet transfusions and thromboembolic events after cardiac surgery in both patients with discontinued and continued antiplatelet therapy. The hypothesis was that transfusion is associated with a higher incidence of adverse events.

METHODS: A cohort study of 6,745 patients undergoing CABG +/- AVR at three university hospitals (2006 - 2012) based on data from the common heart registry. Groups were established based on preoperative exposure to antiplatelet treatment and intraoperative transfusion of platelets. To adjust for possible patient differences the groups were balanced with exact match on 12 parameters (figure 1), resulting in 2 x 955 patients for analysis.

The primary outcome was possible thromboembolic events (in-hospital myocardial infarction and stroke together with re-CABG, coronary angiography or percutaneous coronary intervention) within six month after the primary operation supplemented with 30-day and 6-month mortality and new postoperative dialysis. To adjust for possible confounders, a logistic regression model was performed.

RESULTS: Univariate analysis showed that platelet transfusion was followed by more postoperative thromboembolic events (table 1). By adding mortality and dialysis the differences became more pronounced in the control group (11.8% no platelets vs 22.2% platelets; P=0.011; χ2-test). However the logistic regression showed that only on pump surgery, blood transfusion and postoperative inotropes had independent impact on postoperative thromboembolic events (figure 2).

CONCLUSION: Platelet transfusions possess no independent risk for postoperative thromboembolic events disregarding whether patients are on continued antiplatelet treatment or not.

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Table 1. Total frequency of possible thromboembolic events within 6month. P=0.034; χ2-test.

Antiplatement treatment	No platelets	Platelet transfusion
Discontinued	10.00%	18.50%
Continued treatment	10.70%	11.10%

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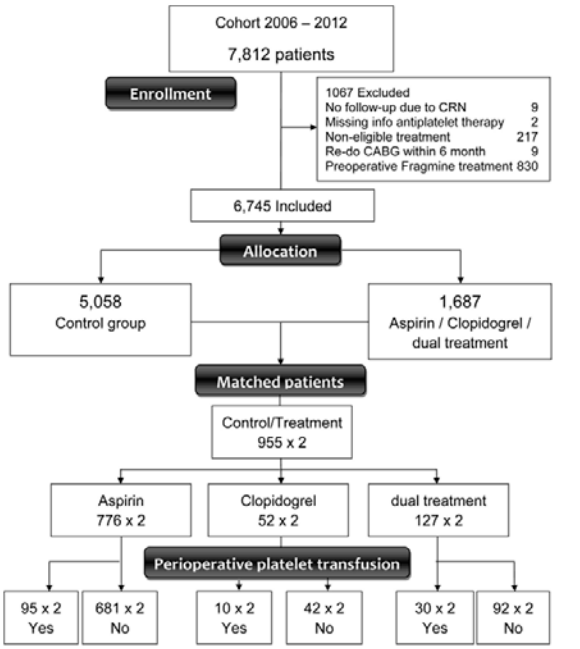
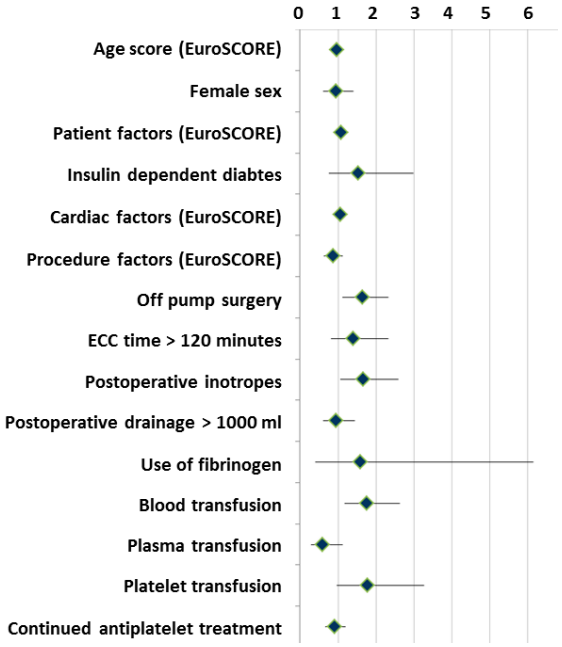
S-68 • continued



Patient cohort. Patients were, besides continued antiplatelet treatment and platelet transfusions, balanced requiring exact match on sex, age score (EuroSCORE), EuroSCORE patient and cardiac factors, procedure type, acute/ elective surgery, insulin dependent diabetes, extra corporal circulation time, perioperative use of aprotinin and fibrinogen and additive EuroSCORE. In case of more than one match patients were further balanced for best match in left ventricular function, unstable/stable angina, year of procedure and institution.



Risk-ratio (95% confidence interval) for combined thromboembolic event within 6 month after surgery. Logistic regression analysis using "enter" method. ECC=extra corporal circulation.

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S-69.

DEXMEDETOMIDINE DOES NOT PREVENT POSTOPERATIVE ATRIAL FIBRILLATION AFTER ESOPHAGEAL CANCER SURGERY

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AFFILIATION:[1]Anesthesiology and Perioperative Medicine, The University of Texas – MD Anderson Cancer Center, Houston, TX, [2]Biostatistics, UT MD Anderson Cancer Center, Houston, TX

INTRODUCTION: The incidence of atrial fibrillation (AF) post esophagectomy ranges from 13% to 46%. Sympathetic stimulation is believed to be a triggering factor for development of AF post cardiac surgery, and β-adrenergic blocker has been used as a prophylaxis for postoperative AF in cardiac surgery[1,2]. Dexmedetomidine (DEX), a selective α2-agonist, can modulate sympathetic system by decreasing norepinephrine activity, which is significantly increased during surgery.[3] We hypothesize that the use of intraoperative DEX during esophageal cancer surgery reduces the incidence of postoperative AF.

METHODS: After Institutional Review Board approval, data from 1149 esophageal cancer resections under general balanced anesthesia was retrieved from electronic medical records from 2000 to 2012. We obtained data regarding demographics preoperative medications, co-morbidities, history of paroxysmal AF and use of DEX intraoperatively. Exclusion criteria included patients younger than 18 years old, incomplete information and history of chronic AF. Mean, standard deviation, median, and range are provided for continuous variables and Wilcoxon rank sum test was used to evaluate the difference in a continuous variable. Frequency counts and percentages are provided for categorical variables and Fisher's exact test or Chi-square test was used to evaluate the association between two categorical variables. Logistic regression models were used for multivariate analysis to include important and significant covariates. A $p < 0.05$ was considered statistically significant

RESULTS: Data from 894 patients was analyzed. The mean age of the population was 60.62 +/- 10.53 years old. The overall incidence of postoperative AF was 12.64% (n= 113) with a mean onset 4.71 +/- 7.93 days after surgery. One hundred and fifty (16.78%) patients received DEX intraoperatively. Our analysis demonstrated that there were more female (23.3%) in the DEX group than in the control group (14.5%, p=0.0072). The incidence of postoperative AF in DEX treatment group was statistically significant higher than that in the group (19.3% vs 11.3%, p=0.0068). The multivariate analysis showed that the use of DEX was a risk factor in the development of AF (OR:2.05, 95%CI:1.25-3.35, p=0.004). The mean onset time of the arrhythmia was similar in both groups of patients (DEX: 5.62 +/- 11.24 days versus non-DEX: 4.39 +/- 6.47 days, p=0.7983). Other factors significantly associated with AF were age and history of paroxysmal AF.

CONCLUSION: The use of dexmedetomidine intraoperatively was associated with an increase incidence of postoperative AF after esophageal cancer surgery.

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Table 1. Demographic and perioperative variables of patient with and without postoperative AF

Covariate		NO Postoperative AF n=781(87.4%)	Posptoperative AF n=113(12.6%)	p-value
Age (years)		59.92 +/- 10.62	65.47 +/- 8.48	<0.0001
Body mass index		27.97 +/- 5.49	27.57 +/- 5.05	0.5794
Gender	F	126(88.1%)	17(11.9%)	0.7679
	M	655(87.2%)	96(12.8%)	
ASA	1/2	98(89.9%)	11(10.1%)	0.1875
	3/3E	654(87.4%)	94(12.6%)	
	4/4E	29(78.4%)	8(21.6%)	
Diabetes mellitus	N	673(88.4%)	88(11.6%)	0.0206
	Y	108(81.2%)	25(18.8%)	
Systemic hypertension	N	426(88.6%)	55(11.4%)	0.2418
	Y	355(86%)	58(14%)	
Coronary artery disease	N	666(88.4%)	87(11.6%)	0.0239
	Y	115(81.6%)	26(18.4%)	
Chronic obstructive pulmonary disease	N	769(87.4%)	111(12.6%)	0.6940
	Y	12(85.7%)	2(14.3%)	
Stroke	N	775(87.7%)	109(12.3%)	0.0277
	Y	6(60%)	4(40%)	
History of paroxysmal AF	N	779(88.5%)	101(11.5%)	0.0001
	Y	2(14.3%)	12(85.7%)	
Preoperative Statins	N	523(89.4%)	62(10.6%)	0.0115
	Y	258(83.5%)	51(16.5%)	
Preoperative CCB (Nondihydropyridine)	N	765(87.6%)	108(12.4%)	0.1707
	Y	16(76.2%)	5(23.8%)	
Preop β-blocker	N	603(89.1%)	74(10.9%)	0.0066
	Y	178(82%)	39(18%)	
Dexmedetomidine	N	660(88.7%)	84(11.3%)	0.0068
	Y	121(80.7%)	29(19.3%)	
Hospital stay (days)		13.25 +/- 14.07	20.09 +/- 18.51	<0.0001

CCB: Calcium channel blocker

Table 2. Multivariate logistic regression model

Effect	Odd Ratio	95% Wald Confidence Limits		P-Value
Age at Surgery	1.054	1.031	1.078	<0.0001
History of Paroxysmal AF Yes vs No	41.328	8.959	190.640	<0.0001
Dexmedetomidine Yes vs No	2.054	1.257	3.355	0.0041
Diabetes mellitus Yes vs No	1.594	0.948	2.682	0.0787
Stroke Yes vs No	3.045	0.709	13.088	0.1344
Diabetes mellitus Yes vs No	1.096	0.604	1.987	0.7630
Preoperative B-blocker Yes vs No	1.203	0.728	1.988	0.4699
Preoperative Statins Yes vs No	1.173	0.731	1.882	0.5092

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S-70.

THE EFFECT OF CHRONIC GARLIC SUPPLEMENT INTAKE ON PLATELET FUNCTION IN HEALTHY VOLUNTEERS: A RANDOMIZED PLACEBO CONTROLLED TRIAL

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INTRODUCTION: Garlic consumption has been associated with an increased perioperative bleeding risk in several case reports. The effect of long-term intake of garlic supplements and the additive effect of non-steroidal drugs on platelet function is not known. The aim of this study was to evaluate the effect of daily garlic supplement intake for 21 days and the additive effect of a single dose of 100mg diclofenac on platelet function in healthy volunteers.

METHODS: Following IRB approval, 32 healthy volunteers were randomly assigned to receive dried garlic powder (KWAI® Forte 600mg, Cassella-med, Germany) or placebo once daily for 21 days. At 21 days, all volunteers received a single oral dose of diclofenac 100mg (Voltaren® retard 100 mg, Novartis Pharma, Austria) and intake of KWAI® or placebo was stopped. After a 7-day washout period all volunteers received a single dose of diclofenac 100mg.

Blood samples were obtained prior to randomization (A); after 21 days of KWAI® or placebo intake before (B) and 5 hours after a single oral dose of diclofenac (C); after the 7-day washout period before -(D) and 5 hours after a single oral dose of diclofenac (E).

Platelet function was evaluated using the PFA-100 platelet function analyser (Siemens, Germany) using collagen/epinephrine as agonists. The primary endpoint was PFA-closure time (CT, normal range <165 s) at timepoint B. Multiple electrode aggregometry (Multiplate®, Roche, Switzerland) using arachidonic acid as an agonist was used as an additional method to determine platelet function. The area under the aggregation curve (AUC, normal range 361–892 AU·min) was used as a secondary endpoint. A fixed effects model was used to test for significance between the two groups. P-values ≤ 0.05 were considered statistically significant. Results are given as mean and 95% confidence interval (CI).

RESULTS: Twenty-seven volunteers completed the study, 5 were lost to follow up.

There was no significant change in platelet function from baseline after 21 days within each group (for CT KWAI: p=0.429, placebo: 0=0.764; for AUC KWAI: p=0.503, placebo: 0=0.472) and no significant difference between the two groups regarding the changes from baseline to day 21. [ΔCT KWAI: 4.50 s (CI -7.04 to 16.04 s), placebo: 1.57 s (CI -9.11 to 12.25 s), p=0.704; ΔAUC KWAI: 49 AU·min (CI -101 to 199 AU·min), placebo: 50 AU·min (CI -91 to 192 AU·min), p=0.994].

After the ingestion of diclofenac, CT increased significantly [ΔCT KWAI: 39.67 s (CI 14.91 to 64.42 s), placebo: 86.29 s (CI 63.39 to 109.20 s)]. The effect on the AUC was only significant in the placebo group [ΔAUC KWAI: 187 AU·min (CI -13 to 387 AU·min), placebo: 423 AU·min (CI 231 to 615 AU·min)].

In the KWAI group, the combined effect of KWAI and diclofenac was less pronounced than the effect of diclofenac alone. (B-C vs. D-E, for CT p=0.012; for AUC p=0.020).

DISCUSSION: In this randomized, the intake of a garlic supplement for 21 days did not impair platelet function. After garlic supplement ingestion, the platelet inhibitory effect of diclofenac was attenuated when compared to diclofenac monotherapy.

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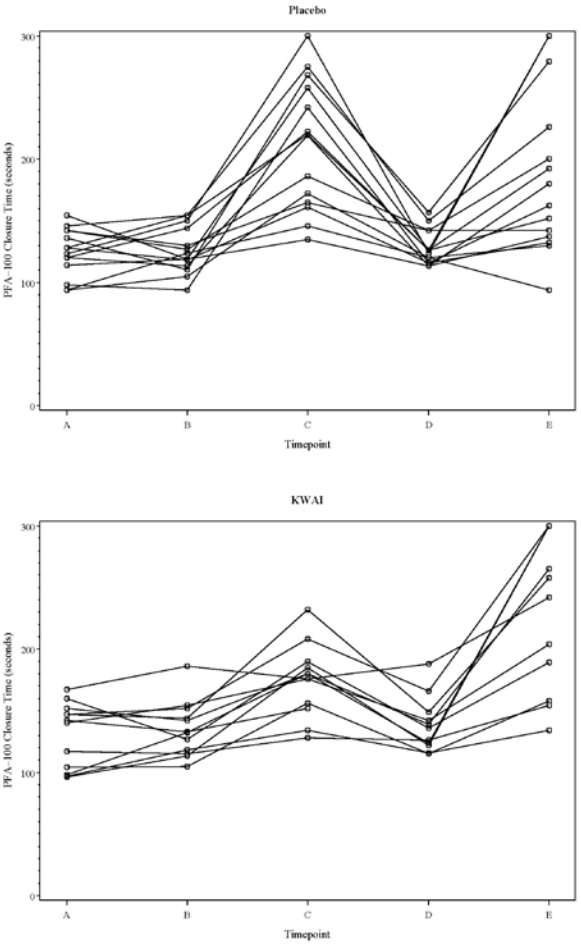

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S-71.

CARDIOPULMONARY BYPASS TRIGGERS DIMINISHED ABILITY OF ANTIGEN PRESENTING CELLS TO PROCESS ANTIGEN IN SOME PATIENTS

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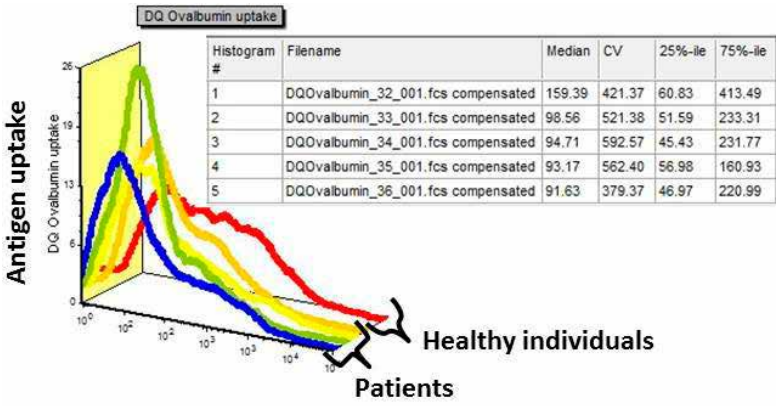
AFFILIATION:[1]Department of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, PA, [2]Neuman University, Neuman University, Philadelphia, PA, [3]Department of Cardiovascular Surgery, University of Pennsylvania, Philadelphia, PA

INTRODUCTION: Antigen presenting cells (APC) are pivotal in regulating the appropriate response of the immune system. Cardiopulmonary Bypass (CPB) triggers an intense inflammatory response that may affect the fate and the function of APC. In the presented study, we focused on monocyte (MO)-derived dendritic cells (DC). Arguably, they are the most potent APC. These cells emerge from precursory peripheral blood monocyte and are primary source of the APC under stress. Alternatively, MO can differentiate into inflammatory macrophage, cells pivotal for promoting inflammatory response and endothelial damage. Here, we conducted a pilot study involving individuals undergoing CPB in which we examined the ability of MO-derived DC obtained to process antigen as a measure of their APC capability. We hypothesize that CPB will diminished APC capability of MO-derived DC due to the large pro-inflammatory insult.

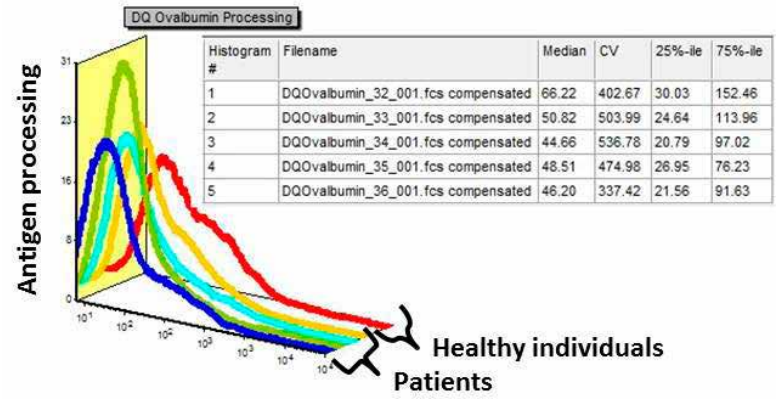
METHODS: Blood from a total of 8 subjects subjected to CPB was obtained. Their isolated MO were subjected to IL-4 & GM-CSF in X-VIVO15™ media in vitro as the optimal environment to generate DC. After 5 days the cells were harvested. The ability to process antigen was measured at 7 day and 28 days using DQ ovalbumin (DQ-OVA) uptake and processing assay. Additionally, MO derived DC were analyzed for surface markers with flow cytometry in term of positive cells (%) or averaged receptor densitiy(MFI). Each of the subjects (n=8) had blood drawn shortly before bypass (t0) and 7 days (t7d) after CPB. Data is presented as mean+standard deviation unless otherwise specified.

RESULTS: The majority of patients had a decreased uptake and processing of the DQ as compared to health control (red line histogram) (Figure 1.) 7 days after undergoing CPB. Interestingly, this diminished capacity to process antigen was not related to altered expression of CD14 (%CD14 t0=8.1+22.1 vs t7d=0.05+0.04), CD1a (%CD1a t0=46.5+27.39 vs t7d=40.6+22.44), or CD86 (MFI CD86 t0=67.2+25.44 vs t7d=56.9+8.06). Only the expression of CD83 was significantly diminished (%CD83 t0=24.5+33.7 vs t7d=0.26+0.22). Observed changes were not related to aberrant sensitivity to IL-4 since the expression of IL-4-inducible marker of CD209 was low in term of percentage of positive cells (%CD209 t0=69+28.8, t+24hr=76+19.3, t+7d=79+13.7) and receptor density (MFI CD209 t0=2780+1910, t+24hr=2337+2110, t+7d=2575+1827).

CONCLUSIONS: Our study confirms that the APC capability of DC-derived from peripheral blood MO to uptake and process antigen is severely diminished up to 7 days after CPB in some individuals. This aberration is not related to the diminished expression of CD86, but seems to be related to aberrant differentiation of the MO into mature DC as signified by diminished expression of CD83.



Histogram #	Filename	Median	CV	25%-ile	75%-ile
1	DQOvalbumin_32_001.fcs compensated	159.39	421.37	60.83	413.49
2	DQOvalbumin_33_001.fcs compensated	98.56	521.38	51.59	233.31
3	DQOvalbumin_34_001.fcs compensated	94.71	592.57	45.43	231.77
4	DQOvalbumin_35_001.fcs compensated	93.17	562.40	56.98	160.93
5	DQOvalbumin_36_001.fcs compensated	91.63	379.37	46.97	220.99



Histogram #	Filename	Median	CV	25%-ile	75%-ile
1	DQOvalbumin_32_001.fcs compensated	66.22	402.67	30.03	152.46
2	DQOvalbumin_33_001.fcs compensated	50.82	503.99	24.64	113.96
3	DQOvalbumin_34_001.fcs compensated	44.66	536.78	20.79	97.02
4	DQOvalbumin_35_001.fcs compensated	48.51	474.98	26.95	76.23
5	DQOvalbumin_36_001.fcs compensated	46.20	337.42	21.56	91.63

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S-72.

TRANSCATHETER AORTIC VALVE REPLACEMENT (TAVI) IN PATIENTS OLDER THAN 90 YEARS: IS AGE RELEVANT FOR THE PERIOPERATIVE THERAPY?

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INTRODUCTION: Transcatheter Aortic Valve Implantation (TAVI) was designed as a therapy for patients with severe aortic stenosis and high peri-operative risk. Different TAVI-registries have shown a mean age of about 81 years for TAVI patients. In 2013, 25 from the 507 million inhabitants (5%) of the European Union (EU) were older than 80 years. With growing experience and increasing obsolescence cardiac anaesthesiologists will most likely face more patients over 90 years of age for this procedure. With an increase of these patients at our university hospital, there was a rising concern whether specific precautions for nonagenarians (NONA) are necessary.

METHODS: Analyzind data from our TAVI-Registry, we compared patients undergoing a transfemoral TAVI aged over 90 years with octogenaric (80 – 89) patients (OCTO). IRB approvement was obtained. Group comparisons were performed by Mann-Whitney-U tests.

RESULTS: Between June 2007 and October 2013 1162 TAVI procedures (all methods of access) were performed. Transfemoral access and a age of at least 80yrs was found in 363 of these patients (31%). Medtronics CoreValve™ was most commonly used 79% (n= 287). Edwards Sapien™ and Sapien XT™ were used in all other patients (n=76).

	OCTO	NONA	p-value
n=	331	32	
m:f ratio	01:01.5	01:01.1	
PREOPERATIVE DATA			
BMI (kg/m²)	26.1±3.9	24.5±3.8	0.013*
LVEF (%)	51±14	52±12	0.725
dPmax (mmHg)	72±29	87±32	0.026*
Aortic valve area (cm2)	0.65±0.2	0.62±0.2	0.417
Haemoglobin (g/dl)	12.4±1.6	12.0±1.1	0.292
Creatinine (mg/dl)	1.2±0.6	1.4±0.8	0.259
STS-Score Mortality (%)	6.7±7.2	10.2±6.0	<0.001*

PERIOPERATIVE DATA			
General Anesthesia	235 (71%)	25 (78%)	0.393
Propofol (mg/kgBW)	3.4±7.1	2.8±3.8	0.955
Remifentanil (µg/kgBW)	0.16±0.32	0.17±0.22	0.51
Norepinephrine (µg/kgBW)	2.83± 5.5	3.2±3.4	0.194
Crystalloid infusion (ml/kgBW)	13.9±10.9	11.7±9.1	0.377
Procedure time (min)	192±55	187±33	0.97

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S-73.

HAPTOGLOBIN 2-2 PHENOTYPE IS ASSOCIATED WITH INCREASED RISK FOR AKI AND 6-MONTH MORTALITY AFTER CORONARY BYPASS GRAFTING SURGERY IN PATIENTS WITH DIABETES

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INTRODUCTION: Post-operative renal insufficiency has been associated with increased morbidity and mortality after cardiac surgery. As a result, serum creatinine level has been used to predict the risk of adverse outcomes after surgery. Moreover, it has been recently published that even subclinical increase in postoperative serum creatinine levels is associated with increased mortality after cardiac surgery[1]. Several studies have reported an association between haptoglobin (Hp) polymorphisms (specifically the Hp 2-2 phenotype) and increased renal morbidity in patients with diabetes. Thus, we sought to determine whether the Hp-2-2 phenotype is independently associated with increased postoperative serum creatinine after coronary artery bypass grafting (CABG) surgery.

METHODS: After IRB approval and written informed consent from all participants, we performed a prospective analysis on 72 consecutive diabetic patients undergoing elective CABG surgery with cardiopulmonary bypass (CPB) at the University of Virginia Medical Center. Haptoglobin phenotypes were determined using gel electrophoresis[2]. Serum creatinine was measured preoperatively and on postoperative days 1-3. Continuous and categorical variables were compared between groups using student t and x2 tests, respectively. A multivariable logistic model was used to derive perioperative and demographic variables associated postoperative kidney injury.

RESULTS: Seventy-two patients were recruited. Twenty eight patients (39%) had the 2-2 phenotype, while forty four patients were either Hp 1-1 (18%) or 2-1 (43%). Mean preoperative creatinine levels did not differ between the patients groups (1.24 mg/dL vs. 1.17 mg/dL, p=NS). On postoperative day 1 the mean serum creatinine level increased by 15 ± 24% in patients with non-2-2 phenotype, whereas in the patients with the 2-2 phenotype mean serum creatinine increased by 37.6 +/- 33.1% (p=0.002). On postoperative day 2 the mean serum creatinine increased by 21.7 +/- 32.3% compared to the pre-operative levels for patients with the non-2-2 phenotype, while in patients with the Hp 2-2 phenotype the creatinine level increased by 45.4 +/- 41.3% (P = 0.014). In addition three patients (10.7%) in the Hp 2-2 group required postoperative dialysis while none of the patients in the non-Hp 2-2 group required dialysis (p<0.001). Furthermore, after 6-month follow up, four patients (14.3%) in the Hp 2-2 group died while only one patient (2.2%) in the non-Hp group died (p<0.0001)

CONCLUSIONS: Diabetic patients with Hp 2-2 phenotype who undergo elective CABG surgery with CPB bypass have significantly higher postoperative creatinine levels and need for dialysis compared to patients with the non-2-2 phenotypes. In addition 6-month mortality after CABG surgery was significantly higher in diabetic patients with the Hp 2-2 phenotype. The Hp 2-2 phenotype may be a significant risk factor for increased morbidity and mortality after CABG in patients with diabetes.

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S-74.

EFFECT OF HYPEROXIA IN CONJUNCTION WITH ISOFLURANE IN THE EXPRESSION OF OXIDATIVE STRESS RESPONSE GENES IN THE HEART AND LUNGS OF MICE

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INTRODUCTION: Volatile anesthetics provide protection to the myocardium against reperfusion injury when applied before ischemia or prior to reperfusion of ischemic myocardium (I/R)[1]. Anesthetic preconditioning (APC) protects against the effects of reperfusion injury[2]. However, since volatile anesthetics are always administered with varying concentrations of oxygen, it is important to determine whether genes potentially relevant to APC are induced by isoflurane in air or are influenced by changes in oxygen concentration[3]. The purpose of this study is to determine whether isoflurane in combination with 60% oxygen induces a differential oxidative stress gene expression profile compared to isoflurane in air in the lungs and hearts of mice.

METHODS: c57BL/6 mice breathed 21% or 60% oxygen with or without 2% isoflurance. An isoflurane vaporizer (Harvard Apparatus) was used to mix oxygen and isoflurane. The animals were exposed for 2 hours to the gas mixture followed by cervical dislocation. The animal use protocol was approved by institutional review (IACUC). Lungs and hearts were removed, perfused in PBS and stored in RNA later (Ambion). Total RNA was isolated from the tissue using Trizol reagent. Equal amounts of RNA were used for RT profile PCR array (mouse oxidative stress and antioxidant defense array, PAMM-0652Z, http://www.sabiosciences.com/genetable.php?pcatn=PAMM-065Z. Real-Time qPCR array was performed and analyzed using manufacturer's protocol (Life Technologies, CA). For each group 3 mice were used.

RESULTS: Expression levels of Ercc6, Gpx4, Gpx5, Prnp, Ptgs1, Ptgs2, Recql4 and Ucp3 genes were increased over 2-fold in the myocardium of the 21%O2/ isoflurane_mice. Ptgs2, Ptgs1 and Ucp3 gene expression was increased three fold in the myocardium of isoflurane breathing mice irrespective of oxygen tension. . These data suggest that cyclooxygenase 1 & 2 (Ptgs1 & Ptgs2 genes) could have a significant role in APC. The increased expression of Ucp 3 suggest that uncoupling of electron transport chain could decrease concentration of O2.- due to isoflurane exposure[1,4]. Increased expression of Gpx4 and Gpx5 could decrease the ROS concentration during reperfusion of the myocardium. When 60% oxygen was included with 2% isoflurane the level of Hspa1a was increased by 14-fold and ccl5 was increased by about 5-fold in the heart. In contrast, in the lung, 60% oxygen and isoflurane mixture induced the following genes: Cyba, Fth1, Gpx4, Gpx5, Hspa1a, Ncf1 by 14, 27, 6, 2.6, 4.33 and 26 fold respectively. Interestingly, these genes were not significantly increased in the lungs of mice breathing only 2% isoflurane with air. Therefore, further studies are required to delineate the role of hyperoxia in isoflurane-mediated APC.

CONCLUSION: These findings demonstrate that gene expression associated with APC is influenced by varying oxygen tension.

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S-75.

IMPACT OF PREOPERATIVE TROPONIN ELEVATION ON 30-DAY MORTALITY

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AFFILIATION: Anesthesiology, University of Michigan, Ann Arbor, MI

INTRODUCTION: Multiple studies have demonstrated that troponin elevations of various magnitudes and from multiple etiologies are associated with increased mortality.[1,2] While the increased risk of surgery after myocardial infraction has long been known,[3] the risk for patients with troponin elevations from all etiologies is currently unknown. For example, it is unclear if small troponin elevations, often attributed to "troponin leaks" contribute to perioperative risk. Therefore, we conducted a single-center, retrospective cohort study to assess the impact of preoperative troponin elevation on 30-day postoperative mortality.

METHODS: Informed consent was waived by the Institutional Review Board due to the minimal level of risk. The study population consisted of all patients greater than 18 years of age who had a troponin measurement within 30 days of surgery. Preoperative subject characteristics were obtained from the anesthesia record. The social security death index was used to determine the incidence of 30-day mortality. Subjects with preoperative troponin concentrations greater than the detectable limit (10 ng/mL) were divided into terciles based on the magnitude of elevation and the time from the maximum troponin concentration and surgery. The relationship between these categories and 30-day mortality was assessed using multivariable logistic regression adjusting for age, gender, ASA classification, surgical duration, and preoperative metabolic acidosis (bicarbonate concentration). The magnitude of associations were expressed as odds ratios (OR) and 95% confidence intervals (CI).

RESULTS: We found that elevated troponin levels were associated with increased risk of death (Figure 1). Even subjects with preoperative troponin levels within the normal range (0.10 - 0.30 ng/mL) were at increased risk for mortality when the surgery occurred within 11 days of this measurement (e.g. OR 1.80, 95% CI 1.02 to 3.17 for surgery within 3 days). For patients with higher levels of preoperative troponin, risk of mortality was increased if surgery occurred anytime within 30-days of the maximum troponin measurement (e.g. OR 1.89, 95% CI 1.06 to 3.38 for surgery within 3 days).

CONCLUSIONS: Patients with preoperative troponin elevation, even of low magnitude, are at increased risk for 30-day postoperative mortality. If possible, surgical procedures should be delayed for any increase in the concentration of serum troponin.

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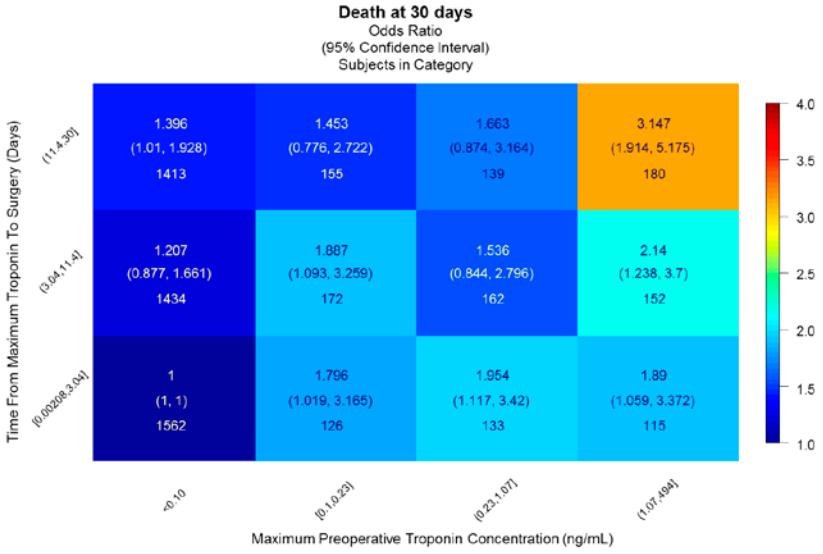

Figure 1: Odds ratio for 30-day postoperative mortality adjusted for age, case duration, gender, ASA status, and preopeartive metabolic acidosis.

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S-76.

ACTIVITIES OF CARDIAC TISSUE MMP-2 AND -9 ARE REDUCED BY REMOTE ISCHEMIC PRECONDITIONING AND CORRELATE WITH SERUM CARDIAC TROPONIN T CONCENTRATIONS IN CARDIOSURGICAL PATIENTS

AUTHORS: K. Zitta[1], P. Meybohm[2], B. Bein1, M. Gruenewald[1], K. Zacharowski[2], M. Steinfath[1], M. Albrecht[1]

AFFILIATION:[1]Department of Anaesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein, Kiel, Germany, [2]Clinic of Anaesthesiology, Intensive Care Medicine and Pain Therapy, University Hospital Frankfurt, Frankfurt, Germany

INTRODUCTION: Transient episodes of ischemia in a remote organ or tissue (remote ischemic preconditioning, RIPC) can reduce myocardial damage resulting in cardioprotection. Myocardial damage is associated with local tissue remodeling and the matrix metalloproteinases 2 and 9 (MMP-2/9) are crucially involved in these events [1,2]. In our recent study we evaluated cellular and molecular effects of RIPC in heart tissue of cardiosurgical patients with cardiopulmonary bypass (CPB) and showed that RIPC regulates HIF-1α levels, apoptosis and inflammation[3]. Here we investigated the effects of RIPC on the activities of heart tissue MMP-2/9 and their correlation with blood concentrations of cardiac troponin T (cTnT) as marker for myocardial damage to gain deeper insight into the RIPC-mediated cellular mechanisms.

METHODS: In cardiosurgical patients with CPB, RIPC was induced by four 5 minute cycles of transient upper limb ischemia/reperfusion using a blood-pressure cuff. Right atrial tissue was obtained from RIPC (N=18) and control (N=17) patients before and directly after CPB (figure 1A). As a marker for myocardial damage cTnT was measured in the patient sera before surgery and at admission to the intensive care unit. Activities of tissue MMP-2/9 were evaluated using gelatin zymography and computer-assisted densitometric analyses. This study was performed in accordance with the Declaration of Helsinki and is registered at ClinicalTrials.gov (NCT00877305).

RESULTS: Serum concentrations of cTnT were 0.63±0.06 ng/ml in the control and 0.20±0.02 ng/ml in the RIPC group (P<0.001; figure 1B). In cardiac biopsies taken before CPB, activities of MMP-2 and MMP-9 were significantly lower in the RIPC group compared to the control (MMP-2: control, 1.13±0.13 a.u.; RIPC, 0.71±0.12 a.u.; P<0.05. MMP-9: control, 1.50±0.16 a.u.; RIPC, 0.87±0.14 a.u.; P<0.01; figure 2 C, G), while activities of the pro-MMPs were not altered (pro-MMP-2: control, 2.21±0.17 a.u.; RIPC, 1.95±0.20 a.u.; P>0.05. Pro-MMP-9: control, 2.27±0.39 a.u.; RIPC, 1.33±0.18 a.u.; P>0.05; figure 2 A, E). In cardiac biopsy samples that were obtained after CPB, activities of pro- and active MMP-2 and MMP-9 were not different between the control and RIPC group (figure 2 B, D, F, H). Spearman's rank tests showed that MMP-2 and MMP-9 activities in cardiac tissue biopsies obtained before CPB were positively correlated with cTnT serum levels (MMP-2/cTnT: Spearman r, 0.40; P=0.016. MMP-9/cTnT: Spearman r, 0.41; P=0.015; figure 3 A, B). No significant correlation between cTnT concentrations and MMP-2/9 activity was found in samples taken after CPB (figure 3 C, D).

CONCLUSION: We propose that an early reduction of tissue MMP-2/9 activities may be involved in RIPC-mediated cardioprotection.

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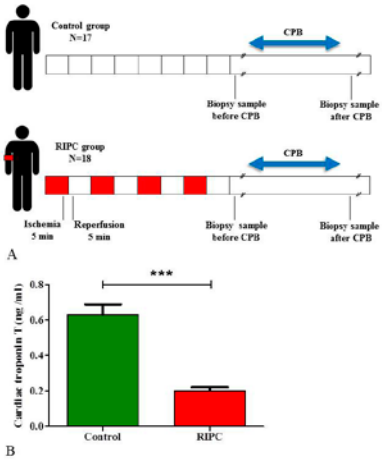

Figure 1: Experimental setting and serum cardiac troponin T (cTnT) concentrations in control and RIPC patients. RIPC was performed by 4 cycles of 5 minutes of upper arm ischemia induced with a blood pressure cuff. Each cycle of ischemia was followed by 5 minutes of reperfusion. Cardiac biopsies were obtained before and after CPB (A). cTnT levels were evaluated at ICU admission in the control and RIPC group (B). Bars denote SEM; ***, P<0.001. CPB, cardiopulmonary bypass; RIPC, remote ischemic preconditioning.

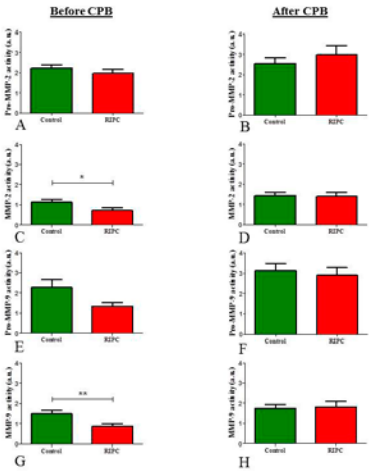

Figure 2: MMP activities in cardiac biopsy samples. The enzymatic activities of pro-MMP-2, MMP-2, pro-MMP-9 and MMP-9 were evaluated in tissue samples taken before CPB (A, C, E, G) and after CPB (B, D, F, H) using gelatin zymography and computer-assisted densitometric analyses. Bars denote SEM; *, P<0.05; **, P<0.01. CPB, cardiopulmonary bypass; RIPC, remote ischemic preconditioning.

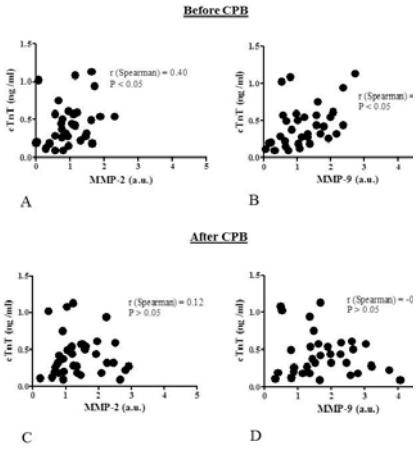

Figure 3: Correlation of cardiac tissue MMP-2/9 activities and serum cardi troponin T (cTnT) levels. cTnT concentrations were measured at admission the intensive care unit (ICU) and were correlated with the activities of MMP and MMP-9 in heart tissue samples obtained before CPB (A, B) and after CI (C, D). CPB, cardiopulmonary bypass; cTnT, cardiac troponin T.

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S-77.

PROPOFOL AMELIORATES HYPERGLYCEMIA-INDUCED CARDIAC HYPERTROPHY AND DYSFUNCTION VIA HEME OXYGENASE-1 /STAT3 SIGNALING PATHWAY IN RATS

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INSTRUCTION AND GENERAL PURPOSE OF THE STUDY: Heme oxygenase-1 (HO-1) is inducible in cardiomyocytes in response to stimuli like oxidative stress, and plays critical roles in combating cardiac hypertrophy and injury[1].Signal transducer and activator of transcription-3(STAT3) plays a pivotal role in HO-1 mediated protection against liver and lung injury under oxidative stress[2]. We hypothesized that propofol, an intravenous anesthetic with antioxidant capacity that has been shown to induce HO-1 expression, may attenuate hyperglycemia-induced oxidative stress in cardiomyocytes via enhancing HO-1 activation and ameliorate hyperglycemia-induced cardiac hypertrophy and apoptosis via HO-1 /STAT3 signaling, and improve cardiac function in diabetes.

METHODS: 8 weeks of streptozotocin-induced Type 1diabetic rats received an i.v. injection of either saline or propofol at a rate of 900μg/kg/min[3] for 45 min. Cardiac function was assayed by pressure-volume loop conduction system and free 15-F2t-isoprostane in plasma and heart tissue was detected by enzyme-linked immunoassay. Primary cultured neonatal rat cardiomyocytes were exposed for 48 hours to either normal glucose (5.5mmol.L-1, Control), a high concentration of glucose (HG, 25.5mmol.L-1) or HG in the presence of propofol (50μmol.L-1).To further confirm the roles of HO-1 and STAT3 played in the beneficial effects of propofol, HO-1 or STAT3 genes expression was respectively knocked down by siRNA in H9c2 cells. Cardiomyocyte cross-sectional area and protein content were used as indices of hypertrophy. Reactive oxygen species (ROS) were detected by DHE fluorescence staining. HO-1 and STAT3 protein expression were detected by Western blot. Cardiomyocytes apoptosis were assessed by TUNEL assay.

RESULTS AND MAJOR FINDINGS: In Type-1 diabetic rats, myocardial 15-F2t-isoprostane was significantly increased, accompanied with cardiomyocytes hypertrophy and impaired left ventricular function that was coincident with reduced HO-1 activity and STAT3 activation despite of an increase in HO-1 protein expression as compared to control. Propofol infusion significantly improved cardiac function with concomitantly enhanced HO-1 activity and STAT3 activation. Similar to the changes seen in diabetic rat hearts, high glucose exposure for 48 hours led to cardiomyocytes hypertrophy and apoptosis in both the primarily cultured neonatal rat cardiomyocyte and in H9c2 cells compared to normal glucose, accompanied by increased ROS. Propofol significantly increased cardiomyocyte HO-1 and p-STAT3 protein expression and HO-1 activity and attenuated HG-mediated cardiomyocyte hypertrophy and apoptosis and reduced ROS production ($P<0.05$). These protective effects of propofol were abolished by HO-1 or STAT3 gene knock down in H9c2 cells.

CONCLUSIONS: Activation of the HO-1/STAT3 signaling path way is major mechanism whereby Propofol mediates amelioration of hyperglycemia-induced cardiomyocyte hypertrophy and apoptosis and cardiac dysfunction.

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S-78.

GENOME-WIDE ASSESSMENT FOR GENETIC VARIANTS ASSOCIATED WITH LONG-TERM HEART FAILURE AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

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INTRODUCTION: Offspring of parents with heart failure (HF) have significantly increased risk of developing HF even after risk adjustment.[1] This risk increases further in offspring of parents with ischemic heart disease, suggesting that myocardial ischemia may potentiate genetic predisposition to develop HF[1] Coronary artery bypass graft (CABG) surgery is performed to prevent complications of ischemic heart disease, yet ~12% of CABG patients experience HF causing hospitalization or death during the 5 yrs after surgery. We performed a genome-wide association study (GWAS) to determine if common genetic variants associate with occurrence of HF hospitalization or HF death after CABG surgery.

METHODS: European ancestry subjects undergoing non-emergency isolated primary CABG surgery with cardiopulmonary bypass at two institutions (2001-2012) were assessed up to 5 yrs after surgery for the outcome of hospitalization or death from HF (mean follow-up 4 yrs ± SD 1.5 yrs). Study IRB approvals obtained at both institutions. Single nucleotide polymorphisms (SNPs; minor allele frequency >1%) were genotyped using DNA from subjects who experienced the study's HF outcome (Illumina Human OmniExpress Array). After employing standard GWAS quality control steps for genotyping quality and population stratification, >500,000 SNPs genotyped in post-CABG HF cases were compared in two separate analyses with control subject GWAS datasets obtained from two ambulatory cohorts (NCBI's dbGaP resources: Analysis #1 eMERGE Geisinger eGenomic Medicine-MyCode Project Controls; Analysis #2 Autopsy-Confirmed Parkinson Disease GWAS Consortium dataset). Chi-squared test (allelic model) or logistic regression analyses (additive, dominant, recessive models) were used to assess SNP associations with HF related hospitalization or death during the 5 yrs after surgery.

RESULTS: Minor allele frequencies for SNPs genotyped in 178 post-CABG HF cases (68 ± SD 11 yrs) were compared with SNPs genotyped in 1261 controls in Analysis #1 and with SNPs genotyped in 785 controls in Analysis #2. SNPs within 14 genetic loci associated in both analyses with risk (P<5x10-5) for developing postoperative HF (Figure 1 allelic model GWAS results). One SNP encoded in the OXTR gene on chromosome 3p25 attained genome-wide significance (Analysis #1 ORadditive model=2.21, P=7.95x10-8; Analysis #2 ORadditive model=2.14, P=2.96x10-6). The two SNPs next most significantly associated with HF were: 1) downstream of the RHBG gene on chromosome 1q22 (Analysis #1 ORadditive model=1.94, P=2.01x10-6; Analysis #2 ORadditive model=1.90, P=2.05x10-5), and 2) at chromosome 14q21 (Analysis #1 ORadditive model=2.17, P=2.63x10-6; Analysis #2 ORadditive model=2.15, P=1.28x10-5).

CONCLUSIONS: We identified novel genetic loci associated with increased risk for development of HF during the 5 yrs after CABG surgery. Replication studies in additional cardiac surgical cohorts are being initiated to assess these loci, and future studies are needed to define biologic mechanisms that link these genetic variants to postoperative HF.

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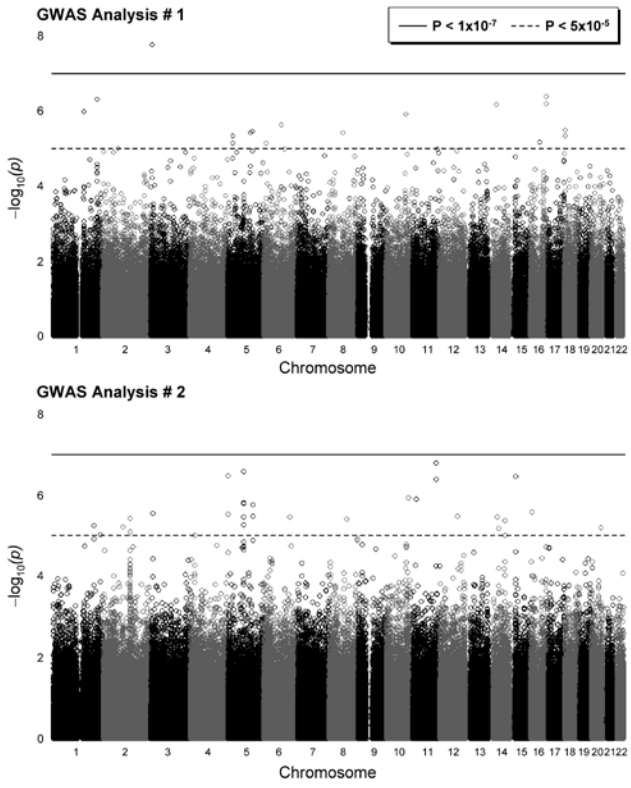
Figure 1



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S-79.

ERYTHROPOIETIN IS A PREDICTOR OF RENAL AFTER AORTIC SURGERY

AUTHORS: Y. kouatli[1], S. N. Neill[2]

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Aortic surgery is associated with acute kidney injury (AKI)[1]. Creatinine and urine output diagnose AKI but these measures can be late [2,3]. Biomarkers could help diagnose AKI[4]. Erythropoietin (EPO) is involved in renal recovery in a rat model of renal injury[5] and could hypothetically be a biomarker for AKI. We evaluated EPO as a biomarker for AKI in patients undergoing aortic surgery.

General Anesthesia was induced. All patients had left femoral and right radial arterial lines and a Swan Ganz catheter. CPB arterial cannulation was in the aorta or in the right axillary artery. A majority of patients had a two stage venous cannula inserted in their right atrium. All patients had a left ventricular decompression cannula. All hypothermic circulatory arrest (HCA) patients were cooled between 16 to 18°C. All other patients were cooled to 28 -32°C. After HCA, antegrade or retrograde cerebral perfusion was provided. Blood samples were obtained after induction, 15 to 20 minutes after cardiopulmonary bypass and 12 to 18 hours post operatively. Samples were frozen at -80° C until completion of the study. EPO samples were analyzed using eBioscience EPO ELISA kits. All were analyzed on Synergy plate reader.

Definitions of renal injury was based on the RIFLE criteria [7]. Univariate comparisons were performed between groups using the Mann-Whitney U tests. EPO medians were compared at each time point between the AKI groups. Additionally, a ratio of draw 3 to draw 1 was calculated for each individual subject in order to assess the magnitude of EPO elevation in AKI. Univariate logistic regressions was performed on the maximum EPO values and the ratios for each subject with AKI as the outcome. Areas under the receiver operating characteristic curves was calculated for each regression.

A total of 13 subjects developed AKI (16.9%). 8 from a population of 31 without HCA (25.8%) and 5 from a population of 46 with HCA (10.9%).

Age, gender, diabetes mellitus, hypertension, smoking, peripheral vascular disease, carotid disease, operative time, CPB time, aortic cross clamp time, HCA, pre-operative hematocrit, total intra-operative units of autologous blood or packed red blood cells, intra-operative units of platelets, fresh frozen plasma and cryoprecipitate, were not significant. Oliguria and length of ICU and hospital stay were significant. EPO levels significantly increased post operatively only in subjects that developed AKI (fig 1). A median of ratios of 3.65 between the last and first level of EPO was statistically significant (Table 1). A logistic regression produced an area under the receiver operator curve (AUC) of 0.69 for EPO (Fig 2) 0.75 for EPO ratios (Fig 3).

Post operative EPO Levels are predictors of renal injury after aortic surgery with or without HCA. EPO ratios could become a clinical tool for the diagnosis of AKI after aortic surgery.

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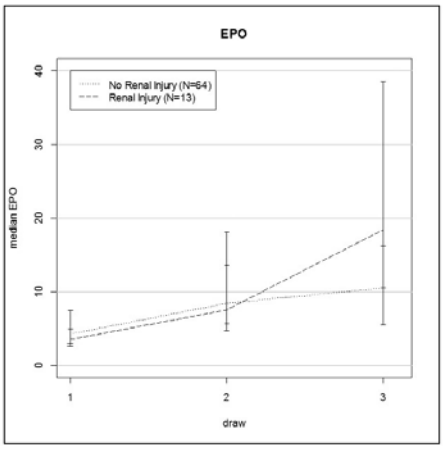
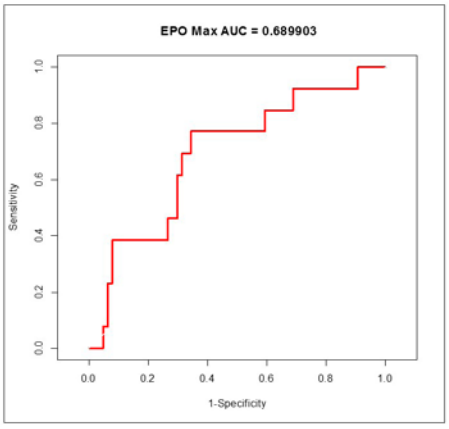
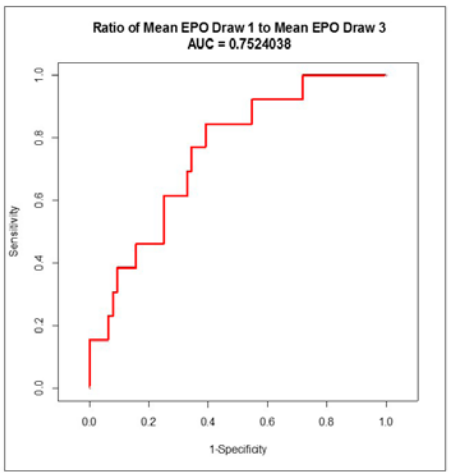


	No renal injury				Renal injury				
	N	Median			N	Median			
EPO DRAW 1	64	4.28	2.59	7.47	13	5.95	3.02	4.96	0.878
EPO DRAW 2	64	8.40	4.73	13.64	13	8.67	3.75	19.05	0.434
EPO DRAW 3	64	10.53	5.54	16.28	13	18.41	10.58	38.53	0.012
EPO draw 3 / EPO draw 1	64	2.59	1.23	3.78	13	3.65	3.33	11.14	0.004





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Critical Care, Trauma and Resuscitation

S-80.

THE AGE OF TRANSFUSED BLOOD PREDICTS HEMATOCRIT CHANGE IN PATIENTS WHO HAVE UNDERGONE ELECTIVE HIP OR KNEE ARTHROPLASTY

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BACKGROUND: Important clinical decisions are based on the standard textbook teaching that there is an expected 3% increase in hematocrit (HCT) following transfusion of a single unit of packed red blood cells (PRBC).[1] There is evidence to suggest that the HCT increase following transfusion in critically ill patients is dependent on the storage time of the transfused blood.[2] Our study is designed to further evaluate this relationship by considering a group of generally healthy patients without concurrent disease processes that could obscure the relationship between HCT change and length of storage of the transfused blood.

METHODS: Charts of the patients that have undergone first-time elective total hip or knee arthroplasty for degenerative joint disease and required blood transfusion for postoperative anemia were included in this study. Included patients received either one or two units of PRBC and there was no cutoff for pre-transfusion HCT values that were considered for this study. Patients that were noted to have postoperative "bleeding" or "hemorrhage" were excluded. Change in HCT level following transfusion was the outcome variable; it was calculated by subtracting the pre-transfusion HCT value from post-transfusion HCT value. When two units of PRBC were transfused to a single patient, resultant change in HCT was divided by two. To interpret the data, duration of blood storage was analyzed as continuous and grouped by weeks of age.

RESULTS: A total of 529 patient's charts were reviewed. Final analysis included 104 patients that received a total of 170 units of PRBCs. Of 104 patients, 38/104 (36.5%) received 1 unit of PRBC and 66/104 (63.5%) received 2 units of PRBC. A statistically significant, linear, inverse relationship was observed between the age of the transfused blood and change in HCT ($r2 = -0.16$, $P < 0.0001$; Figure 1). When transfused blood was grouped by weeks of age, a statistically significant difference in the change in HCT was observed between transfused blood that was ≤3 weeks of age and >3 weeks of age (3.5% vs 2.3%, respectively; $P = 0.001$; Figure 2).

CONCLUSION: Based on our findings we conclude that the change in hematocrit following transfusion in a generally healthy population decreases with increasing age of the transfused blood. Average change in HCT is 3.5% for units of blood that are ≤3 weeks of age and 2.3% for units of blood that are >3 weeks of age. We conclude that the standard teaching that there is an expected 3% increase in HCT following a transfusion of a single unit of PRBCs is no longer accurate.

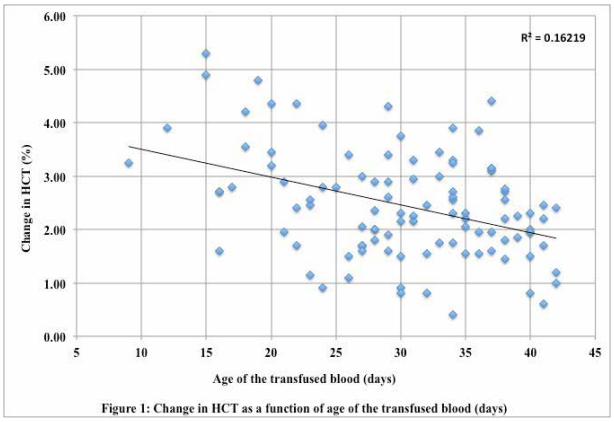

Figure 1: Change in HCT as a function of age of the transfused blood (days)

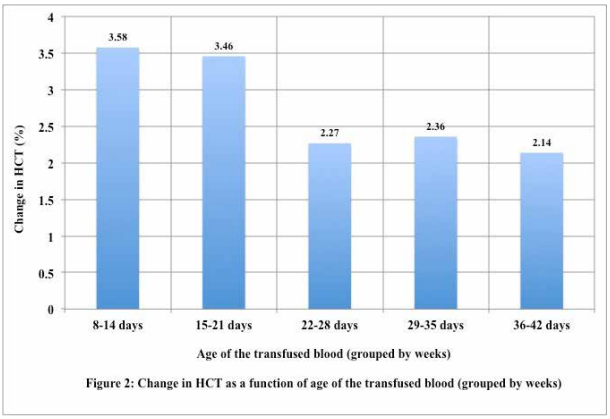

Figure 2: Change in HCT as a function of age of the transfused blood (grouped by weeks)

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S-81.

BLOOD RECOVERY FROM VACUUM-ASSISTED WOUND CLOSURE DEVICES

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INTRODUCTION:

Using negative pressure to assist with wound closure and wound healing has been shown to be highly effective. It is used in many types of surgeries for treatment of a wide variety of wounds. Vacuum-assisted wound closure devices (VAWCDs) are used to apply negative pressure and aid in wound closure and healing by promoting local perfusion. They also promote fluid and blood exudate. The fluid aspirated by VAWCDs is sanguineous and may contain a considerable volume of red blood cells (RBCs). Blood recovery, the perioperative process by which autologous blood is salvaged and retransfused back to the patient, has been shown to reduce the risk of blood transfusions. The aim of this study was to measure the amount of hemoglobin (Hb) lost to VAWCDs in order to evaluate whether or not blood recovery should be considered for VAWCD fluid.

METHODS: Prospective cohort study of the Hb content of VAWCDs in patients with surgical VAWCDs. All canisters of fluid aspirated by the VAWCD were collected. Total fluid volume, total RBC Hb, and free Hb was measured for each canister. Total Hb was calculated from RBC Hb and free Hb. Numbers were totaled for all canisters from a given patient for a given VAWCD site. Microbiology testing was done on all samples for sterility.

RESULTS: Fourteen patients with either large wounds undergoing wound debridement, trauma wounds, or exploratory laparotomy wounds were enrolled in the study. A total of 39 canisters were collected; patients filled one to ten canisters with fluid each, with each canister holding up to 500mL fluid. Patients filling less than one canister (n=4) were excluded. Data from the remaining ten patients showed stratification of patients into either low or high amounts of total Hb: 3.6 +/- 1.3 g Hb (n=8) vs 42.6 +/- 8.8 g Hb (n=2). There was no stratification of free Hb (0.6 +/- 0.4 g Hb, n=10). Mean total fluid volume was 2,033 +/- 202 mL. 23% of canisters (9/39) were not sterile.

CONCLUSIONS: Despite losing high volumes of fluid, most patients with VAWCDs do not lose more than a few grams of Hb. In a small subset of patients there is significantly more bleeding into the wound site and into the VAWCD. These patients lose the equivalent of more than half a unit of packed red cells through their VAWCDs. In terms of sterility, some canisters were contaminated with bacteria, most likely from the wound site. Whether or not red cells can be safely and effectively recovered from VAWCDs will need to be investigated. This study does not support the routine application of blood recovery to VAWCDs.

S-82.

LONG TERM SEDATION WITH VOLATILE ANESTHETICS COMPARED TO PROPOFOL IMPROVES OUTCOME IN A RODENT MODEL OF SEPSIS.

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INTRODUCTION: Sepsis and septic shock are associated with a mortality of approximately 50% and tremendous healthcare costs[1]. Septic patients often require mechanical ventilation and long-term sedation. Due to the known immunomodulatory effects of volatile anesthetics[2] we hypothesized that sedation with these agents would be associated with better outcome compared to sedation with propofol in a rodent model of severe sepsis.

METHODS: Sepsis was induced by cecal ligation and puncture (CLP) in adult male Wistar rats. All animals were mechanically ventilated via a tracheotomy and were instrumented with an arterial and venous line. Sedation was maintained for 24 hours with propofol (5-10mg/kg/h), sevoflurane, desflurane or isoflurane (0.7 MAC). Two sham operated groups received isoflurane or propofol. Arterial blood gases were analyzed every 6h. 0.5ml/kg/h NaCl 0.9% was administered to all rats and doubled in septic animals if mean arterial pressure dropped <55mmHg.

Survival was analyzed using a Log-Rank test; biochemical data was assessed with Student's t-test or ANOVA.

RESULTS:

1. Survival time decreased to 12h (mean) for animals in the CLP-propofol group, whereas survival was >56% after 24h in all other groups ($p<0.001$).
2. After 18h, base excess was significantly lower ($p<0.01$) in the propofol group comparet to the volatile groups (-20.6 for propofol vs. -11.7, -11.8 and -14.2mEq/l for isoflurane, sevoflurane and desflurane).
3. Sham operated animals sedated with propofol showed a 2.7-fold increase in endotoxin levels after 24 hours compared to isoflurane ($p<0.0001$). At 12h endotoxin levels in septic CLP-animals were twice as high in the propofol compared to the isoflurane group ($p<0.0001$).
4. Propofol led to a more pronounced inflammatory reaction when compared to the volatile groups: TNF levels at 12h were 133 vs. 549pg/ml ($p<0.001$) in septic isoflurane animals compared to propofol and 23 vs. 89pg/ml in sham animals after 24h ($p<0.05$).

CONCLUSIONS:

1. Survival of septic rats sedated with the 3 most commonly used volatile anesthetics was significantly higher compared to sedation with propofol.
2. Acidosis developed faster in animals sedated with propofol.
3. The inflammatory response was attenuated in the volatile groups compared to the corresponding propofol groups.
4. Translated into a clinical scenario septic patients might benefit from sedation with volatile anesthetics.

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S-83.

INVESTIGATION OF A NOVEL TURBINE-DRIVEN VENTILATOR FOR USE IN CARDIOPULMONARY RESUSCITATION

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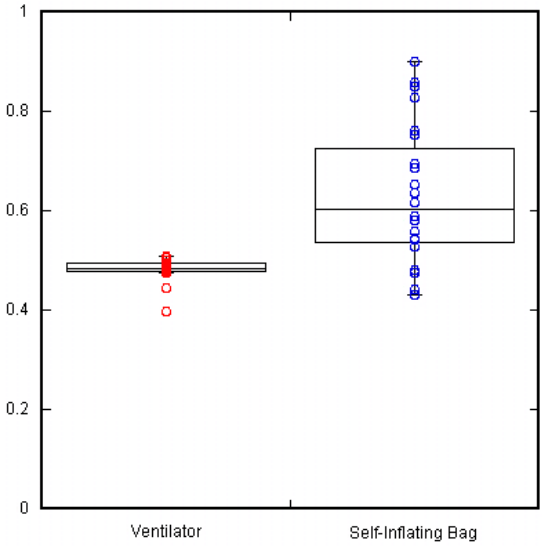
BACKGROUND: Past research has shown that increased respiratory rate during cardiopulmonary resuscitation is inversely correlated with systolic blood pressure. Rescuers often hyperventilate during CPR. Current American Heart Association Advanced Cardiac Life Support (ACLS) recommends a ventilation rate of 8-10 br/min once an advanced airway is established. We hypothesized that a novel, small, turbine-driven ventilator would allow rescuers to adhere more closely to ACLS guidelines.

METHODS: 24 ACLS-certified healthcare professionals were paired into groups of two. Each team performed four randomized rounds of 2-minute cycles of CPR on an intubated manikin, with individuals altering between compressions and breaths. Two rounds of CPR were performed with a self-inflating bag (SIB) and two rounds were with the ventilator. The ventilator was set to deliver 8 br/min, pressure limit 22 cmH20. No coaching of volunteers was given. Respiratory rate (RR), tidal volume (Vt), peak airway pressure (PIP) and compression interruptions (hands-off time) were recorded. Teams also attempted to mask-ventilate the extubated manikin with the ventilator and the SIB. Data were analyzed with a linear mixed model and Welch two-sample t-test.

RESULTS: The mean RR with the ventilator was 7.997 (standard deviation 0.103, 95% confidence interval 7.034-8.958). Mean RR with the SIB was 10.05 (SD 2.15, 95% CI 8.828-11.271). Mean ventilator Vt was 0.482 L (SD 0.022, 95% CI 0.441-0.523). Mean SIB Vt was 0.626 L (SD 0.084, 95% CI 0.568-0.685). Mean ventilator PIP was 22.15 cmH2O (SD 0.314, 95% CI 20.14-24.15). Mean SIB PIP was 31.88 cmH2O (SD 4.47, 95% CI 29.05-34.71). Mean hands-off time for ventilator and SIB were 5.25 sec (SD 2.10) and 6.41 sec (SD 1.45, 95% CI 0.431-1.902), respectively. During the mask leak trial, the mean ventilator delivered Vt was 2.65 L, of which 0.432 L entered the lungs. The mean SIB Vt delivered was 0.448 L, of which 0.262 L entered the lungs.

CONCLUSIONS: When compared to a ventilator with fixed settings in a manikin model, volunteers ventilated with a self-inflating bag within ACLS guidelines. However, volunteers ventilated with increased variation, at higher tidal volumes and higher peak pressures with the SIB. Hands-off time was also significantly lower with the ventilator. In a mask leak simulation, the ventilator provided higher, more consistent tidal volumes. These findings indicate that a turbine-driven ventilator may benefit CPR.



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S-84.

EPINEPHRINE INTRA-MUSCULAR "PENS"

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INTRODUCTION: Intramuscular epinephrine doses of 0.15, 0.3, and 0.5mg are delivered by a variety of devices (pens) containing glass syringes of epinephrine. Delivery of drug is through clothing into the lateral aspect of the thigh in cases of anaphylaxis and life-threatening asthma, and educational institutions in States of the USA have "pens" and training in place following anaphylaxis deaths (see Virginia House Panel ruling HB1107, 2012). Devices have different power springs and needles of different lengths and gauge to pierce clothes, skin, and muscle and to push on the syringe plunger to deliver epinephrine to the patient. We report preliminary investigation of EpiPenR (round barrel model), JextR, and AnapenR.

METHODS: 300 mcg dose pens were either purchased (about $40) by the authors, or donated because they were out-of-date. The manufacturer of AnapenR supplied free pens. We were unable to measure needle thrust power, but measured the length of vertical spray of liquid epinephrine by discharging slightly-angled devices on a wooden floor onto a vertical white wall. The height of the bottom and the top of spread of liquid on the wall was measured from the needle end. Discharge of contents was timed. Needle lengths (protruding from the sheath), diameter, and bevel length were measured, and used devices were dismantled.

RESULTS: Table 1. Anapen uses different concentrations of epinephrine to achieve dosage in a 0.3ml volume, the others have the same epinephrine concentration and utilise a syringe plunger-stop mechanism to change amounts (0.15 and 0.5mg) injected. Jext uses 1mg per ml of epinephrine. Anapen took 2.1 seconds to discharge contents, the others less than 1 second.

CONCLUSION: Jext was the most "powerful" injector with the biggest springs. AnapenR has been withdrawn from use in the UK because the needle was deemed too short, but continues to be used in Canada and mainland Europe. Further research in vitro and vivo is worthwhile, because even multiple doses of epinephrine did not succeed in saving a life[1]. Future ideas may be modification of devices to give more than one dose of epinephrine; advising to have available (and to be ready to use), more than one device for a patient; combining epinephrine with an alpha agonist, (metaraminol or vasopressin), to prevent pooling of blood in muscles and to restore blood pressure[2]. Metaraminol is now part of the Association of Anaesthetists of UK and NI anaphylaxis guideline when intravenous epinephrine does not have a required effect[3].

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Epinephrine "pen" comparison

Pen name	Needle length protruding	Needle diameter	Bevel length	Final needle position	Vertical spray height
Anapen	8mm	0.4mm(27G)	1.25mm	Stays out	13-16cm
EpiPen	13.5mm	0.72mm(22G)	3.28mm	Stays out	58-64cm
Jext	15mm	0.72mm(22G)	2.25mm	Covered	166-180cm

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S-85.

PREDICTION SCORE NOT NECESSARY FOR PATIENTS WITH ATRIAL FIBRILLATION BEFORE CARDIAC SURGERY

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INTRODUCTION: Atrial fibrillation is a common arrhythmia associated with increased morbidity and mortality after cardiac surgery[1]. There are effective treatments available for prophylactic prevention of postoperative atrial fibrillation.[2] The ability to predict which patients are at high risk of developing the arrhythmia will facilitate efficient implementation of a prevention protocol. We recently derived a clinical score to predict new onset postoperative atrial fibrillation (POAF)[2]. The score consists of three simple variables: age ≥65 years old, any mitral valve disease and left atrial dilatation. The predicted probability of developing new onset POAF after heart surgery based on the score is: 15.0% if the score is 0, 19% if 1, 25% if 2; 32% if 3, 39% if 4, 48% if 5, 56% if 6 and 64% if 7. This project aims to test the predictive value of this atrial fibrillation score in patients who already have preoperative atrial fibrillation. We hypothesize that the prediction score is not applicable to patients with preoperative atrial fibrillation since they are inherently at very high risk of developing it after surgery.[4]

METHODS: After research ethics approval, all patients with a history of atrial fibrillation who underwent non-emergent CABG and/or valve surgery from Jan 1st 2010- Dec 31st 2011 were included in this observational cohort study. Using prospectively collected data from a perioperative database supplemented with detailed chart review, eligible patients were assessed for the development of POAF and clinical outcomes in hospital. An atrial fibrillation score was calculated for each patient. Prediction rule validation was performed using the Chi Squared goodness-of-fit test as well as comparison of the area-under-the curve using the Hanley McNeil method.

RESULTS: 293 (81%) of 362 patients developed POAF. The average atrial fibrillation score was 4.5+/-1.9 with a predicted probability of 44+/-14% of developing POAF. 78% of patients had a score at at least 4. All observed rates of POAF were significantly higher than predicted at each level of the score ($p<0.0034$). The AUC under the ROC was 0.573 and was significantly different from the derivation cohort, $p=0.01$. There was no significant difference between the incidence of complications between the two groups. Patients who developed POAF had significantly longer length of hospital stay 18.1 vs 11.5 days, $p=0.001$.

CONCLUSIONS: The majority of patients who have any preoperative atrial fibrillation will also develop it after cardiac surgery. The atrial fibrillation score is not applicable in this population and routine prophylaxis against postoperative atrial fibrillation is recommended in this subset of high risk patients. Prophylaxis may help reduce costs associated with longer hospital stays.

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S-86.

THE EFFECT OF PEEP ON BLOOD LOSS DURING RADICAL PROSTATECTOMY

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INTRODUCTION: Positive end expiratory pressure (PEEP) is commonly applied intraoperatively to prevent atelectasis, and thereby improve oxygenation.[1-2] However, PEEP has been shown to increase vena cava pressures which could result in increased intraoperative blood loss (EBL), especially in prostate surgeries where the bleeding is predominantly venous.[3-4] Known risk factors for EBL during radical retropubic (RRP) and robotic (ROP) prostatectomy include increased BMI and prostate size,[5] but the effect of PEEP on EBL has not been studied. We designed this retrospective database study to investigate the effect of PEEP on EBL in RRP and ROP.

METHODS: We collected data on 240 patients who underwent either RRP or ROP at a single institution between the years 2008 and 2012. Patients were only included in the analysis if their surgery was performed by the 4 surgeons who routinely perform these procedures. Anesthetic records were examined to determine the median PEEP values during surgery. Patient characteristics were compared using t-tests, rank sum, or chi-square tests as appropriate. The association between PEEP (continuous) and EBL (continuous, log-transformed) was tested using linear regression. Models were stratified by surgery type (RRP or ROP) and adjusted for BMI, prostate weight, year of surgery, and surgeon. The interaction between PEEP and type of surgery was tested in the linear regression model.

RESULTS: After excluding patients with missing data, the final sample size was 208 patients. Patients undergoing RRP and ROP were similar with respect to age, race, BMI and prostate size. Median EBL for ROP and RRP were 150ml and 900ml, respectively ($p<0.001$). Patients were classified into low ($\leq$ 1 cmH20) and high ($\geq$ 5 cmH20) PEEP groups. For RRP, median EBL was 725 ml for low PEEP versus 1000 ml for high PEEP ($P = 0.02$). For ROP, median EBL was 250 ml for low PEEP versus 150 ml for high PEEP ($P = 0.06$). After risk adjustment, every cmH20 increase in PEEP was associated with a 7.1% increase in EBL for RRP ($p=0.02$), and a 6.6% decrease in EBL ($P=0.11$) in ROP (Table). Furthermore, the interaction between PEEP and surgery type in predicting EBL was significant ($p=0.004$).

Table: Association between EBL and PEEP by type of surgery

	Open RP		**Robotic RP**	
	Δ% change in EBL** (95% CI)	p-value	Δ% change in EBL**	P-value
			(95% CI)	
Crude	7.2% (1.1,13.6)	0.02	–8.1% (–15.3, –0.4)	0.04
Adjusted*	7.1% (1.1,13.4)	0.02	–6.6% (–14.2, 1.7)	0.113

CONCLUSIONS: We found that the addition of PEEP during radical prostatectomy was associated with differing effects on blood loss, resulting in higher EBL in RRP and a trend towards a lower EBL in ROP. Since PEEP increases venous pressure, our findings of increased EBL during RRP suggest that the benefits of using PEEP should be weighed against the risk of increased EBL. During ROP, it is likely that the extraperitoneal insufflation counteracts the effects of increased venous pressure, thereby preventing blood loss.

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S-87.

COMPARISON OF INTRAVENOUS CONTINUOUS AND BOLUS INFUSION OF FLUIDS IN PATIENTS UNDERGOING MAJOR GASTROINTESTINAL SURGERY.

AUTHORS: L. H. Navarro e Lima[1], R. M. Lima[1], N. Y. Santos[1], W. Meira1, G. R. Rodrigues[1], A. Brinley[2], G. C. Kramer[2]

AFFILIATION: [1]FMB - Anesthesiology Department, Botucatu Medical School - UNESP, Botucatu, Brazil, [2]UTMB - Anesthesiology Department, University of Texas Medical Branch, Galveston, TX

INTRODUCTION: Surgical patients lose large amounts of fluid perioperatively, usually due to blood, urine, and insensible evaporative loss. Optimal management of fluid loss is widely debated as studies show increased mortality with surgery-associated hyper and hypovolemia. Current standard of care (SOC) for surgical fluid administration is continuous intravenous infusion of crystalloid and colloid solutions as well as blood products. This study seeks to determine how bolus infusion of fluids, rather than the SOC infusion, affects patient outcomes. We hypothesize that bolus infusion will reduce total amount of fluid delivery, time to return of bowel function, first feeding, and hospital discharge.

METHODS: Patients between ages 18-65, ASA grades I-III, undergoing major gastrointestinal (GI) surgery were included in this study. Major exclusion criteria included underlying kidney disease. Consecutive patients were randomized to either the control SOC infusion group or the experimental bolus infusion group. The fluid delivery algorithm in the bolus group was based on mean arterial pressure (MAP) and on a pulse pressure variability (PPV) threshold (>12%) (figure 1). The major study outcomes were volume of fluid infused during surgery, time to first intestinal evacuation, time to first oral feeding, and time to hospital discharge. Additional parameters were measured during surgery including the amount and types of fluid, blood product, and urinary output. Blood chemistry values were collected at 60 time intervals. Data with a normal distribution were analyzed using a student's t-test for comparison of the bolus versus SOC groups and presented as mean ± standard deviation.

RESULTS: Data from 58 patients were analyzed. There were no significant differences between groups for age, weight, height, or ASA grade. There were no significant differences for time to first intestinal evacuation (4.8±2.9 vs. 4.5±2.7; p=0.74), time to first oral feeding (3.6±2.1 vs. 3.0±2.2; p=0.27), or time to hospital discharge (11.8±5.8 vs. 11±5.6; p=0.74) between SOC and bolus groups, respectively. However, the volume of fluids (mL) administered was significantly decreased in the bolus group (3,683±2,455) compared to the SOC group (4,487±2,087; p=0.04). Total volume of crystalloids (Lactate's Ringer) delivered (mL) was different between groups (SOC: 3,830±1,445 vs. bolus: 2,828±1,662; p=0.02), as well as the urine output (SOC: 581±315 mL vs. bolus: 421±249 mL; p=0.04). There was no statistically significant difference regarding lactate or central venous oxygen saturation measurements between SOC and bolus groups (figure 2).

CONCLUSIONS: Bolus fluid therapy directed by a PPV algorithm lowered perioperative fluid requirements during major GI surgery compared to patients resuscitated using continuous infusion delivery by SOC per overall clinical assessment. Hemodynamic deficiencies from perioperative fluid losses may be restored using less infused fluid using bolus therapy thereby reducing surgical risks associated with fluid overload.

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Figure 1: Algorithm for fluid delivery in the bolus group.

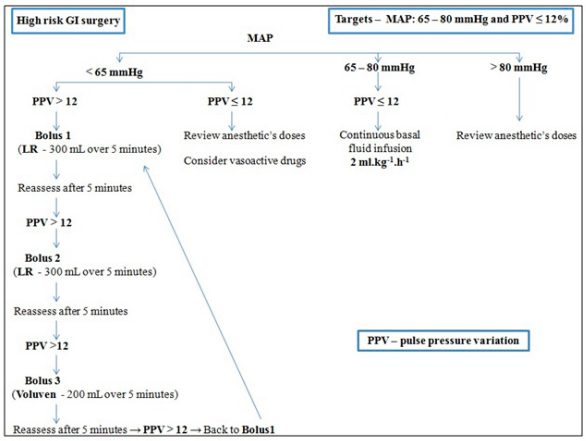
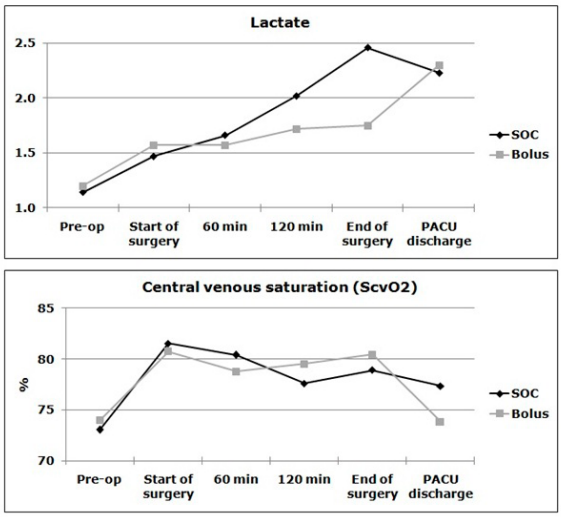


Figure 2: Comparison regarding lactate levels and central venous oxygen saturation throughout the study between SOC and bolus groups.



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S-88.

MEAN PLATELET VOLUME ASSOCIATION WITH POSTOPERATIVE ACUTE KIDNEY INJURY

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INTRODUCTION: Acute kidney injury (AKI) is a frequently encountered clinical problem in the post-surgical population. Its presentation in patients is an independent predictor of morbidity and mortality. Several risk factors for AKI have been reported[1,2] but a complete understanding of AKI remains elusive. Thrombosis due to activated platelets may contribute to microvascular dysfunction that is noted in AKI[3]. An elevated mean platelet volume (MPV) reflects larger platelets, which are believed to be more reactive than smaller platelets. An elevated MPV has been linked to other thrombosis-related disease states[4] including myocardial infarction[5] ischemic stroke[6] and venous thromboembolism[7]. We hypothesize an elevated MPV will be associated with increased incidence of AKI.

METHODS: The AKI database was created by combining our institutional perioperative database, and intermediate outcomes obtained from the institutional Society of Thoracic Surgeons database were used for analysis. For assessment of postoperative AKI, we compared the creatinine values from the last preoperative day vs. the highest postoperative (within 3 days of surgery) value. AKI was defined by KDIGO stage 1 guideline (creatinine increase by 50% or > 0.3 mg/dL). MPV and platelet counts were taken from most recent value prior to surgery. Univariate data comparison used student-t, Wilcoxon rank sum, Fisher's exact test, and Chi square test as appropriate. Variables were then entered into a logistic regression model. 95% confidence intervals that excluded 1 and p values <.05 denoted statistical significance.

RESULTS: A total of 4361 patients were analyzed, and 1207 developed at least stage 1 AKI. After adjustment for demographics, baseline renal function, and co-morbidities, both larger platelets and more platelets were associated with a lower occurrence of AKI. (Table 1) The model has fair discrimination (area under the ROC curve or c-statistic = 0.626 +/- 0.10).

Table 1

Factor	odds ratio	95% confidence interval	p-value
Hypertension	.624	.535 - .728	<.001
Congestive heart failure	.626	.534 - .734	<.001
Creatinine (mg/dL)	1.479	1.286 - 1.700	<.001
Platelet count (K/uL)	.999	.998 - 1.000	.010
Mean platelet volume (fL)	.941	.888 - .996	.037
Constant	.899		.747

CONCLUSIONS: Smaller platelets and fewer platelets pre-operatively are associated with postoperative AKI. This finding is in contradiction to previously described associations between elevated MPV and thrombosis-associated conditions. Further investigation into this association is required, as this finding may eventually help guide AKI prevention strategies in the future.

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S-89.

METHYLENE BLUE ADMINISTRATION FOR ACUTE SEPTIC CARDIOMYOPATHY IN A SEVERELY BURNED PATIENT

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INTRODUCTION: A 60 year old male with no known past medical history was admitted to the Burn Intensive Care Unit with a 45% total body surface area burn secondary to a house fire.

CASE REPORT: During hospitalization, the patient developed septic shock from a pneumonia that was poorly responsive to fluid therapy and vasoactive medications. Transthoracic echocardiography demonstrated a global hypokinesis with an ejection fraction of 10% (from a previous normal 55% ejection fraction). The patient was refractory to infusions of epinephrine, milrinone, norepinephrine, and vasopressin. A pulmonary artery catheter demonstrated a cardiac index of 0.9 L/min/m2 and a systemic vascular resistance of 2100 mmHg. While methylene blue (MB) is typically used for vasoplegia and vasodilatory shock, there is literature that it can improve myocardial performance in the face of septic cardiomyopathy. Therefore we administered methylene blue to improve cardiac performance, weaned our vasoactive medications, and utilized a low-dose furosemide infusion for afterload reduction.

CONCLUSIONS: Nitric oxide (NO) is believed to contribute to the detrimental hemodynamic effects associated with septic shock. NO activates the second messenger guanylate cyclase, which converts cyclic guanosine triphosphate (cGTP) to cyclic guanosine monophosphate (cGMP), resulting in smooth muscle relaxation. In septic patients, bacterial endotoxins and inflammatory cytokines can activate production of an inducible nitric oxide synthase (iNOS), leading to excessive production of NO and cGMP. iNOS is present in both the vasculature and the myocardium. The sustained production of NO from iNOS leads to profound vasodilation, hyporeactivity to catecholamines/vasopressors, and decreased inotropy. Methylene blue (MB) has been used successfully in the treatment of shock and acts through inhibition of eNOS and iNOS. Recent reports have shown that MB increases mean arterial pressure (with or without vasopressors) and reduces adrenergic support requirements in patients with sepsis. In addition, MB has been shown to increase cardiac contractility (increased SVI, LVSWI, RVSWI) through increased sensitivity to catecholamines (endogenous and exogenous) and/or by reducing the attenuating effect of NO on myocyte contraction.

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S-90.

ASA TRAUMA CARE SURVEY: ANESTHESIOLOGY PRACTICES AND OPPORTUNITY FOR EDUCATION

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INTRODUCTION: U.S. hospitals report 39.4 million emergency department (ED) visits for injury annually, and a 14.3% hospital admission rate; 7.3 million of those injured require operative intervention.[1] Anesthesiologists care for injured patients in the ED and/or the operating room (OR). There are no data on acute care anesthesiology practices that incorporate trauma management guidelines.

METHODS: An American Society of Anesthesiologists (ASA) survey of 50 items that questioned participants on preferred techniques, drug use, training, and resuscitation practices for trauma patients in the ED or the OR was distributed by email to 21,491 active anesthesiology attendings.

RESULTS: 2,360 ASA members responded to the survey, with 87.2% saying they provide care for trauma patients. 79% work in a designated trauma center, most of which were private (65.8%) and in urban areas (59.5%). 53.3% of practitioners respond to ED trauma for severely injured patients only and a third (34.1%) not at all. Of those who respond, most (67.4%) only provide airway management; 30% assist with vascular access, resuscitation and/or sedation. Rapid sequence induction (RSI) with direct or video-laryngoscopy was the preferred intubation technique in all patients except those who were hemodynamically stable with known cervical spine deficit (fiberoptic). In hemodynamically unstable patients, etomidate is the induction agent of choice; the majority of respondents reported the use of cricoid pressure (CP) during RSI despite recent literature suggesting no benefit (CP)[2] or potential harm (etomidate)[3,4] from these practices. The majority of respondents reported the use of massive transfusion protocols, but no departmental trauma-anesthesia practice guidelines. 36.2% of respondents have been in practice for > 20 years. One third of the respondents are ATLS certified and 71% desire more ASA educational sessions on trauma care.

CONCLUSIONS: Although anesthesiologists who care for injured patients work in designated trauma centers, the majority are not involved in ED resuscitation. Established trauma guidelines are not always followed. Our results suggest both a need for improved training and an opportunity to expand the peri-operative anesthesiologists' role in the management of patients following traumatic injury.

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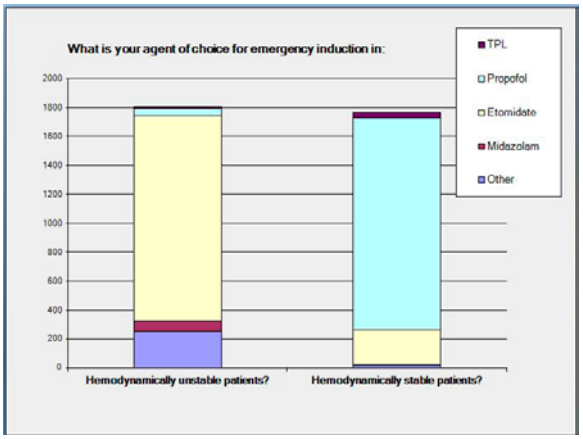
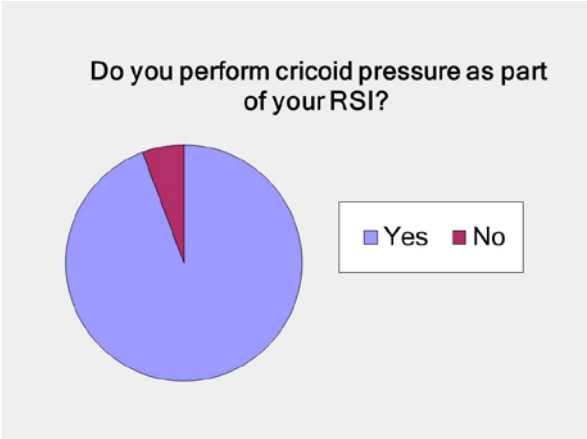
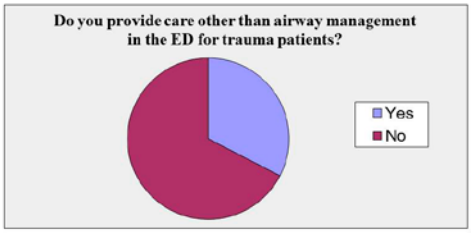




Do you provide care other than airway management in the ED for trauma patients?	Response Percent
Yes	32.6%
No	67.4%



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S-91.

WITHDRAWN.

S-92.

NEEDLELESS CONNECTORS SUBSTANTIALLY REDUCE FLOW OF CRYSTALLOID AND RED BLOOD CELLS DURING LARGE VOLUME RESUSCITATION

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INTRODUCTION: Needleless connectors are widely used in intravenous (IV) tubing in order to reduce blood exposure and bloodstream infection. These connectors have the unintended consequence of decreasing IV fluid flow rates, which is acceptable in many clinical situations. We theorized that needleless connectors produce clinically undesirable flow reduction in cases that require large volume resuscitation of crystalloids and blood products.

METHODS: A Level 1® H-1200 Fast Flow Fluid Warmer was used to deliver crystalloid and red blood cells (RBC) under pressure during simulated massive transfusion. Trials compared flow rates without (control) and with five models of needleless connectors and a variety of IV catheter sizes: 9 french introducer, 7 french Rapid Infusion Catheter, and 14, 16, 18, 20, and 22-gauge IV catheters. Each series of trials consisted of one control and a new needleless connector of each type used with the array of IV catheters and identical transfusion fluid. For each fluid type, five trial series thus tested five individual connectors of each model. Flow rates were measured by timed delivery of 10-100ml volumes in a graduated cylinder. Data are mean +/- SEM.

RESULTS: All five needleless connector models substantially reduced flow of crystalloid and RBCs. Observed flow rates were most affected with the largest IV catheters used. Average RBC flow reductions of 56+/-7% (9 french introducer), 57+/-7% (7 french Rapid Infusion Catheter), 53+/-7% (14 gauge IV), 45+/-8% (16 gauge IV), 31+/-6% (18 gauge IV), 23+/-5% (20 gauge IV), and 11+/-4% (22 gauge IV) were observed (n = 5 series of trials). Average crystalloid flow reductions were 67 +/- 6% (9 french introducer), 69 +/-5% (7 french Rapid Infusion Catheter), 60 +/-6% (14 gauge IV), 51 +/- 7% (16 gauge IV), 33 +/-7% (18 gauge IV), 21+/-6% (20 gauge IV), and 17 +/-5% (22 gauge IV, n = 5 series of trials).

CONCLUSIONS: Needleless connectors in IV tubing greatly reduce the flow of RBC and crystalloid through large-bore IV catheters during simulated large volume resuscitation. Of note, a 9-French introducer with an average needleless connector approximates the flow properties of an 18 gauge IV catheter without. We suggest that providers consider omitting needleless connectors if large-bore IV catheters are placed for the possibility of uncontrolled perioperative hemorrhage.

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S-93.

PRE-BLOCK OF α7ACHRS BY ITS SPECIFIC ANTAGONIST, METHYLLYCACONITINE (MLA) OBLITERATES THE IMMOBILIZATION-INDUCED RESISTANCE TO ROCURONIUM IN MICE

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INTRODUCTION: Resistance to the neuromuscular effects of non-depolarizing muscle relaxants (NDMR) has been reported following immobilization. During this pathologic state, immature type (2α1β1δγ) and neuronal 5α7 acetylcholine receptors (AChRs) are re-expressed in peri- and extra-junctional areas[1,2]. These up-regulated AChRs can potentially contribute to the resistance to NDMRs. In this study using a specific antagonist ligand to the α7AChRs, methyllycaconitine (MLA, Sigma, St. Louis, MO) and NDMR, rocuronium bromide sequentially, we tested the hypothesis that α7AChRs are the cause of the resistance to the neuromuscular effects of rocuronium. To confirm this hypothesis, we preemptively blocked the α7AChRs, and then tested the response to rocuronium on the immobilized and contralateral side.

METHODS: After approval by the Institutional Animal Care and Use Committee, adult male, C57BL/6J, 25-30 g WT (n=13) mice were used. The ankle and knee joints were immobilized by insertion of sterile needles into the joint. The contralateral limb, by sham-immobilization, served as control. At 14 days after immobilization, mice were anesthetized, tracheotomized and mechanically ventilated. The jugular vein was cannulated for drugs and fluids. The sciatic nerve on each side was exposed and stimulated; the resulting contraction of the tibialis anterior muscle on each side was recorded. Supramaximal electrical stimuli of 0.2 msec duration at 2 Hz for 2 sec (train-of-four) were applied every 30 sec. After stabilization of the twitch, MLA (2 ug/g) or saline followed by rocuronium were administered sequentially (MLA+Roc or Sal+Roc groups, respectively) until ≥ 95% twitch depression on both sides. The percent depression of T1 relative to baseline was transformed to logit scale and plotted against the logarithm of the cumulative dose by linear regression analysis to determine the effective dose of rocuronium for 50% and 95% twitch depression (ED50, ED95) on each side.

RESULTS: The weight of the mice were 28.7±5.3 g (n=13). Tibialis and gastrocnemius muscle masses were significantly ($p<0.05$) decreased on the immobilized compared to contralateral side (Table 1). The baseline tibialis twitch tension on the immobilized was significantly ($p<0.05$) decreased compared to that of the contralateral side (Table 1). The ED50 (0.40 ug/g, p=0.0014) and ED95 (0.46 ug/g, p=0.0003) of rocuronium on the immobilized side in the Sal+Roc group (n=6) was significantly increased (Table 1) compared to contralateral side (0.20 ug/g and 0.23 ug/g, respectively). In the MLA+Roc group (n=7), the ED50 and ED95 showed no significant differences between immobilized and contralateral sides (Fig 1).

CONCLUSIONS: This study shows the muscle wasting (decreased tension) and resistance to rocuronium during immobilization for 14 days. The pretreatment (block) of α7AChRs by MLA obliterated the immobilization-induced resistance to rocuronium in mice. We conclude α7AChRs playa pivotal role in the resistance to rocuronium on the immobilized side.

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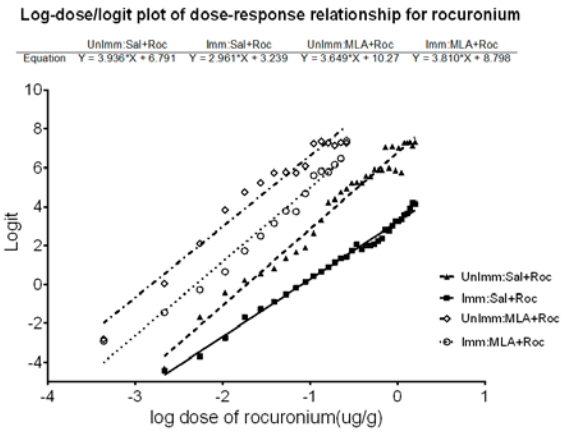

Table 1. † p<0.05 compared with contralateral side within group.				
	MLA+Roc (n=7)		Sal+Roc (n=6)	
	Contralateral	Immobilized	Contralateral	Immobilized
Baseline T1 (g)	15.3±2.3	12.8±2.3†	15.7±4.0	13.2±3.8†
Specific T1 (g/mg/g)	9.79±2.7	10.68±2.3	8.73±1.0	10.62±3.3
TA (mg/g)	1.59±0.3	1.30±0.2†	1.55±0.3	1.13±0.2†
SO (mg/g)	0.32±0.1	0.33±0.1	0.28±0.0	0.36±0.1
GC (mg/g)	5.44±0.5	4.43±0.5†	5.03±1.1	3.91±0.8†
ED50	0.07 (0.06-0.07)	0.11 (0.11-0.12)	0.20 (0.20-0.21)	0.40 (0.39-0.40)†
ED95	0.08 (0.07-0.08)	0.13 (0.12-0.13)	0.23 (0.22-0.23)	0.46 (0.46-0.47)†

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S-94.

ESTIMATED GFR AND AKI OUTCOME PREDICTION MODEL FOR POST CARDIAC SURGERY PATIENTS

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INTRODUCTION: Acute kidney injury (AKI) after cardiac surgery is common (incidence between 1-30%) and is associated with increased health care costs, longer intensive care unit stays, and a higher incidence of complications and mortality.[1,2] Traditional criteria, such as RIFLE, AKIN, and KDIGO, rely on a rise in Cr to diagnose AKI. However, it takes several hours or longer for a change in GFR to be reflected in a rise in Cr. Hence, these traditional criteria may be delayed in recognizing AKI.

A recent publication describes a "kinetic" estimated GFR (keGFR) equation relying on estimated Cr production rate and change in plasma Cr with corrections for fluid balance changes.[3] The purpose of this study is to determine if keGFR predicts AKI staging criteria and mortality.

METHODS: This is a retrospective cohort study of adult patients who underwent cardiac surgery between Jan 4, 2006 and Jan 5, 2012. Exclusion criteria were dialysis and missing baseline or postoperative Cr levels.

KeGFR calculated as:

KeGFR = [(SSPCr x CrCl)/Mean PCr] x [1 – (24xΔPCr)/(ΔTime(h) x MaxΔPCr/day)]

SSPCr = preoperative Cr, CrCl = preoperative Cr clearance by the MDRD formula[4], MeanPCr = mean of preoperative and current Cr, ΔPCr = difference between preoperative and current Cr, ΔTime = time between Cr, MaxΔPCr/day = 1.5 mg/Lday.[3]

AKI was defined as KDIGO stage 1 or worse (creatinine increased by 50% or increased by > 0.3 mg/dL) by the third postoperative day. Death was within 30 days of surgery or in hospital if >30 days. Odds ratios were determined using logistic regression (SPSS 21.0).

RESULTS: 1207 of 4355 patients (28%) developed KDIGO stage 1 or worse AKI with only 269 patients meeting KDIGO criteria for AKI on the first postop creatinine level. Those patients who developed AKI had a mean increase in creatinine of .08 + .29 versus -.121 + .18 mg/dL for those who did not (p<.001) while the GFR decreased 4 + 11 versus an increase of 4 + 7 mL/min/1.73m^2 (p<.001). Change in keGFR had good discrimination in predicting AKI (c-statistic = .765 + 0.11). Using a cutoff value of decrease in keGFR by 5 ml/min/1.73m2 this method had a 90% sensitivity and 45% specificity in predicting AKI.

Both the perioperative change in Cr and keGFR were found to provide good discrimination of AKI based on KDIGO criteria with an area under the ROC curve = 0.733 and 0.765 respectively. The odds ratio for the development of AKI for a 1 mg/dl increase in Cr =2.64 ((95% confidence interval 2.2-3.1, p<.001) and for each 1 ml/min increase in keGFR = 0.861 (95% confidence interval 0.85-0.87, p<.001). Using a combined metric of preop Cr and keGFR the area under the ROC curve for prediction of AKI was 0.800 + .008 (p = 0.008) and death 0.806 + .008 (P = 0.008).

CONCLUSIONS: In a population of cardiac surgery patients, keGFR accurately predicts AKI, and the combination of keGFR and preoperative Cr has good discrimination in predicting death. Future investigations would refine the keGFR equation to improve accuracy and diagnostic utility.

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Discrimination of Key Variables: Area Under the Curve

Variable	Area	P-Value	Asymptotic Sig.b	Asymptotic 95% C.I. Lower Bound	Asymptotic 95% C.I. Upper Bound
Immediate Pre-Op Creatinine	.591	.010	.000	.571	.611
Immediate Post-Op Creatinine	.757	.009	.000	.741	.774
Perioperative Creatinine Change	.733	.010	.000	.714	.752
eGFR Increase	.235	.008	.000	.219	.251

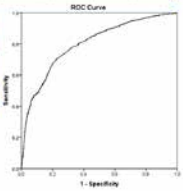
This ROC curve displays graphically the ability of a variety of variables to predict acute kidney injury based on the KDIGO criteria.

Logistic Regression: Discrimination AKI Versus No AKI

	B	S.E.	Wald	df	P-Value	Hazard Ratio	95% C.I. Lower	95% C.I. Upper
Immediate Pre-Op Creatinine	.971	.087	125.522	1	.000	2.640	2.226	3.129
eGFR Increase	-.149	.006	623.747	1	.000	.861	.851	.871
Constant	-1.963	.106	345.174	1	.000	.140		

Area Under the Curve

Variable	Predicted Probability			
Area	Std Error	Asymptotic Sig.b	Asymptotic 95% C.I. Lower Bound	Asymptotic 95% C.I. Upper Bound
.800	.008	.000	.785	.815



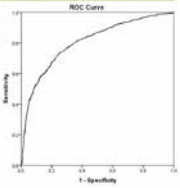
Using a combined metric of immediate pre-op creatinine with change in eGFR, this ROC curve displays graphically the **ability to predict acute kidney injury** based on the KDIGO criteria. The area under the curve has a value of 0.8 with a P value of <0.001 (Confidence interval of 0.785-0.815).

Logistic Regression: Operative Mortality

	B	S.E.	Wald	df	P-Value	Hazard Ratio	95% C.I. Lower	95% C.I. Upper
Immediate Pre-Op Creatinine	.605	.094	41.150	1.000	.000	1.831	1.522	2.203
eGFR Decrease	-.053	.008	44.750	1.000	.000	1.054	1.038	1.071
Constant	-4.324	.160	732.734	1.000	.000	.013		

Area Under the Curve

Variable	Predicted Probability			
Area	Std Error	Asymptotic Sig.b	Asymptotic 95% C.I. Lower Bound	Asymptotic 95% C.I. Upper Bound
.806	.008	.000	.791	.821



Using a combined metric of immediate pre-op creatinine with change in eGFR, this ROC curve displays graphically the **ability to predict post operative death**. The area under the curve has a value of 0.806 with a P value of <.001 (Confidence interval of 0.791-0.821).

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S-95.

COMPLEMENT FACTOR B ACTS DOWNSTREAM OF TLR3 SIGNALING IN THE HEART IN A MOUSE MODEL OF POLYMICROBIAL SEPSIS

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INTRODUCTION: Toll-like receptors (TLRs) and complements are two critical components of the host innate immune system. TLR3, originally identified as a sensor for viral RNA[1] , can also recognize bacterial and host endogenous RNA[2,3] and reportedly plays a role in bacterial sepsis contributing to septic cardiomyopathy and mortality[2,4]. However, the downstream mechanisms responsible for TLR3-mediated cardiac dysfunction is unclear. Complement factor B (cfB) is a necessary component of the alternative pathway of complement activation. We have recently demonstrated an important role for cfB in a mouse model of polymicrobial sepsis. Here, we hypothesize that cfB is specifically regulated by TLR3 signlaing in the heart during polymicrobial sepsis.

METHODS: Bone marrow-derived macrophages (Mϕ) or rat cardiomyocytes were stimulated with the TLR3 ligand, poly (I:C), or the TLR9 ligand, CpG. In vivo, WT and TLR3 KO mice were injected with 100 μg of poly (I:C) i.p.. A mouse model of polymicrobial sepsis was generated by cecal ligantion and puncture (CLP). Complement mRNA expression was assessed by qRT-PCR.

RESULTS: Poly (I:C) induced a robust cfB and moderate C3, but not C4 and C5, mRNA responses (cfB: 103 fold, C3: 22 fold, n=3, ***, P<0.001, #, P<0.01) in WT Mϕ (Fig. A). The effect of poly (I:C) was almost abolished in Mϕ deficient of TLR3. In cardiomyocyte cultures, poly (I:C), but not CpG, induced a marked increase in cfB gene (Fig. B, n=3, *, P<0.05 vs. Con.; PIC: poly (I:C)) and protein expression (Fig. C) in both cells and culture media. Similar results were observed in cardiac fibroblasts (Fig. C). In vivo, poly (I:C) administration specifically led to a marked increase in cardiac cfB gene expression at 24 hours with a minimum effect on C3, C4 and C5 (Fig. D, n=4, *, P<0.05, **, P<0.01, ***, P<0.001; PIC: poly (I:C)). Importantly, the increase in cardiac cfB is TLR3-depedenent as TLR3 deletion abolished the effect of poly (I:C) in vivo (Fig. D). Moreover, the CLP model of polymicrobial sepsis led to a specific cfB gene upregulation in the heart but had no impact on other complements tested (Fig. E, n=4-9, ***, P<0.001 vs. Sham).

CONCLUSIONS: We demonstrate that TLR3 activation leads to specific cfB expression in cultured Mϕ, cardiomyocytes and the heart. This effect seems specific for TLR3 as TLR9 activation fails to induce cfB expression. In vivo, polymicrobial infection leads to specific cardiac cfB gene expression. These data suggest that cfB expression is controlled by TLR3 signaling during bacterial sepsis.

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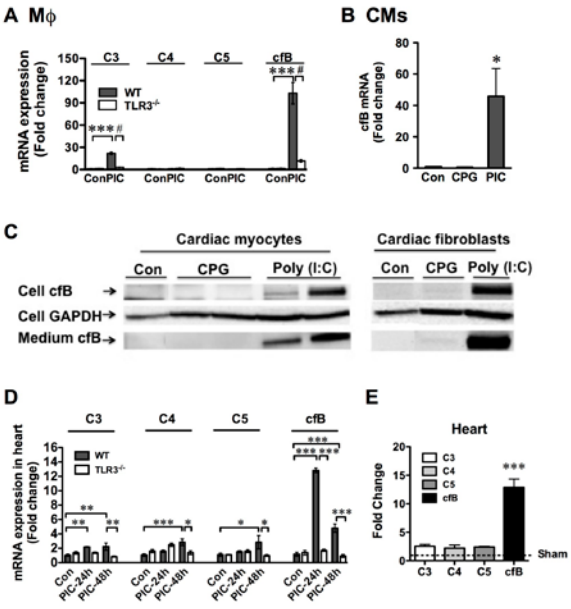

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S-96.

ANESTHESIOLOGISTS' PRACTICES IN CARING FOR PATIENTS WITH TRAUMATIC BRAIN INJURY DIFFERS FROM PUBLISHED GUIDELINES

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OBJECTIVES: Early management of severe traumatic brain injury (TBI) correlates with outcome. The Brain Trauma Foundation and Advanced Trauma Life Support® recommend a target cerebral perfusion pressure of 50-70 mmHg, and hyperventilation only when signs of cerebral herniation occur. We sought to identify practice of anesthesiologists involved in the management of patients with TBI in the emergency department (ED) or operating room (OR).

METHODS: An investigator initiated 50-item survey was distributed by email to American Society of Anesthesiologists (ASA) attending members. Nine items questioned participants on preferred techniques, drug use, training, and resuscitation practices for patients with neurological injuries. We examined frequencies and percentages of responses cross tabulated with demographics.

RESULTS: Of 21,491 surveys, 2,058 ASA members responded that they care for trauma patients. 79% work in a designated trauma center (54.2% Level I). Ninety-four percent of respondents report that they are comfortable managing patients with multiple injuries; a third of survey respondents have been in practice for > 20 years. For patients with TBI, 58.7% of respondents use >70 mmHg as a cerebral perfusion pressure (CPP) goal, and 66.6% use hyperventilation therapy to decrease ICP in the absence of herniation. These responses were more common for those in practice > 20 years and proportions did not change if the cohort was restricted to those that were ATLS certified (36%).

CONCLUSIONS: Whether the guidelines are not known, or are not followed by a majority of anesthesiologists caring for trauma patients remains unclear. There is a need for education and training of existing TBI guidelines.

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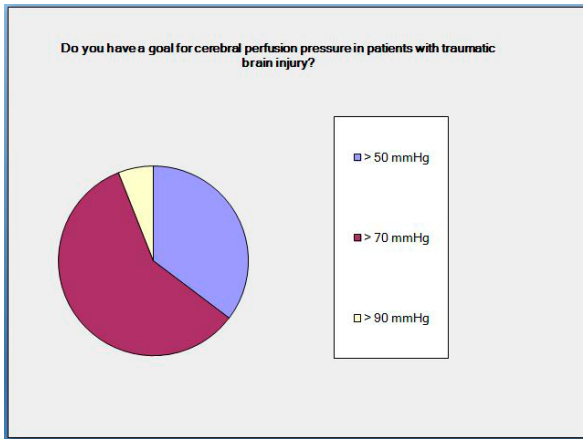

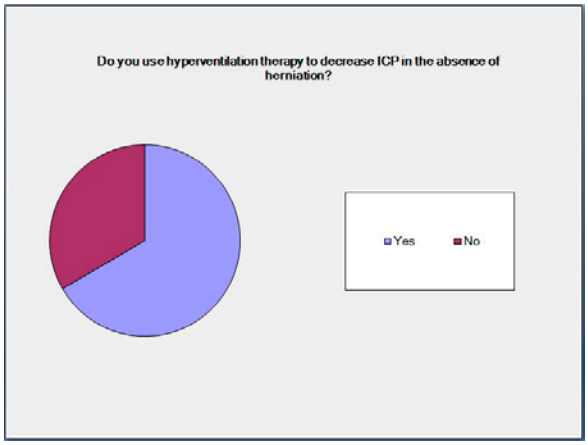

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S-97.

PULMONARY AND CENTRAL VENOUS PRESSURES AS PROGNOSTIC INDICATORS OF POST LUNG TRANSPLANT OUTCOME

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INTRODUCTION: Previous studies have assessed the correlation between the mean pulmonary arterial pressure (mPAP) and primary graft dysfunction (PGD) or mortality[1-4], while another study reported an association with elevated central venous pressure (CVP)[2,3]. We hypothesized that not only the individual values of mPAP and CVP, but also the interaction of these parameters may have a prognostic value in post-operative outcomes of patients undergoing lung transplantation.

METHODS: Perioperative data of 81 patients undergoing lung transplantation at a university hospital was analyzed. The primary outcome was lowest PO2/FiO2 ratio in the first 24 hours after admission to the ICU. Secondary endpoints were ventilation time, in-hospital mortality, length of ICU and hospital stay. We also dichotomized the data by P/F ratio ≥ 200 or < 200 to assess odds ratios. First, negative influence of increased mPAP or CVP on the outcome variables was assessed. Second, assessed the negative impact of discordance of high or low mPAP and high or low CVP (discordance group; DG) compared to concordance of high or low mPAP and high or low CVP (concordance group; CG).

RESULT: For 1 mmHg increase in mPAP and CVP, the lowest 24 hr P/F ratio decreased by 5.1 [95% CI 1.06, 9.12] and 8.48 [95% CI 2.89, 14.07] respectively (Figure 1). When hypoxia was defined as lowest P/F ratio < 200 in the first 24 hrs after admission, 1 mmHg increase in mPAP was associated with higher odds of developing hypoxia [OR 1.12; 95%CI 1.02, 1.23]. There was also a tendency towards higher risk of developing hypoxia in the DG [OR 1.52; 95% CI 0.4, 5.7]. There was significant association between 1 mmHg increase in mPAP and prolonged mechanical ventilation (>27hrs) [OR 1.13; 95%CI 1.02, 1.25]. ICU LOS was significantly extended (>5 days) for 1 mmHg increase in both mPAP and CVP ([OR1.19 ;95% CI 1.06, 1.33] and [OR1.19;95% CI 1.04, 1.37] respectively). There was also a significant difference in ICU LOS between DG vs. CG (OR 6.95 [95% CI 1.37, 35.23]). There was a trend towards increase in odds of extended hospital LOS between DG vs. CG [OR 3.63; 95% CI 0.84, 15,71].

CONCLUSION: Post-operative mPAP, CVP as well as the interaction between these two values may have prognostic values in patients undergoing lung transplantation.

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Figure 1a: Linear correlation of mPAP and lowest P/F ratio in 24 hrs

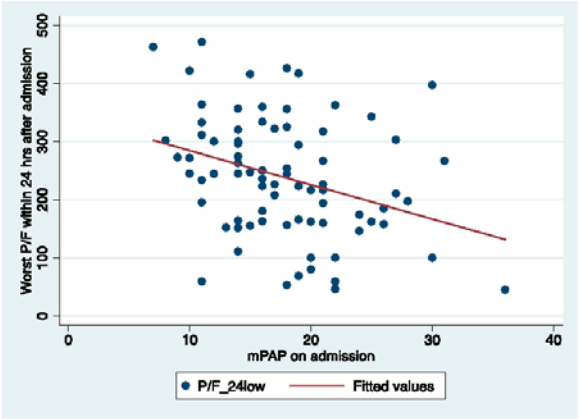
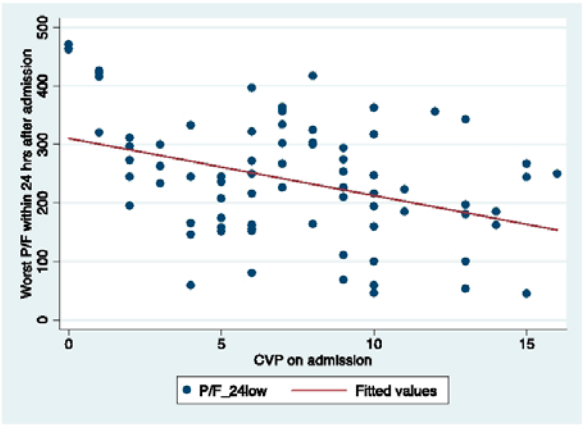


Figure 1b: Linear correlation of CVP and lowest P/F ratio in 24 hrs



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S-98.

ACUTE INCREASE IN HYDROSTATIC PRESSURE STIMULATES THE ENDOCYTOSIS OF ALBUMIN AND PHOSPHORYLATION OF CAV-1 IN LUNG MICROVASCULAR ENDOTHELIAL CELLS AND CHRONIC HEART FAILURE MICE: IMPLICATIONS FOR PRESSURE-INDUCED PULMONARY EDEMA.

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AFFILIATION: [1]Anesthesiology, University of Illinois at Chicago, Chicago, IL, [2]Pharmacology, University of Illinois at Chicago, Chicago, IL

INTRODUCTION: Lung vascular mechanotransduction, activate by elevated hydrostatic pressure, results in endothelial hyper-permeability to water[1,2]. This pathway involves heparan sulfate-dependent NO synthase activation and results in rapid NO-mediated loss of junctional VE-cadherin, contributing to increased paracellular water conductance. Heparanase III and L-NAME attenuate the increase in water permeability by approximately 75%, suggesting that an additional pressure-dependent mechanism is responsible for the remaining increase in permeability. We tested the hypothesis that hydrostatic pressure also increases caveolae-mediated albumin transport, and that this contributes to vascular hyperpermeability.

METHODS: Rat and human lung microvascular endothelial cells (RLMVEC, HLMVEC) were cultured for 5 days on 47 mm diameter polycarbonate filters treated with gelatin and fibronectin. Monolayers were exposed to an acute increase in hydrostatic pressure of 30 cm H2O for 5 min. The effect of heparanase III (15 mU/ml x 30 min) and media albumin concentration on endocytosis was assessed in control vs. pressure-treated RLMVEC for their effect on endocytosis. Western blots of cell lysates were probed for caveolin-1 (cav-1), pTyr14-cav-1, eNOS, pSer1177-eNOS and albumin; all protein bands were normalized to GAPDH. To assess effects of chronically elevated pulmonary vascular pressure on indices of transcytosis, mice (C57/BL6) underwent aortic banding (AoB), which resulted in the development of chronic heart failure after 10 weeks. Lungs were harvested, homogenized and subjected to western blot as described above to assess lung albumin content and syndecan-1 expression.

RESULTS: RLMVEC and HLMVEC exposed to pressure (30 cm H2O) for 5 min had a 10 to 20-fold increase in internalized albumin relative to controls (zero pressure); sample sizes were 3-5 monolayers for all groups. Albumin uptake was directly proportional to the media albumin concentration over the range of 0.0, 0.1 and 1.0 gr/dl. Heparanase III for 30 min increased the endocytosis of albumin. Pressure for 5 min increased pTyr14-cav-1 by 2.3-fold and increased pSer1177-eNOS 10-fold relative to control monolayers. Ao-banded mice lungs had a 2.3-fold increase in lung tissue albumin content relative to non-banded mice lungs whereas syndecan-1 was reduced in Ao-banded mouse lungs.

CONCLUSIONS: Acute increases in hydrostatic pressure rapidly increased the endocytosis of albumin in RLMVEC and HLMVEC, which was associated with an increase in pTyr14-cav-1 and pSer1177-eNOS. Albumin endocytosis was enhanced by heparanase despite the fact that heparanase reduced pressure-induced pSer1177-eNOS. Mice with chronic heart failure induced by Ao-banding also exhibited increased lung tissue albumin levels. Increased albumin transport into the lung interstitial space, and subsequent increase in filtration pressure, may be another pathological mechanism accounting for pressure-induced pulmonary edema[2,3].

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S-99.

MINOCYCLINE FAILS TO IMPROVE NEUROLOGIC AND HISTOLOGIC OUTCOME AFTER VENTRICULAR FIBRILLATION CARDIAC ARREST IN RATS

AUTHORS: T. Drabek[1], I. A. Magnet[2], K. L. Schreiber[1], C. D. Wilson[1], J. P. Stezoski[3], P. Kochanek[1], A. Janata[4]

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INTRODUCTION: Neuro-cognitive disabilities are a well-recognized complication of cardiac arrest (CA). We[1,2] and others [3,4] have reported that prolonged CA produces extensive neuronal death and microglial proliferation and activation. Among other potential mechanisms, microglia have been implicated as triggers of neuronal death and cerebral edema after insults to the CNS. Minocycline is neuroprotective in some brain ischemia models including CA, [3-5] in part by blunting the microglial response,[4] or by a direct effect on neurons.[6] We tested the hypothesis that minocycline would improve survival, as well as attenuate neurologic deficits, neuroinflammation, and histological damage, in our established model of ventricular fibrillation (VF) CA in adult rats.

METHODS: Adult male isoflurane-anesthetized rats were subjected to 6 min VF CA followed by 2 min resuscitation including chest compression, epinephrine, bicarbonate, and defibrillation. After return of spontaneous circulation (ROSC), rats were randomized to two groups: 1) minocycline (M) 90 mg/kg ip at 15 min ROSC; 22.5 mg/kg i.p. q 12 h for 72 h; 2) controls (C), receiving the same volume of vehicle. The rats were kept normothermic during the postoperative course. Neurologic injury was assessed daily using Overall Performance Category (OPC; 1= normal, 5=dead) and Neurologic Deficit Score (NDS; 0%=normal, 100% = dead). Rats were sacrificed at 72 h. Neuronal loss (Fluoro-Jade B staining) and microglia proliferation (anti-Iba-1 staining) were quantified in three selectively vulnerable brain regions (hippocampus, HIP; striatum, STRI; cerebellum, CEREB) by three independent reviewers masked to the group assignment.

RESULTS: In the M group, 7 out of 13 rats survived to 72 h compared to 8 out of 20 rats in the C group (p=NS). Degree of neurologic injury (OPC) was not different between groups (Fig 1). Neurological outcome was not different between all studied rats (Fig 2) or survivors (Fig 3). Number of degenerating neurons or proliferating microglia was not different between groups in any region (Fig 4). Numerically, there were ~ 20% less degenerating neurons and proliferating microglia in HIP and STRI in the minocycline group, with considerable variability in the histological damage.

CONCLUSION: Minocycline did not improve survival and failed to confer substantial benefits on neurologic injury, neuronal loss or microglial proliferation in multiple brain regions in our model of rat VF CA. The relative lack of effect of minocycline in this normothermic VF CA model is in line with our prior results from deep hypothermic CA,[2] and further corroborated by others in asphyxial CA in adult rats.[3] In contrast, minocycline has previously showed benefits in immature rats subjected to asphyxial CA,[5] suggesting significant age-dependent differences in neuroinflammation after CA

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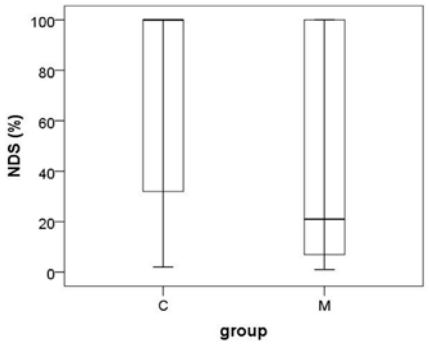

Fig. 2 Neurologic deficit score at 72 h in all rats studied. Boxes represent interquartile ranges. The line across each box indicates the median, and the whiskers are the highest and lowest values.

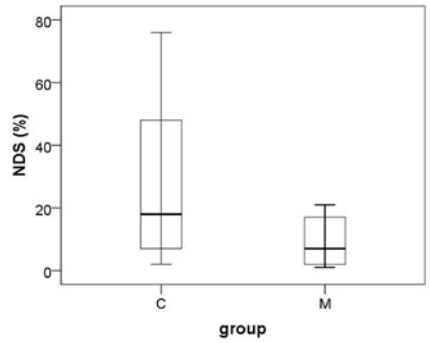

Fig. 3 Neurologic deficit score at 72 h in survivors. Boxes represent interquartile ranges. The line across each box indicates the median, and the whiskers are the highest and lowest values.

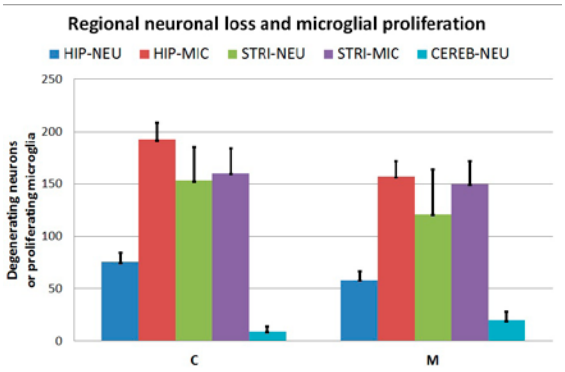

Fig. 4 Regional neuronal loss and microglial proliferation (mean±SEM) were not different between groups in any region.

	control	minocycline
OPC 5 Death / brain death	●●●●●●●●●●●●	●●●●●●
OPC 4 Severe disability		
OPC 3 Moderate disability	●●●	●
OPC 2 Mild disability	●●●	●●
OPC 1 Normal	●●	●●●●

Fig.1 Overall performance categories (OPC) after VF CA in rats. Each dot represents one rat. No difference between groups.

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S-100

LIBERAL INTRAOPERATIVE FLUID RESUSCITATION IS ASSOCIATED WITH REINTUBATION AND UNPLANNED MECHANICAL VENTILATION ON THE INTENSIVE CARE UNIT

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AFFILIATION:[1]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, [2]Anesthesia, Vanderbilt University, Nashville, TN, [3]Inserm, French National Institute of Health and Medical Research, Bordeaux, France

INTRODUCTION: Adverse respiratory outcomes are the most common non-surgical complications following surgery[1]. This results in longer hospital stays, increased morbidity, mortality, and financial costs[2]. Unplanned reintubation within 72 hours of postoperative extubation is an accepted marker of respiratory compromise[1]. Liberal fluid regimes have been associated with improved outcomes for pain and nausea in healthy patients for routine surgeries[3]. However in thoracic surgery, restrictive regimes are associated with fewer postoperative respiratory complications[4]. No large, well-controlled studies have focused on the association between intraoperative fluid management and adverse respiratory outcomes.

Our primary hypothesis is that liberal intraoperative fluid use is associated with unplanned reintubation and ventilation on the ICU. Our secondary hypothesis is that liberal intraoperative fluid resuscitation is associated with postoperative respiratory failure, pulmonary edema, pneumonia and post-extubation O_2 desaturation.

METHODS: Prospective analysis of electronic patient data from patients who underwent surgery under general anesthesia between January 2007 and November 2012. Pre-, intra- and postoperative data was integrated from the Anesthesia Information Management System and the hospital's billing database. We included 90,993 patients aged 18 and up who were extubated at the end of the case. We evaluated the effects of intraoperative fluids administered (crystalloids and colloids, weighted by effectiveness, categorized by quartiles). The primary outcome was unplanned reintubation leading to mechanical ventilation on the ICU within 72 hours after surgery. Secondary outcomes were respiratory failure, pulmonary edema and pneumonia within 72 hours after surgery, and post-extubation O_2 desaturation <90%. We controlled for age, gender, BMI, procedure length, ASA score, Charlson Comorbidity Index, SPORC score1, depth of anesthesia, neuromuscular blocker use, median vasopressor dose/hour, opioid dose, surgical service, admission type and blood products.

RESULTS: Liberal (upper quartile) fluid resuscitation was associated with reintubation and ventilation on the ICU (OR 2.43, [CI 1.53-3.86]), postoperative respiratory failure (OR 2.26, [CI 1.79-2.85]), pulmonary edema (OR 1.76, [CI 1.50-2.06]), pneumonia (OR 1.54, [CI 1.17-2.04]), ICU admission (OR 2.80, [CI 2.37-3.31]) and post-extubation desaturation<90% (OR 1.21, [CI 1.10-1.34]). The effect of liberal fluid volumes (median 3.75L [2.51-286.9L]) on the likelihood of reintubation and mechanical ventilation was higher in low-risk patients (ASA risk score 1+2 vs >2), (OR 3.77 [CI 1.27-11.16], vs 2.12[CI 1.25-3.60]).

CONCLUSIONS Liberal fluid resuscitation during surgery is associated with unplanned reintubation and mechanical ventilation on the ICU. Exploratory analysis suggests that this association is of particular importance in low risk patients (ASA score 1+2).

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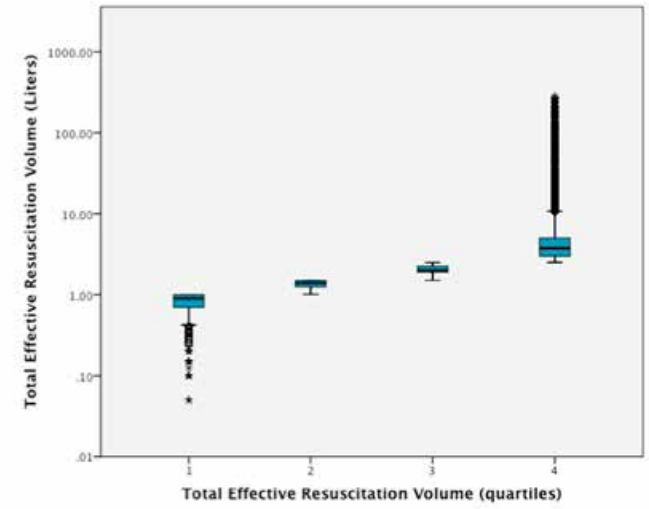

Figure 1: Median, quartiles, 10/90 per cent percentile (error bars), and outer fence of normalized fluid resuscitation volume (crystalloids+colloids times factor 3)

Table 1: Odds Ratios of adverse outcomes for upper quartile volumes of intraoperative fluid resuscitation

OR	ASA: all (n=84,585)	ASA: 1 and 2 (n=59,874)	ASA 3 and higher (n=24,711)
Reintubation	**2.43** (1.53-3.86)	**3.77** (1.27-11.16)	**2.12** (1.25-3.60)
Respiratory failure	**2.26** (1.79-2.85)	**3.57** (2.32-5.47)	**1.93** (1.47-2.55)
Pulmonary edema	**1.76** (1.50-2.06)	**2.25** (1.68-3.02)	**1.61** (1.34-1.95)
Pneumonia	**1.54** (1.17-2.04)	**1.78** (1.11-2.82)	**1.38** (0.96-1.97)
ICU admission	**2.80** (2.37-3.31)	**2.55** (1.87-3.47)	**2.93** (2.39-3.60)
O_2 desaturation (1)	**1.21** (1.10-1.34)	**1.24** (1.10-1.41)	**1.13** (0.98-1.33)

(1) Post-extubation

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Economics, Education and Policy

S-101.

THE IMPACT OF A FLIPPED CLASSROOM ON INTERN WELLNESS AND BURNOUT: A PILOT STUDY

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AFFILIATION: Department of Anesthesiology, Pain and Perioperative Medicine, Stanford Hospital and Clinics, Palo Alto, CA

INTRODUCTION: The incidence of intern burnout approaches 75%[1]. Recognizing the issue of intern burnout has developed wellness programs that increase self-reported well-being[2].

ImPRINT, a yearlong blended curriculum for interns matriculating into anesthesiology residency includes monthly courses based on the "flipped classroom." Assigned didactics are viewed from home, and classroom time is reserved for interactive discussions, part task training, and case simulations. We hypothesized that such a course would promote intern wellness.

METHODS: After IRB approval, all anesthesiology interns were invited to participate. A modified Meslach Burnout Inventory (MBI) was completed in the first and last months of internship. Additionally, for each module, responses to the following statement were recorded: "We define wellbeing as a sense of wholeness and balance (of mind, body, and spirit) that creates an inner resilience to meet the challenges of living without being overwhelmed. On a scale of 1 to 100, please score your wellbeing at this particular moment: 100 being the most and 1 being the least."

Our primary hypothesis is that higher rates of burnout would be present at the end of intern year and that participation in ImPRINT would be a protective factor. For the primary outcome, we case matched students by gender and age. Our secondary hypothesis is that participation in the monthly modules would promote an improvement in reported well-being through facilitating a sense of community. Normality of distribution was determined using the Kolmogorov-Smirnov test. Primary outcome data were normally distributed and were compared using Student's t test. Secondary outcome data, pre- and post- scores for each module were compared using repeated measures ANOVA with post-hoc Tukey-Kramer multiple comparisons testing. A two-side $p<0.05$ was considered statistically-significant for all analyses.

RESULTS: All 22 anesthesia interns were enrolled. For the primary outcome, a control group of 5 interns did not participate in ImPRINT (group 1) and were case-matched to the interns that did participate in ImPRINT (group 2).

PRIMARY OUTCOME: Mean[SD] score on modified MBI of 2.2[2.9] vs. 2.8[2.8] for groups 1 and 2, respectively ($p=0.749$).

SECONDARY OUTCOME: Within module pre- vs. post- scores were not statistically-significant.

Post-hoc power calculation revealed that the sample size of 5 subjects per group had 6% power to detect the 0.6 difference between means at a 0.05 significance level, and a sample size of 34 per group would have been required to achieve 80% power.

CONCLUSIONS: Based on this pilot study, a blended learning curriculum did not show a significant impact on intern wellness or burnout. Scores greater than 4 on the MBI suggest a high risk of burnout and the rationale for our post-hoc power calculation. In theory, utilizing classroom time for interactive learning activities promotes socializing and peer-to-peer support. Future research should focus on a multi-center prospective study to further elucidate of the impact of blended learning on physician wellness.

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S-102.

LESS FRESH IS MORE GREEN

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INTRODUCTION: Low flow anesthesia, as defined by fresh gas flow totaling 1 L/minute, has been shown to have benefits to the patient and the environment. Reductions in waste and expenditure on volatile anesthetics has also been shown. The purpose of this study was to assess average usage at our institution, consider it's potential role in the Perioperative Surgical Home Model and reinforce the benefits of using low flow anesthesia with anesthesia providers.

METHODS: Fresh gas flow rates and volatile anesthetic concentrations were observed over a six month period by residents and trained medical students. Cases that were recorded during induction and emergence were excluded to more accurately approximate usage during the maintenance phase of anesthesia. Based on the average flow rates obtained, the amount of volatile agent wasted, by exceeding the threshold of 1 L/minute fresh gas flow, was determined.

RESULTS: As a result of studying 156 cases, the average concentration of sevoflurane and desflurane were 1.66% and 4.66%, respectively. The average fresh gas flow rate used in the observed cases was 3.09 L/minute. The results of this study, along with the benefits of using low fresh gas flow anesthesia, were presented to the institution's anesthesiologists, residents and medical students.

DISCUSSION: Implementing a practice of low fresh gas flow rates could reduce volatile anesthetic agent usage significantly. Simply by reducing fresh gas flow rates to 1 L/min, volatile agent usage could be reduced by up to 66% at this institution. A second set of data will be recorded to assess the extent of the initial educational effort. In considering the advent of the Perioperative Surgical Home Model, simple proposals such as low fresh gas flow rates leading to cost reduction could, in fact, help leverage Anesthesiology Departments for future initiatives. This study challenges the field to increase the frequency with which low fresh gas flow rates are used. Usage of low fresh gas flow is a simple way for physicians to conserve resources, help the environment and enhance patient care.

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S-103.

RELATED FACTORS FOR MECHANICAL COMPLICATIONS IN ULTRASOUND GUIDED CENTRAL VENOUS CATHETERIZATION

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INTRODUCTION: Contrary to our expectations regarding efficacy of ultrasound guided central venous catheterization (CVC), mechanical complications increased using ultrasound devices in our hospital[1]. Based on our findings, we recommend that doctors in our hospital utilize ultrasound devices for vascular visualization followed by conventional landmark technique, and utilize real time ultrasound guidance only following adequate training. In this study, we focused on the differences in mechanical complications between these two techniques and investigated the efficacy of ultrasound guided CVC. The purpose of this study was to elucidate the principal factors underlying mechanical complications in two techniques in CVC; real time ultrasound guidance (Dynamic method; Dm) and ultrasound vascular visualization followed by conventional landmark technique (Static method; Sm).

METHODS: This retrospective, observational study was approved by the ethical committee in our university. Observational records of CVC over a period of 10 months, which were mandatory and submitted to our safety department, were examined. Factors analyzed were insertion sites, level of doctor according to CVC clinical experience, and risk factors. Comparison of mechanical complications between Dm and Sm were analyzed using Chi square tests.

RESULTS: A total of 788 observation records were analyzed. Cases of CVC with Dm, Sm and without ultrasound devices were 255, 392 and 141, respectively. Total mechanical complication rates were 3.5, 1.5 and 0%, respectively. Comparison of mechanical complication rates between Dm and Sm are shown in the Table. A greater number of mechanical complications occurred in Dm compared to Sm with puncture sites of femoral vein and with patients that exhibited no risk factors ($p<0.05$). A greater number of complications tended to occur when doctors with less experience utilized Dm compared to Sm ($p=0.06$).

CONCLUSION: When real time ultrasound guidance is applied in CVC, precautions should be taken, even for patients with no risk factors. Real time ultrasound guided CVC in internal jugular vein may be performed safely compared to femoral vein. Therefore, visualization followed by conventional method is recommended for femoral approach, unless the operator is well trained with ultrasound devices, in accordance with National Institute for Health and Clinical Excellence (NICE) guidance in the UK.

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Table Comparison of mechanical complication rates between Dm and Sm

		Dm (dynamic methods)	Sm (static methods)	P value
Insertion sites	IJV	2.1% (4/194)	2.6% (5/191)	0.7
	SCV	22.2% (2/9)	0% (0/4)	0.3
	FV	4.7% (2/43)	0.5% (1/190)	0.03
Level of doctors	JR	7.1% (2/28)	1.4% (2/146)	0.06
	SD	2.9% (3/103)	0.8% (1/122)	0.2
	INS	2.8% (3/108)	2.1% (2/97)	0.7
Risk factors	Yes	0% (0/69)	3.8% (3/78)	0.1
	No	4.8% (9/187)	1.0% (3/314)	0.02

The number in the parenthesis shows the number of patients. Dm: dynamic methods; real time ultrasound guidance, Sm: static methods; vascular visualization using ultrasound devices followed by landmark technique, IJV: internal jugular vein, SCV: subclavian vein, FV: femoral vein; JR: junior residents less than two year clinical experience, SD: senior doctors more than three year clinical experience, INS: instructors more than five year experience and certified as instructors in CVC.

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S-104.

ANALYSIS OF PATIENT PREFERENCES FOR DIFFERENT TYPES OF PREOPERATIVE ORAL REHYDRATION THERAPY PRODUCTS

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INTRODUCTION: Since 2012, when local preoperative fasting guidelines were established by a professional body, medical policy in our country has favored extending the period of clear fluid consumption by patients. Many hospitals now also routinely administer preoperative oral rehydration solution (ORS) during oral rehydration therapy (ORT). While the safety, effectiveness, and cost of liquid and gel ORS products have been well studied, little is known about patient preference. Obviously, understanding this would ease administration of ORT.

METHODS: In our hospital, on the evening before surgery, informed of the significance of preoperative ORT and encouraged to consume as much as they are comfortable with, each preoperative patient weighing over 20 kg is routinely given one 500 ml bottle of liquid and one 200 g pouch of gel. Our hospital provides only OS-1® (Otsuka Pharmaceutical Factory, Inc.) products for preoperative ORT. Officially approved by the Consumer Affairs Agency as a 'Food for special dietary uses', OS-1® also conforms to formulation values recommended for ORS by the American Academy of Pediatrics. Homogenous without shaking, both product types have the same nutritional and electrolyte composition and the same specific gravity (1.01). During the study period (Sep., 2012 to Dec. 2013), before patients were taken for surgery, we collected the bottles and pouches that had been left with them the night before. After weighing remnants of liquid and gel to ascertain the amounts consumed, we analyzed the data.

RESULTS: Preoperative ORT was indicated for 321/403 surgical patients (79.7%; mean age, 43 years; otolaryngological/dental cases, 158/163; male/female cases, 161/160; average liquid/gel intake, 313/102 g). We found no statistically significant differences in consumption related to surgery type, or sex, or season. Patients <20 years (n = 37), however, consumed statistically significantly more gel (average, 168 g) and less liquid (156 g) than patients ≥20 years (n = 284; gel, 100g; liquid, 363 g; both $P < 0.01$, Mann-Whitney U-test).

CONCLUSIONS: Patients <20 years consumed more gel and less liquid than patients ≥20 years.

DISCUSSION: Although patients are informed of the significance of preoperative ORT and actively encouraged to consume it, they are not forced to consume the total amount. While preoperative ORT reduces patient discomfort and improves physical condition; forceful administration may cause stress and negate the positive effect. Striving to ensure optimal intake for appropriate replenishment of water and electrolyte levels, we need to match provision to patient preference.

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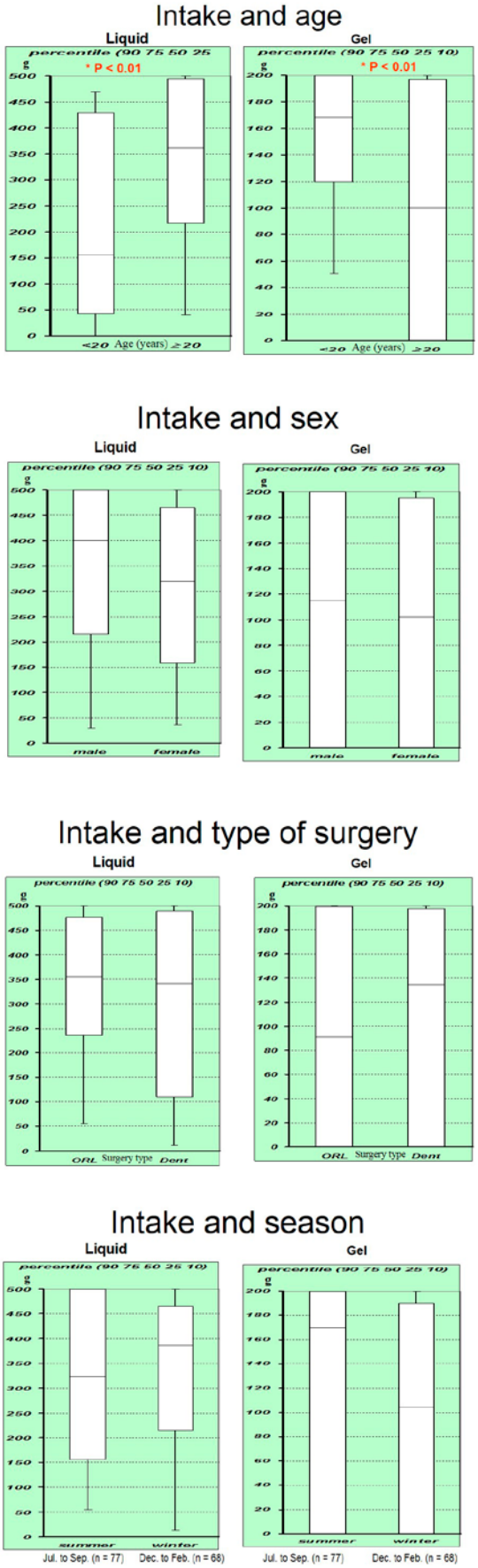

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S-105.

INTRODUCTION OF 2ND SIMULATION SESSION DURING 3RD YEAR UNDERGRADUATE ANAESTHESIA CORE ROTATION- "EXIT SIMULATION"

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INTRODUCTION: All 3rd year medical students rotate through the Simulation centre on day 2 of core Anesthesiology. Every year, learner feedback has highlighted the wish for "more simulation". Core seminars prohibited time available until our recent adoption of the Flipped Classroom.

METHODS: All core seminars were converted to interactive e-modules thereby freeing up an extra half day. As the first simulation day occurred early on in the rotation, it was felt that the second session should be an "Exit Sim". This would serve 2 purposes- to consolidate learning objectives of the rotation and as a revision aid for final examination. Course objectives were mapped for clinical areas where Anesthesiologists care for patients ie. Preoperative, Intraoperative and Postoperative scenarios.

The Undergraduate working party consisted of Simulation coordinators, Anesthesiology Residents, Staff and Simulation Fellows. Presentation of original work[1], participation at international simulation conferences, plus medical literature review lead to the following innovative educational tools.

During the preoperative scenario, risk analysis and critical thinking were incorporated. In 2 subgroups the students performed real time preoperative assessment of a Standardized Patient. After collaboration and communication the teams had to come to management consensus.

In the Intraoperative scenario, Mental practice was introduced[2]. Roles were assigned to reflect a working operating room adding physical barriers to communication, increased cognitive load eg.suturing "s"s , surgical drapes, attire and surgical safety checklist.

Postoperatively we utilized SAGAT stops- Situational Awareness Group Awareness Technique to provide perceptual and cognitive feedback.[3]

Teams were scored throughout to introduce healthy competition.

RESULTS: Initial learner feedback is categorized by each scenario. **Preoperative:** "Very realistic patient and co-morbidities", "Great to have the opportunity to think through the patient plan on our own". "I liked the complexity of the case, it incorporated a number of important anesthetic considerations"

Intraoperative: "Good at giving first-hand look at intra-op communication. I will certainly remember some valuable lessons from this scenario". "The visualization before the simulation was helpful". "I really enjoyed thinking through the case before it started, I will use this technique in the future". "Scenario demonstrated the importance of inter-team communication well". "Reinforced what we have seen throughout the rotation".

Postoperative: "Taught me to avoid fixating on a problem maintaining the big picture". "Reinforced the learning done throughout". "This highlighted many good learning points".

CONCLUSION: We are excited about the launch of our new

Undergraduate Anesthesia curriculum after our initial positive feedback and we hope that this additional simulation day helps "close the loop" on their core rotation.

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S-106.

SURVEY ON USE OF PHARMACOKINETIC SIMULATION SOFTWARE FOR ANESTHESIA RESIDENT EDUCATION

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INTRODUCTION: This study was undertaken to determine the frequency of use and perception of efficacy of pharmacokinetic simulation software for education in anesthesiology residency programs. Pharmacokinetic simulators, such as Gas Man (Med Man Simulations, Inc., Boston, MA), depict inhalational anesthetic concentration in various body compartments and the changes caused by altering minute ventilation, cardiac output, vaporizer concentration, and fresh gas flows.

METHODS: A survey was sent to US anesthesia residency program directors, inquiring about: (1) how pharmacokinetics is taught; (2) how they see pharmacokinetic simulation as contributing to residents' education: (a) understanding of the specialty of anesthesia, (b) insight into pharmacokinetics, and (c) improvement of clinical performance; (3) their own experience using pharmacokinetic simulation for personal or resident education; and (4) impediments to using simulation programs. At our institution, a similar survey was sent to the anesthesia faculty and another survey was given to junior residents after their participation in a simulation session using the Gas Man program. To assess the efficacy of the Gas Man program, a test, containing questions about basic anesthesia pharmacokinetics, was administered before and after the Gas Man simulation session.

RESULTS: Responses were received from 16 anesthesia residency program directors and 19 anesthesia faculty members. Nearly all respondents believed pharmacokinetic simulation programs can contribute to greater understanding of the specialty of anesthesia, improved clinical performance, and a better grasp of pharmacokinetics. Few have used these programs personally and even fewer have used them in resident education, yet most would like to use them more frequently. Program directors said cost was the greatest impediment to use, while our faculty saw limited time as the greatest barrier. The 23 participating residents rated the simulator very highly after a one hour simulation session and believed the program contributed greatly to their understanding of pharmacokinetics, the specialty of anesthesia, and clinical care. Residents scored slightly higher on the post-test, given seven days after the simulation session, than on the pre-test.

CONCLUSIONS: Anesthesia residency program directors, anesthesia faculty and anesthesia residents all agree that pharmacokinetic simulation used in resident education can contribute to a greater understanding of the specialty of anesthesia, clinical care, and pharmacokinetic concepts. They would like to use these programs more frequently as a supplement to lectures, independent reading, and intraoperative teaching, but have encountered impediments to doing so, including cost and time limitations. Further efforts to overcome these barriers by increasing familiarity and access to pharmacokinetic simulation software may improve the education of anesthesia residents and, ultimately, patient care.

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WITHDRAWN.

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S-108.

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S-109.

TEACHING METHODS FOR AIRWAY MANAGEMENT SKILLS

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INTRODUCTION: Airway management skill is fundamental to junior doctors. In the UK, foundation programme is an interface between under graduation and post-graduation. Foundation doctors (FD) often face airway emergencies. Teaching basic airway management skills to large cohort group can be a challenge. There is no single best method to teach airway management skills. Several teaching methods have been evaluated to teach airway management skills[1]. Our aim was to devise and develop a teaching programme for basic airway management for the most junior doctors.

METHODS: We devised learning outcomes to teach airway management for a group of 40 FD. Three hours are allocated for didactic teaching of FD. We identified 3 learning domains - Cognitive (knowledge), psychomotor (skills) and affective (attitude) important to learn airway management[2]. We formulated learning outcomes. We linked learning outcomes to learning domains as below

(1)To describe aetiology of airway compromise and its management (Knowledge and comprehension)

(2) Be able to demonstrate use of airway devices (application) and

(3) Practical management of airway compromise in simulated scenarios (cognitive, affective, psychomotor domains).

A specific feedback form was used to evaluate teaching programme. Feedback form used scale 1-5 (5 = excellent and 1=poor).

RESULTS: We adopted several teaching methods (table 1). Careful planning for several teaching methods and grouping of learners were done to achieve learning outcomes (table 1).

We achieved 4.4, 4.3 and 4.3 score for presentation, content and relevance. There were specific comments to increase number of teachers and simulated scenarios. Demonstrations followed by hands on experience were also found to be useful.

DISCUSSION: Teaching airway management skills for large group of inexperienced junior doctors is difficult. There is a variability in airway management teaching programme[3]. Learning outcomes helped us to choose appropriate teaching methods. We used various methods to improve understanding and apply learnt knowledge. Each teaching method has advantages and disadvantages (table 2). Airway management skills also require use of psychomotor skills and positive attitude. 'Hands on' experience and simulation facilitated to achieve these domains. We also use peer feedback to encourage active participation in learning. In addition, we facilitate the reflection on action to improve learning experience and airway management performance.

We are planning to improve our teaching by recruiting 2 more teachers. This would allow us to use more simulated scenarios.

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Duration and contents of individual teaching method

	Number of teachers	Number of foundation doctors	Duration in minutes	Content
Lecture	1	40	25	Overview of airway assessment and basic devices for airway management e.g. airways, bag-mask-ventilation, Laryngeal mask airways and endotracheal intubation
Demonstration using mannequins	2	2 groups (20 in each group)	45	Practical demonstration of technical and safe use of basic airway devices. Discussion of indications, contraindications and complications
Hands on experience	2. Each support 4 stations	8 equipped stations. 5 students at each station.	50 minutes (10 minutes for each learner while other learners observe)	Practical use. Peer and teacher give feedback on the skill.
Simulation- based scenarios	2	8 groups. Out of 5 in each group, 3 learners get opportunity to face scenario. Two learners given responsibility for feedback.	40 minutes. 10 minutes for each of the 4 airway problem scenarios including timing for feedback.	40 minutes. 10 minutes for each of the 4 airway problem scenarios including timing for feedback.

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S-109 • continued

Learning outcome achieved and advantages and disadvantages of individual teaching method				
	Learning outcome achieved	Advantages	Disadvantages	Comments
Lecture	1	-Sequential and logical information	-Teaching depends on knowledge and skills of presenter	Interaction promotes active participation
		-Suitable for large group	-Resources required e.g. time, space	
Demonstation	1 and 2	-Active engagement	-Requires attention and observation	-Plan and execute carefully
		-May stimulate interest	-In large group some may not be able to do close observation	
		-Can provide useful clinical tips		
Hands on mannequins	2	-Improves confidence	-Requires supervision for optimal use	-Integrate feedback and reflection
		-Opportunity to correct mistakes	-Not possible to provide details of all airway problems	
Simulation-based scenarios	1, 2 and 3	-Repetition possible	-Validity to teach airway management controversial	-Integrate feedback and reflection
		-Increasing difficulty / complexity of a case in step-wise approach	-May lead to over confidence	
		-Useful for evaluation	-Not a substitute for real life scenarios	
		-No risk to patients		

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S-110.

IMPACT OF FRESH GAS FLOW RATES ON VOLATILE ANESTHETIC AGENT USAGE: A COST ANALYSIS

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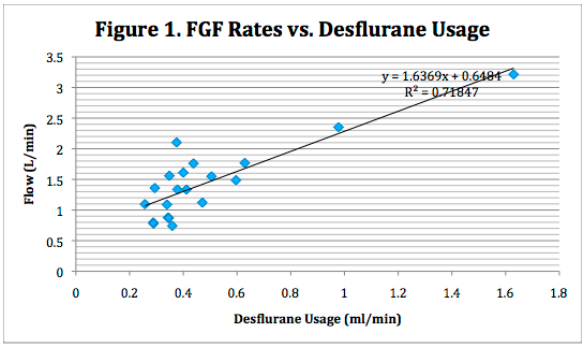
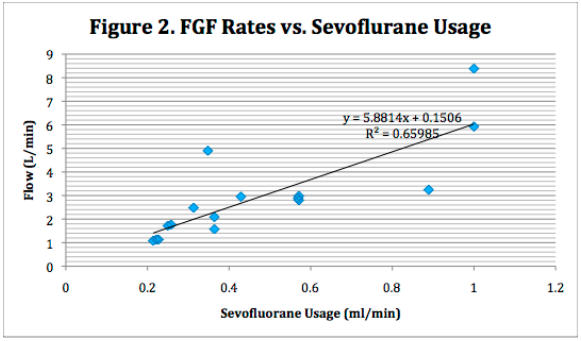
INTRODUCTION: Hospital and departmental operating budgets are an increasing concern for anesthesiologists. Volatile gasses represent approximately 20% of anesthetic department drug costs1. Volatile usage is a particularly feasible target for cost savings since it can be easily reduced by decreasing fresh gas flow (FGF) rates 2,3,4. With newer carbon dioxide absorbents, concerns over the generation of toxic by-products using low FGF rates are of little clinical relevance 4,5. Excess volatile usage due to excessive FGF rates results in increased costs and atmospheric pollution without clinical benefit6.

The objectives of this study were to determine the impact of FGF rates on Desflurane and Sevoflurane usage, and to estimate potential cost savings if lower flows were used.

METHODS: FGF rates and volatile usage data were recorded from our OR anesthesia machines during one week. FGF rates were plotted against volatile usage to show the relationship between them. OR cases were separated into lower FGF (less than 1L/min total flow for Desflurane; less than 2L/min for Sevofluorane) and higher FGF groups (greater than 1L for Desflurane; greater than 2L/min for Sevoflurane). Median FGF rates from the two groups, after adjustment for length of cases, were used to estimate the differences in costs between using median higher FGF rates vs. median lower FGF rates. Results were extrapolated to represent cost savings for an entire year. Cases using both Sevoflurane and Desflurane, or Nitrous Oxide were excluded.

RESULTS: The relationship between FGF rates (L/min) to volatile usage (ml/min) is illustrated in Figure 1. for Desflurane and in Figure 2. for Sevoflurane.





The proportion of cases in the low and high FGF groups for each volatile, their FGF ranges, and median FGF values are shown in Table 1. The relationship between FGF rates and Desflurane usage was represented by y=1.6369x + 0.6484 (Figure 1). Rearranging this formula to solve for x and inserting FGF rates yields median low-flow Desflurane usage of: x=0.828/1.6369 - 0.3961 = 0.110ml/min, while median high-flow Desflurane usage would be x=1.549/1.6369 - 0.3961 = 0.550ml/min. The same calculation was used for Sevofluorane cases. The costs of using high versus low FGF rates, and estimated cost savings using median lower FGF rates, were calculated using a representative* cost per ml of volatile (Table 2). *Cost shown is approximate and proportional, since exact cost is a trade secret.

Table 1. Summary of Case Data	**Desflurane**	**Sevoflurane**
Number of cases	40	29
Hours of usage	86:05:00	41:15:00
FGF range (L/min)	0.713-7.707	1.079-9.7
Number of cases in low-flow group	14	13
Median FGF rate for low-flow group (L/min)	0.828	1.573
Number of cases in high-flow group	26	16
Median FGF rate for high-flow group (L/min)	1.549	3.001

Table 2. Summary of Cost Data	**Desflurane**	**Sevoflurane**
Cost *	$0.44/ml	$1.20/ml
Cost of volatile using median low flow rates	$0.05/min	$0.29/min
Cost of volatile using median high flow rates	$0.24/min	$0.58/min
Cost savings using median low flow rates	$0.19/min	$0.29/min
Cost savings for a 120 min. case	$23	$35

The cost savings if high-flow cases were substituted with low-flow cases was conservatively estimated at $81,250 per year.

CONCLUSIONS: A minority of anesthesiologists at our institution use lower flows, despite the fact that using lower FGF rates represents a potentially significant cost savings. The importance of reducing FGF rates is not trivial, and measures should be adopted to promote this practice whenever possible.

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S-111.

DO STRUCTURED COMMERCIAL INTENSIVE WEEKEND MOCK ORAL BOARD EXAMS IMPROVE EXAM PERFORMANCE?

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INTRODUCTION: While all candidates who present for ABA certification have undertaken exhaustive learning and written testing to achieve candidacy, there is little significant experience in presenting in an oral exam. The purpose of the oral exams is to attest to the candidate's soundness of judgment, rationale, ability to assimilate and analyze data, define priorities, recognize and respond to complications and communicate effectively. Few milestones provoke more anxiety in the course of becoming an anesthesiologist than the oral exam.

HYPOTHOSIS: The authors, (partners and owners of a private oral board preparation company, Board Stiff Live, Inc.) sought to determine if their intensive weekend course of mock oral exams and feedback improved the candidates' performance.

METHOD: Candidates did a three day mock oral exams course with academic faculty. Each candidate did nine exams and participated/critiqued in 27 others. We compared the scores in knowledge, content and delivery for the first exam and their last exam.

RESULTS: First we tested the normality of the variable by drawing the histogram and qqplot of the variables. The histogram didn't reveal any skewed behavior, and therefore normality of the variables is verified.

Equality of the variance between the pre and post measurements was checked using F statistic. The test showed that the variance between pre and post measurements for all variables were equal. Equality of means between the pre and post measurements was tested using the paired t-test. This test confirms that the mean values for the pre and post measurement are significantly different, suggesting that post measurements have on an average higher values compared to pre measurements.

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S-112.

DEVELOPMENT OF CLINICAL PERFORMANCE METRICS FOR RESIDENTS

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INTRODUCTION: The ACGME now requires residency training programs to give residents feedback regarding their personal clinical effectiveness. Having previously described our development of an automated, near-real-time performance capture and feedback tool that provides objective performance data,[1] we now describe our efforts to develop ongoing clinical performance metrics for trainees.

METHODS: We began by reviewing the proposed ACGME milestones, our existing departmental performance metrics, and published works in the literature.[2] We then developed a list of potential metrics, which could be automatically obtained from our routine clinical documentation, which include a) glucose monitoring (every hour if receiving insulin and every 2 hours if diabetic but no insulin intraoperatively), b) central line insertion practices (documentation of sterile technique and all steps), c) temperature management (>36C), d) immediate postoperative pain scores (<=7), e) antibiotic administration (within 60 minutes prior to incision), f) measurement of a blood pressure prior to induction of general anesthesia (in a non-pediatric inhalational induction case), g) administration of antiemetic medications in high risk patients, and h) completion of electronic post-operative orders prior to patient arrival in the PACU. Each metric is scored in a binary pass/fail system, and if any applicable metric for a case is failed, then the case is flagged as a 'fail.' This case then appears in the resident dashboard and they can select it in order to immediately pull up the anesthesia care record in order to review why they might have not performed on this quality metric (Figure 1).

RESULTS: Resident performance on 55,269 completed cases has been incorporated into our automated dashboard, and trainees now have access to their own performance data on these metrics as well as aggregated data concerning the performance of their residency class and the residency as a whole in order to provide individual-group comparisons, as shown in Figure 1.

CONCLUSIONS: We demonstrate the development of eight clinical performance metrics for anesthesiology trainees. These metrics have been implemented into a near real-time feedback dashboard that satisfies one component of the ACGME requirements to provide trainees with information concerning their personal clinical effectiveness, which will be an integral part of the Milestones system. We are in the process of developing additional clinical performance metrics, such as rate of postoperative nausea and vomiting, need for re-intubation, post-operative residual neuromuscular blockade, unanticipated ICU admissions, length of time in a hypotensive state, surgical apgar score, and postoperative elevations in creatinine and troponin. We believe that such ongoing performance feedback will improve clinical and professional assessment and performance.

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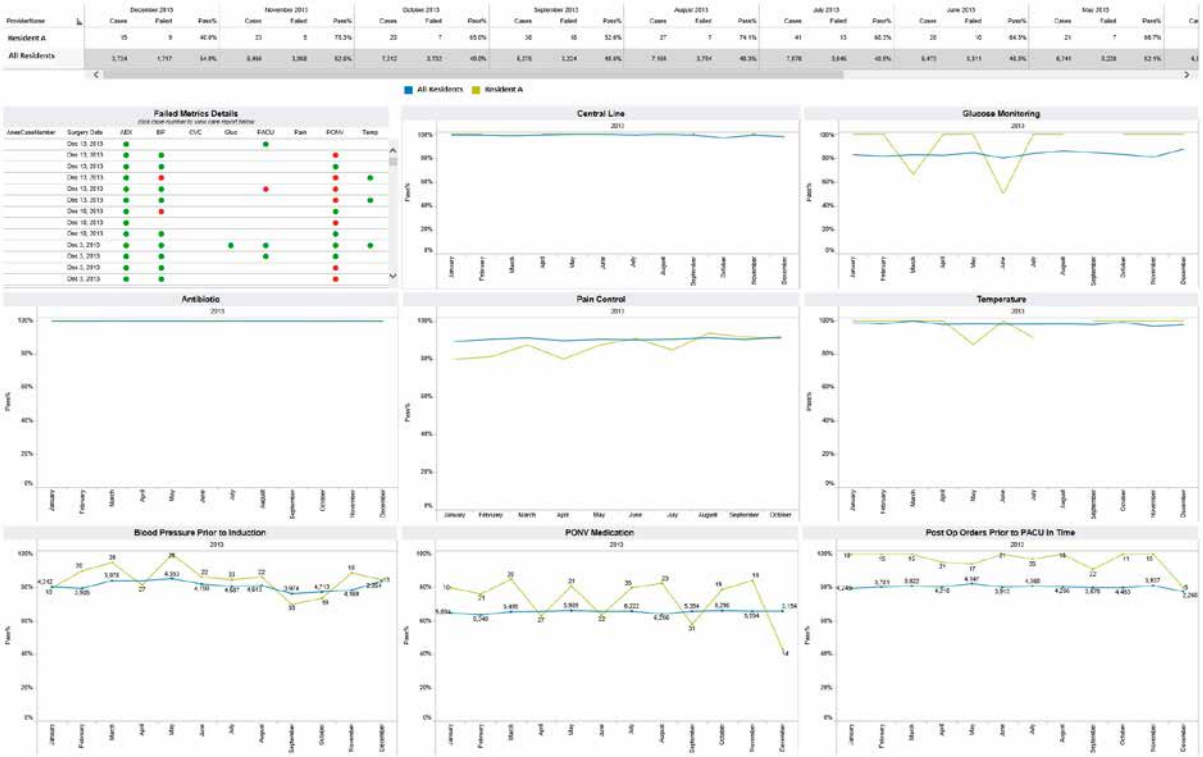
Figure 1



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S-113.

QUANTIFICATION OF VARIABILITY IN ANESTHESIA RESIDENCY AIRWAY TRAINING

AUTHORS: J. P. Wanderer[1], S. T. Jennings[2], J. M. Ehrenfeld[1], M. D. McEvoy[1]

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BACKGROUND: The Accreditation Council for Graduate Medical Education (ACGME) maintains sets of core program requirements which describe the guidelines for anesthesiology residency training. Airway management is a key skill for a practicing anesthesiologist. While the ACGME's current system describes the minimum number of cases that residents are required to complete for specific case types, little guidance is provided for airway management beyond "significant experience with a broad spectrum of airway management techniques," and less is known about the variability in resident airway experience. Here we describe the variability in airway experience of CA3 (PGY-4) residents in performing four essential, but non-routine, airway management techniques: awake intubation, fiberoptic intubation, nasal intubation and intubating LMA.

METHODS: We extracted airway management techniques from the ACGME Residency Case Log system as well as from our perioperative information management system (PIMS). Fifteen CA3 residents were analyzed after completion of their residency. Airway management techniques were attributed to specific residents when they documented the airway management technique described and were the initial (or only anesthesia) provider for the case. Additionally, we determined the total number of each airway management technique performed at our institution during their residency.

RESULTS: Experience varied widely among anesthesiology residents. The experience with nasal intubations reported to the ACGME ranged from 4 to 32 (mean 16.3 ± standard deviation 7.5), awake intubations from 0 to 10 (3.8 ± 3.2), fiberoptic intubations from 11 to 51 (31.4 ± 10.4) and intubating LMAs from 0 to 4 (1.7 ± 1.5). In total during this three year period of time at our institution including all anesthesia provider types, there were 4,759 nasal intubations, 171 awake intubations, 2,014 fiberoptic intubations, and 160 intubations performed with an LMA. Comparison of the experiences reported to the ACGME with our PIMS anesthesia charts revealed largely correlated data with evidence of both under- and over-reporting.

CONCLUSION: The results of this study demonstrate that airway management experience varies substantially among anesthesiology residents within the same residency class. For each airway management technique, ample training opportunities existed at our institution during this period. Decision support software has been described for anesthesiology trainee assignments1 that provides supervising anesthesiologists with airway management experience data extracted from PIMS. As these airway management techniques are normally planned for ahead of time, utilization of this type of software might facilitate clinical scheduling of trainees in order to ensure that all anesthesiology residents graduate with a significant and consistent exposure to the full spectrum of airway management techniques.

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S-114.

JOB INSECURITY PREDICTS BURNOUT IN PAIN MEDICINE SPECIALISTS

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INTRODUCTION: Burnout is a prolonged response to chronic emotional and interpersonal stressors on the job, defined by 3 dimensions: exhaustion, cynicism, and inefficacy.[1] Burnout can affect quality of care, job turnover, and negatively influence others in the group.[2] This study aimed to determine the incidence of burnout amongst pain medicine specialists and whether there are demographic or social/psychological characteristics of the job setting that predicts burnout.

METHODS: Recruitment to participate in a Survey Monkey was via email invitation to the membership of the American Society of Interventional Pain Physicians. The survey consisted of demographics, Maslach Burnout Inventory-Human Services Survey (MBI-HSS), and Job Content Questionnaire (JCQ). MBI-HSS assesses for burnout in helping professions and is composed of 3 subscales: Emotional Exhaustion (EE), Depersonalization (DP), and Personal Accomplishment (PA). JCQ is designed to measure social and psychological characteristics of jobs, revealing high-demand/low control/low support models of job strain development.[3] Three multivariable linear regressions were performed to determine whether age, gender, marital status, average hours worked per week, job decisional authority, job insecurity, and type of current practice predicted the three subscales of the MBI.

RESULTS: A total of 266 surveys were completed between June 10, 2013 and November 4, 2013. 141 (61.3%) and 82 (35.6%) of respondents scored high EE and DP respectively, and 98 (42.6%) had low PA-the 3 essential indicators of burnout. Across all three models (EE, DP, and DP) only one variable significantly predicted burnout; job insecurity. Higher levels of job insecurity predicted more emotional exhaustion, more depersonalization, and less personal accomplishment. Specifically, for every 1 unit increase in job insecurity, there was a 1.74 point increase in EE, a 1.09 point increase in DP, and a 1.03 point decrease in PA (Tables 1, 2, and 3).

Analyses of Predictors and MBI-EE

Covariate	MBI-EE estimate (*SE*)	MBI-EE *p* value
Age	-0.03 (0.11)	.81
Gender	0.30 (2.57)	.91
Marital status		.59
Divorced/separated	0.91 (4.78)	
Married/significant other	-2.20 (3.35)	
Never married/ single	Referent category	
Average hours worked per week	0.10 (0.07)	.16
JCQ: Decisional Authority	-0.23 (0.13)	.08
JCQ: Job Insecurity	1.74 (0.55)	**.002**
Current Practice		.49
Community Hospital	5.87 (3.98)	
Group Practice	6.64 (4.18)	
Private Practice (<20 Providers)	3.29 (3.13)	
Other	3.32 (4.71)	
University Practice	Referent category	

Note. $n = 215$, $df = 203$, JCQ = Job Content Questionnaire

Analyses of Predictors and MBI-DP

Covariate	MBI-DP estimate (*SE*)	MBI-DP *p* value
Age	-0.11 (0.06)	.07
Gender	-0.96 (1.38)	.49
Marital status		.32
Divorced/separated	-2.30 (2.58)	
Married/significant other	-2.73 (1.80)	
Never married/ single	Referent category	
Average hours worked per week	-0.05 (0.04)	.19
JCQ: Decisional Authority	-0.08 (0.07)	.24
JCQ: Job Insecurity	1.09 (0.30)	**<.001**
Current Practice		.62
Community Hospital	0.64 (2.14)	
Group Practice	1.04 (2.25)	
Private Practice (<20 Providers)	-0.99 (1.68)	
Other	-2.13 (2.53)	
University Practice	Referent category	

Note. $n = 215$, $df = 203$, JCQ = Job Content Questionnaire

Analyses of Predictors and MBI-PA

Covariate	MBI-PA estimate (*SE*)	MBI-PA *p* value
Age	-0.04 (0.06)	.50
Gender	0.38 (1.32)	.77
Marital status		.11
Divorced/separated	4.03 (2.46)	
Married/significant other	3.54 (1.72)	
Never married/ single	Referent category	
Average hours worked per week	0.01 (0.04)	.84
JCQ: Decisional Authority	0.12 (0.07)	.08
JCQ: Job Insecurity	-1.03 (0.28)	**<.001**
Current Practice		.20
Community Hospital	-3.61 (2.05)	
Group Practice	1.44 (2.15)	
Private Practice (<20 Providers)	-0.06 (1.61)	
Other	0.06 (2.42)	
University Practice	Referent category	

Note. $n = 215$, $df = 203$, JCQ = Job Content Questionnaire

CONCLUSIONS: The high incidence of burnout amongst pain medicine specialists is quite worrisome as it places them at risk for substance abuse, interpersonal difficulties, suicidal ideation, and increases the risk for medical error. In all 3 subscales the incidence is higher than the overall US physician population.[4] Unlike other studies; a younger, single clinician did not predict burnout. High levels of job insecurity, as measured by the JCQ, were a predictor of burnout in our population. These results should be used to create preventative and management programs to mitigate burnout, while increasing clinician engagement.

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S-115.

EXAMINING THE POTENTIAL BENEFITS OF PERIPHERAL NERVE BLOCKADE IN A RESOURCE-LIMITED INTERNATIONAL SETTING: THE EXAMPLE OF RWANDA.

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INTRODUCTION: Surgical intervention can play a significant role in the public health scheme of a developing country; as much as 11% of disease is amenable to treatment, cure or palliation with surgery. Concurrently, anesthesia capacity in limited resource settings is an important public health issue that recently has received increased attention. Using Rwanda as an example, we explore the potential impact of a regional anesthesia service in a developing country setting.

METHODS: Using a literature review and an in-country hospital assessment, the potential clinical, economic, and educational impact of peripheral nerve blockade were assessed. Two public referral hospitals in Rwanda were assessed: Centre Hospitalier Universitaire, Kigali (CHUK) and Centre Hospitalier Universitaire, Butare (CHUB). Limitations and barriers to the establishment of a consistent peripheral nerve block service were identified.

RESULTS: The majority of orthopedic surgery is carried out in the public referral hospitals, CHUK and CHUB. Referral hospitals, while more equipped than the district hospitals, face important limitations such as inconsistent central oxygen and electrical supplies, which delay or cancel surgical cases. Whereas 99% of lower extremity surgery at both CHUB and CHUK is performed under spinal anesthesia, only 10-15% of these patients receive supplemental peripheral nerve blockade. Although approximately 55% of orthopedic cases at CHUB involve upper extremity fractures, very few upper extremity surgery patients are offered brachial plexus blockade. In the setting of inconsistent central oxygen or electricity, surgery performed under peripheral nerve block with reliance on small-cylinder-sourced oxygen and battery-operated monitors is poised to be economically advantageous. Clinically, the use of peripheral nerve blockade could improve postoperative pain control, and decrease postoperative nausea and vomiting, as well as length of stay in the post-anesthesia care unit. Finally, consistent use of peripheral nerve blockade could enhance the national anesthesia training program, therefore improving local capacity. Limitations include lack of equipment and limited skills regarding peripheral nerve block techniques among local anesthesiologists.

CONCLUSION: The establishment of a regional anesthesia service in a limited resource setting such as Rwanda may positively impact local anesthesia capacity as well as clinical, economical, and training aspects. Continued international collaboration and research is needed to properly improve anesthesia capacity in nations with limited resources.

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S-116.

WITHDRAWN.

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S-117.

PERIOPERATIVE SURGICAL HOME FOR THE SAME DAY ADMISSION CARDIAC SURGICAL PATIENT: IMPROVING CARE, SATISFACTION, AND ENROLLMENT IN RESEARCH

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INTRODUCTION: With evolving legislature and reimbursements for anesthesiologists, the perioperative surgical home has evolved as a tool to improve patient care, quality and satisfaction. While the perioperative home has been shown to create a marked improvement in several patient factors, one critical area that may also improve is with research study enrollment. Enrolling patients in clinical research can be a challenging endeavor, and numerous studies have shown that the comfort of the patient can influence their decision to consent to participating in a clinical study.

Undergoing a surgical procedure is a very stressful experience for a patient. Many attempts have been made to elucidate the reasons for this stress, as well as the various facets of patient satisfaction in the perioperative period. Interventions such as a preoperative visit from an anesthesiologist, coordinated visits between the surgical and anesthesia team, and decreased waiting time can all increase patient satisfaction and decrease patient stress. Furthermore, thorough preoperative visits can provide optimal information about all phases of the perioperative period.

Given the improvement with satisfaction and the ability to spend more time with the patient, the perioperative surgical home can be an invaluable tool to improve patient comfort towards a research study, and thereby foster enrollment.

METHODS: We conducted a retrospective review of all cardiac surgical cases at our institution from January 2012 - November 2013. Patients were categorized as to whether they were seen in the preoperative clinic 3-6 days prior to surgery and admitted on the day of surgery, or were inpatients and seen by the anesthesia team in the hospital.

Surveys were presented to all same day cardiac surgery patients with the goal of observationally evaluating patient satisfaction with the preoperative process.

RESULTS: Out of a total of 2963 cardiac surgical cases from January 2012 - November 2013, 1153 were admitted on the day of surgery (38.9%).

In observational reports, patients reported an 87% satisfaction rating with their overall experience in the preoperative clinic, 95% reported that they were comfortable, and 90% reported receiving adequate information regarding surgery and associated research projects.

CONCLUSIONS: The perioperative surgical home for day of admission elective cardiac surgical patients provides an arena to overcome several barriers involved in consent to clinical research. Our patients reported overwhelming satisfaction with the salient information provided regarding their entire hospitalization and associated research, as well as with the overall preoperative evaluation process. Based on our findings, we recommend a prospective randomized trial to further explore the increase in enrollment in research studies with the establishment of a perioperative surgical home.

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S-118.

ANESTHESIOLOGIST STAFFING CONSIDERATIONS CONSEQUENT TO THE TEMPORAL DISTRIBUTION OF HYPOXEMIC EPISODES IN THE POST ANESTHEISA CARE UNIT

AUTHORS: M. G. Lopez[1], R. H. Epstein[2], J. M. Ehrenfeld[3], F. Dexter[4]

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INTRODUCTION: Hypoxemia (SpO2 < 90%) is common in post anesthesia care unit (PACU) patients.[1-4] The temporal distribution of desaturation has managerial implications, as treatment may necessitate an anesthesiologist's presence. However, prior studies (from 20 years ago) evaluated the incidence of PACU hypoxemia, not when episodes occurred, and workload attendant to the management of such episodes (possibly multiple interventions in individual patients) cannot be inferred. More recent studies of hypoxemia in the PACU in the context of residual neuromuscular blockade (NMB) truncated SpO_2 observations at 15 or 30 min.[5-7] We evaluated 3 hypotheses: (1) most (i.e., > 50%) PACU hypoxemia lasting ≥ 2 min occurs < 30 min following admission; (2) episodes resolve more slowly than operating room hypoxemia; and (3) most (i.e., > 50%) PACU intubations occur < 30 min following admission.

METHODS: Electronically recorded SpO2 values recorded every 30 to 60 sec were retrieved from 137,757 PACU patients over N = 80 4-week periods at an academic medical center. Onset times of hypoxemic episodes were determined and resolution at 3, 5, and 10 min was assessed. Episodes were compared occurring < 30 min and ≥ 30 min following PACU admission. Patients undergoing intubation in the PACU were identified by doing a free text search for comments suggesting intubation, followed by a confirmatory manual chart review. Intervals from PACU admission to intubation were determined.

RESULTS: Hypothesis #1 was rejected, as only 31.2% ± 0.05% of hypoxemic episodes occurred < 30 min after PACU admission (P < 0.0001) (Fig. 1). Few (< 1%) transporting anesthesia providers were still present in the PACU 30 min following exit from the operating room (Fig. 2). Hypothesis #2 was accepted, as hypoxemic episodes were unresolved in the PACU vs. the OR after 3 min in 40.9% ± 0.6% vs. 21.2% (P < 0.0001), and after 5 min in 32.6% ± 0.5% vs. 8.1% (P < 0.0001). Hypothesis #3 was rejected, as 63%, (95% CI 51.2% to 72.6%) of PACU intubations occurred ≥ 30 min following admission (P = 0.029).

CONCLUSIONS: Because most (i.e., > 50%) hypoxemic episodes in the PACU occur ≥ 30 min after admission, a time when the anesthesia provider who transported the patient usually would no longer be present (> 99% of cases), the PACU needs to be considered when anesthesiologist OR staffing and assignment decisions are made. Future studies of NMB evaluating respiratory complications in the PACU should extend their observation period beyond 30 min.

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Figure 1. Time Course of PACU Hypoxemic Episodes

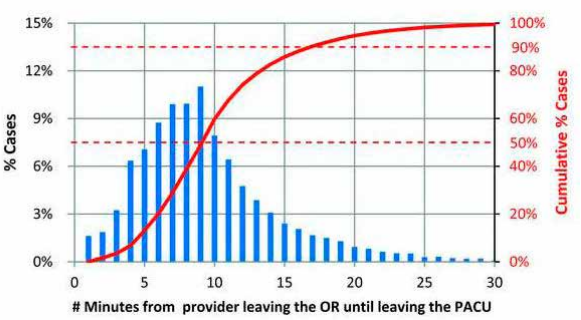
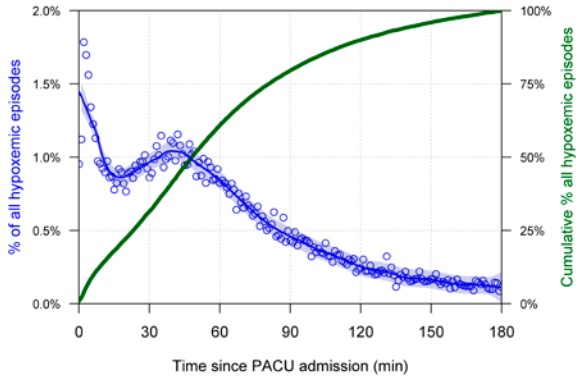


Figure 2. Anesthesia Provider Presence in the PACU



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S-119.

THE EFFECT OF PRE-DRAWN SYRINGES ON INTRAOPERATIVE MEDICATION USAGE

AUTHORS: K. S. Ladha[1], K. Nanji[1], E. Pierce[1], J. A. Hyder[2]

AFFILIATION: [1]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, [2]Department of Anesthesiology, Mayo Clinic, Rochester, MN

INTRODUCTION: Medication shortages have become increasingly common in the United States and have been implicated in unplanned treatment changes and poor outcomes. At the same time little is known regarding the impact of pre-packaged syringes on medication usage rates. We tested if a local shortage of pre-packaged ephedrine sterile injectables, replaced by provider-diluted ephedrine, was associated with changes in ephedrine and phenylephrine use and intraoperative hemodynamics.

METHODS: Consecutive patients undergoing general surgery (colectomy, hernia repair, parathyroidectomy and thyroidectomy) and orthopedic surgery (primary total knee and hip arthoplasty) at a tertiary care center were included one month prior to and one month after the start of the pre-packaged ephedrine syringe shortage. Patient demographics and information regarding a patient's anesthetic were obtained from the anesthesia information management system. Lowest mean arterial pressure and lowest heart rate were calculated as measures of hemodynamics. The induction dosage of propofol and median minimum alveolar concentrations (MAC) were also collected. Associations between syringe shortage, hemodynamics and medication use were tested in univariate and multivariate linear and logistic regression models.

RESULTS: A total of 304 patients were included prior to the pre-packaged syringe shortage and 298 patients were included after the shortage began. Ephedrine bolus use differed significantly before and after the absence of pre-packaged syringes [148/304 (48.7)% vs 117/298 (39.3)%, p=.020]. In multivariate analyses adjusting for age, sex, American Society of Anesthesiologists status, surgical procedure, primary anesthesia provider and surgical duration, patients were significantly less likely to receive ephedrine during the shortage [OR=0.67 (95%CI 0.48-0.95), p=0.0245) and patients' average phenylephrine bolus dosage was significantly greater [+27.80mcg, (95%CI 1.43-54.18) p=0.0389]. Patients' hemodynamics assessed by lowest heart rate or lowest mean arterial pressure did not differ significantly during the shortage. There was also no significant difference in the median MAC during the case and the dose of propofol before and during the shortage.

CONCLUSION: The events at our institution created a natural experiment to study changes in anesthesia provider behavior and patient effects in response to a shortage of pre-packaged syringes. Our findings confirm that providers altered their medication administration patterns, as patients were significantly less likely to receive ephedrine during the shortage. This was associated with a significant increase in the dosage of phenylephrine boluses. There was no detectable difference in MAC, propofol dosage or hemodynamics.

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S-120.

COMPARISON OF ANESTHESIA TRAINING EXPERIENCE AT A RURAL REFERRAL HOSPITAL IN WESTERN KENYA TO AN ACGME-APPROVED PROGRAM IN THE UNITED STATES

AUTHORS: M. D. McEvoy[1], M. W. Newton[1], J. Ehrenfeld[1], J. P. Wanderer[1], M. Higgins[2], K. A. McQueen[1], W. S. Sandberg[1]

AFFILIATION: [1]Anesthesiology, Vanderbilt University, Nashville, TN, [2]Anesthesiology, VUMC, Nashville, TN

INTRODUCTION: It is well recognized that there is a lack of anesthesia care providers in many resource-poor countries, especially in rural areas. This often is a barrier to providing adequate care for large numbers of patients requiring surgery in those settings.[1] We have previously reported on the development of a nurse anesthetist training program in Western Kenya.[2] However, there is little objective data comparing anesthesia training in low-income countries versus programs in the United States. This study reports on 12-months of cases performed by anesthesia trainees at a hospital in Western Kenya (Kijabe Hospital) compared to the experience of their counterparts in an ACGME-approved program in the U.S.

METHODS: We constructed a database to capture case log data from trainees in Kenya in the 2012 academic year. This database contained the same fields as those in the ACGME Case Log system for anesthesiology residents. Additional fields were added for type of surgery in order to delineate the experience in Kenya. This dataset was compared in aggregate to the information from our residency training program.

RESULTS: We collected data on 872 cases performed by 6 anesthesia trainees at a rural Kenyan hospital (Kijabe Hospital) and 7,883 cases performed by 42 residents (CA1-3) at our institution in the same time period. Figures 1-5 show the comparison in trainee experience by percentage (%) between training programs concerning patient age, gender, type of case, patient status (ASA), anesthesia type, and airway management. Patient gender was identical between programs, whereas Kenyan trainees cared for roughly half as many patients >65 years but almost 3 times as many patients <12 years (fig 1 & 2). ASA ≥3 represented 5% of cases performed by Kenyan trainees and 65% of cases by those in our program (fig 3). Case types (fig 4) were fairly similar between programs, except that gynecologic, obstetric, and other intra-abdominal cases represented a larger percentage for Kenyan trainees. Finally, Kenyan trainees performed a greater percentage of cases under neuraxial or regional anesthesia than residents in our program (fig 5).

CONCLUSIONS: These results detail the experience of anesthesia trainees in a rural referral hospital in Kenya. While the training program has been successful for over a decade concerning capacity building, a quantifiable comparison of trainee experience has not previously been known. These results highlight the context-specific similarities and differences in training based on the patient populations served. Future research needs to compare this experience to government-sponsored and administered nurse anesthetist and anesthesiology resident training programs in Kenya and East Africa.

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Figure 1: Comparison of Trainee Experience by Patient Age

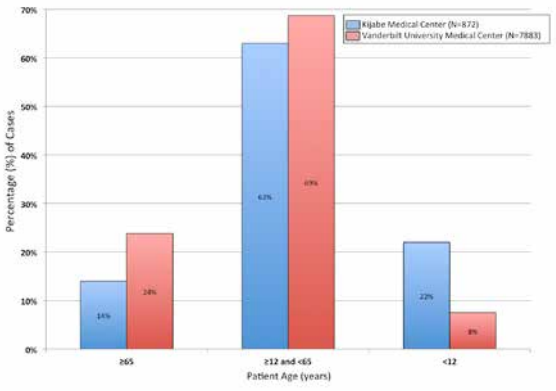


Figure 2: Comparison of Trainee Experience by Patient Gender

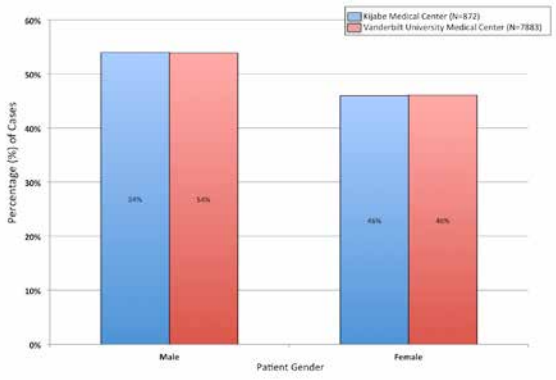
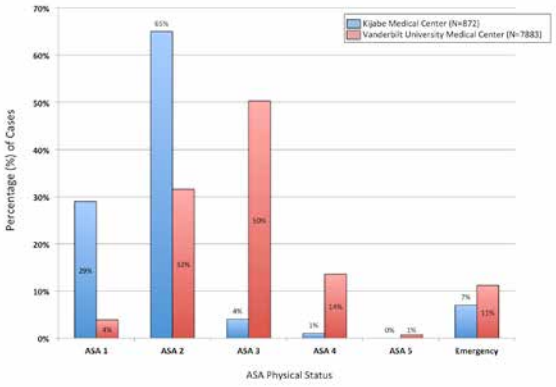


Figure 3: Comparison of Trainee Experience by ASA Physical Status of Patients



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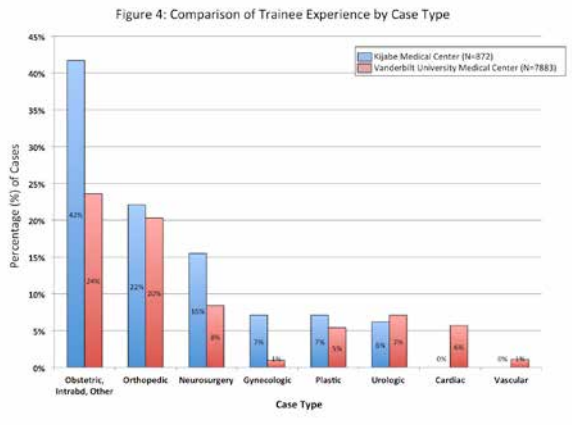

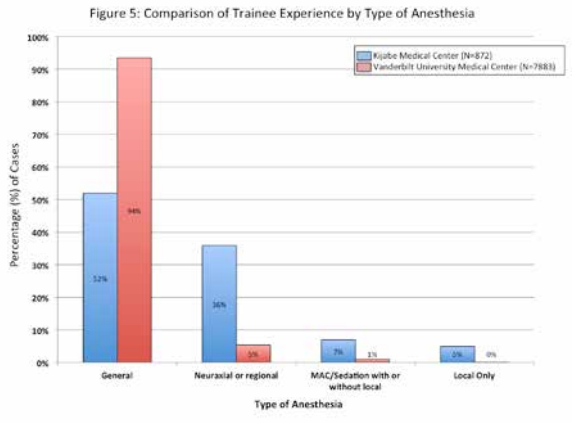

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S-121.

EVALUATION OF A PATHOLOGY SPECIFIC APPROACH TO DATABASE TEE TRAINING FOR ANESTHESIOLOGY RESIDENTS

AUTHORS: C. D. Key[1], O. Klimkina[2], A. DiLorenzo[2], P. Zephyr[2]

AFFILIATION: [1]Anesthesiology, University of Alabama Birmingham, Birmingham, AL, [2]Anesthesiology, University of Kentucky, Lexington, KY

BACKGROUND: Transesophageal echocardiography (TEE) has become an increasingly used tool for the anesthesiologist. Questions related to basic knowledge of TEE are included on the American Board of Anesthesiology certification exam, and curriculum incorporating this topic is encouraged by the ACGME. Currently, there are no standardized requirements for TEE learning time or defined learning outcomes, and there is a minimal amount of literature dedicated to the teaching of TEE in residency training programs.

Our anesthesiology program requires a TEE rotation in the CA-3 year and uses a combination of teaching methods including intraoperative TEE, simulator training, self-study, and TEE database study reading.

The database contains TEE studies completed by anesthesia faculty in a variety of cases. During the TEE rotation, training has traditionally been done by reading random studies from the database. Our research was conducted to compare a pathology specific training approach with the current random approach.

METHODS: IRB exemption was obtained. The study group consisted of 12 residents from the PGY1 and PGY2 years. All PGY 3 and 4 residents who had completed cardiothoracic or TEE rotations were excluded. The two groups were randomized into a pathology specific study group (group 1) and a random mixture study group (group 2).

After an introductory lecture on TEE standard views, both groups received four 45-minute teaching sessions moderated by a senior resident. Sessions were presented in Power Point format and composed with TEE images and clips from database chosen by the primary investigator.

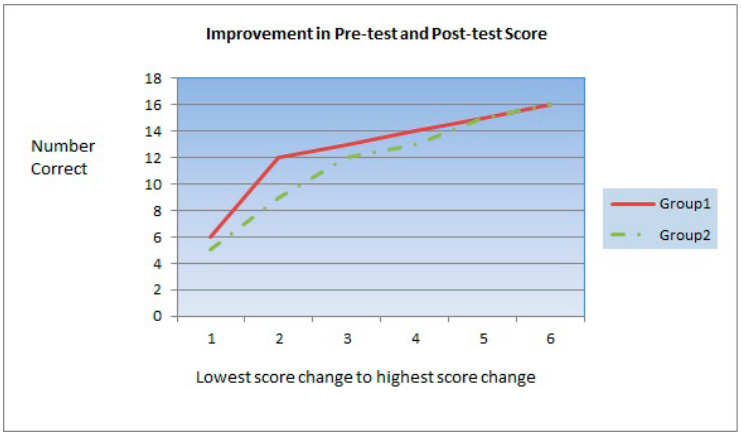
Group 1 received teaching in a pathology organized approach including left ventricular and right ventricular performance, pathology of aortic valve, pathology of mitral valve, and common emergency conditions (hypovolemia, cardiac tamponade, aortic dissection). Group 2 received teaching consisting of identical images and clips introduced as a random mixture.

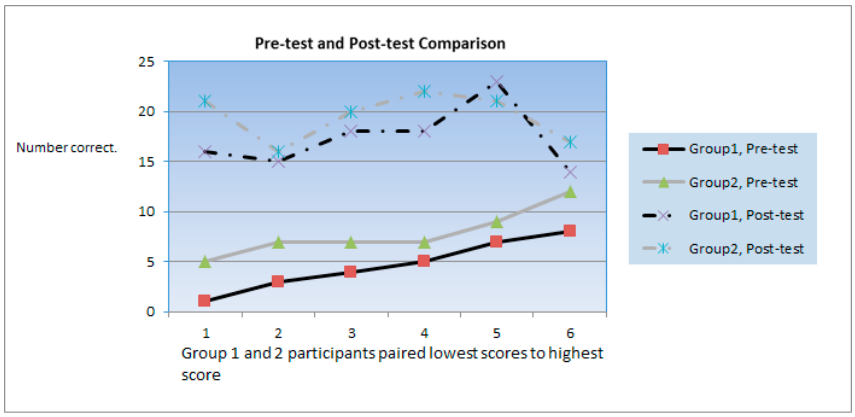
RESULTS: Resident's performance was evaluated by the same written pre-study and post-study test. The test included 26 open-answer questions. Participants were expected to identify TEE standard views, basic cardiac anatomy, or pathology previously discussed during teaching sessions. The average percentage of performance improvement of two groups for the post-study test was: 48.3% for group 1 and 44.7% in group 2 (no significant difference between groups, a p-value of 0.691).

The pre-test average for both groups was 24.22%, and the post-test average was 70.82% (significant difference in performance with a p-value of less than 0.005).

CONCLUSION: There was no statistically significant difference seen in teaching technique (pathology specific or random approach to database TEE training), although group 1 (pathology specific approach) showed a greater degree of improvement than group 2 (random approach).

A statistically significant difference was found in the overall improvement in the scores of the post-test compared to pre-test for both groups, indicating that database instruction for 1st and 2nd year residents is an effective method for introductory TEE training.





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S-122.

IMPLEMENTATION OF A JOINT SURGICAL HOME MODEL: A CASE STUDY AT THE UNIVERSITY OF CALIFORNIA IRVINE

AUTHORS: L. Garson[1], S. Vakharia1, R. Schwarzkopf[2], M. Cannesson[1], Z. Kain[1]

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INTRODUCTION: Healthcare in the US is noted for variability of care, high cost, and poor outcomes[1]. In the perioperative setting, variable and fragmented care increases the chance for operational mistakes and the overall cost of the perioperative care[2].

Recently, the American Society of Anesthesiologists (ASA) that the Perioperative Surgical Home (PSH) concept is a potential solution to this problem[3]. Today, while the PSH concept has already been described and discussed by several authors, the actual "real life" implementation of this new model has never been reported.

In this abstract we describe the development and implementation of the Joint-PSH at our institution and we present the evaluation of this program after 12-months of experience.

METHODS: On October 1st, 2012, our group at UC Irvine Health has started a Perioperative Surgical Home that was aimed at providing services to patients undergoing elective primary hip (THA) and knee (TNA) arthroplasties. Under the Joint-PSH initiative, members of the Departments of Anesthesiology & Perioperative Care and Orthopedic Surgery along with members of all perioperative hospital services developed and implemented a series of clinical pathways defining and standardizing preoperative, intraoperative and postoperative management for these patients. We report length of stay in the hospital (LOS), incidence of perioperative blood transfusions, postoperative complications (based on national benchmarks: mechanical complications, surgical site infection and bleeding, pulmonary embolism, myocardial infarction, pneumonia, and sepsis) 30-day readmission, mortality, and patient satisfaction.

RESULTS: Between October 1st 2012 and October 1st, 2013, 49 Primary THA and 89 TKA were included in the joint-PSH. The mean LOS for TKA and THA were respectively 2.5±0.7 and 2.6±0.7 days. The incidence of perioperative blood transfusion was 4%. In -hospital mortality was 0% and 30-day readmission was 1%. We observed one post-operative complication (hip dislocation). Our Press Ganey Score for overall Patient Satisfaction was 98 percentile.

CONCLUSION: Our institution's Joint-PSH outperformed national benchmarks in most primary and secondary study endpoints. We believe a key component of the PSH is the role of the anesthesiologist. Additionally, our PSH program emphasizes the patient centered continuum of care that is an essential component of a PSH. We believe that our experience with the Joint-PSH program for total joint arthroplasty supports the PSH model to foster collaboration across disciplines, strong communication between all stakeholders from the preoperative evaluation process through postoperative care on into discharge in order to lead to excellent patient outcomes and high patient satisfaction.

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S-123.

DATA-DRIVEN ANALYSIS OF RACIAL AND ETHNIC DIFFERENCES IN REPORTED PAIN

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INTRODUCTION: The growing problem of pain in America is compounded by health disparities in pain assessment and management. Prior efforts to define the scope of pain disparities have generally focused on the role of race and ethnicity in a single disease, symptom, clinical setting, or patient population. No study, however, has broadly evaluated the association of race and ethnicity in reported pain.

METHODS: In this single-center study we use existing data-driven methods to analyze 199,069 clinical encounters representing visits from 84,821 patients to examine the association between race, ethnicity, and initial pain scores across a broad range of primary diseases and presenting symptoms.

RESULTS: In a multivariate logistic regression model including terms for age, gender, race, and ethnicity, Black (OR 1.46, 95% CI 1.40-1.53, $P < 0.001$), American Indian (OR 1.57, 95% CI 1.29-1.90, $P < 0.001$), and Hispanic (OR 1.38, 95% CI 1.34-1.43, $P < 0.001$) patients were more likely to report pain than their White and Non-Hispanic counterparts. Asian race and male gender were associated with a lower likelihood of reporting moderate-to-severe pain.

CONCLUSIONS: Our results demonstrate that reported pain differs by race and ethnicity independent of primary disease or presenting symptom. This study adds context to the growing body of literature describing the impact of gender, race, and ethnicity on acute pain management. By demonstrating that Black, American Indian, and Hispanic patients report higher initial pain, this study suggests that previously reported disparities in pain are, at least in part, influenced by racial and ethnic differences in reported pain.

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S-124.

WITHDRAWN.

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S-125.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS (ASA) PHYSICAL STATUS CLASSIFICATION PREDICTS LENGTH OF STAY IN PATIENTS UNDERGOING ROBOTIC ASSISTED LAPAROSCOPIC PROSTATECTOMIES

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AFFILIATION: [1]Anesthesiology, Maimonides Medical Center, Brooklyn, NY, [2]Urology, Maimonides Medical Center, Brooklyn, NY

INTRODUCTION: Robotically assisted laparoscopic radical prostatectomies (RALRP) offer several advantages to patients including earlier ambulation, decreased pain and a quicker post operative recovery. In our institution most patients are discharged on post operative day 1 following RALRP. Our goal was to look at preoperative factors that predicted length of stay.

METHODS: A retrospective review of all RALRP by a single surgeon between July 1, 2009 and December 31, 2010 was performed. We used generalized linear modeling with SAS statistical software to examine the relationship between length of stay and preoperative and perioperative factors. Preoperative clinical variables included age, body mass index, American Society of Anesthesiologists (ASA) physical status classification, hemoglobin, hematocrit, and creatinine. Perioperative parameters included trendelenberg time, intraoperative intravenous fluids and post-operative pain score. Univariate and multivariate analyses were performed.

RESULTS: The cohort included 95 cases of RALRP. The majority of patients (n=82) were discharged home on post operative day 1, while the remainder of cases (n=13) stayed for greater than one day (range 2-7 days). On univariate analysis, two factors were significantly correlated with LOS: ASA Score ($p < 0.001$,) and preoperative hemoglobin ($p = 0.03$). On multivariate analysis, ASA score ($p = <0.01$) remained statistically significant.

CONCLUSIONS: In our cohort, ASA physical status significantly influenced length of stay following RALRP. Based on this data, patients with greater ASA physical status should be optimized prior to surgery and may require more intensive post operative care.

Descriptive Table of Significant Predictors of LOS

Factor		LOS = 1 Day	LOS > 1 Day	p-value
ASA Score	1	8 (10 %) a	0	< 0.001 (< 0.001) b
	2	67 (82 %)	11 (85 %)	
	3	7 (8 %)	2 (15 %)	

[a]frequency (%) [b]univariate p-value (multivariate p-value)

Descriptive preoperative and intraoperative characteristics. [mean (s.d.)]

Factor	LOS = 1 (n=82)	LOS>1 (n=13)
Age	59.4 (7.3)	57.4 (7.9)
BMI	28.4 (4.2)	26.9 (3.4)
Hemoglobin	14.3 (1.4)	13.9 (1.5)
Creatinine	0.96 (0.2)	1.03 (0.2)
ASA Physical Status	1.99 (0.4)	2.15 (0.4)
Trendelenburg time (min)	179.7 (32)	186.2 (31.4)
IV Fluids (ml)	1883 (524.6)	1815 (651.7)

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S-126.

WOMEN'S INTEREST IN ANESTHESIOLOGY RESIDENCY: THE EFFECT OF THE EIGHTY-HOUR WORK RULE

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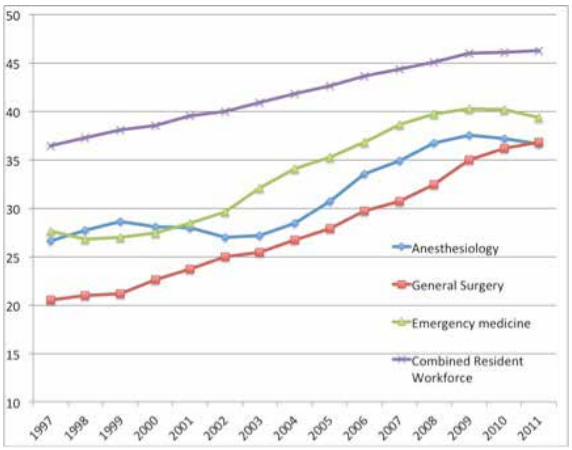
INTRODUCTION: Currently, women represent about 50 % of medical student graduates. However, some specialties still have low representation of female trainees[1,2]. The number of hours worked per week during residency may be one of the factors influencing residency choice among women. The aim of the study was to assess the effect of the implementation of the 80-hour work restrictions mandated by Accreditation Council for Graduate Medical Education (ACGME) in 2003 on enrollment of women in anesthesiology and other specialties characterized as high intensity work-hour during residencies.

METHODS: The number of residents and the proportion of women enrolled in specialty residency programs in the USA between 1997 and 2011were obtained from reports from the National Graduate Medical Education Census on physicians enrolled in programs accredited by the ACGME. Specialties characterized as high-intensity work-hour residencies such as anesthesiology, general surgery, and emergency medicine, were selected for the study. The combined resident workforce, (pool of residents enrolled in all the specialties combined) was used as a comparison group. Differences in trends of enrollment of women before and after 2003 were assessed using linear regression tests and analyses of covariance. P values are presented to assess differences in the slopes representing the rate of change in enrollment of women before vs. after 2003.

RESULTS: There were significant increases in the rate of enrollment of women in anesthesiology, general surgery, and emergency medicine after 2003 (Figure). The proportion of female residents in anesthesiology increased at a rate close to 0% per year, from 26.6% to 27.2%, between 1997 and 2003. After 2003, in contrast, female residents in anesthesiology increased at an average rate of 1.23% per year, becoming 36.6% of the residents in 2011 (P for difference in slopes = 0.002). Women in general surgery programs increased at an annual rate of 0.90% between 1997 and 2003 (from 20.5% to 25.4%) and at a higher annual rate of 1.54% after 2003 (P =0.0001), reaching a proportion of 36.8% in 2011. Similarly, the rate of enrollment of women in emergency medicine increased from 0.43% per year between 1997 and 2003 (from 27.6% to 32.1%) to 1.22% per year between 2003 and 2011, when they represented 39.4% of all the residents (P =0.004). The rate of change in proportion of women in the combined resident workforce remained stable throughout the study period with women representing 36.4% of all the residents in 1997 and 40.9% in 2003, for an annual increase of 0.72%. In 2011 women represented 46.3% of the combined resident workforce, for an increase rate of 0.68% per year between 2003 and 2011 (P =0.521).



CONCLUSIONS: This study suggests that the 80-hour rule implemented in 2003 has contributed to improving the interest of women in specialties characterized previously by longer working hours during residency training. Other factors affecting the under-representation of women in some specialties need to be investigated.

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S-127.

VALIDATING A VETERANS AFFAIRS PERIOPERATIVE SURGICAL HOME: OPTIMIZING PATIENTS WITH CORONARY ARTERY DISEASE IN THE PREOPERATIVE CLINIC

AUTHORS: L. Yarmush

AFFILIATION: Anesthesiology, Houston VAMC, Houston, TX

INTRODUCTION: The American Society of Anesthesiologists (ASA) recently proposed the creation of the Perioperative Surgical Home (PSH) to provide high quality, patient-centric care from preoperative booking to postoperative discharge[i].

The challenge now for anesthesiologists is to extend their medical knowledge into the preoperative period. This retrospective chart review was undertaken to validate how well anesthesiologists in the Anesthesiology Preoperative Clinic (APOC) optimize patients with coronary artery disease (CAD).

METHODS: With IRB approval, all patients presenting to APOC from January through June 2013 prior to outpatient, non-cardiac surgery were reviewed. Patients were risk stratified with strict adherence to published AHA/ACCF guidelines[ii]. Patients presenting with signs and/or symptoms of new or unstable CAD were deemed not optimized. They underwent stress testing scheduled by APOC. Patients who had high-risk results on stress testing were referred to the cardiology department for further workup.

RESULTS: A total of 2959 patients were seen in APOC during the review period. 38 patients were considered not optimized due to concern for CAD. 25 patients had a positive stress test (true positive), while 13 had a negative stress test (false positive). No patient in this group of 38 had a perioperative myocardial infarction (MI). 2917 patients deemed optimized by APOC had no perioperative myocardial infarction (true negative) while only 4 patients deemed optimized by APOC had a perioperative MI (false negative). Sensitivity of a diagnosis of CAD was 86% and specificity was 99%. Positive predictive value was 66% and negative predictive value was 99%. Positive likelihood ratio was 194 (110-340 95% CI). Negative predictive value was 0.14 (0.05-0.34 95% CI).

CONCLUSIONS: Patients with occult blockages of the coronary arteries and patients with known CAD who have asymptomatic progression of their disease are at risk for perioperative ischemia[iii]. Using diagnostic acumen and following AHA/ACCF guidelines, APOC staff correctly identified patients needing further cardiology evaluation. These numbers validate the anesthesiologist's claim to be the physician providing preoperative medical optimization as part of the Perioperative Surgical Home.

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ii. J Am Coll Cardiol 2009, 54(22):e13-118

iii. JAMA 2012, 307(21):2295-304

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Liver

S-128.

DISCOVERY OF A FUNCTIONAL CYP2E1 EPITOPE WITH IMPLICATIONS IN THE PATHOGENESIS OF HEPATIC DILI AND INFECTION

AUTHORS: D. Njoku[1], D. Thomas[2], A. Vakos[2], J. Mantilla[2], L. Santhanam[2], N. Rose[3], D. Njoku[1]

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INTRODUCTION: CYP2E1 is a key enzyme in drug metabolism. CYP2E1 autoantibodies are a marker for immune-mediated-DILI (Im-DILI) from anesthetics and severe necroinflmation in chronic hepatitis C (CHC). CYP2E1 epitopes that trigger autoantibodies remain elusive; moreover, we do not know whether CYP2E1 epitope autoantibodies affect hepatocellular homeostasis as measured by alterations in enzyme activity or gross markers of mitochondrial stress. Our aim was to uncover CYP2E1 epitopes responsible for hepatitis and autoantibodies in anesthetic Im-DILI as well as autoantibodies in CHC and then determine whether anti-CYP2E1 epitope autoantibodies alter hepatocellular homeostasis. We hypothesized that key CYP2E1 epitopes would be recognized by immune cells from experimental Im-DILI mice that had been immunized with liver proteins covalently modified by a model trifluoroacetyl chloride hapten (TFA).

METHODS: We tested 15-18 mer CYP2E1 candidate epitopes for recognition by sera from patients with anesthetic Im-DILI and CHC, and then assessed for H2-Ad recognition using H2-Ad DO11.10 T cell hybridomas or H2-Ed recognition using splenocyte proliferation assays from anesthetic DILI-modeled BALB/c mice. Hepatitis, cytokines and antibodies were assessed following epitope immunizations to BALB/c mice. Hepatocyte homeostasis was measured using Vivid® CYP2E1 Blue screening platform, HepaRG™ cells in culture, fluorescent-labeled epitope antibody and CellRox®Deep Red reagent (Life Technologies).

RESULTS: One epitope (JHDN5) induced proliferation in splenocytes from BALB/c mice in vitro that had been immunized with TFA-altered liver proteins ($p<0.05$). IgG4 subclass-specific JHDN5 autoantibodies were detected by ELISA in sera from anesthetic DILI ($p<0.05$) and CHC patients ($p<0.001$). TFA-altered JHDN5, induced significant IL-4, levels in spleens from immunized mice after 2 weeks as well as proinflammatory cytokines, hepatitis, TFA and CYP2E1 antibodies in BALB/c but not IL-4 -/- mice by 3 weeks ($p< 0.05$). JHDN5 antisera (JHDN5Ab) inhibited CYP2E1 microsomal activity up to 50% in vitro. AlexaFluor488-labeled JHDN5Ab co-localized with the endoplasmic reticulum and mitochondria in hepatocytes in vitro suggesting that JHDN5 autoantibodies may directly inhibit CYP2E1 activity or indirectly by altering mitochondrial homeostasis. JHDN5Ab induced mitochondrial stress detected by CellRox® detection in hepatocytes cultured in vitro.

CONCLUSIONS: Prior studies demonstrated critical relationships between IL-4 and CYP2E1. Diminished CYP2E1 activity has been demonstrated in anesthetic Im-DILI patients but not consistently in CHC. This is the first demonstration of a common CYP2E1 epitope in anesthetic DILI and CHC that induces hepatitis and antibodies in mice as well as the first demonstration of diminished hepatic CYP2E1 enzymatic activity induced by JHDN5Ab in vitro that may explain diminished CYP2E1 activities in some patients. These findings may have implications in drug metabolism during hepatic pathological states.

S-129.

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S-130.

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S-131.

ENOLATE-FORMING COMPOUNDS PROVIDE HEPATOPROTECTION IN A MOUSE MODEL OF ACETAMINOPHEN TOXICITY.

AUTHORS: A. Vydyanathan[1], B. Kosharskyy[1], N. Shaparin[1], L. Zhang[1], R. LoPachin[2], T. Gavin[3]

AFFILIATION: [1]Anesthesiology and Pain Medicine, Montefiore Medical center, New York, NY, [2]Department of Anesthesiology, Albert Einstein College of Medicine, New York, NY, [3]Department of Chemistry, Iona college, New Rochelle, NY

INTRODUCTION: We have shown previously[1] that 1,3-dicarbonyl enols such as 2-acetylcyclopentanone (2-ACP) provide complete protection in a mouse model of acetaminophen (APAP) hepatototoxicity. This protection is based on the ability of 2-ACP to form a highly nucleophilic enolate that can scavenge N-acetyl-p-benzoquinone imine (NAPQI), the toxic electrophile metabolite of APAP[1,2]. Resveratrol (red wine), phloretin (apple skins) and other plant-derived polyphenols are antioxidants (free radical scavengers) that also have enolate-forming enol moieties. To further investigate the enolate role in hepatoprotection, the respective abilities of resveratrol and phloretin to prevent APAP toxicity in mice were determined and compared to the hepatoprotective efficacies of 2-ACP and N-acetyl cysteine (NAC, Mucomyst™).

METHODS: Male C57BL/6N mice (20-25g) were divided into groups (n=12) based on corresponding treatment. Test compounds (2.4 mmol/kg) or vehicle (phosphate buffered PEG) were administered by the intraperitoneal (ip) route 20 minutes prior to oral APAP (500 mg/kg). For all groups, survival was assessed over 7 days post-APAP and indices of oxidative stress (e.g., glutathione depletion) and liver cell death (e.g., serum ALT levels) were measured.

RESULTS: APAP-treated mice exhibited substantial lethality by day 3 (85%; Fig. 1), which was associated with significant oxidative stress and hepatocyte death. 2-ACP given ip provided complete protection against APAP-induced hepatotoxicity. Resveratrol by the same route provided modest hepatoprotection (~40% lethality at day 3), while phloretin and NAC were ineffective (Fig. 1). Corroborative studies (not shown) indicated that ip administration of 2-ACP (alone) was not toxic and provided dose-dependent protection (0.8 - 2.4 mmol/kg) against APAP hepatotoxicity. In contrast, ip phloretin administered alone over a broad dose-range (0.4-2.4 mmol/kg) was highly toxic and provided only limited protection against APAP hepatoxicity at 0.2 mmol/kg; i.e., 60% survival at day 7. Increasing the i.p. NAC dose-rate (4.8 - 7.2 mmol/kg) was also toxic when given ip alone and, when administered with APAP, these doses accelerated hepatoxicity.

CONCLUSIONS: Results show that 2-ACP and resveratrol administered ip can provide hepatoprotection in an animal model of APAP poisoning, whereas NAC and phloretin were ineffective and exhibited dose-dependent toxicity. These findings suggest that enolate-forming compounds might be effective in treating acetaminophen poisoning and other hepatotoxic conditions involving conversion of parent compounds to reactive electrophilic intermediates; e.g., diclofenac.

Acknowledgement Research supported by NIH grant ES03830-26 (to RL).

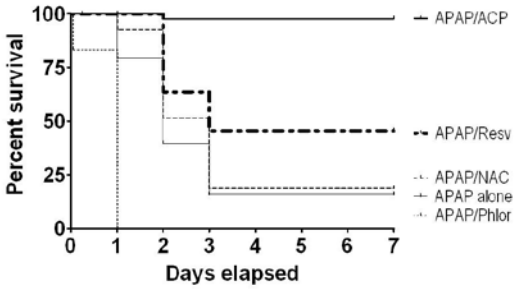

Figure 1: Effects of resveratrol, phloretin, 2-ACP and NAC on the survival of AAP-intoxicated mice. Kaplan-Meier survival curves are presented for the different experimental groups of mice; i.e., oral APAP alone or APAP administered ip 20 mins after test compound (2.4 mmol/kg). Both the APAP/2-ACP and AAP/Resv data sets are statistically different from AAP alone; $p<0.05$, Mantel-Cox test.

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S-132.

HYDROXYETHYL STARCH AND ACUTE KIDNEY INJURY IN ORTHOTOPIC LIVER TRANSPLANTATION: A SINGLE CENTER RETROSPECTIVE REVIEW

AUTHORS: W. R. Hand, J. R. Whiteley

AFFILIATION: Anesthesiology and Perioperative Medicine, Medical University of South Carolina, Charleston, SC

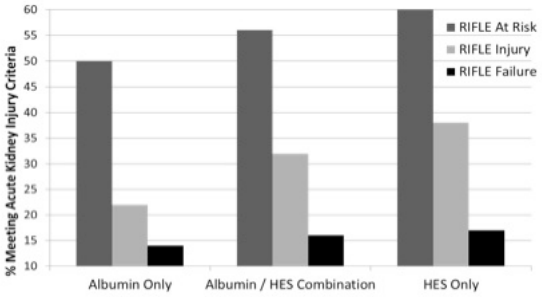
INTRODUCTION: Acute Kidney Injury (AKI) is a frequent complication of orthotopic liver transplantation (OLT).[1] Colloids are routinely used to maintain intravascular volume during OLT. Recent evidence has implicated 6% hydroxyethyl starch (HES) (130/0.4) with AKI in critically ill patients.[2] Since HES is still commonly used, we wished to confirm whether HES does lead to AKI.

METHODS: We performed a retrospective cross-sectional analysis of electronic anesthesia records, surgical dictations, and perioperative lab results. Postoperative AKI incidence was determined by RIFLE criteria. AKI was staged into Risk, Injury, and Failure based on change in serum creatinine from preoperative baseline to peak level by postoperative day 7. Uni- and multivariate analysis was used to evaluate the association between type of intraoperative colloid administered and AKI.

RESULTS: 174 adult patients underwent OLT and had complete records for review. Of these, 50 received only 5% albumin, 25 received both 5% albumin and HES, and 99 received only HES. Albumin only, albumin and HES, and HES only groups were otherwise homogenous based on patient characteristics and intraoperative variables. There was a statistically significant linear by linear association between type of colloid(s) administered and AKI (Rifle Criteria - Injury Stage). Patients administered HES were 3 times more likely to develop AKI within 7 days after OLT compared to albumin (adjusted odds ratio 2.94, 95% CI: 1.13-7.7, p=0.027). The linear association between colloidal use (5% albumin only vs. albumin/HES vs. HES only, ranked ordering) and "Injury" was statistically significant (p=0.048).

CONCLUSIONS: Patients receiving 6% HES (130/0.4) had an increased risk of AKI compared to patients receiving 5% albumin during OLT. These retrospective findings are consistent with recent clinical trials that found an association between 6% HES (130/0.4) and renal injury in critically ill patients. HES should not be used during OLT. that developed acute kidney injury by the three designated RIFLE criteria (risk, injury and failure) based on intra-operative colloidal agent type. There was a linear association (p=0.048) between colloidal use and development of AKI. After adjusting for baseline confounding variables, patients that received HES were nearly three times more likely to develop AKI compared to those that received albumin (Adjusted Hazard Ratio 2.97, 95% CI: 1.13 - 7.7, p=0.027)

Figure 1: Percent of patients



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Neuroscience in Anesthesiology and Perioperative Medicine

S-133.

PERIOPERATIVE CYTOKINE PATTERNS IN CSF AND PLASMA DURING AND AFTER KNEE REPLACEMENT SURGERY

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INTRODUCTION: Postoperative Delirium has been associated with worsened functional and cognitive decline, and other adverse sequelae[1-4], in particular in older patients[5]. Recent data in animal studies demonstrate increases in inflammatory markers in serum and cerebrospinal fluid (CSF) even after aseptic surgery, suggesting that inflammation of the central nervous system may be part of the pathogenesis of postoperative cognitive changes[6-8]. Mediators that have been identified include Il-1β[6,8], TNFα[7] and IL-6[1,9].

METHODS: We investigated the hypothesis that neuroinflammation is an important cause for postoperative delirium after major non-cardiac surgery. After IRB approval and informed consent, we included patients undergoing total knee arthroplasty, who received spinal anesthesia and femoral nerve block using convenience sampling. Specifically for the study, all study patients had an indwelling spinal catheter placed at the time of spinal anesthesia which was left in place for up to 24 hours for the sampling of CSF. Plasma and CSF samples were collected preoperatively and at 3h, 6h and 18h postoperatively. Cytokine levels were measured using Enzyme Linked Immunosorbent Assays and Luminex. Postoperative delirium was measured using the Confusion Assessment Method (CAM) via a structured protocol. Measured cytokines were IFNα2 and IFNγ, IL-1β, IL-4, IL-5, Il-6, IL-8, IL-10 and IL-12p70, MCP1, MIP1α and MIP1β, and TNFα in plasma and CSF and Amyloid β40 and β42 as well as RAGE in CSF only.

RESULTS: Eleven patients were studied. One patient developed postoperative delirium. Cytokine analysis was performed in 10 patients with complete sample sets. We observed an universal increase in proinflammatory cytokines in particular in CSF (Table 1 and 2). In the patient with delirium a persistence of the increase in pro-inflammatory cytokines IL-6, IL-8, MCP1 was observed in the CSF, while the early anti-inflammatory IL-10 response was minimal (Table 2).

CONCLUSIONS: In this pilot study, alterations in cytokine courses were identified. This indicates substantial pro-and anti-inflammatory activity in the central neural system during aseptic surgery. The data on individual cytokines may provide a starting point for future research to diagnose and possibly treat surgery-induced cognitive changes. In particular, CSF IL-6, IL-8 and MCP-1 levels had inter-individually highly variable courses in the perioperative period and/or were altered in the patient who developed postoperative delirium.

	Plasma IL-5					Plasma IL-8				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	0.81	1.57	*100*	0.04	*100*	4.83	2.26	*100*	5.34	*100*
3h	0.52	0.85	*64*	0.05	*125*	7.13	2.84	*148*	9.18	*172*
6h	1.00	1.19	*124*	0.11	*275*	14.69	5.80	*304*	12.36	*231*
18h	2.38	2.49	*295*	0.14	*350*	15.22	6.54	*315*	16.19	*303*
	Plasma IL-6					Plasma TNFα				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	5.40	5.53	*100*	79.09	*100*	6.77	2.91	*100*	13.63	100
3h	17.79	20.51	*329*	211.95	*268*	7.18	2.77	*106*	18.9	139
6h	209.03	145.69	*3869*	272.06	*344*	7.13	3.14	*105*	34.22	251
18h	285.33	148.69	*5281*	317.99	*402*	7.39	2.97	*109*	35.32	259
	Plasma IL-10					Plasma Il 12p70				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	17.32	23.32	*100*	13.63	100	5.15	12.40	*100*	0.06	*100*
3h	20.31	13.00	*117*	18.9	139	3.98	9.74	*77*	0.06	*100*
6h	41.36	28.34	*239*	34.22	251	4.59	10.82	*89*	0.06	*100*
18h	63.45	43.16	*366*	35.32	259	4.06	11.21	*79*	0.06	*100*

Table 1: In the perioperative period an increase in Plasma IL-5, IL-6 and IL-8 was observed in all patients, while IL12p70 was constant. The patient who developed postoperative delirium was the only patient with substantially increased plasma TNFα. For the antinflammatory plasma IL-10 trends were similar in all patients. All units are in pg/ml. The percentages express changes in the cytokine based on the preoperative value.

	CSF IL-6					CSF IL-8				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	7.67	2.79	*100*	7.56	100	41.40	5.29	*100*	30.75	*100*
3h	16.09	10.90	*210*	26.39	349	80.49	34.99	*194*	130.98	*426*
6h	83.02	90.39	*1083*	243.36	3219	432.46	611.73	*1044*	889.37	*2892*
18h	149.22	156.33	*1946*	355.14	4698	362.27	280.67	*875*	1333.34	*4336*
	CSF Il-12(p70)					CSF MCP1				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	0.84	0.58	*100*	0.76	100	2042.88	1008.99	*100*	945.56	*100*
3h	0.84	0.51	*100*	1.05	138	2316.62	945.47	*113*	1847.94	*195*
6h	1.15	0.43	*137*	1.6	211	5522.37	3075.97	*270*	8542.12	*903*
18h	0.92	0.51	*110*	1.53	201	4146.53	2608.86	*203*	8167.86	*864*
	CSF TNFα					CSF IL-10				
	Average	SD	%	Delirium	%	Average	SD	%	Delirium	%
Preop	1.32	0.53	*100*	1.69	100	0.77	0.61	*100*	0.29	100
3h	1.87	1.92	*142*	3.45	204	9.06	12.54	*1175*	0.29	100
6h	1.83	0.89	*139*	3.21	190	18.61	34.89	*2412*	15.58	5467
18h	1.89	0.59	*143*	1.42	84	16.96	19.59	*2198*	16.74	5874

Table 2: In the patient who developed postoperative delirium, at the end of the observation period several CSF cytokines continued to be two-fold higher compared to the patients without delirium. These included proinflammatory MCP1, IL-6, IL-8 and the anti-inflammatory IL-10. Less pronounced changes were present in IL12p70 and TNFα. All units are in pg/mL The percentages express changes in the cytokine relative to the preoperative value.

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S-134.

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S-136.

MEASUREMENT OF THE GASOTRANSMITTER HYDROGEN SULFIDE IN HUMANS USING THE FLUORESCENT MOIETY DANSYL AZIDE

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INTRODUCTION: Gasotransmitters are endogenously made, biologically active gases with unique physiologic properties. At present the best studied gasotransmitters are the inorganic compounds nitric oxide (NO), carbon monoxide (CO), and hydrogen sulfide (H2S). As small molecules these agents are innately highly permeable to the cell membrane and both directly, and indirectly, modify cellular activities. Furthermore synthesis and degradation is rapid and discrete when compared to larger molecular agents; characteristics that explain much of their exhibited temporal and site specificity.

While NO has been studied for decades the endogenously made gases CO and H2S have only more recently been appreciated as agents purposefully synthesized by organisms for physiologic purposes. In particular the elucidation of the relationship between CO and H2S in regulation of the hypoxic respiratory drive has offered valuable insight into the way that this neurochemical reflex functions. Extrapolation into localized hypoxic response is now an area of active research in the field.

Of the two gases most directly associated with confined hypoxic tissue response H2S appears to be the primary vasodilator while CO acts as a tonic vasoconstrictor and modulator of H2S synthesis. The vasodilatory properties of H2S, in conjunction with the molecules' reductive capacity and short half-life, make it an intriguing and challenging target for monitoring. To this end a number of direct and indirect methods have been proposed, all with variable results as regards estimation of species-specific background activity and sensitivity of the model to detect change. Reliable human in vivo methodology for H2S activity has in particular been poorly described.

METHODS: Initial protocol development was performed on serum collected at room air from a single volunteer. Internal standards of Na2Sx9H2O were applied to serum aliquots loaded with 200µmol dansyl azide and submitted to fluorescence readings (excitation 340nm, emission 517nm). Once correlation between internal standards in human serum had been verified a pilot project was proposed. This ongoing pilot project consists of ten healthy male volunteers who breathe room air, hypoxic (15% oxygen, 85% nitrogen), and hyperoxic (100%) gas mixtures on a non-rebreather system until equilibrated. Venous whole blood samples are collected at each oxygen sampling and treated as described in the protocol development.

RESULTS: Preliminary findings show notable differences between individual serum samples collected under variable oxygen exposure (Figure 1) and good response to internal standards (Table 1).

CONCLUSION: In order to study the role of H2S as a hypoxic responder in humans a reliable, robust, and safe protocol amenable to standard hospital laboratory procedures is needed. The fluorescent moiety dansyl azide was chosen for this study due to its simple synthesis and ease of use. Though still underway initial findings from our pilot project show measurable differences in fluorescence between the tested oxygen states, suggesting that this protocol may prove useful in the study of hypoxic response in humans.

Figure 1: Subject B Response to Variable Oxygen Conditions

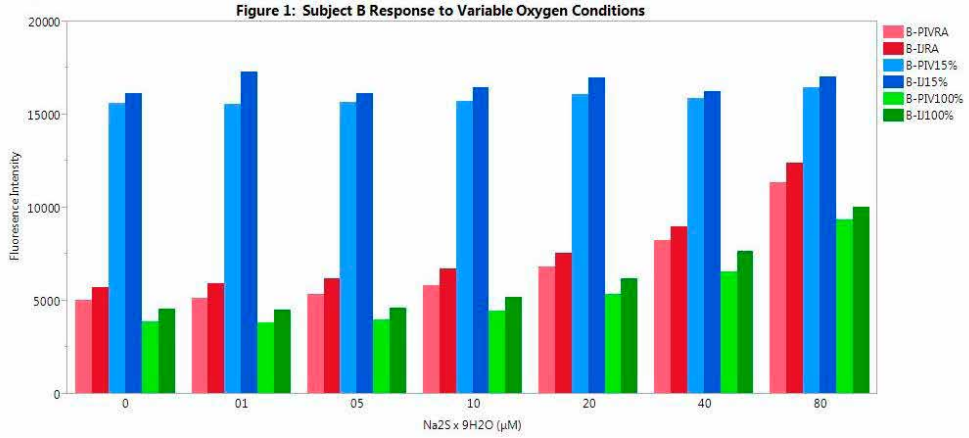

Table 1: Subject B Serum Fluorescence Response to Internal Standards

	Na_2S x $9H_2O$ (µM)							
Sample ID	0	1	5	10	20	40	80	R^2
Buffer-1	48	35	82	60	50	279	604	0.945
Buffer-2	47	32	24	20	84	235	458	0.968
B-PIVRA	5077	5171	5353	5868	6821	8244	11381	0.999
B-IJRA	5727	5960	6217	6742	7565	8997	12420	0.999
B-PIV15%*	15625	15587	15672	15762	16111	15899	16483	0.842
B-IJ15%*	16168	17305	16135	16490	16996	16273	17054	0.080
B-PIV100%	3875	3817	3981	4470	5370	6579	9388	0.997
B-IJ100%	4556	4533	4641	5192	6213	7672	10043	0.990

PIV: antecubital intravenous phlebotomy site, IJ: internal jugular intravenous phlebotomy site, RA: room air, 15%: 15% oxygen, 85% nitrogen, 100%: 100% oxygen

*PIV and IJ samples collected under 15% oxygen consumed baseline dansyl azide (200µM), preventing full capture of internal standards

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S-137.

EFFECTS OF ISOFLURANE ON THALAMO-CORTICAL AND CORTICO-CORTICAL TRIGGERED UP STATES IN MURINE BRAIN SLICES

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INTRODUCTION: Loss of consciousness under volatile anesthetics is likely mediated via direct actions on the cortico-thalamic network. The molecular targets of these agents are well described, and end effects on cortically mediated behaviors are similarly well known, but how these agents alter activity at the network level is unclear. Previous studies suggest that these mechanisms may be related to depression of the thalamic activity, impairment of the cortical information integration ability, preferential inhibition of cortical feedback connectivity, or a combination of these. Little is known about the effects of anesthetics at the level of the cortical network. A well-known component of the cortical network activity is the UP state. UP states are all-or-none, propagating bouts of network activity that appear during sleep and anesthesia. UP states can be triggered and studied in brain slices, and may reveal the complex interaction of multiple neurons throughout the cortical layers. We compared the effects of isoflurane (ISO) on UP states triggered by either thalamocortical (TC) or corticocortical (CC) stimulation in a TC brain slice.

METHODS: The study was approved by the institutional animal care and use committee. Acute auditory TC brain slices were prepared from 4-13 week-old mice. Afferent stimuli were applied using bipolar tungsten electrodes either at the superior thalamic radiation, just rostral to the hippocampus (TC) or in layer 1 or 2 (L1/2) of neocortex, 0.5 - 1 mm caudal to the recording site in auditory cortex (ACx; CC). Local field potentials (LFPs) and multiunit activity (MUA) were recorded using multielectrodes (16 shanks, 100µm spacing, 1 site/shank) oriented either perpendicular to the pial surface to estimate the laminar profile of the UP states, or rostro-caudally in L5 of ACx, to measure the lag time, propagation and firing rate of the UP states. ISO was dissolved in the aCSF and bath applied to the slice. Propagation velocity was computed from the linear fit of the lag time vs. distance along the horizontal array.

RESULTS: TC and CC afferent stimulation reliably evoked UP states in all slices following both TC and CC stimulation. For each slice both stimuli led to UP states with similar firing rate (20-170Hz) and duration (100-350ms). UP states usually originated in L5 and spread to L2/3, and propagated several millimeters along the layers at a rate dependent on stimulus Intensity (range 8 - 42 µm/ms). ISO (0.1 - 0.5%) increased the threshold for evoking UP states in a dose dependent manner. It slowed the horizontal propagation, and decreased the firing rate of both TC and CC induced UP states. UP state latency following TC stimulation was always prolonged, whereas following CC stimulation it could be either prolonged or shortened. The threshold to induce UP states by CC stimulation was significantly more sensitive to ISO then TC stimulation. CC stimulation could not elicit Up states even at low doses of ISO.

CONCLUSIONS: ISO suppresses and slows UP state activity in cortical networks. Initiation of UP states by CC stimulation was very sensitive to ISO, suggesting a strong effect of ISO on long range CC and not TC connections.

S-138.

MAXIMUM DAILY SODIUM IS A PREDICTOR OF ACUTE KIDNEY INJURY IN PATIENTS FOLLOWING SUBARACHNOID HEMORRHAGE

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BACKGROUND: Hypertonic saline therapy is often used in critically ill SAH patients for indications ranging from control of intracranial hypertension to managing symptomatic hyponatremia. The risk factors for developing AKI in this patient population are not well defined, especially the role of sodium therapeutics on kidney function.

SPECIFIC AIM: To study the role of serum sodium and risk for developing AKI (based on the new validated definition) in the SAH population admitted to a large academic neurocritical care unit.

METHODS: This is an IRB-approved, retrospective cohort study of patients admitted to a tertiary academic neurologic intensive care unit. The patient cohort included adult (age>18Y) patients admitted to the Neurocritical care unit following SAH who were admitted for more than 72 hrs. Development of AKI after admission to the ICU was defined using the AKIN serum creatinine criteria between 72 hours and 14 days following admission. A Cox proportional hazards survival model with multiple time varying covariates was developed to evaluate the effect of maximum sodium exposure on the risk of AKI. Sodium exposure was captured as the running maximum daily serum sodium concentration (mEq/L). Sodium exposure was used as a surrogate for hypertonic saline therapy.

RESULTS: The final cohort of patients included 736 adults admitted to the neurosciences ICU between 2006-2012. The number of patients who developed AKI was 64 (9%). Patients in the AKI cohort had an increased length of stay (15.6 ± 9.4 vs. 12.5 ± 8.7) and risk of death. The odds of death were more than two fold greater among patients who developed AKI (odds ratio 2.33 95% CI 1.27, 4.3).

Sodium exposure was significantly associated with the hazard of developing AKI, adjusting for age, sex, preexisting renal disease, diabetes mellitus, count of radiocontrast exposures, number of days on mechanical ventilation, and Glasgow Coma Scale score. For each 1mEq/L increase in the running maximum daily serum sodium, the hazard of developing AKI was increased by 5.4% (95% CI 1.4, 9.7).

CONCLUSION: The running maximum daily sodium (surrogate for hypertonic saline therapy) is a significant risk factor for developing AKI in an otherwise low risk patient population.

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S-139.

NITROUS OXIDE-INDUCED SLOW AND DELTA OSCILLATIONS

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INTRODUCTION: Characterizing the electroencephalogram (EEG) activity in healthy volunteers receiving nitrous is challenging because concentrations of 60% or greater induces significant nausea and emesis.[1] However switching from ether anesthetic to nitrous oxide is a common practice used to facilitate emergence from general anesthesia (GA) in the operating room. Since the transition from ether anesthetic to nitrous oxide is associated with a switch in the mechanisms and sites of drug action, it provides an avenue to explore the EEG signatures associated with nitrous oxide-mediated hypnosis.

METHODS: This retrospective observational study was approved by the Human Research Committee at MGH. We reviewed our database of anesthesia and EEG recordings and identified 12 subjects who received a conversion from sevoflurane to nitrous oxide (60-70%) during routine surgery. EEG activity was recorded using the Sedline monitor (Masimo, Irvine CA). GA was maintained with sevoflurane, oxygen and air and intravenous narcotics (n=9), or with sevoflurane, oxygen and air along with epidurally administered opioids with local anesthetics (n=3). The maintenance concentration of sevoflurane ranged from 1.6% to 2.8% with a median of 1.95%. For the duration of skin closure, nitrous oxide and oxygen were administered at approximately 7 and 3 liters per minute respectively and the sevoflurane concentration was decreased to less than 1.0% or turned off. We used multitaper spectral method to compare the EEG signature during sevoflurane anesthesia to high dose nitrous oxide anesthesia.

RESULTS: Sevoflurane GA was characterized by alpha (8 to 13 Hz) oscillations (Fig 1A). Following the transition to nitrous oxide, the alpha oscillations associated with sevoflurane dissipated, and was replaced with large-amplitude slow (0.1-1 Hz) and delta (1-4 Hz) oscillations (Fig 1B). The EEG power of the slow and delta oscillations elicited by nitrous oxide were significantly larger than those associated with sevoflurane ($P < 0.05$ for both; Wilcoxon Test). We also found that there was no difference in EEG power of gamma (20-30 Hz) oscillations during the period when these large amplitude slow and delta oscillations were present ($P > 0.05$; Wilcoxon Test).

CONCLUSIONS: These observations differ from what is typically reported for nitrous oxide, namely a decrease in slow-delta wave activity with the higher frequency remaining constant.[2] These observations are the first report of large amplitude slow-delta oscillations induced by high dose nitrous oxide administration. They suggest a different mechanism and brain state relative to sevoflurane and lower doses of nitrous oxide. Further study of these oscillations may offer new insights into the neural circuit mechanisms of nitrous oxide and new strategies for managing emergence from GA.

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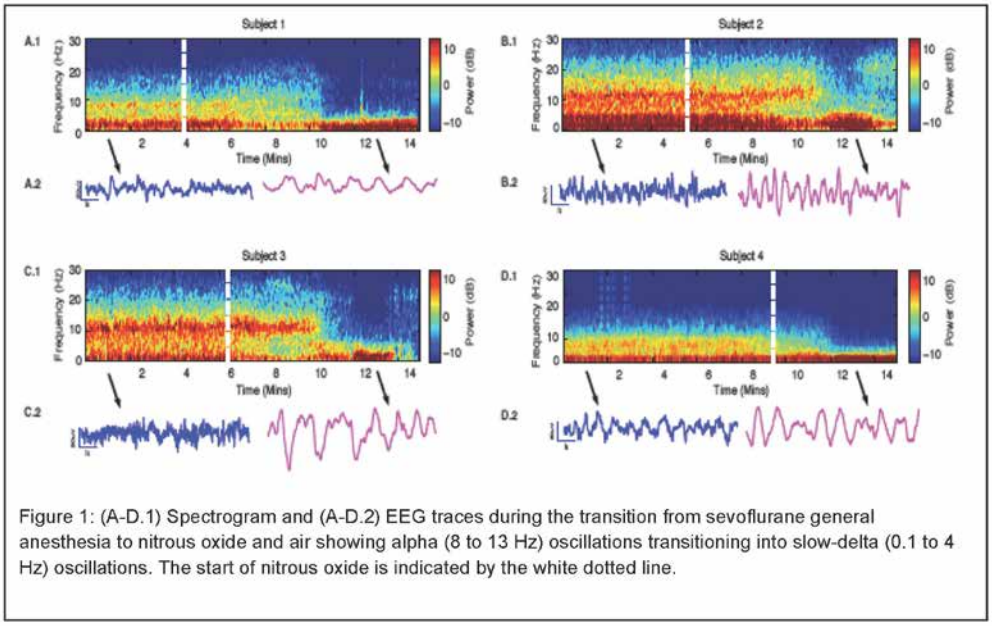

Figure 1: (A-D.1) Spectrogram and (A-D.2) EEG traces during the transition from sevoflurane general anesthesia to nitrous oxide and air showing alpha (8 to 13 Hz) oscillations transitioning into slow-delta (0.1 to 4 Hz) oscillations. The start of nitrous oxide is indicated by the white dotted line.

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S-140.

DEVELOPMENT AND EVALUATION OF A TRAINING PROTOCOL FOR ASSESSING DELIRIUM AS AN OUTCOME IN CLINICAL TRIALS

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INTRODUCTION: A challenge in conducting multicenter trials is ensuring the reliability of outcome assessments across sites. The lack of objective measures for certain outcomes impacts the feasibility of their inclusion in such studies. Postoperative delirium depends on clinician diagnosis, and is therefore vulnerable to subjective interpretation. Delirium is a common and costly[1] complication that warrants inclusion in perioperative studies. The Confusion Assessment Method (CAM)[2] is based on key diagnostic criteria described in the DSM[3] (acute onset or fluctuating course, inattention, and disorganized thinking or altered level of consciousness) and has provided a reliable framework for delirium assessment. It is 94% sensitive and 89% specific for detecting delirium, when used by an experienced evaluator.[4] The goals of this study were to evaluate whether a structured CAM training protocol achieved reliable scoring and to identify areas for improvement.

METHODS: As part of a large, multicenter RCT led by our site (NCT01690988), we developed a methodology to train researchers to use the CAM to assess delirium. Lead researchers attended a one-day seminar led by Dr. Sharon Inouye, the creator of the CAM. This seminar included instruction in conducting standardized, scripted patient interviews and in the scoring of the CAM. Lead researchers then instructed additional trainees. Trainees were required to conduct at least two satisfactory interviews in the presence of a lead researcher. Then, all researchers conducted a total of 35 practice interviews in rotating small groups or pairs, scoring each CAM independently, and then comparing and discussing reasons for discrepancies. To evaluate the success of the training process, all researchers were required to independently view and score nine videos of interviews of actors depicting delirious and non-delirious patients. We quantified overall agreement on the presence or absence of delirium using Fleiss' kappa statistic. We quantified agreement on all five key criteria of the CAM using total agreement, the kappa statistic, and concordance.

RESULTS: Eight raters independently viewed and scored nine patient scenarios. Overall agreement for the presence or absence of delirium (CAM +/-) was good (71.7%). Total agreement for the presence or absence of each of the key criteria of the CAM, across all scenarios, was also good (74%; kappa = 0.71, concordance = 0.84). When comparing raw scores, the majority of inter-rater discrepancies were found in scores for two CAM criteria: disorganized thinking and altered level of consciousness.

CONCLUSION: With training and experience, researchers can reliably assess delirium using the CAM. Limitations in reliability were observed primarily in two domains of the CAM, which should be the focus of further rater training.

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S-142.

IDENTIFICATION OF POTENTIAL TARGET PROTEINS LEADING TO REDUCED SURGICAL BLEEDING FROM PRETREATMENT OF SPRAGUE DAWLEY RATS WITH C. ATROX VENOM

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INTRODUCTION: The venom of the Western Diamondback rattlesnake, *Crotalus atrox*, possesses cytotoxic, myotoxic, and hemorrhagic properties.[1] The venom is known to include proteins in a few major families including serine proteases, zinc metalloproteases, L-amino oxidase and PLA_2 as well as several non-enzymatic proteins.[2] These enzymatic and non-enzymatic toxins represent a largely untapped source of target-specific bioactive molecules which have great potential as therapeutic precursors in the clinical arena. Metalloproteases and serine proteases affect platelet aggregation, blood coagulation, and fibrinolysis.[3] Snake venom metalloproteases in particular have been shown to specifically alter fibrinogen, greatly reducing its ability to form a clot.[4] We have shown that rats preconditioned with 1/50 LD50 of *Crotalus atrox* venom demonstrate decreased bleeding in a surgical brain injury model.[5] We have also observed increased fibrinogen levels in these preconditioned rats. Our current work is focused on identifying the specific protein(s) present in venom which are responsible for these hematologic changes.

METHODS: Whole *Crotalus atrox* venom was separated into ten major fractions by size exclusion chromatography using a HiLoad 16/60 Superdex 75 prep grade column (Figure 1).

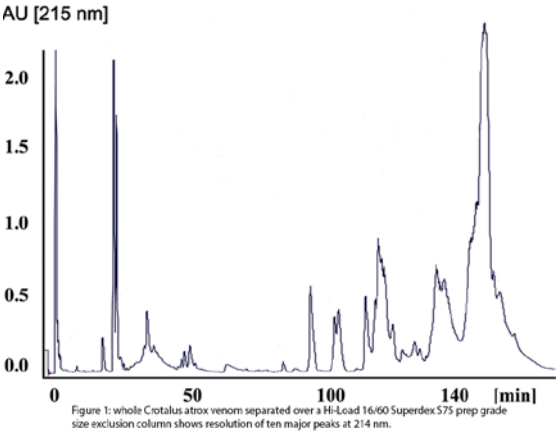


Figure 1: whole Crotalus atrox venom separated over a Hi-Load 16/60 Superdex 575 prep grade size exclusion column shows resolution of ten major peaks at 214 nm.

The fractions were lyophilized, and then resuspended in phosphate-buffered saline to a concentration of 8 mcg/ml. These fractions were run on SDS-PAGE and compared to both a standard molecular weight marker as well as published mass spectrometry data for C. atrox venom protein (Figure 2).

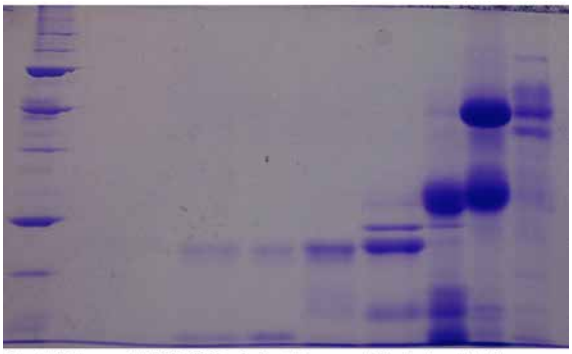
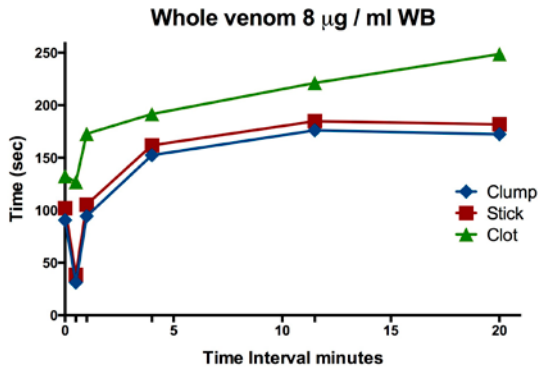
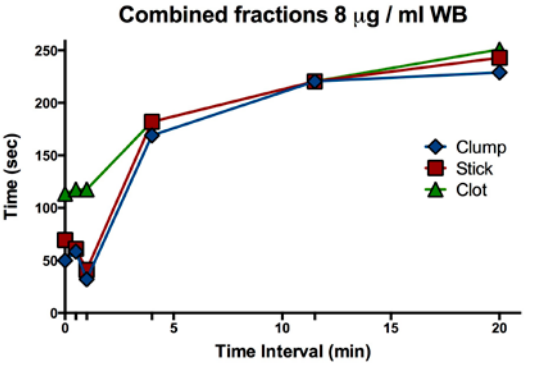


Figure 2: Proteins separated by SDS_PAGE from fractions 2-19 correspond with molecular weights of known C. atrox proteins including L-amino acid oxidase; SVMP atrolysin C, B, D and hemorrhagic toxin A (lanes 2, 3, 4); SVSP catroxase-2 and 1; CRVP (lanes 5, 6, 7, 8); PLA2; and C-type natriuretic protein (lanes 7,8)

The fractions were then combined and incubated with whole human blood for measurement of coagulation parameters. These measurements were then compared to coagulation parameters of whole C. *atrox* venom.





RESULTS: Both commercially available whole C. atrox venom and the combined fractions obtained by size exclusion chromatography displayed a particular pattern of activity as measured by coagulation parameters in whole human blood (Figure 3).

Initially clotting time was reduced and shortly thereafter clotting time was extended in a time dependent manner for both whole C. *atrox* venom and the reconstituted combined fractions of venom.

CONCLUSIONS: The unique pattern of initial pro-coagulant and subsequent anti-coagulant effects observed with whole C. *atrox* venom have been shown to be consistent with combined fractions of venom isolated by size-exclusion chromatography and reconstituted in a biologic buffer. We have thus developed a framework for analysis of distinct fractions of venom with the ultimate goal of isolating the protein(s) which confer this effect, as well as determination of the protein(s) resulting in decreased surgical bleeding in the surgical brain injury model. Work to identify the active protein(s) is ongoing.

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S-143.

RELATIONSHIP OF AWAKE BISPECTRAL INDEX TO PREOPERATIVE MEMORY FORMATION

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INTRODUCTION: Anesthesia awareness is a rare but significant complication of general anesthesia. As such, "awareness" monitors have been developed to target to the appropriate depth of anesthesia. One such monitor, the Bispectral Index (BIS) (Covidien) uses an algorithmically processed EEG and EMG to output a dimensionless integer ranging from 0 (no brain activity) to 100 (complete wakefulness). Initial studies indicated that BIS improved upon other anesthetic monitoring techniques in preventing awareness[1], but subsequent studies have indicated that BIS is no better[2] or worse[3] than control protocols. This study was designed to characterize whether BIS is correlated with a subject's ability to form memories, a prerequisite for reporting awareness events, by assessing recall of words spoken to the subject in the preoperative time period. Additionally, BIS values and word recall relative to timing of midazolam administration were considered.

METHODS: Following IRB approval and informed consent, 168 adult subjects were enrolled in the study. All subjects were undergoing procedures involving administration of preoperative midazolam prior to general anesthesia. BIS values were recorded at five, three, and one minute prior to midazolam administration; at the time of administration; and at one, three and five minutes post-administration. At all of these time points except the final one, a unique word was spoken and the subject was asked to remember the word. Word recall was assessed post-operatively and relationship of BIS to recall was analyzed via Wilcoxon Rank sum test.

RESULTS: Differences in BIS for subjects remembering versus not remembering a word were statistically significant ($p<0.05$) for three of the six words. These included the word spoken at midazolam administration (Word 4), and the words spoken one minute and three minutes after midazolam administration (Words 5 and 6, respectively). Word 4 had lower average BIS values by one point for those recalling the word as compared to those not recalling the word. Words 5 and 6 had higher average BIS values for those recalling the words as compared to those not recalling the word by three and four points, respectively. For other words, there were no statistically significant differences in BIS scores. Across time relative to midazolam administration, a small decrease in average BIS was seen one minute after midazolam administration, whereas a significant decrease in percentage of subjects recalling a word began one minute prior to midazolam administration.

CONCLUSIONS: While statistically significant differences in BIS were found for certain words recalled versus not recalled, these results do not reflect a clinically significant difference in BIS, precluding its use to predict a subject's ability to form memories in the preoperative setting. The temporal findings suggest that memory formation may decline even before the administration of a pre-operative sedative, a phenomenon not reflected by a statistically or clinically significant change in BIS.

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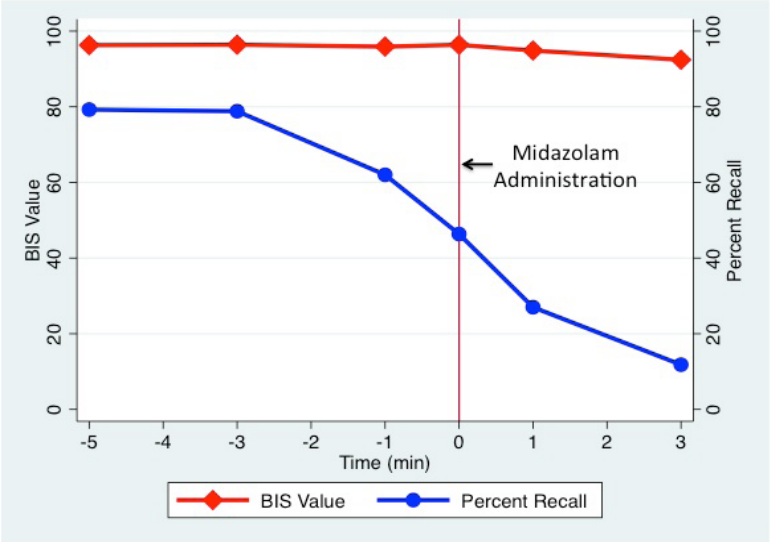

Figure 1: Temporal comparison of mean BIS value and word recall

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S-144.

CRITICAL ROLE OF INFLAMMATORY CYTOKINES IN IMPAIRING BIOCEHMICAL PROCESSES FOR LEARNING AND MEMORY AFTER SURGERY IN RATS

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BACKGROUND: Patients with postoperative cognitive dysfunction have poor outcome. Neuroinflammation is proposed as the underlying pathophysiology for this dysfunction. We determined whether proinflammaory cytokines affected the trafficking of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors to the plasma membrane, a fundamental biochemical process for learning and memory.

METHODS: Four-month-old male Fischer 344 rats were subjected to right carotid exposure under isoflurane anesthesia. Some rats received intravenous lidocaine infusion during anesthesia. Rats were tested two weeks later by Barnes maze. Hippocampus was harvested at 6 h after the surgery for Western blotting of interleukin (IL)-1β or IL-6. Hippocampal slices were prepared from rats 2 weeks after the surgery or hippocampal slices were from control rats. These slices were incubated with or without tetraethylammonium, an agent that can induce long-term potentiation, for determining trafficking of GluR1, an α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor subunit.

RESULTS: Surgery increased the time to identify the target box in the Barnes maze when tested 1 and 8 days after the training sessions. Surgery increased IL-1β and IL-6 in the hippocampus. The tetraethylammonium-induced GluR1 phosphorylation and trafficking was abolished in the hippocampal slices prepared from rats after surgery. These surgical effects were minimally affected by lidocaine. Incubation of control hippocampal slices with IL-1β and IL-6 also abolished tetraethylammonium-induced GluR1 trafficking.

CONCLUSIONS: Our results suggest that surgery increases proinflammatory cytokines that then inhibits GluR1 trafficking to lead to learning and memory impairment.

S-145.

HIPPOCAMPAL GABAERGIC FIELD POTENTIALS: A NOVEL HIGH THROUGHPUT SCREEN FOR GENERAL ANESTHETICS IN RAT

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INTRODUCTION: Concern for anesthetic toxicity is growing. It is vital that we can rapidly screen for safe, effective anesthetics with minimal adverse effects on cognition. At the cellular level, anesthetics alter the behavior of neurons, often by enhancing inhibitory signals through interactions with the GABAA receptor (GABAR). We describe a novel, high throughput method to directly measure a compound's effect on aggregate GABAAR mediated inhibition within area CA1 of rat hippocampus, an area crucial for learning and memory, without the need for whole cell recordings. We found these field inhibitory postsynaptic potentials (fIPSPs) by cutting brain slices to preserve coherent current sources and sinks, stimulating basket cell interneurons, and recording CA1 pyramidal cell hyperpolarization. We further isolated the fIPSP using NMDA and AMPA receptor antagonists to block excitatory transmission. We validated our assay with two common GABAergic anesthetics, and have begun screening compounds identified by in silico methods of molecular docking and computational chemistry for their potential as anesthetics.

METHODS: 24-28 day old Sprague Dawley rats were anesthetized with isofluorane and decapitated. Brains were submerged in chilled artificial Cerebrospinal Fluid (aCSF). 400 μm thick slices were cut and placed in aCSF, and bubbled with 95% O2 and 5% CO2. Field potentials were evoked through a bipolar tungsten stimulating electrode placed in the stratum pyramidale (SP) of the CA1 region. Recordings were conducted through a glass microelectrode 150 μm away in the SP of CA1. Drugs used to isolate fIPSPs include antagonists for the following receptors: d-APV (NMDA), NBQX (AMPA), kynurenic acid (AMPA, NMDA, Kainate). GABAergic dependence of the fIPSP was confirmed by fIPSP disappearance in picrotoxin (GABAAR antagonist). The validity of the screen was tested on known anesthetics, propofol and midazolam. Benzodiazepine dependence of fIPSP was tested with flumazenil.

RESULTS: A significant change in the magnitude of the fIPSP is evident upon application of propofol. Application of low concentrations of propofol (1-5 um) produces a small increase in the size in the fIPSP (<5%), consistent with enhancement of phasic inhibition. Interestingly, larger doses of propofol (20 μM) decreased the fIPSP significantly (35-40%), consistent with enhanced tonic inhibition and net hyperpolarization of the slice. Midazolam, on the other hand, produced an enhancement of the fIPSP, suggesting a greater role of phasic inhibition in its anesthetic effect. In all cases,50 μM picrotoxin the fIPSP to the level of background noise.

CONCLUSIONS: The isolated fIPSP gives predictable, fast results with propofol and midazolam, and exhibits sensitivity to varying concentrations of these drugs. Thus, isolated fIPSPs allow for direct measurement of an anesthetic's effect on GABAA transmission. Combining this fast, minimally invasive, neural population based approach affords a unique opportunity to assay multiple lead compounds for anesthetic efficacy in an intact, well characterized neural circuit with clear relevance to learning and memory.

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S-146.

POST-DISCHARGE NAUSEA AND VOMITING AFTER ORTHOGNATIC SURGERY REMAINS FREQUENT DESPITE IMPLEMENTATION OF MULTIMODAL PROTOCOL EFFECTIVE IN REDUCING POST-OPERATIVE NAUSEA AND VOMITING

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AFFILIATION: [1]Anesthesiology, University of North Carolina, Chapel Hill, NC, [2]Oral & Maxillofacial Surgery, UNC Hospitals, Chapel Hill, NC

INTRODUCTION: Post-operative nausea and vomiting (PONV) has received considerable attention in the anesthesia literature. Post-discharge nausea and vomiting (PDNV) is less well understood and can result in readmission, wound complications, and patient dissatisfaction. The purpose of this study is to assess the impact of a multimodal protocol that has successfully decreased PONV on experience of PDNV after LeFort I osteotomy.

METHODS: Consecutive subjects undergoing LeFort I osteotomy with or without additional procedures at a single academic institution were recruited as the intervention cohort for an IRB-approved study. This cohort was managed with a multimodal antiemetic protocol including total intravenous anesthesia; prophylactic ondansetron, steroids, scopolamine, and droperidol; gastric decompression at surgery end; opioid-sparing analgesia; avoidance of morphine and codeine; prokinetic erythromycin; and minimum 25 mL/kg fluids. Consecutive subjects from a larger study who underwent similar procedures prior to protocol implementation formed the comparison group. Data were extracted from medical records. Data regarding occurrence of PDNV was derived from patient diaries Data were analyzed with Fisher's Exact Test and Wilcoxon Rank Sum Test. $P<0.05$ was considered significant.

RESULTS: The intervention (n=70) and comparison (n=137) groups were similar in terms of gender (61% and 65% female, P=0.65), race (67% and 69% Caucasian, P=0.63), proportion of subjects with known risk factors for PONV (P=0.59), and percentage undergoing bimaxillary surgery (63% and 60%). Surgery time was over 180 minutes for more subjects in the intervention group (67% versus 59%) but the difference was not significant (P=0.26). Prevalence of PON was significantly lower in the intervention group than the comparison group (26% versus 70%, $P<0.0001$). Incidence of POV was likewise significantly lower in the intervention group (11% versus 29%, P=0.0056). Prevalence of PDNV, though, was unaffected by the protocol. PDN was reported by 71% of the intervention subjects and 60% of the comparison subjects (P 0.18). PDV was reported by 27% of the intervention subjects and 29% of the comparison subjects (P 0.79).

CONCLUSIONS: Modalities that successfully address PONV may fail to impact PDNV. Additional investigation into PDNV is merited.

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S-147.

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S-148.

CARDIAC SAFETY OF SABER®BUPIVACAINE IN PATIENTS UNDERGOING ABDOMINAL SURGERY IN THE BESST TRIAL

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INTRODUCTION: Bupivacaine is commonly used as a part of postsurgical multimodal pain management, but its use is limited by a short duration of action. SABER®-bupivacaine was developed to provide a sustained release formulation of bupivacaine for 72 hours in order to maximize analgesia during the period of maximal postoperative pain. To evaluate any clinical evidence of cardiovascular-related bupivacaine systemic toxicity with SABER®-bupivacaine treatment, cardiac safety was assessed in the phase 3 Bupivacaine Effectiveness in SABER™ Surgical Trial (BESST).

METHODS: BESST was an international, multicenter, double-blind trial evaluating the safety and efficacy of SABER®-bupivacaine 5 mL (660 mg) instilled into surgical wounds prior to closing. Eligible patients were randomized into 3 cohorts depending on surgical procedure; cohort 1 (n = 48) for open laparotomy (long incisions; mean, 20 cm); cohort 2 (n = 50) for laparoscopic cholecystectomy (small incisions; mean, 4 cm); and cohort 3 (n = 207) for laparoscopic colectomy (medium incisions; mean, 8-9 cm). Control for cohorts 1 and 2 was bupivacaine HCl (150 mg); cohort 3 was placebo controlled. Safety assessments included treatment-emergent adverse events (TEAEs), laboratory monitoring, wound healing, vital signs, and physical exam. Cardiac safety was assessed by digital 12-lead Holter monitoring from 1 hour before surgery until 72 hours after surgery. A 24-hour baseline Holter was obtained on an ambulatory basis before surgery. ECGs and PK samples were taken before and 0.5, 1, 2, 4, 8, 12, 16, 24, 30, 48, and 72 hours after dose. ECGs extracted from the Holter recordings were assessed for changes in heart rate, RR, PR, QRS, QT, QTcF (Fridericia formula-corrected QT interval), QTcB (Bazett corrected QT interval), QTbtb (QT beat-to-beat) and percentage QTbtb outliers. The primary ECG end point was SABER®-placebo -corrected baseline-adjusted effect on QTcF (ΔΔQTcF) for SABER®-bupivacaine in cohort 3. The relationship of plasma bupivacaine concentration to ΔΔQTcF was also evaluated in cohort 3. Bupivacaine plasma concentration was assessed via a validated liquid chromatography/mass spectrometry (LC-MS/MS) method.

RESULTS: Most patients reported at least 1 TEAE, most commonly gastrointestinal symptoms (nausea, vomiting, or constipation), likely to due to anesthetic, surgery, or opioid use. Cardiovascular and neurologic TEAEs were similar between treatments with no signs of bupivacaine toxicity. There were no consistent effects on any of the ECG intervals, including QTcF, observed in the Holter data. PK-PD modeling showed that SABER®-bupivacaine did not prolong the QT interval as the slope of the ΔΔQTcF versus bupivacaine concentration regression was essentially flat. No proarrhythmic events were observed in any of the Holter recordings for all 3 cohorts.

CONCLUSIONS: SABER®-bupivacaine (5 mL instilled into a variety of abdominal surgical wounds) was well tolerated, with no evidence of systemic bupivacaine cardiac toxicity, no effect on ECG intervals, and no ventricular arrhythmias.

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S-151.

CORTICAL RISK FACTORS RELATED TO SURGERY FROM ADNI DATABASE BLOOD AND IMAGING BIOMARKERS

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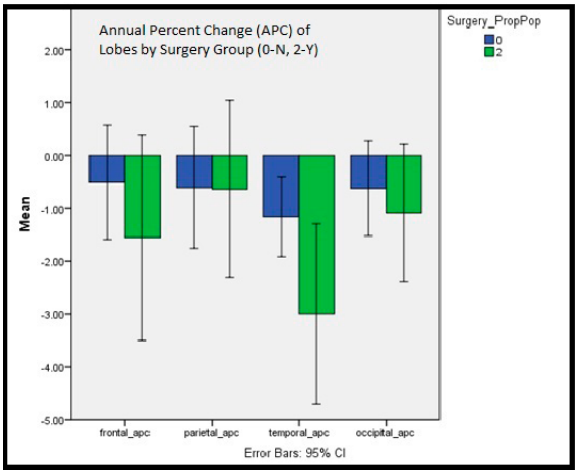
INTRODUCTION: It has previously been reported, based on analysis of the Alzheimer's Disease Neuroimaging (ADNI) database, that subjects who incidentally had surgery during their participation had more rapid hippocampal (hip) and gray matter atrophy in the interval between imaging visits when surgery occurred than controls. Furthermore, long term volume changes showed dependence on surgical type. We examined blood biomarkers (BMs) in these same ADNI surgical groups for impact on cortical volumes to identify prognostic factors for postoperative cognitive dysfunction (POCD).

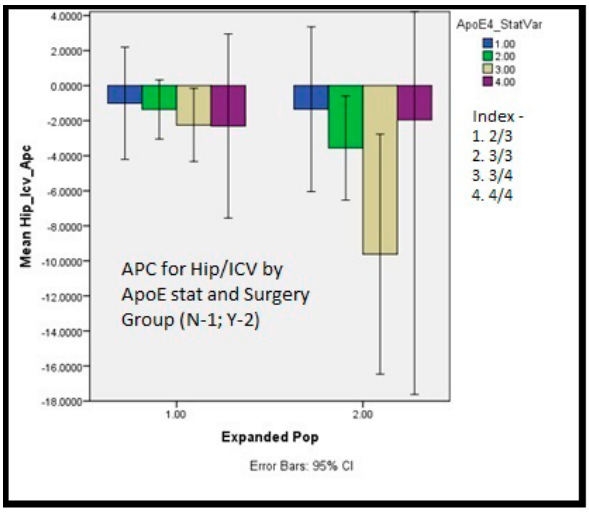
METHODS: We selected 3 candidates (C reactive protein - CRP; Leptin; Interleukin 6 (IL-6)) from over 30 populated in ADNI, by examining dependence on gender, age, BMI, diagnosis (Dx), intracranial volume (ICV), ApoE4 gene status and each other. Depending on their distribution (all log transformed), we used ANOVA based analysis (T-Test, univariate, multivariate, Pearson correlation) or rank based methods. Principal component analysis was used to group biomarkers. IL-6 was converted to a 3 value categorical since ~1/3 of data points were below resolution. We used baseline BM values (prior to surgery).

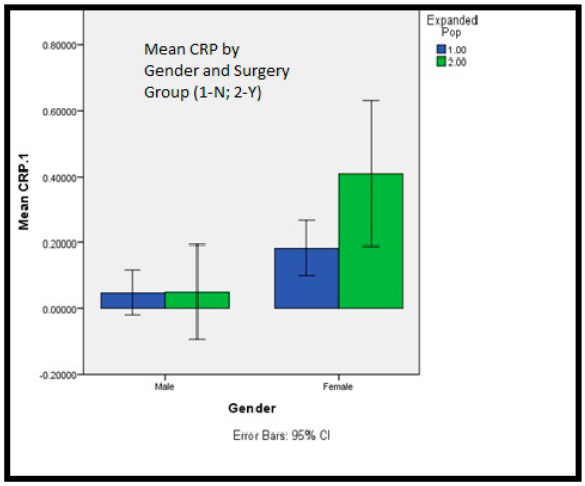
RESULTS: The greatest atrophy risk groups were defined by surgery type (non-orthopedic), lobes (temporal; fig. 1), Dx (MCI) and genotype (ApoE = ¾ [#3]; fig 2). An indicator of inflammation/infection, with marked elevation post surgery, CRP had an anomalous response (decrease) to Alzheimer's progression. CRP had pronounced dependence on ApoE4 status (neg corr.;p=0.001), gender (F > M; p<0.05), education (yrs; p=0.009; neg. corr.), BMI (pos. corr., p<=0.005) and IL-6 (p=0.000). Dependence on Dx was not significant (p>0.5) in the presence of an ApoE4 term. Subjects later having non-orthopedic surgery showed elevated CRP vs. controls (p=0.02). Elevation of CRP among all surgical subjects (p=0.045) was due to females (gender*surgery group interaction, p=0.01; fig 3).

A metabolic modulator, leptin had pronounced dependence on gender (females > male) and BMI (p=0.000); and is a significant covariate in cortical and Hip volume (with IL-6, diagnosis, and gender; p<0.01). It trends lower with Dx progression, and is reduced by surgery in a high risk (MCI; ApoE = 3/4) surgery group (p=0.001; fig 4). An inflammatory cytokine, IL-6 elevation speeds cortical atrophy (p=0.047), and cognitive loss (p=0.046). It correlates with baseline temporal lobe volume (p=0.002) and Dx (p=0.003, $\chi 2$), but not the ApoE4 genotype (opposite to CRP result). It is elevated by surgery amongst MCI subjects (fig 5).

DISCUSSION: All 3 BMs affect baseline values of cortical volume and vary with Dx and/or ApoE4 status; where ApoE4 itself is a cofactor for the surgical effect on atrophy. They dramatically depend on such factors as gender, BMI, ICV and age. Surgical group changes predate actual surgery. More routine study of these BMs and ApoE genotype perioperatively could support better understanding of surgically related atrophy; as well as identifying targets for enhancing neuroprotection (Leptin), or blocking the deleterious effects of inflammation (IL-6, CRP).







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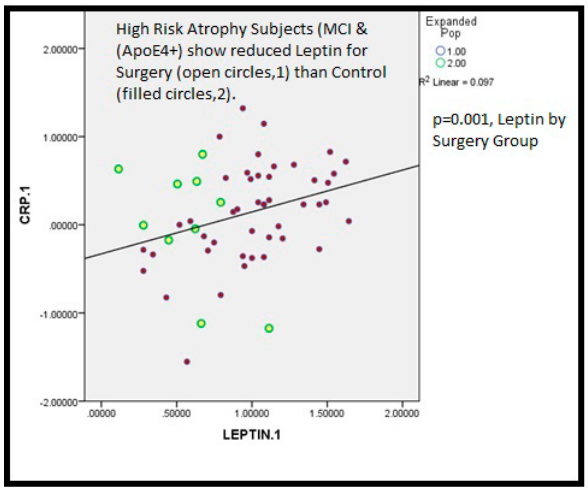

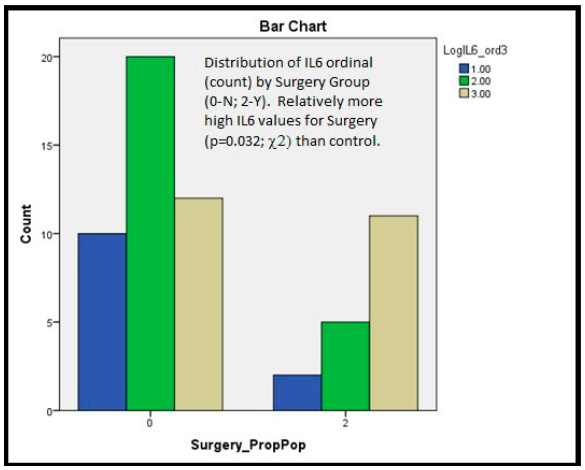

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S-152.

SYNAPTIC PLASTICITY IN THE CA3 SUBFIELD OF THE HIPPOCAMPUS IS FACILITATED BY δGABAA RECEPTORS IN MICE

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INTRODUCTION: γ-Aminobutyric acid type A ($GABA_A$) receptors are well known modulators of memory processes and are novel targets for memory-enhancing drugs. We recently showed that increasing the activity of δ subunit-containing GABAA ($\delta GABA_A$) receptors enhances performance for certain types of hippocampus-dependent memory tasks and promotes neurogenesis (1). Long-term potentiation (LTP) of synaptic transmission in the hippocampus, a major cellular correlate of memory, is modulated by GABAA receptor activity (2). In the CA3 subfield of the hippocampus, LTP at Mossy fiber-CA3 pyramidal cell synapses is facilitated by presynaptic GABAA receptors (2). $\delta GABA_A$ receptors may be expressed at presynaptic Mossy fiber terminals and could have an excitatory action that facilitates Mossy fiber-CA3 LTP. Here, we test the hypothesis that $\delta GABA_A$ receptors facilitate Mossy fiber-CA3 LTP.

METHODS: Hippocampal slices were prepared from wild-type (WT) and transgenic $\delta GABA_A$ receptor null mutant (*Gabrd-/-*) mice. Extracellular field postsynaptic potentials (fPSPs) were recorded from the CA3 subfield, where Mossy fiber-CA3 pyramidal cell synapses are located. Basal neurotransmission and presynaptic plasticity were compared in slices from WT and *Gabrd-/-* mice using input-output plots and paired pulse responses, respectively. LTP at Mossy Fiber-CA3 synapses was generated in slice using a tetanic stimulation protocol (3 trains of 100 Hz stimulation for 1 sec). fPSPs recorded in the first minute following tetanic stimulation were used to measure post-tetanic potentiation (PTP) while fPSPs recorded during the last five minutes were used to measure long-term potentiation (LTP). All experiments wereperformed in the presence of the selective n-methyl-D-aspartate (NMDA) receptor antagonist (2*R*)-amino-5-phosphonopentanoate (50 μM), to prevent the induction of NMDA receptor-dependent LTP. Values are expressed as mean ±standard error of the mean (SEM).

RESULTS: A pronounced PTP of the fPSPs was observed in both genotypes; however, PTP was greater in the WT slices compared to *Gabrd-/-* slices: (WT: 178.3 ± 16.1%, n = 16 versus *Gabrd-/-*: 126.3 ± 6.9%, n = 19; $t = 3.15$, $df = 33$, $p < 0.01$). Similarly, at 1 hr following tetanic stimulation, LTP was greater in WT slices (WT: 168.3 ± 13.1%, n = 16 versus Gabrd-/-: 128.0 ± 4.3%, n = 19; $t = 3.18$, $df = 33$, $p < 0.01$). The input-output plots and the paired pulse ratios were similar in WT and Gabrd-/- slices, suggesting there was no differences in basal neurotransmission or presynaptic function between the genotypes.

CONCLUSIONS: Here we show that the expression of $\delta GABA_A$ receptors facilitates LTP at Mossy fiber-CA3 synapses without significantly affecting basal neurotransmission or presynaptic plasticity. It is possible that selectively enhancing the function of $\delta GABA_A$ receptors with drugs such as 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol (THIP), could improve specific types of memory such as spatial working memory that are regulated by the CA3 subfield of the hippocampus.

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S-153.

POSTOPERATIVE COGNITIVE DYSFUNCTION; EXECUTIVE FUNCTION VS. MEMORY AFTER GENERAL ANESTHESIA

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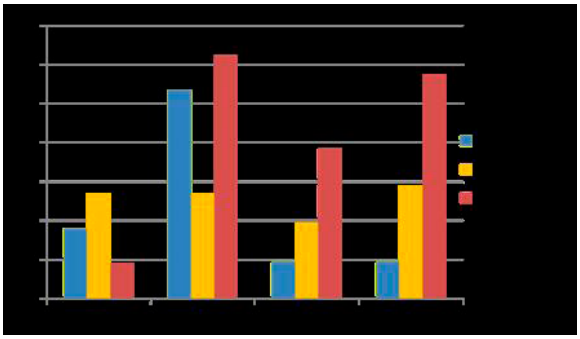
BACKGROUND: Postoperative cognitive dysfunction (POCD) is a common complication of the elderly, and can be diagnosed by performance on a battery of neuropsychological tests. More than 40% of surgical patients >60 years old had POCD at discharge, and12.7% at 3 months[1]. The 1995 POCD Consensus Conference suggested that research should include the domains of learning and memory, attention, executive functioning and language. However, most have focused on memory and only a very small percent included executive function[2]. While memory deficits predict incipient dementia[3,4] executive dysfunction is often predictive of loss of ADL and independent function[4]. Here we report the performance of a battery comparing the perioperative performance of memory vs. executive domains.

METHODS: After IRB approval we administered a full Uniform Dataset (UDS) battery to 76 elderly patients prior to major noncardiac surgery, and at 3 and 6 months after surgery. The UDS battery is the standard Alzheimer's Disease Research Center battery and includes 12 tests of 7 domains[5]. We performed a factor analysis on the baseline tests which identified 2 groups: executive function/attention/processing speed (Trails A/B, Digit Span Forwards/Backwards) and memory/language (Logical Memory Immediate/Delayed, Category Fluency). For each subject and test a raw and change score was calculated and normalized (raw score divided by standard deviation of the baseline score), then averaged to create the domain composite. Impairment was defined as: 0.5 SD (mild), .75 (moderate), or ≥ 1 SD (severe).

RESULTS: Overall 26.8% had impaired executive function, 8.9% had a decline in memory, and 1.8% had both. At 3 months 10% had decline in memory, most mild or moderate and 30% of patients had decline in executive function, most severe. At 6 months 13% declined in memory vs. 20% in executive function. Decline of both was rare at 3 and 6 months. (Fig1).



DISCUSSION: Our data demonstrates that POCD is characterized by impairment in both executive and memory functions. This suggests that the use of composite scores which combine multiple domains may obscure impairment, because not all are sensitive to the postoperative state. Studies of memory alone may miss a large proportion of patients who are suffering from POCD characterized by executive dysfunction.

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S-154.

THREE-HOUR EXPOSURE TO ISOFLURANE CAUSES SIGNIFICANT DEATH OF BRAIN CELLS IN NEONATAL MACAQUES

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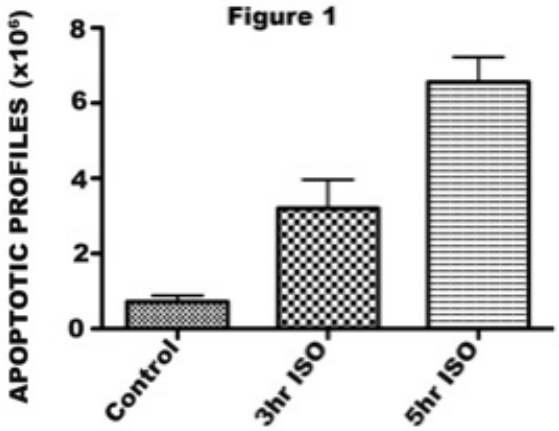
INTRODUCTION: We have shown previously that isoflurane anesthesia for 5 hrs triggers widespread apoptosis of neurons and oligodendrocytes (OLs) in the neonatal nonhuman primate (NHP) brain. Shorter durations of isoflurane have not been studied in this model, but others have reported that ketamine for 3 hrs in neonatal NHPs, did not cause neuroapoptosis in the frontal cortex. Recently, several retrospective cohort studies in humans have suggested that brief anesthesia at a young age increases the risk for long-term neurobehavioral disturbances, including attention deficit disorder and learning disability. However, in view of the negative findings with brief exposure to ketamine, it is unclear whether neuroapoptosis could be a plausible explanation for these deficits. We designed this study to determine whether a 3-hour exposure to isoflurane causes cellular injury in the developing NHP brain.

METHODS: With institutional approval (IACUC), rhesus macaques (Macaca mullata) on postnatal day 6 (P6) were exposed to isoflurane anesthesia for 3 hrs maintaining a moderate surgical plane (n=5), or no anesthesia (controls; n=5). At 6-8 hrs after time zero animals were re-anesthetized and perfusion-fixed to prepare the brain for histopathologic analysis. Serial sections through the entire brain were stained to determine cell death and identify affected cell types. For quantitative assessment, activated caspase 3 (AC3)-positive profiles in each section (at 2 mm intervals across the brain) were identified as either neurons or OLs and plotted and counted using a computer-assisted Microbrightfield Stereo Investigator system. The data was compared to that from a NHP cohort (n=5) that had been exposed to isoflurane for 5 hrs, using the same model.

RESULTS: Compared to the control group, the mean number of apoptotic profiles (neurons + OLs) per brain was 4.8-fold higher ($P < 0.001$) in the group exposed to isoflurane for 3 hrs (Figure 1). Isoflurane exposure for 5 hrs resulted in a 9-fold increase ($P<0.0001$). At both 3 and 5 hrs, the neuronal populations most severely affected were those in the parietal, temporal and occipital cortices, which are critical for somatosensory, auditory and visual information processing. Caspase-positive profiles identified as OLs were present across all white matter.

CONCLUSION: Exposure of neonatal NHPs to isofurane for 3 hrs at a moderate surgical plane induced significant apoptosis of both neurons and OLs, in brain regions critical for sensory information processing. Exposure to isoflurane for 5 hrs caused more cell death than exposure for 3 hrs, suggesting a dose-dependent effect. The results demonstrate the toxic effects of isoflurane in primates with shorter exposure times than previously thought, and are concerning as many operative or diagnostic procedures in pediatric medicine require effective anesthesia times in the range tested in this study.



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S-155.

NEUROENDOCRINE LONG-TERM DEVELOPMENTAL EFFECTS OF EXPOSURE OF NEONATAL RATS TO ANESTHESIA WITH PROPOFOL OR ETOMIDATE

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AFFILIATION: [1]Anesthesiology, University of Florida, Gainesville, FL, [2]Anesthesiology and the McKnight Brain Institute, University of Florida, Gainesville, FL

INTRODUCTION: Developmental consequences and mediating mechanisms of exposure to neonatal anesthetics were studied by investigating the effects of propofol and etomidate - anesthetics with similar gamma-aminobutyric acid type A receptor (GABAAR)-mediated mechanism of action. During the anesthesia, propofol causes a greater increase in corticoid levels.

METHODS: All experimental procedures were approved by the authors' IRB for animal research. Postnatal days 4, 5 or 6 (P4-6) Sprague Dawley rats were anesthetized for 5 hrs by administering intraperitoneally (IP) propofol or etomidate 40 or 8 mg/kg for induction and 20 or 4 mg/kg/60 min for maintenance, respectively. Control rats received equal numbers of saline injections. In order to study the roles of GABAAR-mediated excitation and systemic corticosterone, additional groups received either the Na+-K+-2Cl- co-transporter inhibitor bumetanide (1.82 mg/kg, IP) prior to propofol or a single injection of corticosterone (0.2 mg/kg, IP), respectively. All pups, except the negative control, were separated from the dams for 5 hrs. The elevated plus maze (EPM) test to assess anxiety-like behavior and prepulse inhibition (PPI) of the acoustic startle response measurements to evaluate sensorimotor gating function were performed at ~P70 and ~P80, respectively. Trunk blood samples to measure stress-related and baseline serum levels of corticoids were collected either 5 min or several days after completion of the PPI test, respectively. The synaptic activity in brain hippocampal slices was studied at >P80 in rats that underwent the PPI test.

RESULTS AND MAJOR FINDINGS: Maternally separated saline treated rats exhibited anxiety-like EPM behavior, but normal PPI responses. Only in male rats did both anesthetics exert anxiolytic effects, but impaired the PPI responses. Levels of corticosterone and aldosterone at baseline and after stress were increased in rats previously anesthetized with each anesthetic with greater effect of propofol over etomidate for post-PPI corticosterone and baseline aldosterone (Fig. 1). Only propofol increased the frequency of miniature inhibitory postsynaptic currents in the CA1 pyramidal neurons. Bumetanide did not alter endocrine and synaptic responses, moderately enhanced anxiolytic and reversed PPI effects of propofol. Corticosterone did not affect the PPI of the startle response, but caused anxiogenic, synaptic and endocrine effects similar to those of propofol.

CONCLUSIONS: Neonatal anesthesia results not only in behavioral but also long-term neuroendocrine abnormalities. The effects of bumetanide suggest mechanistic involvement of GABAAR-mediated excitatory signaling. The heightened baseline and stress-related levels of corticoids months after exposure to general anesthesia suggest that functional consequences of exposure to neonatal anesthetics may result, at least in part, from a combination of the acute effects of anesthetics at the time of anesthesia and continuous exacerbated endocrine responses to stress initiated by exposure of an immature CNS to these anesthetics.

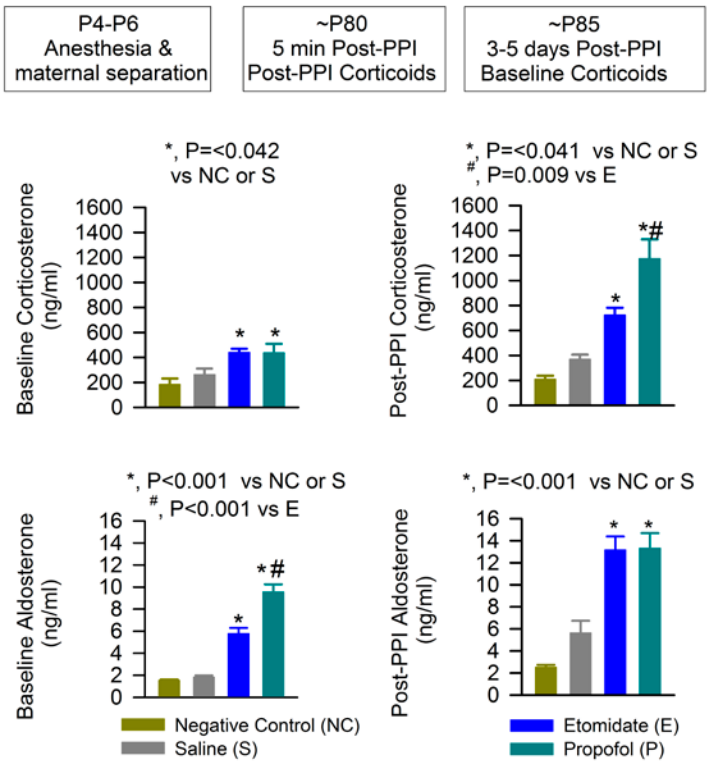

Figure 1.

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S-156.

THE EFFECT OF VENTILATION ON CEREBRAL OXYGENATION IN PATIENTS UNDERGOING SURGERY IN THE BEACH CHAIR POSITION: A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Surgery in the beach chair position (BCP) may reduce cerebral blood flow and oxygenation, resulting in neurologic injuries. Recent case reports have raised concerns that the BCP may be a risk factor for the development of cerebral and spinal cord ischemia and infarction[1,2]. Near-infrared spectroscopy is a non-invasive technology that allows real-time assessment of the adequacy of cerebral tissue oxygenation (and, indirectly, of cerebral blood flow). The authors tested the hypothesis that a ventilation strategy designed to achieve end-tidal carbon dioxide (EtCO2) values of 40 to 42 mmHg would increase cerebral oxygenation (SctO2) during BCP shoulder surgery compared to a ventilation strategy designed to achieve EtCO2 values of 30 to 32 mmHg.

METHODS: Seventy patients undergoing shoulder surgery in the BCP with general anesthesia were enrolled in this randomized controlled trial. All anesthetic management was standardized. Mechanical ventilation was adjusted to maintain an EtCO2 of 30 to 32 mmHg in the control group (control 30 to 32) and an EtCO2 of 40 to 42 mm Hg in the study group (study 40 to 42). Cerebral oxygenation was monitored continuously in the operating room using near-infrared spectroscopy. Baseline heart rate (HR), mean arterial blood pressure (MAP), peripheral oxygen saturation (SpO2), and SctO2 were obtained before induction of anesthesia, and these values were then measured continuously and recorded into a laptop computer from induction of anesthesia until tracheal extubation. The number of cerebral desaturation events (CDEs) (defined as a ≥ 20% reduction in SctO2 from baseline values) was recorded. Clinical recovery was assessed.

RESULTS: Baseline demographic characteristics did not differ between the two groups. No significant differences between groups were observed in hemodynamic variables or phenylephrine interventions during the surgical procedure. Sct02 values in the study 40-42 group did not decrease over time. In contrast, Sct02 measurements in the control 30-32 group were lower than baseline values from 10 minutes postinduction until 60 minutes ($P < 0.01$ across time). Furthermore, SctO2 was significantly lower in the control 30-32 group than the study 40-42 group from 16 minutes postinduction until 60 minutes ($P < 0.01$ across time). The incidence of CDEs was higher in the control 30-32 group (55.6%) than it was in the study 40-42 group (8.8%, $P < 0.0001$). The majority (67.7%) of CDEs occurred during episodes of hypotension (≥ 20% decrease in MAP). The incidence of nausea was 33.3% in the control 30-32 group and 8.8% the study 40-42 group ($P = 0.019$) during the PACU admission.

CONCLUSIONS: Cerebral oxygenation is significantly improved during BCP surgery when ventilation is adjusted to maintain EtCO2 at 40 to 42 mmHg compared to 30 to 32 mmHg. A lower incidence of nausea was also observed in the study 40 to 42 group.

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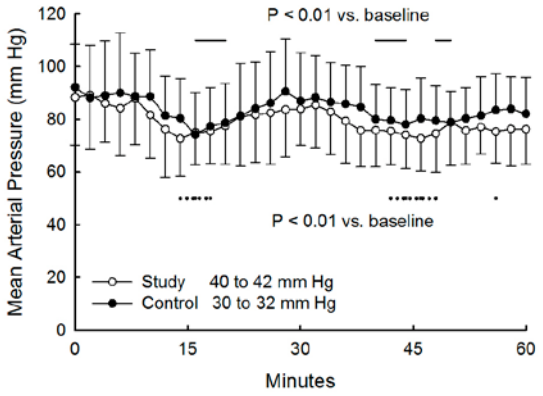

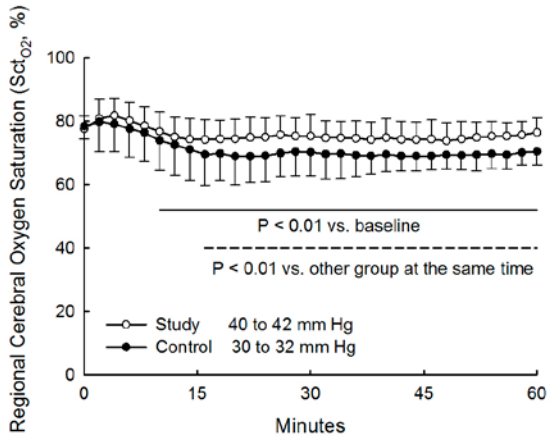

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S-157.

WITHDRAWN.

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S-158.

SEVOFLURANE AND PROPOFOL INDUCE DISTINCT EEG BURST-SUPPRESSION PATTERNS IN RATS

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AFFILIATION: [1]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, [2]Neurology, Massachusetts General Hospital, Boston, MA

INTRODUCTION: Burst-suppression is an EEG pattern seen during deep anesthesia that is characterized by alternating periods of high amplitude (bursts) and isoelectric periods (suppressions). The burst-suppression probability (BSP) algorithm[1] can be used to quantize the depth of anesthesia, with 0 indicating no EEG suppression and 1.0 indicating complete suppression. Burst-suppression is widely treated as a uniform process across different general anesthetics. In this study, we compared burst-suppression durations and energy in rats anesthetized with sevoflurane and propofol.

METHODS: After institutional approval, rats (n=4) with extradural EEG electrodes underwent general anesthesia with propofol and sevoflurane in separate experiments at least 3 days apart. Propofol was administered IV to maintain BSP levels of 0.4, 0.65, and 0.9 for at least 15 minutes each[2]. For sevoflurane experiments, rats were placed in an anesthetizing chamber and the inhaled sevoflurane concentration was increased from 3.6% to 4.2% by increments of 0.2% every 30 minutes. EEG recordings were manually threshold into a binary sequence of burst and suppressions. This series was used as an input in the BSP algorithm (Fig. 1). Burst-suppression time durations and energy were calculated and separated by BSP into their corresponding bin size. Median burst-suppression time duration and energy values were computed, and 95% confidence intervals were used for all BSP values to test for statistical significance.

RESULTS: Empirical cumulative distribution function plots (Fig. 2) for all BSP values and bin sizes reveal that sevoflurane induces longer burst-suppression durations than propofol ($p < 0.001$, KS Test). For propofol, the overall median burst duration was 0.28s and the median suppression duration was 0.22s. For sevoflurane, the overall median burst duration was 1.50s and the median suppression duration was 1.58s (Fig. 3A). The median difference between propofol and sevoflurane burst durations was 1.22s, and between suppression durations it was 1.36s. For propofol, the overall median burst energy was 130.15μV2 and the median suppression energy was 85.45μV2. For sevoflurane, the overall median burst energy was 204.05μV2 and the median suppression energy was 3437.5μV2 (Fig. 3B). The median difference between propofol and sevoflurane burst energy was 73.63μV2, and the median difference between suppression energy was 3351.4μV2. 95% confidence intervals for the differences between sevoflurane and propofol were greater than 0, indicating that burst-suppression energy and duration were significantly higher for sevoflurane than propofol.

CONCLUSIONS: Burst-suppression durations and energy were significantly different between sevoflurane and propofol, regardless of BSP. At all depths of general anesthesia, sevoflurane induced longer bursts and suppressions than propofol. Our results suggest that propofol and sevoflurane induce distinct brain states, with different physiological mechanisms underlying their burst-suppression patterns.

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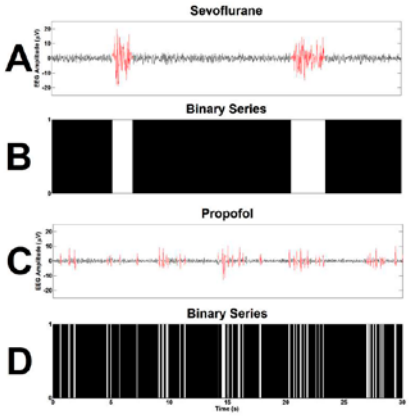

Figure 1: Raw EEG traces and binary series from the same rat at BSP of 0.8. (A) 30-second EEG recorded during sevoflurane general anesthesia, where black indicates suppression, and red indicates a burst. (B) Binary series of the EEG trace from (A), showing suppressions as black and bursts as white. (C) 30-second EEG recorded during propofol general anesthesia. (D) Binary series of the EEG trace from (C), showing suppressions as black and bursts as white. Although the BSP is equivalent at 0.8, propofol induced shorter bursts and suppressions than sevoflurane.

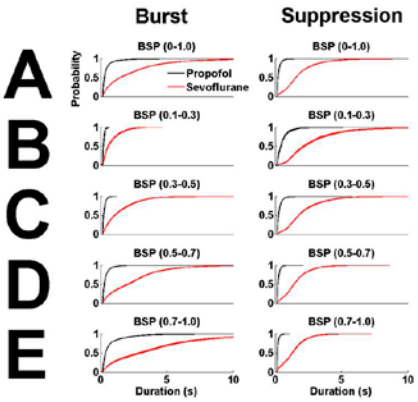

Figure 2: Empirical cumulative distribution function plots of burst and suppression durations for propofol (black trace) and sevoflurane (gray trace). (A) Distributions for all BSP levels show the majority of propofol bursts and suppressions are <1 second in duration. (B-E) Distributions sorted by BSP show sevoflurane having significantly longer durations than propofol ($p < 0.001$, Kolmogorov-Smirnoff test).

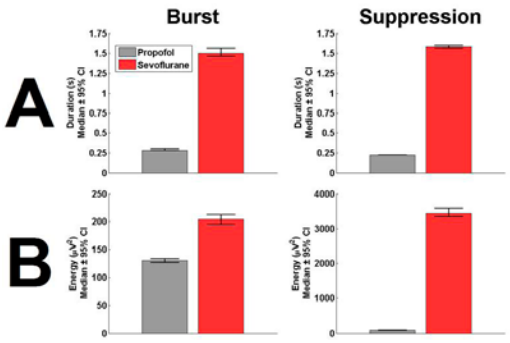

Figure 3: Bar graphs of median duration and energy for bursts and suppressions for propofol and sevoflurane. (A) Median burst and suppression durations are longer for sevoflurane than propofol. Median difference between bursts is 1.22s (95% CI 1.18-1.27) and suppressions is 1.36s (95% CI 1.34-1.38), with 95% CI greater than zero. (B) Median burst and suppression energy is larger for sevoflurane than propofol. Median difference between bursts is 73.63μV2 (95% CI 64.53-81.89) and suppressions is 3351.4μV2 (95% CI 3253.5-3496.7), with 95% CI greater than zero.

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S-159.

SELECTIVE INHIBITION OF PHOSPHOINOSITIDE 3-KINASE (PI3K)γ IS NEUROPROTECTIVE IN A RAT MODEL OF SURGICAL BRAIN INJURY

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INTRODUCTION: Surgical brain injury (SBI) attributable exclusively to the neurosurgical procedure itself could cause early postoperative complications, thus exacerbating neurological/behavioral outcomes[1]. To date, the issue of specific perioperative neuroprotection against SBI has not been well studied. Our group established a clinically relevant rodent model of SBI and demonstrated the important role of inflammation in SBI pathophysiology[2]. PI3Kγ is predominately expressed in immune cells, regulating inflammatory responses[3]. PI3Kγ deficiency was neuroprotective in acute experimental stroke[4]. In the present study, we investigated the treatment effect of AS252424, a selective PI3Kγ inhibitor in a rat model of SBI.

METHODS: All protocols were approved by the Animal Health and Safety Committees of Loma Linda University and were in compliance with Federal regulations. Sprague Dawley adult male rats were randomized into following 4 groups (n=6/group): Sham, SBI+Vehicle, SBI+AS252424 Low dose (3 mg/kg) and SBI+AS252424 High dose (10mg/kg). SBI was induced in anesthetized rats by partially resecting the right frontal lobe guided by stereotaxic coordinates. Shams underwent identical surgical procedure without brain resection. AS252424 or vehicle was administered intraperitoneally at both 1 hr prior to and 30 min after SBI. At 24 hrs and 72 hrs post-SBI, 1) neurobehavior were assessed by modified Garcia test; 2) brain water content within both sides of frontal lobes and parietal lobes, cerebellum and brain stem were measured, as an indicator of brain edema.

RESULTS: There were significantly higher brain water contents within right frontal lobe and worse neurobehavioral performance in SBI rats than shams. Compared to vehicle treated SBI, the high dose but not low dose AS252424 treatment significantly reduced brain edema (Fig. 1) and improved the scores of modified Garcia test (Fig. 2) at 24 hrs post-SBI. The neuroprotective effects persisted to 72 hrs post-SBI.

CONCLUSIONS: High dose of AS252424 attenuated brain edema after SBI and was associated with neurobehavioral benefit. Selective inhibition of PI3Kγ may provide a potential neuroprotective strategy that can be applied to neurosurgical patients.

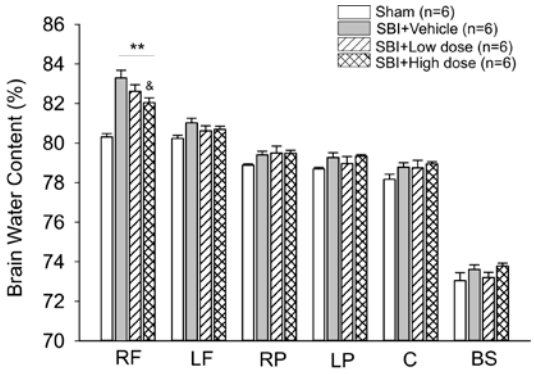

Fig. 1 Brain water content at 24 hours post-SBI. SBI was associated with significantly higher brain water content in right frontal lobe (RF) than Sham. High dose (10 mg/kg) AS252424 treatment significantly reduced brain edema compared to non-treated SBI rats. Data=Mean±SD, **p<0.01 vs Sham; &p<0.05 vs SBI+Vehicle. RF=Right frontal lobe, LF=Left frontal lobe, RP=Right parietal lobe, LP=Left parietal lobe, C=cerebellum, BS=Brain stem.

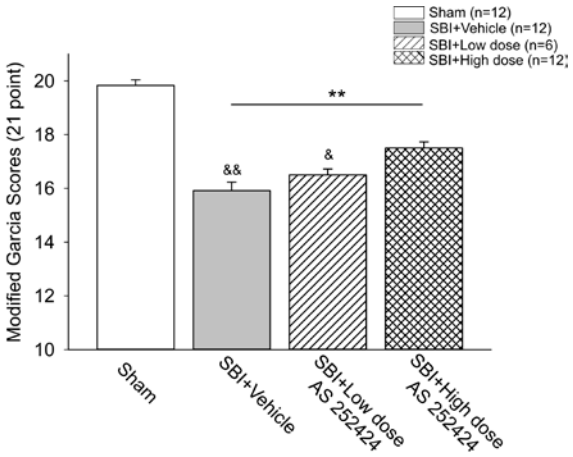

Fig. 2 Modified Garcia test at 24 hours post-SBI. SBI was associated with significantly lower modified Garcia scores than Sham. High dose (10 mg/kg) AS252424 treatment significantly improved the modified Garcia scores compared to non-treated and low dose (3 mg/kg) AS252424 treated SBI rats. Data=Mean±SD **p<0.01 vs Sham; &&p<0.01, &p<0.05 vs SBI+High dose AS252424.

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S-161.

THE EFFECT OF SEVOFLURANE ANESTHESIA ON INDIVIDUAL INTRAOPERATIVE CEREBRAL BLOOD FLOW AUTOREGULATION

AUTHORS: N. Goettel[1], M. Czosnyka[2], S. P. Strebel[1], L. A. Steiner[1]

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INTRODUCTION: Autoregulation of blood flow is a key feature of the human cerebral vasculature to assure adequate oxygenation and metabolism of the brain under changing physiologic conditions[1,2]. Impaired cerebral blood flow (CBF) autoregulation is associated with various pathological and pharmacological states, and may be at origin of poor neurological outcome such as silent ischemia[3] and/or postoperative cognitive decline[4], which is more common in elderly patients. Little is known about the effect of inhalational anesthetic agents and advanced age on CBF autoregulation.

METHODS: We conducted a prospective observational multicenter study to determine the effect of sevoflurane anesthesia on individual CBF autoregulation in two age groups. All patients underwent a standardized sevoflurane anesthesia for a major surgical intervention. Recorded by transcranial Doppler ultrasonography, cerebral hemodynamic data were computed to provide an individual CBF autoregulation curve for each patient. CBF autoregulation indices, thresholds and ranges were compared in young and elderly patient groups.

RESULTS: One-hundred and thirty-three patients were included in the study, 49 patients (37%) aged 18 to 40 years and 84 patients (63%) older than 65 years. Intraoperative minimum alveolar concentrations of sevoflurane were 0.94 ± 0.09 in young and 0.81 ± 0.12 in older subjects. Overall, the index of CBF autoregulation was significantly higher in older patients (0.5 vs. 0.41, $P = 0.011$), indicating a decreased autoregulatory capacity in the elderly. In both young and older patients, effective cerebral autoregulation was found only in a very narrow blood pressure range of 13.8 ± 9.8 mmHg and 10.2 ± 8.6 mmHg respectively. The lower threshold of autoregulation was 66 ± 12 mmHg in young and 73 ± 14 mmHg in older patients.

CONCLUSION: Our data shows that the autoregulatory plateau is significantly shortened in both young and elderly patients under sevoflurane anesthesia using approximately 1 MAC. Whether this reduction of the human brain's capacity to autoregulate CBF has an impact on the vulnerability for intraoperative cerebral ischemic events remains unclear.

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PROPOFOL AFFECTS DIFFERENT HUMAN BRAIN REGIONS DEPENDING ON DEPTH OF SEDATION

AUTHORS: X. Quan, J. Yi, T. H. Ye, S. F. Lin, L. Zou, S. Y. Tian, Y. G. Huang

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INTRODUCTION: Blood oxygen level-dependent functional magnetic resonance imaging (BOLD-fMRI) provides a novel method for non-invasive real-time exploration of the brain areas that are activated under sedation or anesthesia . The target areas in human brain underlying propofol-induced behavioral changes such as loss of consciousness and amnesia are particularly investigated[1,2]. Recent studies implied the inhibition of temporal lobe and thalamus could result in a reduction of the level of consciousness[1,3]. However, these studies did not use objective monitor, such as bispectral index (BIS), to measure the depth of sedation and to make a significant distinction between different levels of consciousness. In the present study, we used BIS and modified observer's assessment of alertness/ sedation (OAA/S) score to monitor depth of sedation and to make sure the loss of consciousness, and used BOLD-fMRI to explore the brain areas underlying the sedative effect of propofol and to delineate brain areas that are associated with loss of consciousness.

METHODS: Forty-eight volunteers were randomly divided into 2 groups based on BIS and Observer's Assessment of Alertness/ Sedation score (OAA/S): a mild sedation group (BIS 60 to 80, OAA/S 3) and deep sedation group (BIS 40 to 60, OAA/S 1). In tests preliminary to BOLD-fMRI scanning, propofol was administrated with a target-controlled infusion system to determine target effect-site concentrations of propofol to achieve the desired sedation level. Within one week of the preliminary tests, BOLD-fMRI was used to examine brain activation during wakeful baseline and desired sedation level with propofol infusion.

RESULTS: Mild propofol sedation inhibited left inferior parietal lobe activation (T value 7.22, voxel 22). Deep sedation inhibited left insula (T value 14.09, voxel 163), left superior temporal gyrus (T value 9.68, voxel 19), and right middle temporal gyrus (T value 31.65, voxel 46) activation. Compared with mild sedation, deep propofol sedation inhibited activation in left thalamus (T value 16.76, voxel 185), precentral gyrus (T value 10.99, voxel 26), anterior cingulate (T value 8.16, voxel 19), and right basal nuclei (T value 7.92, voxel 56).

CONCLUSIONS: The left inferior parietal lobe is associated with mild propofol sedation. The left insula, superior temporal gyrus, and right middle temporal gyrus are associated with deep propofol sedation. As deepening sedation induced loss of consciousness, concluded from decreasing BIS and OAA/S, the inhibition of activation in the left thalamus, precentral gyrus, anterior cingulate and right basal nuclei while increasing the depth of sedation suggest that these regions may be involved in loss of consciousness.

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Fig. 1. Brain areas activated in the wakeful baseline but inhibited during mild propofol sedation.

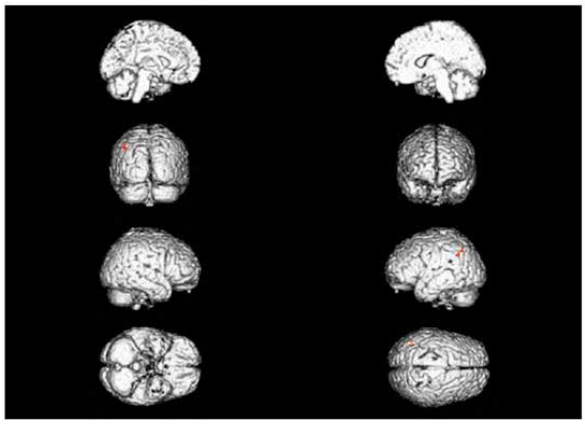


Fig. 2. Brain areas activated in the wakeful baseline but inhibited during deep propofol sedation.

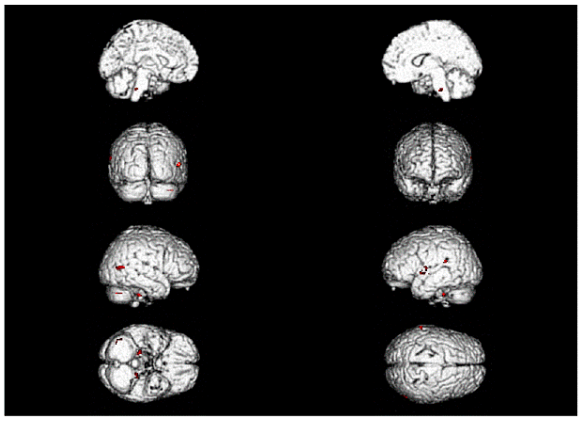
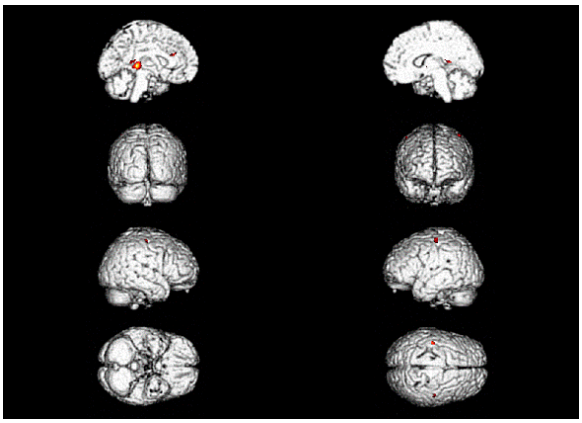


Fig. 3. Brain areas activated during mild sedation but inhibited during deep sedation.



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S-163.

EFFECT OF ANESTHESIA AND SURGERY ON TAU PATHOLOGY AND COGNITION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Alzheimer's disease (AD) is the leading form of dementia. The neuropathological hallmarks of AD include senile plaques of β-amyloid (Aβ) peptides and neurofibrillary tangles (NFT) resulting from hyperphosphorylated tau protein. Tau pathology is important because it is correlated to dementia in AD, and to memory loss in normal aging and mild cognitive impairment [1]. The large majority of cases (~99%) of AD is late onset and sporadic in origin. The causes of sporadic AD are considered multifactorial, with external factors interacting with biological or genetic susceptibilities to accelerate the manifestation of the disease. Anesthesia and/or surgery might be such factors, as several reports suggest increased incidence of AD after anesthesia/surgery[2].

We have previously demonstrated that different types of anesthetics result in tau hyperphosphorylation either directly or indirectly by inducing hypothermia[3]. In the present study, our goal was to investigate the effect of a minor abdominal surgery on tau pathology. Our hypothesis was that peripheral surgery but not brief anesthesia would induce tau hyperphosphorylation through the activation of inflammation pathways, resulting in memory impairment.

METHODS: We used young and old B6 mice as well as young and old hTau mice, a model of AD-like tau pathology overexpressing non-mutant human tau on a murine tau knock-out background. The two mice strains were separated in two groups, one control group undergoing brief isoflurane anesthesia and the other anesthesia and a minor abdominal surgery. Spatial memory was assessed with the Barnes maze. Tau pathology and inflammation markers were examined from hippocampal extracts by Western blot. This study was approved by the Comité de Protection des Animaux du CHUL.

RESULTS AND MAJOR FINDINGS: We did not find any difference in tau phosphorylation between control and surgery groups in B6 or hTau mice at either age. There was no effect of surgery on spatial memory and on central inflammation.

CONCLUSIONS: We conclude that in our experimental settings, a minor abdominal surgery has no effect on memory and AD-like tau pathology. While there has been clinical interest on the consequences of surgery and anesthesia on cognitive decline, their biochemical consequences on AD neuropathogenic pathways have only begun to be studied very recently. Overall, more studies are warranted to further understand the cognitive consequences of different types of surgery on the elderly.

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S-164.

POST-SEDATIVE TREATMENT WITH THE MGLUR5 ANTAGONIST MTEP BLOCKS KETAMINE-INDUCED NEURONAL APOPTOSIS IN POSTNATAL 7-DAY RATS

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INTRODUCTION: Inhaled or injected anesthetics cause altered brain development in neonatal rats and possibly in infants and young children[1]. In neonatal rats, ketamine (KET) sedation elicits neuronal apoptosis, possibly due to an increase in extra-synaptic glutamate. We hypothesized that the metabotropic glutamate receptor 5 (mGluR5), localized in astrocytes, mediates homeostatic rebalancing of excitatory drive after prolonged reduction in brain activity by KET. In postnatal 7-day (PND7) KET-sedated rats, we assessed the ability of post-sedation injection of the mGluR5 antagonist MTEP to: (1) reduce neuronal apotosis,(2) increase astrocyte-mediated transport of glutamate.

METHODS: After IACUC approval, PND7 rats received 6 s.c. injections at 2 hr intervals of: saline (Sal, n=3) or KET (20 mg/kg, n=6). 1 hour after the last injection, KET-injected rats received intraperitoneal injections of saline (KET-Sal, n=3), or MTEP, 3 mg/Kg (KET-M, n=3). 5 hours after the last Sal or KET injection, rats were sacrificed and brains were processed histochemically for caspase-3 (Casp-3), mGluR5, and the astrocyte glutamate transporter, EAAT2. Casp-3 labeled neurons were quantitated in: prefrontal ctx (Pfr), restrosplenial ctx (Rsp), hippocampus (Hipp) and lateral dorsal thalamus (LD). Internalization of EAAT2 was assessed by the presence of densely-stained intracellular EAAT2 label. Regional differences in Casp-3 cells over the different groups were compared using one-way ANOVA.

RESULTS: In the PND7 brain, KET induced a significant increase in Casp-3 cells, compared to saline, in Prf, RSp, Hipp and LD ($p < .05$). Post-sedation MTEP injection in KET-sedated animals significantly reduced the number of Casp-3 cells in all 4 regions, compared to post-sedation Sal treatment. Immuno-labeling for both mGluR5 and EAAT2 was predominantly localized to astrocytes. In Sal injected rats, EAAT2 label was localized primarily to the cell membrane, whereas in KET-SAL rats EAAT2 label was localized to densely-labeled cytoplasmic endosomes, indicating reduced glutamate transport resulting in increased extra-synaptic glutamate (2). In contrast, in KET-MTEP injected rats EAAT2 was localized to the cell membrane, similar to Sal injected rats, indicating that MTEP treatment restores glutamate transport and reduces extra-synaptic glutamate levels.

CONCLUSIONS: The brain engages a variety of strategies to maintain the dynamic range of global and synapse-specific activity. EAAT2 and mGluR5 have both been implicated in brain homeostasis [2], and in PND7 rats, both are expressed in astrocytes. The current results suggest that the mGluR5 antagonist MTEP blocks post-ketamine apoptosis by blocking mGluR5-induced cytoplasmic trafficking of the glutamate transporter EAAT2, leading to decreased excitotoxic extrasynaptic glutamate levels and reduced neuronal apoptosis. Pharmacological targeting of mGluR5 and EAAT2 may ameliorate the deleterious effects of ketamine in the neonatal brain, and should be further studied.

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S-165.

CRITICAL ROLE OF GLUTAMATE TRANSPORTER TYPE 3 IN DETERMINING ISOFLURANE EFFECTS ON HIPPOCAMPAL GLUR1 TRAFFICKING AND CONTEXT-RELATED LEARNING AND MEMORY IN MICE

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INTRODUCTION: Glutamate transporter type 3 (EAAT3), the major neuronal EAAT, may play a role in learning and memory. Isoflurane, a commonly used volatile anesthetic, enhances the trafficking of EAAT3 to the plasma membrane. We determined whether isoflurane affected biochemical processes for learning and memory via EAAT3.

METHODS: Hippocampus from wild-type or EAAT3 knockout mice was incubated with 2% isoflurane for 5 min. The trafficking of GluR1, an α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor subunit, to the plasma membrane, which is a fundamental process for learning and memory, was determined.

RESULTS: We showed that isoflurane increased EAAT3 but did not change the amount of GluR1 in the plasma membrane of wild-type mice. Isoflurane increased protein kinase A (PKA) in the immunoprecipitates prepared by an anti-EAAT3 antibody in the wild-type mouse hippocampus. Also, isoflurane increased protein phosphatase activity in the hippocampus of wild-type and EAAT3 knockout mice. The anesthetic reduced GluR1 in the plasma membrane of the EAAT3 knockout mouse hippocampus and decreased phosphorylated GluR1 at ser845 in these mouse hippocampi. Although the PKA inhibitor KT5720 did not affect the isoflurane effects on GluR1 trafficking and phosphorylation in the EAAT3 knockout mice, the phosphatase inhibitor okadaic acid attenuated these isoflurane effects. The PKA activator 6-BNZ-cAMP-AM increased GluR1 trafficking to the plasma membrane of EAAT3 knockout mouse hippocampus. Finally, isoflurane inhibited the context-related fear conditioning in the EAAT3 knockout mice.

CONCLUSION: These results suggest that isoflurane may increase GluR1 trafficking to the plasma membrane via EAAT3 and inhibit GluR1 trafficking via enhancing protein phosphatase activity. Lack of EAAT3 effects leads to the decreased GluR1 trafficking and impaired learning and memory after isoflurane exposure in the EAAT3 knockout mice.

ACKNOWLEDGEMENTS: This study was supported by grants (R01 GM065211 and R01 GM098308 to Z Zuo, 2007 Frontiers in Anesthesia Research Award to Z Zuo, 10GRNT3900019 to Z Zuo, Epstein Professorship endowment, University of Virginia).

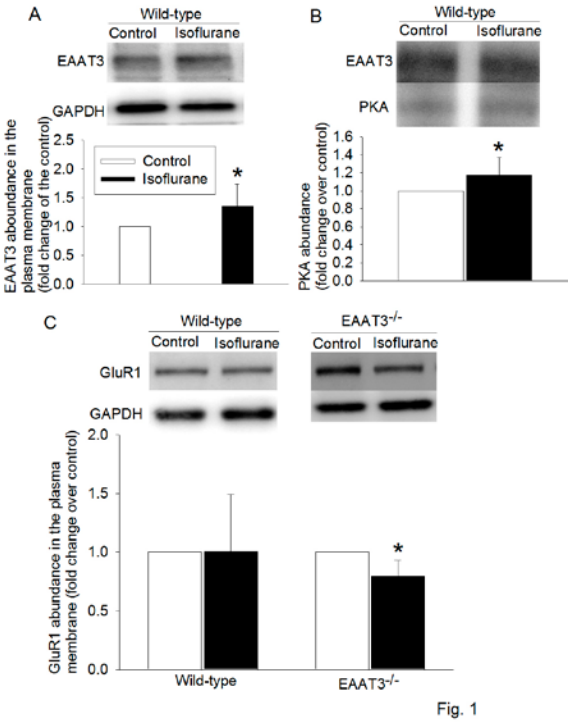

Fig. 1

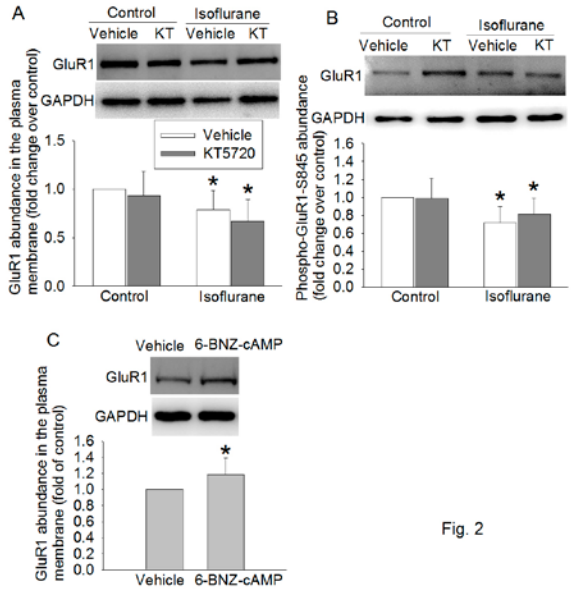

Fig. 2

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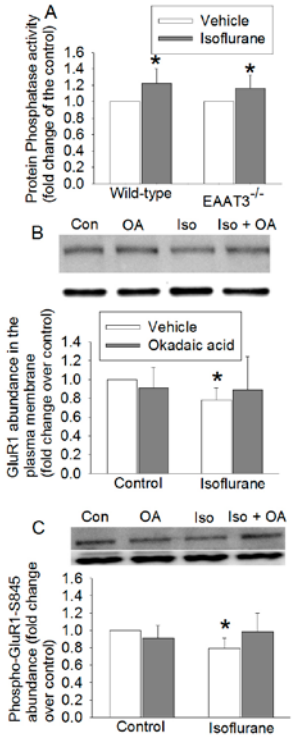

Fig. 3

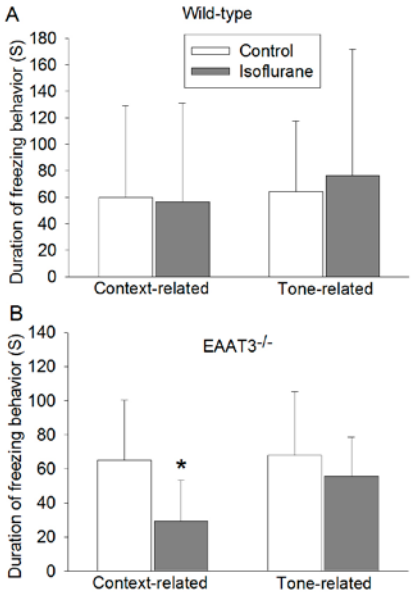

Fig. 4

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S-166.

BAX IS REQUIRED FOR ANESTHESIA INDUCED NEURONAL APOPTOSIS IN NEONATAL MICE

AUTHORS: D. Jardine

AFFILIATION: Anesthesiology and Pediatrics, University of Washington, Seattle, WA

INTRODUCTION: Exposure to anesthetics increases apoptosis during rapid brain growth in neonatal animals. Epidemiologic investigations of human infants exposed to anesthesia suggest that anesthetic exposure may be associated with subtle developmental deficits.

Anesthetic neurotoxicity may be induced via the intrinsic or extrinsic apoptotic pathways[1]. We hypothesized that BAX, a well-characterized proapoptotic protein, could have an important role in the induction of neuroapoptosis after exposure to isoflurane in infant mice. To test this hypothesis, we exposed a strain of BAX deficient mouse pups to isoflurane anesthesia and quantitated neuroapoptosis in BAX deficient mice and BAX wild type mice.

METHODS: IACUC approval was obtained for all procedures. BAX deficient transgenic mice were obtained from Jackson Labs (strain B6.129X1-Baxtm1Sjk/J). PCR genotyping was performed using primers specified by Jackson Labs. BAX wild type (WT) and homozygous BAX deficient (BAX KO) mice were used for these experiments. Mouse pups (P6) were exposed to either 0.75% isoflurane in room air or room air (no isoflurane) for 240 minutes in a temperature controlled chamber that was adjusted to maintain a rectal temperature of 37°C in the mouse pups. The mice were sacrificed by intraperitoneal pentobarbital injection and underwent trans-cardiac perfusion with PBS followed by 4% paraformaldehyde for 7 minutes each. After 48 hours of fixation in 4% paraformaldehyde, the right hemisphere of the brain was sectioned sagittally (50 µm slices). Every 5th slice was collected for histology. Staining was performed with an antibody to cleaved caspase-3 (Asp175). Secondary staining was accomplished with a fluorescent goat anti-rabbit IgG. Stereological counting procedures (optical fractionator) were used to count apoptotic cells in the cortex and caudate-putamen regions.

RESULTS: At baseline conditions, BAX KO mice had less apoptosis in the cortex and caudate-putamen than WT mice. BAX KO mice had no increase in neuroapoptosis after exposure to four hours of isoflurane anesthesia.

CONCLUSIONS: BAX KO infant mice are completely protected from neuroapoptosis induced by four house of isoflurane exposure. This suggests that transient disruption of the apoptotic cascade could be exploited as a therapy to reduce or eliminate anesthesia induced neurotoxicity during critical periods of development.

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Figure 1: Apoptotic cells in the cortex. BAX KO: homozygous BAX deficient mice; WT: wild type mice. Error bars: ± 1 SD.

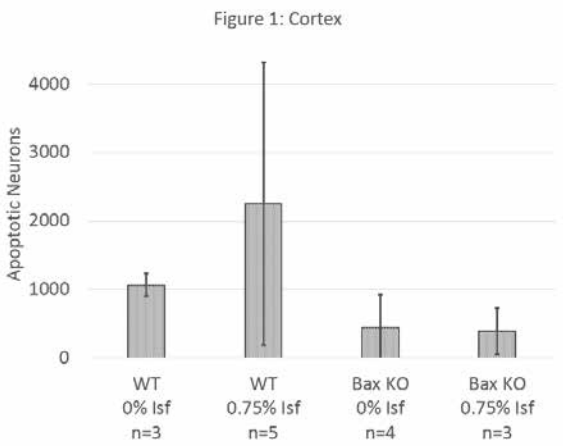
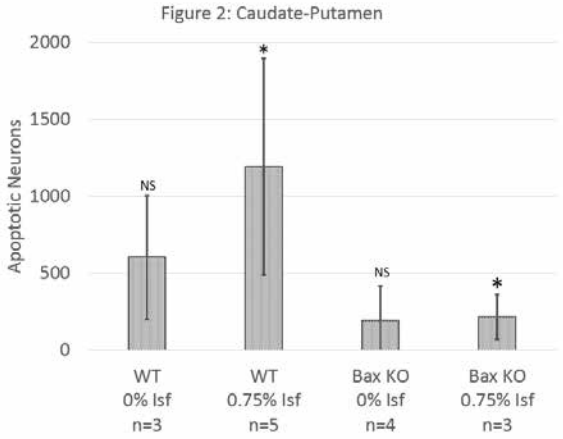


Figure 2: Apoptotic cells in the caudate-putamen. BAX KO: homozygous BAX deficient mice; WT: wild type mice. Error bars: ± 1 SD.



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S-167.

HYPOTHERMIA PROVIDES MODEST PROTECTION AGAINST ANESTHESIA INDUCED NEURONAL APOPTOSIS IN NEONATAL MICE

AUTHORS: D. Jardine

AFFILIATION: Anesthesiology and Pediatrics, University of Washington, Seattle, WA

INTRODUCTION: Exposure to anesthetics increases apoptosis during rapid brain growth in neonatal animals. Epidemiologic investigations of human infants exposed to anesthesia suggest that exposure may be associated with subtle developmental deficits.

A recent report indicated that maintaining brain temperature at 31.9°C may provide complete protection against anesthesia induced neuroapoptosis in mouse pups[1]. Because deep hypothermia is difficult to safely maintain in human patients, we elected to investigate whether cooling to 33°C could provide equivalent protection against neuroapoptosis.

METHODS: IACUC approval was obtained. Mouse pups (P6) were exposed to either 0.75% isoflurane in room air or room air (no isoflurane) for 240 minutes in a temperature controlled chamber. Rectal temperature was continuously monitored and the chamber was adjusted to achieve the target rectal temperature (30°C, 33°C, or 37°C). The mice were sacrificed by intraperitoneal pentobarbital injection and underwent trans-cardiac perfusion with PBS followed by 4% paraformaldehyde for 7 minutes each. After 48 hours of fixation in 4% paraformaldehyde, the right hemisphere of the brain was sectioned sagittally (50 µm slices). Every 5th slice was collected for histology. Staining was performed with an antibody to cleaved caspase-3 (Asp175). Secondary staining was accomplished with a fluorescent goat anti-rabbit IgG. Stereological counting procedures (optical fractionator) were used to count apoptotic cells in the cortex and caudate-putamen regions. One way ANOVA analysis was performed with the SPSS software.

RESULTS: During the experiment, mouse pups remained active; although the isoflurane exposed pups lost their righting reflex. Animals exposed to isoflurane exhibited a 10 fold (cortex) or 21 fold (caudate-putamen) increase in neuroapoptosis at 37°C compared to baseline conditions (no isoflurane exposure, temperature 37°C). Induction of hypothermia to 33°C reduced neuroapoptosis by approximately 30% (29% in cortex, 32% in caudate-putamen). Induction of hypothermia to 30°C further reduced apoptosis in cortical neurons (57% reduction compared to baseline); however, little additional benefit was observed in the caudate-putamen at 30°C.

CONCLUSIONS: We were unable to replicate an earlier study which showed complete neuroprotection provided by 31.9°C. Our data demonstrate a modest reduction in neuroapoptosis at 33°C with further reduction at 30°C in the cortex. Although these findings indicate that hypothermia provides modest protection against anesthesia induced neuroapoptosis, a safer, more effective and easier to implement intervention is desirable.

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Figure 1: Apoptotic cells in the cortex. All animals except controls were exposed to 0.75% isoflurane. Differences of $P<0.05$ (ANOVA, Tukey post hoc) are indicated by asterisks. Error bars: ± 1 SD.

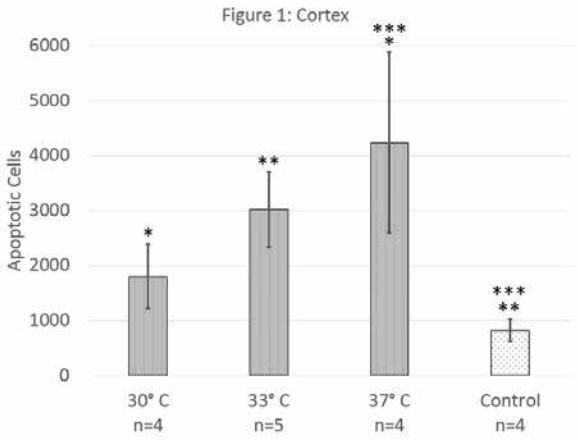
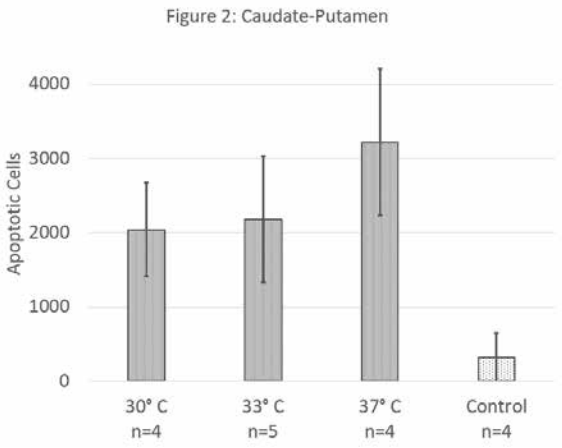


Figure 2: Apoptotic cells in the caudate-putamen. All animals except controls were exposed to 0.75% isoflurane. Differences between groups were not statistically significant. Error bars: ± 1 SD.



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S-168.

PRESYNAPTIC ROLE OF α2 ADRENERGIC RECEPTORS IN RAT HIPPOCAMPAL NEURONS

AUTHORS: M. Hara[1], J. P. Baumgart[1], Z. Zhou1, H. C. Hemmings[2]

AFFILIATION: [1]Anesthesiology, Weill Cornell Medical College, New York, NY, [2]Anesthesiology, Pharmacology, Weill Cornell Medical College, New York, NY

INTRODUCTION: α2 adrenergic agonists have sedative and analgesic effects through modulation of the release of norepinephrine in noradrenergic neurons of the pons and medulla oblongata. Although α2 adrenergic receptors are distributed widely throughout the central nervous system, their functions within non-noradrenergic neurons is poorly understood. Conventional electrophysiologic recordings in brain slices cannot remove the influence of noradrenergic nerve terminals. Therefore we studied individual nerve terminals in isolated hippocampal neurons to determine the presynaptic effects of α2 receptors independent of their effects on noradrenergic afferents.

METHODS: Hippocampal CA3-CA1 regions were dissected from 1-2 day old Sprague Dawley rats, dissociated, and plated onto poly-ornithine coated glass. 7-8 days after plating, neurons were transfected with cDNA to express two genetically encoded optical probes in presynaptic boutons. Laser-scanning fluorescence image measurements of action potential-evoked neurotransmitter release were made using synaptophysin-pHluorin, a reporter of synaptic vesicle exocytosis, and intracellular $[Ca^{2+}]$ ($[Ca^{2+}]i$) was measured using the Ca^{2+}-indicator GCaMP6. Exocytosis and $[Ca^{2+}]i$ were quantified as a function of number of action potentials.

RESULTS: Treatment of cultured hippocampal neurons with the α2 adrenergic agonist clonidine (0.5 μM) decreased neurotransmitter release to ~70% of control; this inhibitory effect was abolished by the selective $\alpha2_A$ antagonist BRL 44408 (3 μM), but not by the selective $\alpha2_C$ antagonist JP 1302 (3 μM). Clonidine also inhibited action potential evoked increases in $[Ca^{2+}]i$; the effect of clonidine on $[Ca^{2+}]i$ correlated with its effect on exocytosis across a varying number of action potentials.

CONCLUSION: In addition to their well known effects in modulating norepinephrine release from noradrenergic neurons, α2 adrenergic agonists also suppress neurotransmitter release by inhibiting presynaptic Ca^{2+} influx upstream of the exocytotic release machinery in hippocampal neurons. This provides another mechanism of action for their sedative and amnestic effects.

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S-169.

THE BENZODIAZEPINE ANTAGONIST, FLUMAZENIL, MITIGATES POST-ANESTHESIA EFFECTS OF ISOFLURANE BY IMPROVING VIGILANCE IN A RAT MODEL

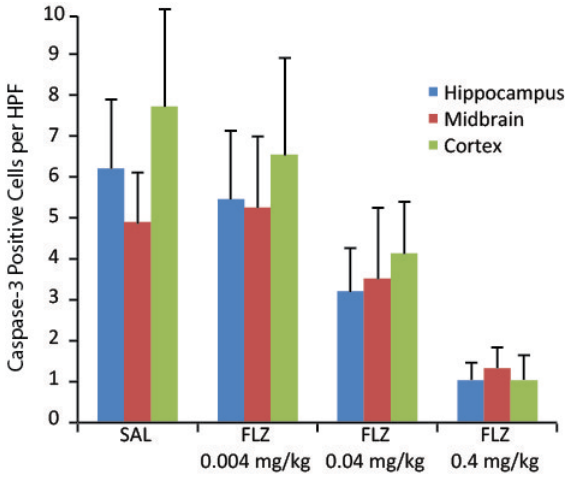
AUTHORS: P. S. Garcia[1], S. C. Burke[1], B. L. Raymond[1], G. L. Keating[2], S. R. Baber[1], C. Karlapalem[1], J. A. Fidler[1]

AFFILIATION: [1]Anesthesiology, Emory University / Atlanta VA Medical Center, Atlanta, GA, [2]Neurology, Emory University, Atlanta, GA

INTRODUCTION: Recently, pharmacologic inhibition of GABA activity using flumazenil has been shown to improve vigilance in hypersomnic patients[1]. In this study, the authors further explored the overlap between sleep and anesthesia by testing the hypothesis that flumazenil - widely considered a rescue drug for benzodiazepine toxicity - improves recovery following isoflurane anesthesia.

METHODS: Using adult rats anesthetized for 30 minutes with isoflurane, a GABA-enhancing inhaled anesthetic, the authors tested the effect of pre-emergence administration of flumazenil on time to recover the righting reflex (RR), as well as its effect on physiologic parameters, general activity, and memory in the post-anesthesia state. A histological examination of anesthetic-induced neuro-apoptosis was also performed. Similar experiments were performed in animals instrumented with EEG/EMG electrodes for assessing sleep during recovery from general anesthesia. Sleep-wake data was scored automatically using Somnologica Science software and then reviewed and edited for artifact removal (if necessary) on an epoch-by-epoch basis. All animals were housed in a 12:12 h light-dark cycle lights off at 7 p.m. Memory testing was performed during the active period.

RESULTS: Flumazenil (0.4 mg/kg) decreased mean time to RR by a modest amount, and improved performance on a novel object recognition memory task performed 5 hours after anesthetic recovery. Flumazenil had little effect on general activity or physiologic and respiratory factors under general anesthesia. But, flumazenil-treated animals spent more time awake in the first active period following their anesthetic than the saline-treated animals. Histologic examination revealed a dose-dependent decrease in caspase-3 positive cells in the hippocampus, midbrain, and cortex in animals administered flumazenil upon cessation of isoflurane anesthesia (Figure).



DISCUSSION: The authors conclude that flumazenil actively promotes emergence from isoflurane anesthesia while mitigating some of the deleterious effects of this anesthetic on memory and neuronal viability. These findings suggest that flumazenil may be a useful clinical adjunct to anesthetic practice to rapidly reverse general anesthesia and to possibly prevent cognitive problems after anesthesia. The authors also conclude that different post-anesthesia emergence trajectories can influence cognition beyond the immediate recovery period and emergence could be a critical time to pharmacologically intervene for improved post-anesthesia cognitive recovery.

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S-170.

PATHOPHYSIOLOGIC DEFICITS IN THE HIPPOCAMPUS OF THE SPRAGUE DAWLEY RAT AFTER REPEATED ISOFLURANE EXPOSURE

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INTRODUCTION: General anesthesia is delivered to nearly 21 million patients [1] annually; approximately 31-40% of patients experience postoperative cognitive dysfunction (POCD) - a transient deterioration in cognitive performance following surgery under anesthesia[3,4] - at time of discharge and a significant number continue to experience POCD three months after surgical intervention[2]. Transient impairments in cognitive and behavioral function have been characterized in patients following a single exposure to volatile anesthesia [5,6]. Similarly, learning and memory deficits have been observed in young and aged animals after exposure to a single volatile anesthesia [7,8]. However, the cumulative effects of repeated exposure to a volatile general anesthetic remain unknown, as this is often employed in individuals requiring multiple surgical interventions.

METHODS: We investigated the effects of repeated isoflurane exposure on learning and memory in spontaneous ventilating 10-week-old Sprague Dawley rats. Animals were exposed to an induction dose of isoflurane of 3-5% in 100% oxygen. Once animals lost their ability to maintain righting-reflex isoflurane concentration was lowered to 1.5% in 100% oxygen. Animals remained under general anesthesia for one-hour every other day, for a total of three exposures in one week. Using electrophysiological techniques we examined the effects of repeated exposures to isoflurane on the induction and maintenance of long-term potentiation (LTP), a cellular model of learning and memory, in the rat hippocampal CA1 region. In addition, we investigated whether repeated isoflurane affected spatial learning and memory using the Morris water maze.

RESULTS: One-day following repeated isoflurane exposure, LTP was significantly increased compared with naïve controls ($p = 0.023$) in the CA1 hippocampal region, while at one-week after the final session, LTP was inhibited compared to baseline recordings ($p = 0.038$). LTP recovered to baseline levels one-month after the final isoflurane exposure ($p = 0.079$). One week after exposure, animals spent less time in the hidden platform quadrant ($p = 0.007$), did not travel as far in total distance ($p = 0.021$), and took longer to reach the quadrant ($p = 0.015$). 30 days after exposure, however, a complete recovery in spatial learning and memory were observed as exposed animals did not differ from controls.

CONCLUSIONS: These data suggest that repeated exposure to volatile agent general anesthesia may produce adverse effects on hippocampal-dependent memory and learning, but over time animals will recover.

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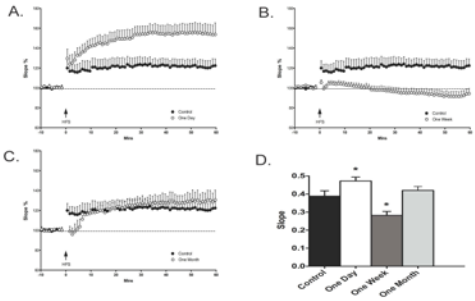

Figure One. Long term Potentiation, cellular memory and learning, is altered one-day and one-week following repeated isoflurane exposure and returns to control levels in 30 days. Using electrophysiological techniques, we examined the effects of repeated exposures to isoflurane on the induction and maintenance of long-term potentiation (LTP) in the rat hippocampus. Male Sprague-Dawley rats, ages 7-14 weeks (n = 21), were anesthetized with 1.5% isoflurane and 100% oxygen for one hour every other day, for a total of three exposures in one week. Recordings of the CA1 region at one day, one week and one month following repeated exposure to isoflurane. Repeated-measures ANOVA overall statistical significance was achieved ($p < 0.05$). Post hoc comparisons revealed at one-day following the repeated isoflurane exposure,(A.) LTP was significantly increased compared with naïve controls ($p=0.023$), (B.) one-week after the final session; LTP was inhibited compared to baseline recordings ($p=0.038$). (C.) one-month LTP was not significantly different from control ($p=0.794$).

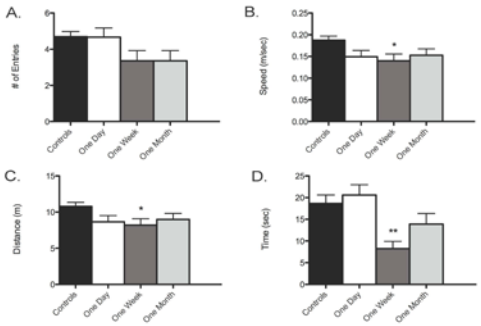

Figure Two. Spatial memory and learning is impaired one week following repeated isoflurane exposure and returns to control levels in 30 days. To investigate whether repeated isoflurane affected spatial learning the Morris water maze was used. One-way repeated-measures ANOVA, of probe trial data, revealed a significance in total distance traveled, speed and time spent in the hidden platform quadrant (all $p < 0.05$) and (A.) no significant difference in number of entries into the NW quadrant. Post hoc analysis further demonstrated a significant difference after one week in animals that received repeated isoflurane exposures in (B.) distance traveled ($p = 0.021$), (C.) speed through the maze ($p = 0.015$), and (D.) total time spent in the NW quadrant ($p = 0.007$). All values returned to not significant levels at the one-month time point.

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S-171.

WITHDRAWN.

S-172.

MOPPS: MEMORIES OF THE PERIOPERATIVE PERIOD STUDY

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INTRODUCTION: The extent to which patients remember the perioperative period has implications for assessing patient satisfaction with individual anesthesiologists, for timing of informed consent, and for provision of medical information. The primary hypothesis was that the majority of surgical patients do not remember the operating room (OR). Secondary hypotheses were that many patients only remember events prior to the preoperative holding area, and that amnesic medication doses as well as patient factors impact memories of perioperative locations.

METHODS: This was a retrospective study of patients from two clinical trials (n=8100) that focused on prevention of awareness during intended general anesthesia. A modified Brice questionnaire was administered at 1-3 and 30 days postoperatively. Patient responses to the questions "What was the last thing you remembered before going to sleep?" and "What was the first thing you remembered after waking up?" were analyzed, and locations were coded (e.g. holding area, OR, recovery area) based on patient descriptions. The proportions of patients who, at 30 days after their surgery, did not remember perioperative locations of interest were ascertained. Logistic regression analyses were performed for patients not remembering the OR before surgery and for patients remembering the OR after surgery, both at 30 days postoperatively. To assess the stability of memories, reports on locations recalled between 1-3 days were compared with those recalled at 30 days postoperatively.

RESULTS: More than half the patients did not remember the OR both before and after surgery ($P < 0.0001$; 2187/4067; 95% CI, 52.2% to 55.3%). Fifty-six percent of patients did not remember the OR before surgery (3353/5990; 95% CI, 54.7% to 57.2%), and 95% did not remember the OR after surgery (4327/4564; 95% CI, 94.1% to 95.4%). Fifteen percent of patients (892/5990; 95% CI, 14.0% to 15.8%) not only did not remember the OR, they did not even remember being in the preoperative holding area.

Midazolam dose, administered in the preoperative holding area or in the OR before induction, and increased age were independent predictors of not remembering the OR before surgery (both $P<0.002$). No variable significantly predicted remembering the OR after surgery (all $P>0.11$).

Forty-one percent of patients (2077/5122; 95% CI, 39.2% to 41.9%) changed their answer regarding memory of last location before surgery between 1-3 and 30 days postoperatively, and 40% of patients (1388/3517; 95% CI, 37.9% to 41.1%) changed their answer regarding memory of first location after surgery.

CONCLUSIONS: There is likely to be absence of content validity for postoperative assessment of satisfaction with individual anesthesiologists' care among patients undergoing general anesthesia. Preventing many patients from experiencing perioperative amnesia (e.g., to facilitate assessment of anesthesiologists) might not be achievable or indeed desirable. The extent of perioperative amnesia may argue against obtaining consent and providing information just before surgery among sicker patients.

REFERENCES: N/A

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S-173.

POSTANESTHETIC MEMORY DEFICITS IN MICE ARE CAUSED BY INCREASED ACTIVITY OF EXTRASYNAPTIC GABA(A) RECEPTORS

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BACKGROUND: General anesthetics cause memory deficits that persist long after the anesthetic has been eliminated. The cellular mechanisms underlying these deficits are unknown and to date, no specific treatments have been developed. It is assumed that anesthetics do not affect the function of their target receptors once they are eliminated. However, we previously showed that pharmacologically inhibiting γ-aminobutyric acid type A receptors that contain the α5 subunit (α5GABA-A receptor) both prevents and reverses memory deficits after anesthesia in mice (Anesthesiology 2010: 113 (5): 1061-71, Anesth Analg 2012: 114 (4): 843-55). Here, we tested the hypothesis that α5GABA-A receptors are necessary for the development of anesthetic-induced memory deficits and that the expression and activity of these receptors is enhanced after anesthesia.

METHODS: Wild-type (WT) and α5GABA-A receptor null-mutant (Gabra5-/-) mice were treated with the intravenous anesthetic etomidate (8 mg/kg i.p.). Memory was assessed 24 h, 72 h and 1 week later with the object recognition task. In other studies, mice were treated with etomidate and hippocampal slices were prepared 24 h later. Activity of α5GABA-A receptors in these slices was studied by measuring the amplitude of a tonic inhibitory conductance in CA1 pyramidal neurons using whole cell recording methods. Additionally, surface biotinylation and Western blotting were used detect potential changes in surface expression of the α5 subunit in hippocampal slices.

RESULTS: WT but not Gabra5–/– mice exhibit impaired recognition memory for at least 72 h after etomidate. The amplitude of the tonic conductance is increased after etomidate in WT slices but not Gabra5–/– slices. Similarly, the surface expression of α5GABA-A receptors was increased 24 h after etomidate treatment.

DISCUSSION: These results show that α5GABA-A receptors are necessary for post-anesthetic memory deficits. Further, the memory deficits are associated with a long-term increase in the expression and function of α5GABA-A receptors. Here, we provide the first evidence that a commonly used general anesthetic increases the cell-surface expression of a target receptors and this increase persists long after the anesthetic has been eliminated.

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S-174.

NEONATAL EXPOSURE TO NITROUS OXIDE DISTURBS GRANULE CELL MIGRATION IN THE RAT DENTATE GYRUS

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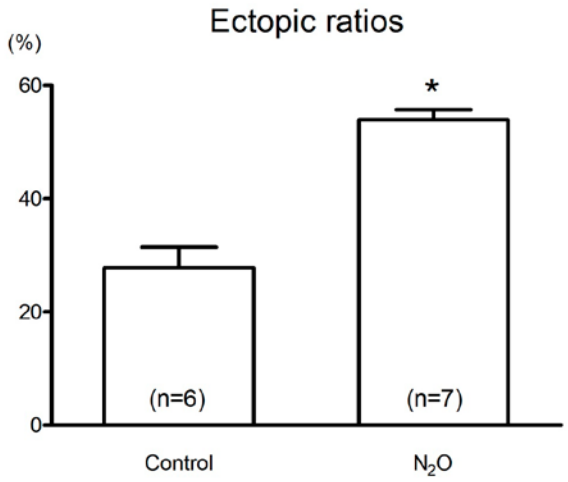
INTRODUCTION: In the early postnatal period, granule cell (GC) progenitors of the hippocampal dentate gyrus (DG) are generated in the dentate hilus area, and then GCs migrate to the granule cell layer (GCL). On the other hand, it has been reported that the signal via N-methyl-D-aspartate (NMDA) receptor regulates neural cell migration in synaptogenesis period. Since nitrous oxide (N_2O), which is one of the commonly used anesthetics, has anti-NMDA property; neonatal N_2O exposure has the potential to influence the migration of GCs.

METHODS: To evaluate the influence of neonatal N_2O exposure on the migration of neonatally generated GCs, we examined the localization of GCs by histological method. This experiment was approved by the Committee for Animal Research of the Hokkaido University Graduate School of Medicine. At postnatal day 6 (P6), Wistar strain male rat pups were subcutaneously administered 5-bromo-2'-deoxyuridine (BrdU) as the neurogenesis marker. At P7, rats were exposed to 50% nitrous oxide with 50% oxygen (N group) or to air (Control group) for 2 h. At P21, under deep anesthesia, rats were transcardially perfused with phosphate buffered saline followed by 4% paraformaldehyde. After the perfusion, the brains were removed and postfixed, then cryosectioned. In the double immunofluorescent staining, antibodies against BrdU and the GC marker prospero-related homeobox 1 (Prox1) were used. The localization of BrdU/Prox1 co-labeled cells was assessed by confocal microscopy. All the co-labeled cells were counted for the hilus and the GCL in 6-10 sections from each rat, and then the ratio of hilar/total GCs (ectopic ratio) was calculated in each rat, and the data were analyzed using unpaired t test.

RESULTS: The ectopic ratio of the N group (N=7, 53.9±4.7%) was significantly higher than the control group (N=6, 27.8±8.1%) ($P<0.0001$, figure 1).



CONCLUSIONS: This result suggests that neonatal N2O exposure causes the derangement of the GC migration in the neonatal rat DG. As described above, it has been indicated that the appropriate NMDA signal during synaptogenesis period is necessary to regulate the neural cell migration normally. Excessive anti-NMDA signaling evoked by neonatal N2O exposure may disturb the GC cell migration in the rat DG.

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S-175.

GESTATIONAL PROPOFOL EXPOSURE INDUCES NEUROAPOPTOSIS AND LONG-TERM BEHAVIORAL DEFICITS IN OFFSPRING RATS

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INTRODUCTION: Drugs that inhibit γ-aminobutyric acid type A (GABAA) and N-methyld-aspartate (NMDA) receptors have been shown to cause neurotoxicity in animal models. A recent study on rhesus macaques demonstrates that prenatal propofol exposure may cause apoptosis in the fetal brain[1]. The long-term consequences of prenatal propofol exposure, however, are unknown. The present study explored the effect of maternal propofol exposure on the fetal brain, in addition to learning and memory in offspring rats.

METHODS: With IACUC approval, we conducted experiments on 30 pregnant Sprague-Dawley rats, which were randomly divided into three groups which received propofol, intralipid emulsion (the vehicle of propofol) and saline (control). Propofol, intralipid or saline was administered to pregnant rats (gestational day 18) by continuous infusion via tail vein (IV) catheters. In order to avoid hypoxia and hypercapnia, the dams undergoing propofol treatment were intubated and supported with controlled mechanical ventilation at 60-70% FiO2. Vital signs such as heart rate, arterial oxygen saturation, and pulse distention were continuously monitored using a Pulse Oximeter. The temperature was maintained at 37± 0.5°C with a heating lamp and temperature controller. Arterial blood gases were analyzed at 15 minute intervals. Dams treated with intralipid or saline were allowed to move freely in the home cage during infusion. C-sections were performed 6 hours post infusion and fetal brain tissue was harvested. The tissue samples were subjected to the Western blot and immunohistochemistry to assess for interleukin-6 (IL-6) and caspase-3 levels. Learning and memory function in a different cohort of offspring rats was assessed in a radial 8-arm maze.

RESULTS: The maternal vital signs and blood gas analysis indicated that the dams undergoing general anesthesia were stable. (Fig. 1 and Table 1) This suggests that the methods used to support the pregnant rats during propofol general anesthesia effectively eliminate hypoxia and hyper- or hypo-glycemia as confounding variables. Propofol anesthesia, but not intralipid emulsion increased cleaved caspase-3 levels (propofol 404 ± 42.23% [mean ± S.M.E.] VS. control 100% ± 21.58%) and IL-6 levels (propofol 139 ± 8.10% [mean ± S.M.E.] VS. control 100% ± 5.82%) in the fetal rats. (Fig. 2) Caspase-3 activation occurred primarily in the cerebral cortex and thalamic regions of the exposed rodent brains. Double staining with antibodies to cleaved caspase-3 and antibodies to NeuN demonstrated that most of the cleaved caspase-3 positive cells were neurons. (Fig. 3). Moreover, the offspring from propofol treated dams made more errors and took longer to complete the maze task across five days of testing and made less correct choices prior to the first error compared to age matched controls on postnatal day 28 in the radial 8-arm maze. (Fig. 4)

CONCLUSION: These results indicate that prenatal propofol exposure may induce neuroapoptosis in the fetal brain, and lead to learning and memory deficits in offspring rats.

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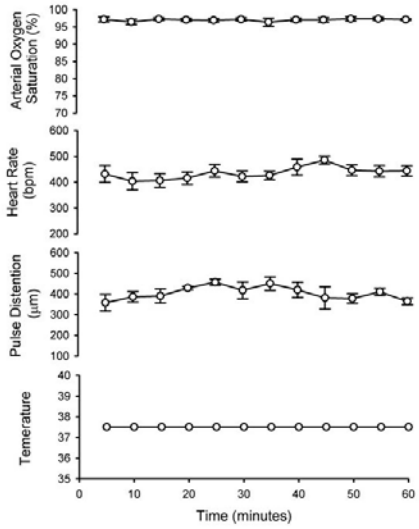

Figure 1 Vital signs of rats during general anesthesia induced by propofol. Arterial oxygen saturation, heart rate and pulse distention were monitored by pulse oximeter. The data were averaged every 5 minutes during propofol infusion. Temperature was maintained in the range of 37.5 °C using temperature controller. These data indicated that vital signs can be keep stable during general anesthesia induced by propofol (n = 10).

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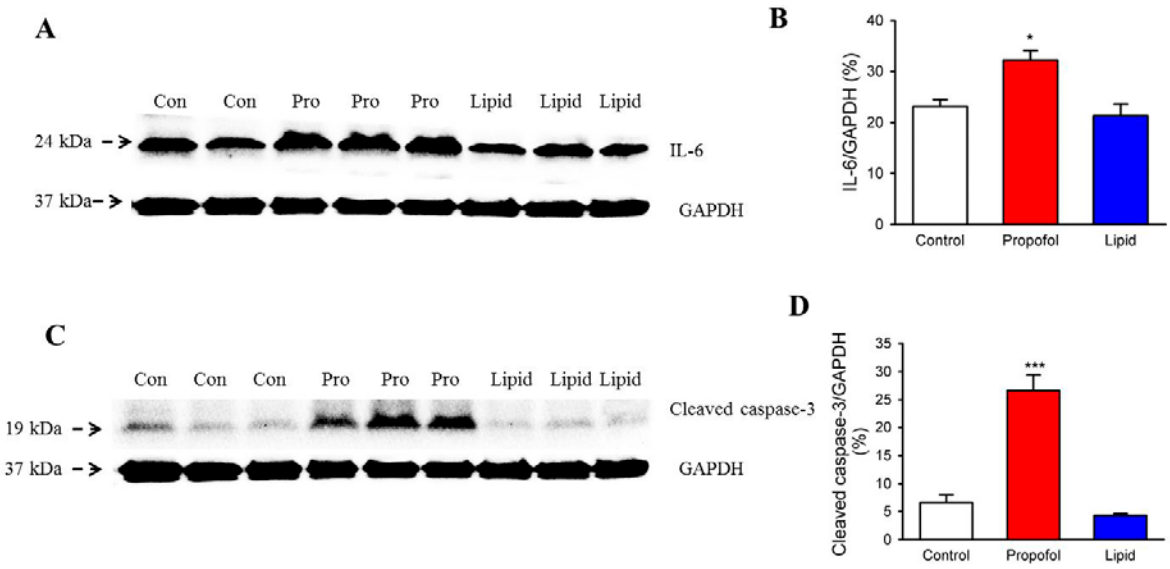

Figure 2. Propofol anesthesia for 1 h in pregnant rats at E18 increase IL-6 levels induces caspase-3 activation in the brain tissues of fetal rats. Propofol general anesthesia (IV, 1h), intralipid (IV infusion, 1 h) was administered to pregnant rats on gestational day 18. Control pregnant rats were only set up IV in the tail, but do not infusion. Fetus was taken out six hours after stopping infusion. The brain tissues of fetal rats were harvested for Western blot. (*A*) Propofol anesthesia, but not intralipid, increases IL-6 levels in the brain tissues of fetal rats as compared with the control condition on Western blot analysis. There is no statistically significant difference in the amounts of GAPDH in the rat brain tissues following the propofol anesthesia, intralipid treatment or control condition. (*B*) Quantification of the Western blot shows that propofol anesthesia increases IL-6 levels in the rat brain tissues as compared with the control condition (**P*<0.05). Furthermore, Intralipid infusion does not affect the IL-6 levels in brain tissues of fatal rats. (*C*) Propofol anesthesia, but not intralipid, induces caspase-3 activation in the brain tissues of fetal rats as compared with the control condition on Western blot analysis. There is no statistically significant difference in the amounts of GAPDH in the rat brain tissues following the propofol anesthesia, intralipid treatment or control condition. (*B*) Quantification of the Western blot shows that propofol anesthesia increases cleaved caspase-3 levels in the rat brain tissues as compared with the control condition (****P*<0.001). However, intralipid infusion does not affect the IL-6 levels in brain tissues of fatal rats.

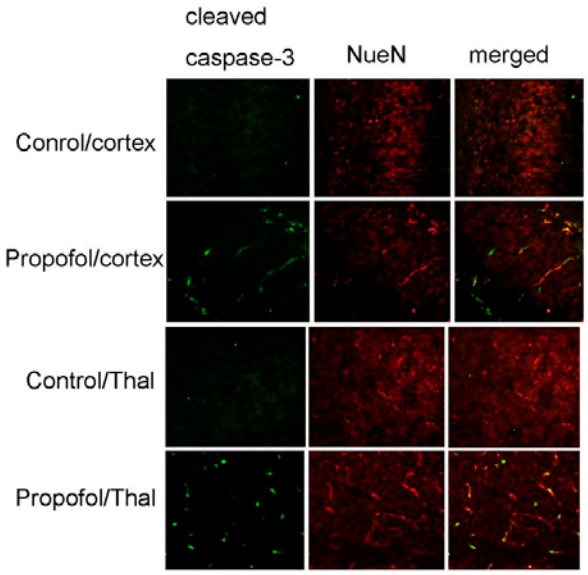

Figure 3. Caspase-3 activation occurred primarily in neurons in the cerebral cortex and thalamus regions. Double staining with antibodies to cleaved caspase-3 (*green) and* antibodies to NeuN, a neuron-specific nuclear protein (*red), demonstrated that most of the cleaved caspase-3 positive cells* were neurons. Thal: Thalumus

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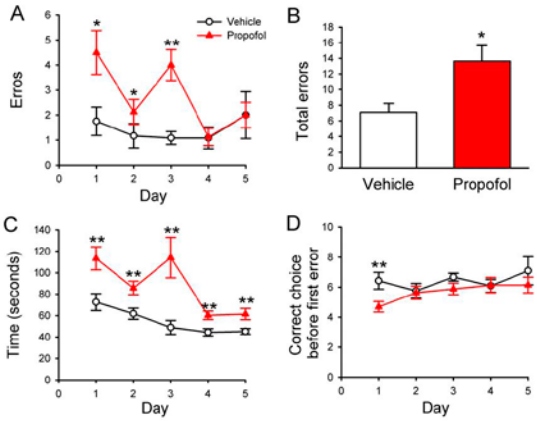

Figure 4. Anesthesia with propofol for 1 h in pregnant rats at E18 induces learning and memory impairment in offspring rats tested at P35. (A) Rats prenatally exposed to propofol made more errors relative to the controls across 5 days of testing (A). There was also a significant difference between groups in terms of the total number of errors over the 5 days of testing (B). Rats prenatally exposed to propofol also took longer time to complete the maze task (C) and made less correct choice prior to first error in the first day (D) than age-matched controls. Data are expressed as mean ± S.E.M. n = 16, *$P < 0.05$, *$P < 0.01$ *vs*. vehicle.

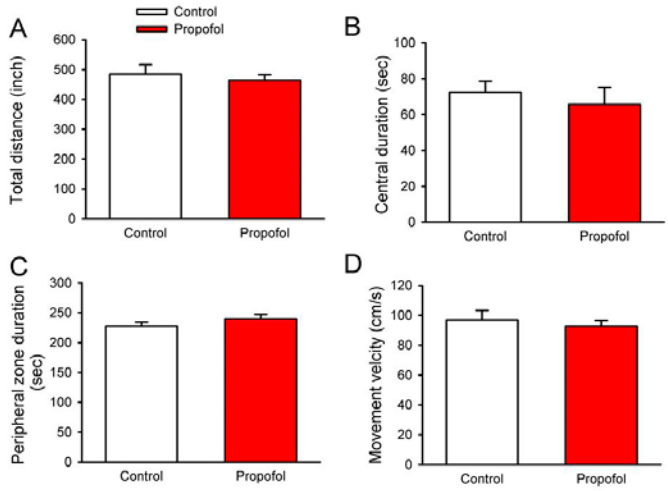

Figure 5. Propofol anesthesia for 1 h in pregnant rats at E18 does not change locomotor activities in offspring rats tested at P28. Data are expressed as mean ± S.E.M. n = 16.

Table 1 Physiologic Variable of Pregnant Rats during Propofol Anesthesia

	Anethesia Time			
----	15 min	30 min	45 min	60 min
ET CO2				
pH (arterial)	7.37 (7.36-7.37)	7.38 (7.36-7.41)	7.37 (7.35-7.41)	7.39 (7.35-7.46)
P_{ACO2} (mmHg)	44 (43-46)	50 (44-55)	48 (43-52)	46 (40-51)
P_{AO2} (mmHg)	310 (237-384)	298 (205-416)	299 (279-396)	283 (244-323)
$HCO3^-$	31.3 (27.1-35.5)	31.3 (28.5-31.6)	30.6 (28.7-32.5)	28.3 (27.7-28.6)
Na^+	141 (140-143)	140 (139-141)	140 (139-141)	141 (141-143)
K^+	4.5 (4.2-4.9)	5.1 (4.7-5.7)	5.2 (4.9-5.7)	4.9 (4.7-5.4)
Glucose (mM)	127 (118-137)	135 (119-154)	133 (129-140)	141 (124-148)
Hb (mg/dl)	13 (11-13)	13 (12-13)	13 (12-14)	13 (12-14)

Data are presented as median (range: min-max). P_{ACO2} = arterial carbon dioxide tension; P_{AO2} = arterial oxygen tension; Hb = hemoglobin. n = 4

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S-176.

SOLUBLE EPOXIDE HYDROLASE POLYMORPHISMS ARE ASSOCIATED WITH OUTCOME AFTER ANEURYSMAL SUBARACHNOID HEMORRHAGE

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INTRODUCTION: Pathologic alterations in cerebral blood flow are common after aneurysmal subarachnoid hemorrhage (SAH), and often manifest as delayed cerebral ischemia (DCI), stroke, and poor outcome. Epoxyeicosatrienoic acids (EETs) are arachidonic acid metabolites that play an important role in cerebral blood flow regulation and neuroprotection after brain injury. EETs have properties that may mitigate the risk of DCI after SAH, including cerebral vasodilation and inhibition of inflammation. Single-nucleotide polymorphisms in the gene for the enzyme soluble epoxide hydrolase (sEH), which inactivates EETs, have been shown to alter baseline EETs levels via enzyme activity variation. These polymorphisms are common in humans and have been linked to ischemic stroke risk and outcome, but their role in SAH has not previously been evaluated. In this prospective observational study of patients with SAH, we compare vital and neurologic outcomes based on functional genetic polymorphisms of sEH.

METHODS: Blood samples were obtained after informed consent. Allelic discrimination based on quantitative real-time PCR was used to differentiate wild-type (WT) sEH from K55R heterozygotes (predictive of increased sEH activity and reduced EETs; thus, harmful genotype) and R287Q heterozygotes (predictive of decreased sEH activity and increased EETs; thus, protective genotype). Medical records were reviewed for demographics and important physiologic and outcome data. The primary outcome was new stroke after SAH. Secondary outcomes were mortality, Glasgow outcome scale (GOS) score and neurologic deterioration attributable to DCI, based on recent multicenter consensus guidelines.

RESULTS: There were no differences in demographic characteristics between the groups. Multivariable logistic regression models adjusted for admission age and Glasgow coma scale revealed an increase in the odds of new stroke (OR 5.48; 1.51-19.91) and mortality (OR 7.62; 1.19-48.7) in the K55R group, but no change in the odds of new stroke (0.56; 0.16-1.96) or death (3.09; 0.51-18.52) compared to WT sEH group. R287Q genotype was associated with reduced odds of having a GOS ≤ 3 (0.23; 0.06-0.82)). There were no significant differences among genotypes in the odds of neurologic deterioration due to DCI.

CONCLUSIONS: Genetic polymorphisms of sEH are associated with, and may predict neurologic and vital outcomes after aneurysmal SAH. The link between sEH polymorphisms and EETs levels after injury remains unknown, as does the relationship between EETs and outcomes after injury. Elucidating these relationships may identify a role for sEH inhibitor drug therapy in the treatment of DCI after SAH.

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S-177.

INFLAMMATION INCREASES NEURONAL SENSITIVITY TO GENERAL ANESTHETICS IN MICE

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: The sensitivity to general anesthetics is often enhanced in critically ill patients through mechanisms that are poorly understood[1]. This hypersensitivity is frequently attributed to altered drug pharmacokinetics[2] or patient hemodynamic instability[3]. Most general anesthetics are positive allosteric modulators of the inhibitory γ-aminobutyric acid type A (GABAA) receptor[4]. Recent evidence shows that inflammation, which usually accompanies critical illnesses, increases the surface expression of GABAA receptors[5]. Here, we studied the hypothesis that inflammatory factors increase the sensitivity of neurons to anesthetics.

METHODS: Cultured hippocampal neurons were pre-treated with the pro-inflammatory cytokine IL-1β or a control solution. GABA-evoked currents were recorded in the absence and presence of an intravenous anesthetic (etomidate) or an inhalational anesthetic (isoflurane) using whole-cell patch clamp techniques. In addition, we studied the effects of systemic inflammation on behavioural sensitivity to etomidate and isoflurane in adult male mice in vivo. Animals were treated with the pro-inflammatory agent lipopolysaccharide (LPS) and anesthetic-induced loss of righting reflex (LORR) and loss of tail-clamp withdrawal reflex (LOTW) were measured.

RESULTS AND MAJOR FINDINGS: The amplitude of GABA-evoked current was 2-fold greater in IL-1β-treated neurons compared to controls. Etomidate further increased the GABA current up to 3.5-fold in IL-1β treated cells compared to controls. Similarly, isoflurane-mediated GABA conductance was 4-fold greater in IL-1β-treated neurons compared to controls. The concentration-response plots for etomidate and isoflurane showed that the EC50 values were similar (Control etomidate 10.7 ± 6.7 μM, n=5 versus IL-1β etomidate 13 ± 2.9 μM, n=9, p=0.7; Control isoflurane 314.3 ± 37.5 μM, n=8 versus IL-1β isoflurane 347.5 ± 28.9 μM, n=10, p=0.5) whereas the maximal responses were increased (Control etomidate 1017 ± 202.2 pA, n=5 versus IL-1β etomidate 3314 ± 260.3 pA, n=9, $p<0.001$; Control isoflurane 1037 ± 92.3 pA, n=8 versus IL-1β isoflurane 1544 ± 145 pA, n=10; $p<0.05$). LPS increased the sensitivity to etomidate- and isoflurane-induced LORR and etomidate-induced LOTW. Isoflurane-induced LOTW, which is not a GABAA receptor dependent behavioural endpoint, was unaffected by LPS.

CONCLUSIONS: Neuronal sensitivity to both an injectable and inhaled anesthetic was much greater in cells treated with IL-1β compare to controls. Behavioural studies corroborated our in vitro findings. These results need to be considered when selecting an appropriate dose of anesthetics for critically ill patients.

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S-178.

OPTOGENETIC DISSECTION OF THE NEURONAL CIRCUITS OF THE MOUSE RESPIRATORY NETWORK

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INTRODUCTION: Neural circuitry controlling breathing in mammals is organized within brainstem compartments, which regulate its own activity by feedback loops, and extend from the pons to the lower medulla. The core network, that generates the respiratory rhythm and shapes inspiratory and expiratory motor patterns, is distributed among three adjacent functional structures in the ventrolateral medulla: the Bötzinger complex (BötC), pre-Bötzinger complex (preBötC) and rostral ventral respiratory group (rVRG).

METHODS: We sought to investigate the role of a genetically defined population of inhibitory glycinergic neurons of this network, located in the BötC and preBötC, by combining optogenetics using the in-situ working heart-brainstem preparation. In order to achieve selective expressions of the Channelrhodopsin-2 (ChR2) transgene in restricted population of glycinergic neurons, we combined mice genetics (GlyT2-Cre mice;[1]) with stereotactical AAV-virus injection (DIO-Chr2-EYFP) allowing Cre-mediated expression of ChR2 in inhibitory neurons. Animals were incubated at least 2 weeks post injection (usually 2-4 weeks), and then were used for in situ experiments. Working heart-brainstem preparation is an arterially perfused, decorticated preparation that produces in vivo-like respiratory rhythm and is widely used to study autonomic nervous system. For the purpose of this study, ventral medullary surface was exposed, to allow blue light stimulation (473 nm, delivered by a fiber optic) through the ventral medullary surface, at the level of BötC and preBötC.

RESULTS: Tonic (30-45s, 33Hz pulses) stimulation of the glycinergic neurons of the BötC and pre-BötC resulted in depression of the inspiratory frequency of about 45%, independent of the level of baseline activity. The effect on the PND amplitude was variable. Burst stimulation (1.5s, 33Hz, variable interval) had the capacity to stabilize or disrupt the rhythm, dependent of the frequency of stimulation.

CONCLUSIONS: This work shows that glycinergic neurons located in the BötC /preBötC are important components of the circuitry controlling breathing. The activity of these cells seems to be especially vital for the control of the duration of the expiratory period and transition from expiration to inspiration. Taken together our technique with selective activation of identified neuronal populations allows not only the detailed analysis the respiratory network but also represents a novel tool for the functional analysis of anesthetics and the action on the respiratory network.

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S-179.

DIFFERENTIAL NEURONAL DYNAMICS IN SOMATOSENSORY VERSUS HIGHER-ORDER CORTICES DURING RECOVERY FROM PROPOFOL ANESTHESIA IN PRIMATES

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INTRODUCTION: The mechanisms of neural recovery from anesthetic-induced unconsciousness are poorly understood. Elucidating the neural substrate of recovery is an essential step for eliminating postoperative neurocognitive problems and potentially catastrophic complications.

METHODS: Here we studied the neuronal dynamics during a transition from propofol-induced unconsciousness into consciousness by directly recording intracortical local field potentials (LFPs) in the primary somatosensory cortex (S1) and a frontal higher-order cortex (ventral premotor cortex, PM) in non-human primates. Two monkeys were trained in a behavioral task in which they were required to hold a push-button until the end of each trial. Propofol was infused for 60 minutes through a surgically implanted vascular port and no other sedatives or anesthetics were used. The animal's trial-by-trial behavioral response was recorded as a correct response, failed attempt, or no response (Fig.1A). The animal's loss of consciousness (LOC) was defined as the first no-response trial followed by the complete lack of response for the remainder of anesthesia (Fig.1 a black arrow and dotted lines) and the return of consciousness (ROC) as the first trial after which there were at least five consecutive attempts (correct or failure) (Fig.1 a brown arrow and dotted lines). Neural activity was recorded in the alert - anesthetized - emerging continuum simultaneously from these cortices through surgically implanted microelectrode arrays. All experiments were approved by IACUC and performed in compliance with the NIH guidelines.

RESULTS: In PM, we found a transient increase in the LFP alpha/beta power and a decrease in the slow oscillations during early recovery (between the termination of propofol and ROC) (Fig.1C) while slow oscillations remained increased in S1 until ROC (Fig.1B), suggesting a frequency-specific regional difference during early recovery. At the ROC, there was a discontinuous shift to beta oscillations in both S1 and PM (Fig.1B,C). These beta oscillations appeared to become coherent between regions as soon as they appeared during emergence (Fig.1D). On the contrary, during anesthetic induction the regionally coherent beta oscillations were disrupted while the animal was still performing (Fig.1D). Further comparison of the spectral profiles between LOC and ROC suggested that the oscillatory dynamics were not simply mirror opposite. In addition, these sequential neural changes were identified in animals that were not performing the task, suggesting that the observed neural changes at ROC were not the results of returning task performance.

CONCLUSIONS: Our results demonstrate that the ROC from propofol anesthesia is associated with an abrupt return of synchronized beta oscillations in this cortical network. However, during the early recovery period prior to ROC, the higher-order cortex and the primary sensory cortex appear to be dissociated. Together with previously reported neuronal dynamics at LOC, our results suggest distinctively unique neural processes during the transition into and out of propofol-induced unconsciousness.

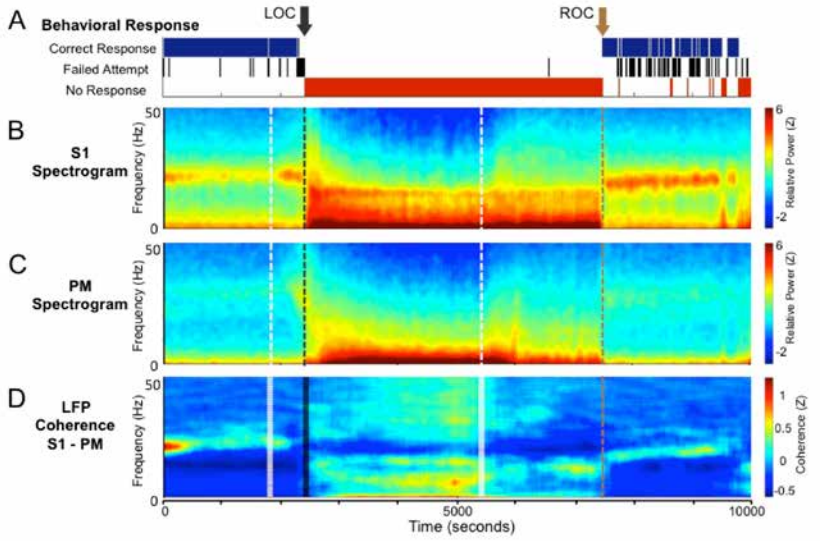

Figure 1. Behavioral response and the local field potential (LFP) change during induction and emergence from propofol anesthesia in a primate. **A.** Behavioral responses: correct (blue), failed attempt (black), and no response (red). **B.** LFP spectrogram in S1. **C.** LFP spectrogram in PM. **D.** Time-frequency LFP coherence plots between S1 and PM. LOC occurred at 2425 sec (a black arrow and dotted lines) and ROC at 7483 sec (a brown arrow and dotted lines). Propofol was infused from 1800 sec to 5400 sec at a rate of 200 μg/kg/min (white dotted lines).

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S-180.

MATERNAL-FETAL ANESTHESIA AND FETAL NEUROTOXICITY USING THE OVINE MODEL

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Advances in surgery and technology have led to an increase in procedures performed in utero. However, there is limited knowledge on the effect of anesthesia on the fetal brain. Fetal neurotoxicity following anesthetic exposure has been previously demonstrated in small animal models exposed to Isoflurane.[1,2] The purpose of this study was to examine the effects of Isoflurane on the fetal brain in a larger ovine animal model.

METHODS: With Animal Care and Use Committee approval, pregnant Western Cross sheep at 70 days gestation (term = 145 days) were exposed to Isoflurane to simulate the effect of anesthetic exposure during mid-gestation human fetal procedures. The effect of dose, duration and repeated episodes of anesthesia were assessed (table 1). Age appropriate fetuses not exposed to anesthesia served as controls. Pregnant ewes received a preassigned anesthetic, were maintained on mechanical ventilation and monitored for peripheral oxygen saturation, blood pressure, heart rate and temperature. Serial arterial blood gases were monitored. Once the designated anesthetic was complete, the animals were euthanized and fetal brain processed for histology. Neuroapoptosis in the frontal cortex and hippocampus (dentate gyrus, end plate, and pyramidal cortex) was detected using anti-caspase-3 antibodies and analyzed by Aperio digital imaging. To determine the late effects of anesthesia on neuronal loss, one group had fetuses exposed at mid gestation that were euthanized 60 days later at day 130 and compared to control day 130 fetuses. Data were analyzed using ANOVA with post-hoc analysis as appropriate.

RESULTS: Thirty-two fetuses were studied (Table 1). There was a substantial amount of developmental neuroapoptosis in the fetal brain at day 70 of gestation. Anesthetic exposure did not result in an increase in neuroapoptosis in the hippocampus. However, the frontal cortex showed an increase in neuroapoptosis with exposure to anesthesia that was most pronounced in the fetuses with multiple exposures to anesthesia (Figure 1). Repeated exposure of small amounts appears to be more injurious that a single long exposure of a higher dose. The fetuses with multiple exposure to anesthesia at mid gestation also showed remarkable neuronal loss in the frontal cortex by day 130 when compared to age appropriate controls (Figure 2). The neuronal loss paralleled the increase in neuroapoptosis seen in the acute preparation as they were noted only in the frontal cortex and not in the hippocampus.

CONCLUSIONS: In our fetal ovine model, there is a selective vulnerability to anesthetic insult in the brain that was more apparent in the frontal cortex than the hippocampus. Repeated exposure to anesthesia appeared to be more injurious than the dose or duration of anesthesia at this stage of development. Anesthetic toxicity manifested as increased neuroapoptosis acutely, persisted over time as increased neuronal loss in the frontal cortex. Further studies are needed to better understand the short, medium and long term effects of exposure to anesthesia in-utero on brain development.

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Sheep Exposure to Isoflurane			
Group	Gestational Age	Isoflurane	N
A	70 days	Control (No Isoflurane)	5
B	70 days	Isoflurane 2% for 1 hour	6
C	70 days	Isoflurane 4% for 3 hours	6
D	70 days	Isoflurane 2% for 1 hour every other day x 3	6
E	70 days	Isoflurane 2% for 1 hour every other day x 3 and euthanized at day 130	6
F	130 days	Control (No Isoflurane)	3

Figure 1a-d: Effect of Isoflurane Exposure on Neuroapoptosis in the Mid-gestation Fetal Ovine Brain. Number of Apoptotic nuclei per mm³ of brain tissue. Data presented as mean ± standard deviation.
** = p<0.05 compared to control.*

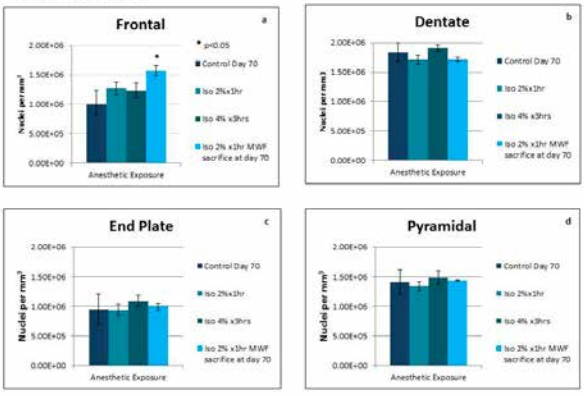
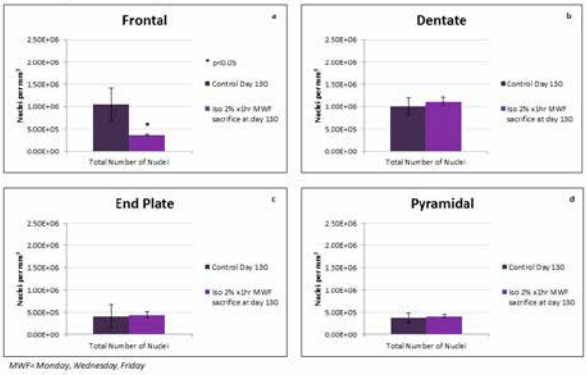


Figure 2a-d: Effect Of Isoflurane Exposureat Day 70 On Neuronal Cell Content at Day 130 of Gestation (Term = 145 Days). Total nuclei per mm³ for control fetuses at 130 days of gestation compared to fetuses exposed to Isoflurane at 2% for 1 hour every other day x3 at 70 days of gestation and then sacrificed at 130 days of gestation. Data presented as mean ±SEM. *p<0.05 vs. Control,



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S-181.

MIDAZOLAM INCREASES TAU PHOSPHORYLATION IN THE MOUSE HIPPOCAMPUS

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INTRODUCTION: In Alzheimer's disease, the microtubule-associated protein tau can undergo aberrant hyperphosphorylation leading to the development of neurofibrillary pathology. It has been previously demonstrated that propofol[1] and dexmedetomidine[2] increase tau phosphorylation in the absence of hypothermia. However, the impact of midazolam on tau phosphorylation is unknown; hence, the aim of this study was to test the hypothesis that midazolam also increases tau phosphorylation under normothermic conditions.

METHODS: Following IACUC approval, male C57BL6/J mice (8-10 week old) received midazolam (Mid) 10 mg/kg (n=5), 25 mg/kg (n=5) or an equal volume of 0.9% saline (control (Ctl), n=4) i.p (STUDY 1). The mice were sacrificed 30 min later. Furthermore, to examine the duration of tau phosphorylation, male C57BL6/J mice received Mid 25 mg/kg (Mid 6h, n=5) or 0.9% saline (control, n= 4) i.p. and were sacrificed 6h later (STUDY 2). Lastly, the mechanism underlying tau hyperphosphorylation was examined by screening for the activation pattern of a panel of tau kinases and phosphatases in the hippocampi of the Mid 25 mg/kg and saline mice from STUDY 1. Normothermia was maintained throughout the study, and hippocampal tissue was harvested immediately at the end of each specified treatment period. Levels of phosphorylated tau (p-tau) at the AT8 (pSer202/pThr205), PHF-1 (pSer396/pSer404) and CP13 (pSer202) phosphoepitopes as well as total tau (Tau 46) were determined using immunoblotting. Protein bands were visualized by enhanced chemoluminescence, and densitometric analysis of the immunoblot bands was performed using MultiGauge® software. Band immunoreactivity levels for all epitopes were normalized to total tau, after being controlled for gel loading with β-actin. Statistical comparisons were made using an unpaired t-test or ANOVA with Newman-Keuls post hoc test applied when appropriate. Data are expressed as mean ± SD and $P < 0.05$ was considered statistically significant.

RESULTS: At 30 min, Mid 10mg/kg and 25 mg/kg produced similar, significant increases in hippocampal p-tau levels at the AT8 (247 ± 70 and 225 ± 89% of Ctl, respectively), and CP13 (215 ± 65 and 223 ± 81% of Ctl, respectively), phosphoepitopes (Fig. 1). No significant changes in p-tau levels at PHF-1 or total tau were observed. Interestingly, 6h following midazolam 25 mg/kg, tau phosphorylation was still present, as increases were observed at all 3 phosphoepitopes (Fig. 2). Decreased levels of phosphorylated-GSK-3β at the serine 9 residue, which correlates with GSK-3β activation, paralleled the observed tau hyperphosphorylation. No other significant changes in tau kinases and phosphatases were observed.

CONCLUSIONS: Acute midazolam administration increases hippocampal tau phosphorylation in mice under normothermic conditions, and this response persists for at least 6h. The activation of GSK-3β may underlie the observed hyperphosphorylation. The impact of these changes on tau function and neurobehavior warrant further investigation.

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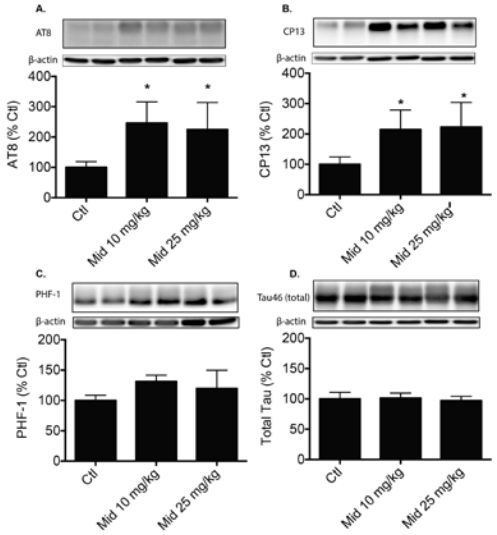
Supported by NIGMS 1R01GM101698



Rectal Temperatures (ºC): Ctl 37.4 ± 0.3, Mid 10 mg/kg 37.3 ± 0.3, Mid 25 mg/kg 37.4 ± 0.2

Fig 1. Hippocampal tau phosphorylation (%CTL) at the AT8, CP13, and PHF-1 phosphoepitopes (A-C) in mice treated with midazolam (Mid) 10 mg/kg (n = 5) or 25 mg/kg (n =5). Control mice (Ctl, n =4) were treated with an equal volume of 0.9% saline. Normothermia was maintained throughout and all mice were sacrificed 30 min after treatment. Phosphorylated tau levels were normalized to total tau (D) after controlling for gel loading with β-actin. Data are expressed as mean ± SD and $P < 0.05$ vs. Ctl.

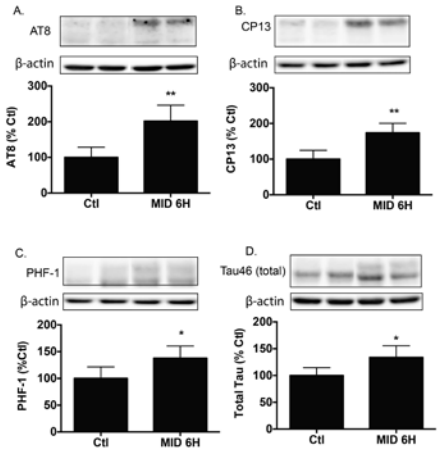


Fig 2. Hippocampal tau phosphorylation (%Ctl) at the AT8, CP13, and PHF-1 phosphoepitopes (A-C) in mice treated with midazolam 25 mg/kg (MID 6h, n = 5) or 0.9% saline (Ctl, n =4) i.p. and sacrificed 6h later. Normothermia was maintained throughout the study. Phosphorylated tau levels were normalized to total tau (Tau46, D), after controlling for gel loading with β-actin. Data are expressed as mean ± SD and *, **, *** $P < 0.05$, 0.01, and 0.001, respectively vs. Ctl.
Rectal temperatures: Ctl 36.4 ± 0.3°C and MID 6h 36.9 ± 0.2°C.

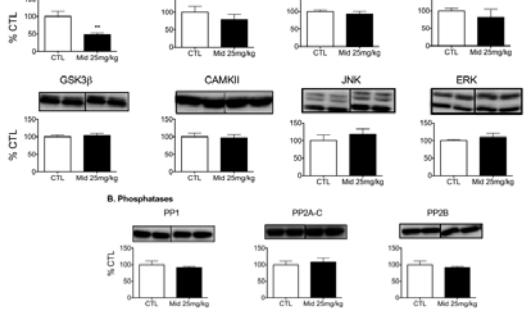


Fig. 3: Hippocampal levels of tau kinases (A) and phosphatases (B) in mice, 30 min after treatment with midazolam 25 mg/kg or saline (CTL) i.p. A significant decrease in the level of phospho-GSK-3β Serine 9 was observed. The decreased Ser 9 phosphorylation is associated with the activation of GSK-3β and correlates with the midazolam-induced increase in tau phosphorylation. No significant changes in phosphatase levels were observed. Data are expressed as mean ± SD and ** $P < 0.01$ vs. CTL.

Abbreviations: GSK-3β (glycogen synthase kinases-3β), CAMKII (calmodulin-dependent kinase II), ERK (extracellular signal-regulated kinase), JNK (c-Jun N-terminal kinase), PP1 (protein phosphatase 1), PP2A-C (protein phosphatase -catalytic subunit), PP2B (protein phosphatase 2B)

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Obstetric Anesthesiology

S-183.

POST CESAREAN SECTION EPIDURAL FENTANYL INFUSION AND MORPHINE PROVIDE SIMILAR ANALGESIA, BUT EPIDURAL MORPHINE CAN CAUSE MORE NAUSEA AND PRURITIS

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AFFILIATION: Anesthesiology, University Hospitals Case Medical Center, Cleveland, OH

INTRODUCTION: This study compares the analgesic efficacy and frequency of side effects of an epidural fentanyl infusion, which use to be our standard post-C-section analgesic, with the popular epidural preservative free morphine dose[1-3] following Cesarean section surgery.

METHODS: After IRB approval was obtained, charts of all patients during a 6 month period (1/11-6/11) who had an epidural fentanyl infusion or who received an epidural dose of preservative free morphine after their Cesarean section were reviewed. The fentanyl infusions consisted of 4mcg/ml fentanyl with epinephrine 1.25mcg/ml delivered by epidural PCA with a 15ml basal rate, 4ml demand dose and a 15 min lockout time. The epidural morphine dose was determined by the anesthesia team involved, and it was assumed to last 17-24hrs.[1,3] The epidural catheter was removed after the morphine dose was administered, and it was left in for up to two days for the fentanyl infusion. The following information was collected from each chart: age, gestational age, height, weight, dose of morphine administered, hours after the Cesarean section the epidural catheter was left in place, pain level (0-10 scale) and respiratory rate at 8 and 16 hrs after the end of the Cesarean section, number of doses of pain, nausea and pruritis medications the patient received in the 16 hrs after the Cesarean section, and the number of pain medication doses during that period excluding acetaminophen and NSAIDS.

RESULTS: A total of 381 women met the criteria to be in the study, with 108 receiving epidural fentanyl infusions and 273 having received a dose of epidural morphine after their Cesarean section. The fentanyl infusion was discontinued at an average of 38.6 (±9.9) hrs after the surgery. Epidemiological statistics were similar for the two groups. Pain scores at 8 and 16 hrs after the procedure were comparable for the two groups (F: 2.8±2.6, 3.7±2.6; M: 1.9±2.5, 2.5±2.6 for 8 and 16 hrs, respectively). All respiratory rates for the study period were at least 14/min. More patients (26% vs 15%) required over two doses of pain medications during the 16hrs in the morphine group, and this was significant (p=0.03). However, patients requiring pain medications other than NSAIDS and acetaminophen during this period did not differ significantly between the groups (18% vs 25%, p=0.13). The number of patients requiring more than two medications for nausea or pruritis was significantly greater for the morphine group (21% vs 8%, p=0.003).

CONCLUSION: For the first 16hrs after a Cesarean section, epidural morphine and an epidural fentanyl infusion deliver approximately the same pain relief without depressing respirations. Epidural morphine may cause more nausea and/or pruritis that may need to be treated. Epidural fentanyl infusions can be continued past the time that the single dose of epidural morphine will have worn off.

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S-184.

REGIONAL ANESTHESIA IN HIGH-RISK PARTURIENTS: EFFICACY IN PARTURIENTS WITH LOW PLATELET COUNTS.

AUTHORS: B. Hua, S. Nair, J. Bernstein

AFFILIATION: Anesthesiology, Montefiore Medical Center, Bronx, NY

INTRODUCTION: Regional anesthesia as a standard of care for labor pain relief or for Cesarean section in Obstetric anesthesia is widely practiced. In the high-risk obese parturient, it is even more crucial to provide a safe regional anesthetic in order to avoid the risks of general anesthesia. Obesity in women of reproductive age is associated with obstructive sleep apnea, preeclampsia, and a greater likelihood for difficult intubation. Since thrombocytopenia of < 100 X $10^9.L^{-1}$ affects about 1% of parturients, the current literature suggested a platelet count cut-off at 75 to 80 x $10^9.L^{-1}$ for the safe placement of regional anesthesia. But, one study by Tanaka et al, advocated for a lower cut-off at 50 x $10^9.L^{-1}$ which excluded pre-eclamptic patients.

In this study, our goal was to integrate the incidence of obesity, preeclampsia, and thrombocytopenia, given the large, high risk patient population seen at our institution, and further investigate the safety and efficacy of regional anesthesia for the support of lowering the safe platelet count to as low as 50 x $10^9.L^{-1}$.

METHODS: The Clinical Looking Glass (CLG), the patented hospital software program, was utilized to identify 20,244 obstetric patients who delivered in our hospital between September 2009 - 2013. A retrospective, detailed chart review was then performed for 256 parturients (1.3%) who had platelet counts </= 100 x $10^9.L^{-1}$ noted at the time of pre-anesthesia assessment. The etiology of the thrombocytopenia, type of anesthetic technique, mode of delivery, major neurological and anesthetic complications, and BMI were also collected. There were no exclusion criteria.

RESULTS: Of the 256 parturients, 151 (59%) had received regional anesthesia. From 80 - 100 x $10^9.L^{-1}$, 75% of the patients (131/175) received regional anesthesia (89 epidural/37 spinal/5 CSE) and the mean BMI was 31.37 +/- 5.65. From 50 - 79 x $10^9.L^{-1}$, 25% of the patients (19/76) received regional anesthesia (10 epidural/9 spinal) and the mean BMI was 31.41 +/- 4.94. One out of 13 patients below 50 x $10^9.L^{-1}$ received an epidural regional anesthetic and the mean BMI was 35.82 +/- 10.20. There were no neurological complications found.

CONCLUSION: From our high risk parturient population, an average BMI of > 30 was found in all the subgroups, with the highest present with a platelet count < 50 x 10 9.L-1. The lack of complication with regional anesthesia placed in our parturients supports the need to promote its safe use for a platelet count > 50 x 10 9.L-1. In the future, the supplemental look at the platelet function with the count can further help identify those with a greater risk for complications from regional anesthesia.

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S-185.

WITHDRAWN.

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S-186.

IS 6% HETASTARCH PREFERRED OVER PROPHYLACTIC IV EPHEDRINE FOR PREVENTION OF HYPOTENSION FROM INTRATHECAL ROPIVACAINE FOR CESAREAN SECTION?

AUTHORS: A. Sakr[1], S. Cohen[1], D. Ramos[1], K. Rah[1], S. Syed[2], S. Syed[1], C. W. Hunter[1]

AFFILIATION: [1]Anesthesiology, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ, [2]Anesthesiology, ZMAR LLC, Sugar Land, TX

INTRODUCTION: The use of prophylactic IV ephedrine or 6% Hetastarch is effective for prevention of hypotension from spinal anesthesia for cesarean section (C/S) when compared with Lactated Ringer's solution (LR) alone. From a financial standpoint the cost of 1L of LR is $0.86, 1 Ampule of ephedrine is $0.32, and 500mL of 6% Hetastarch is $16.16. We examined which treatment is the most effective for the prevention of hypotension from combined spinal-epidural (CSE) anesthesia for C/S.

METHODS: Following IRB approval and informed consent 244 parturients scheduled for elective C/S with CSE were studied. In all patients, the epidural space was located at L3-4 or L4-5 interspace using an epidural needle in the lateral decubitus position. The epidural catheter was inserted immediately following administration of 10mg ropivacaine with 100mcg epinephrine and 25mcg fentanyl intrathecally.

The patients were randomized into 4 groups. GI (n=60) received IV 2L LR prior to induction of CSE. GII (n=66) received IV 1L LR and upon the spinal injection, received IV ephedrine 30mg for 15min. GIII (n=57) received IV 500mL 6% Hetastarch + 1L LR prior to spinal injection. GIV (n=61) received IV 500mL 6% Hetastarch + 1L LR prior to spinal injection, and upon the spinal injection also received IV ephedrine 30mg for 15min.

Immediately after the spinal induction, the patients were positioned supine with left uterine displacement. BP was measured with automatic BP device every 2min for the duration of the surgery. Hypotension was defined as a systolic BP (SBP) < 100mmHg and < 80% of the baseline BP. Hypotension was treated with IV boluses of ephedrine 5mg q2min. Reactive hypertension was defined as an increase in SBP > 20% above baseline. Values are mean ± SD. P value <0.05 was considered significant.

RESULTS: 26 patients (43.3%) in Group I had hypotension compared to 10 patients (15.2%) in Group II, 15 patients (26.3%) in Group III, and 13 patients (21.3%) in Group IV (Table 1). 24 patients (40%) in Group I required treatment of hypotension with IV ephedrine, compared to 8 patients (12.1%) in Group II, 9 patients (15.8%) in Group III, and 10 patients (16.4%) in Group IV (Table 1).

CONCLUSIONS: IV prophylactic ephedrine is more cost effective and is as effective as 6% Hetastarch for the treatment of hypotension from intrathecal ropivacaine for cesarean section.

Table 1:

	GI n= 60	GII n= 66	GIII n=57	GIV n= 61
Age (yrs)	31.7 ± 4.9	30.7 ± 6.2*	32.2 ± 5.8	32.8 ± 4.9
Weight (lbs)	180.3 ± 38.0	181.2 ± 39.8	179.8 ± 41.5	181.3 ± 41.3
Height (in)	63.2 ± 8.9	63.5 ± 2.5	63.3 ± 2.6	63.5 ± 2.3
Primi n (%)	14 (23.3)	13 (19.7)	20 (35.1)	11 (18.0)
Multi n (%)	46 (76.7)	53 (80.3)	37 (64.9)	50 (82.0)
1. Efficacy n (%)	55 (91.7)	61 (92.4)	54 (94.7)	58 (95.1)
2. Uncomfort. n (%)	1 (1.7)	3 (4.5)	1 (1.8)	2 (3.3)
3. +Sedation n (%)	3 (5.0)	2 (3.0)	2 (3.5)	1 (1.6)
4. G/A	0	0	0	0
Nausea Rx n (%)	19 (31.7)	13 (19.7)	16 (28.1)	28 (45.9)
Vomiting n (%)	9 (15.0)	16 (24.2)	6 (10.5)	16 (26.2)
Hypotension n (%)	26 (43.3)**	10 (15.2)	15 (26.3)	13 (21.3)
Hypotension Rx (IV ephedrine boluses) n (%)	24 (40.0)***	8 (12.1)	9 (15.8)	10 (16.4)
Overall Satisfaction	9.6 ± 1.0	9.8 ± 0.6	9.6 ± 0.8	9.6 ± 0.9

*II<IV, p<0.04, **I>II, III & IV, p<0.02, ***I>II, III & IV, p<0.001.

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S-187.

DOES INCREASING THE CONCENTRATION OF EPIDURAL-PCA FENTANYL FOR LABOR IMPROVE ANALGESIA WITHOUT EFFECT TO NEONATE?

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INTRODUCTION: Epidural fentanyl 2mcg/mL with bupivacaine 0.015% and epinephrine 2mcg/mL required frequent rescue doses of 0.25% epidural bupivacaine for satisfactory labor analgesia, whereas less anesthetic was needed with sufentanil. This study analyzed whether increasing the concentration of less expensive fentanyl would provide adequate analgesia with less local anesthetic and without neonatal impact.

METHODS: Seventy-five primiparae and 75 multiparae evaluated during labor and delivery (L&D) were divided into 3 groups. Patients received no systemic opioids and were randomized in a double-blinded design to groups with either 2, 4 or 6mcg/mL of fentanyl. All groups received 0.015% bupivacaine and 2mcg/mL of epinephrine. After a dose of 3mL 1.5% lidocaine and 5mcg/mL epinephrine they received a 12mL loading dose of the study solution. An infusion was started at 6mL/hr with PCA boluses of 2mL and a lockout time of 10min. For inadequate analgesia, up to 4 boluses of 5mL study solution were given 10min apart and infusion rate was increased by 2mL/hr up to 3 times. If analgesia was still inadequate (pain score > 5), up to 4 boluses of 5mL of 0.25% bupivacaine were given. Pain scores, side effects, and overall patient satisfaction were assessed hourly with a 10-point VAS (Visual Analog Scale). Values are mean ± SD. P value <0.05 was considered significant.

RESULTS: There were no differences among the groups regarding demographic data, outcome of L&D, instrumental delivery, infusion duration, pain scores, satisfaction scores, or side effects. Apgar scores did not differ among groups and was <7 at 1 min in 4 and 1 patients for primiparae and multiparae, respectively; and was >7 for all patients at 5 min. Neonatal neuro-behavioral assessment total scores at 1 and 24 hrs were > 35 (max score = 40) for all infants. Infusion characteristics are shown in Table 1. Maternal and cord plasma concentrations of fentanyl upon delivery are depicted in Table 2

CONCLUSIONS: Increasing the concentration of fentanyl did not impact the neonates or the outcome of labor and delivery. Increasing the concentration of fentanyl significantly decreased the bolus volume of study solution. However, total 0.25% bupivacaine required remained high.

Table 1: Infusion Characteristics

	Total PCA Vol. (mL)	Study Solution Bolus Vol. (mL)	Total Study Solution Vol. (mL)	# of Pts. Requiring 0.25% Bup. (#)	Total Vol. of 0.25% Bup. (mL)
Primiparae					
Group I	12.1 ± 12.0	13.4 ± 8.0*	71.4 ± 40.5	15	5.8 ± 7.2
Group II	8.6 ± 5.9	10.3 ± 9.8	58.2 ± 38.8	10	3.9 ± 5.4
Group III	9.2 ± 8.9	7.5 ± 6.6	57.9 ± 31.5	13	3.9 ± 4.9
Multiparae					
Group I	7.8 ± 8.2	11.6 ± 8.6**	50.1 ± 34.9	13**	4.8 ± 5.7
Group II	4.5 ± 3.5	9.4 ± 8.1	38.2 ± 28.1	9	4.0 ± 7.5
Group III	4.9 ± 4.3	6.2 ± 8.0	33.8 ± 31.4	5	2.4 ± 5.9
*Significantly greater than Group III, p<0.007, ** Significantly greater than Group III, p<0.03					

Table 2: Maternal and Cord Plasma Concentrations of Fentanyl Concentration (ng/mL) Upon Delivery

Mother's Baseline		Mother's Post-delivery		Placental		Cord Blood
	P	M	P	M	P	M
Group I	0	0	0.5 ± 0.9	0.09 ± 0.09	0.50 ± 0.8**	0.07 ± 0.06
Group II	0	0	0.2 ± 0.2	0.13 ± 0.1	0.08 ± 0.08	0.03 ± 0.07
Group III	0	0	0.3 ± 0.2	0.32 ± 0.27*	0.10 ± 0.08	0.07 ± 0.06
*Significantly greater than Group I & Group II, p<0.04, ** Significantly greater than Group II, p<0.04						

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S-188.

CSE FOR CESAREAN SECTION: GERTIE MARX VERSUS PENCAN SPINAL NEEDLES

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INTRODUCTION: PENCAN spinal needles along with ESPOCAN epidural needles are used routinely for combined spinal-epidural anesthesia for cesarean delivery. However, we frequently encountered difficulty piercing the dura forcing us to switch to epidural block. We compared Gertie Marx spinal needle with PENCAN needle to determine which one is preferred by our obstetric patients.

METHODS: Following IRB approval and informed consent, 124 ASA I-II parturients, who requested neuraxial block for C/S, were included. The epidural space was located with ESPOCAN 18 gauge epidural "Braun" needle (B. Braun Medical Inc.) at L3-4 or L4-5 interspace with loss of resistance to air technique using a midline approach in the lateral or sitting flexed position. Patients were then randomized to one of two groups. Group I: 59 patients had a 25 gauge PENCAN spinal needle placed in the subarachnoid space. Group II: 65 had a 26 gauge Gertie Marx spinal needle (IMD Inc. USA) placed in the subarachnoid space. Patients received intrathecally 10mg isobaric bupivacaine with 25mcg fentanyl and 100mcg epinephrine. When the dura could not be pierced by the spinal needle, the epidural needle was rotated 45 degree at a time for further attempts. If still unsuccessful, the spinal needle was removed and an epidural block was applied. All patients had a 19g Arrow FlexTip plus (Arrow international Inc.) open-end tip catheter placed 4cm in the epidural space. An investigator recorded patients' height, weight, parity, patients' position, the distance of the epidural space from the skin, technical problems, paresthesia and pain upon insertion of the spinal needle, time to incision, difficulty with catheter insertion, post-dural-puncture headache, transient radicular irritability, duration of procedure, and overall satisfaction from the technique use. Values are represented as mean ± SD, $p < 0.05$ considered significant.

RESULTS: The groups did not differ in age, weight, height, parity, distance of epidural space from the skin, duration of surgery, previous neuraxial block, need to rotate or reinsert the epidural needle, efficacy of the block, side effects from the block, difficulty with catheter insertion, sensory level, overall satisfaction, or APGAR score. Time to incision was 33 ± 8 min and 24 ± 6 min for Group I and II respectively ($p = 0.0001$). Time to T6 was 6 ± 4 min and 2.6 ± 2 min for Group I and II respectively ($p = 0.0001$).

CONCLUSIONS: Application of PENCAN spinal needle when compared to Gertie Marx needle for C/S had less success piercing the dura, caused more paresthesia and pain during insertion, prolonged time to incision, and required switch to epidural block more often.

	PENCAN n=59	Gertie Marx n=65	P-Value
Lateral Position n (%)	55 (93.2)	48 (73.8)	0.002
Spinal needle problem n (%)	34 (57.6)	19 (29.2)	0.001
Leg jerk upon needle insertion n (%)	24 (40.7)	10 (15.4)	0.001
Paresthesia upon needle insertion (0-10)	3 ± 3.8	1.4 ± 3.0	0.02
Pierced dura with successful block n (%)	36 (61.0)	56 (86.2)	0.001
Switched to epidural n (%)	23 (39.0)	8 (12.3)	0.001
Sedation (0-10)	0.1 ± 0.5	3.3 ± 3.9	0.0001
Overall Satisfaction (0-10)	9.3 ± 1.1	9.6 ± 1.0	0.09

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S-189.

PREVENTION OF HYPOTENSION DURING CESAREAN SECTION UNDER SPINAL ANESTHESIA: INCREMENTAL ADMINISTRATION OF 0.2% BUPIVACAINE

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INTRODUCTION: Patients undergoing spinal anesthesia for cesarean section are at great risk of supine hypotension. In addition to aortocaval compression and the extent of sympathetic blockade produced by spinal anesthesia [1], the total amount of local anesthetic may play a role in determining the intensity of arterial hypotension[2]. In this study, incidence and intensity of hypotension during cesarean section under spinal anesthesia were determined by using incremental doses of 0.2%bupivacaine.

MATERIALS AND METHODS: Four ml of 0.5% hyperbaric bupivacaine solution (20 mg) were diluted with 6 ml of normal saline to produce a 0.2% approximately isobaric local anesthetic solution (20 mg/10 ml=2 mg/ml). Forty-three non-hypertensive patients undergoing cesarean section were studied. A combined spinal-epidural needle was inserted at the L3-L4 interspace with the patient lying on her right side. Bupivacaine solution (1 ml, 2 mg) was injected incrementally at intervals of 2 min or over to a total of 3 ml (6 mg), then an epidural catheter was placed via the epidural needle. A blood pressure decrease of greater than 20% in baseline pressure or below 90 mmHg was treated with phenylephrine.

RESULTS: The anesthetic level at proceeding to surgery was T5-T3. Only 3 of the 43 patients needed vasopressor treatment. Each of the 3 patients needed only 0.05 mg of phenylephrine. None of them complained of the respiratory discomfort.

CONCLUSIONS: The dose of bupivacaine for cesarean section is reported to be 12 to15 mg[3]. This study showed that when 0.2% bupivacaine was given in incremental doses, 1 ml (2 mg) by 1 ml (2 mg), a total of 6 mg was sufficient to produce satisfactory anesthesia for cesarean section. This lower dose can minimize the risk of spinal anesthesia for cesarean section. Prolonged surgery and postoperative pain can be controlled by the combined spinal-epidural anesthesia.

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S-190.

CAN WE APPLY ELECTRICAL MEDIAN NERVE STIMULATION FOR PROPHYLACTIC TREATMENT OF NAUSEA AND VOMITING (N/V) IN PARTURIENTS UNDERGOING CESAREAN SECTION (C/S) WITH COMBINED SPINAL-EPIDURAL TECHNIQUE (CSE)?

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INTRODUCTION: At our institution we routinely administer IV 8mg Ondansetron and 10mg metoclopramide upon induction of CSE for treatment of N/V during C/S. Application of electrical median nerve stimulation helps reduce the incidence of N/V during general anesthesia.[1] In this study we are comparing electrical median nerve stimulation to no treatment to determine if electrical median nerve stimulation is effective in the prophylactic treatment of N/V in our parturients undergoing C/S with CSE.

METHODS: This is a retrospective review of anesthesia records of 153 parturients undergoing induction of CSE for C/S. Group I (GI, n= 76) received no therapy. Group II (GII, n= 77) received median nerve stimulation from procedure onset until arrival at the PACU. An investigator recorded patients' height, weight, ASA status, gestational age in weeks, Apfel score (1-4), hypertension (>140/90), hypotension (<90 systolic), hypoxia (O2 Sat <85%), blood loss >700mL, efficacy of sensory block for C/S, evidence of N/V during procedure (after administration of epidural medications, after eversion of uterus, after replacement of uterus, upon arrival to PACU), N/V treatment satisfaction, and overall satisfaction. The student's t-test, Chi-squared test, and Fisher's exact test were used for statistical analysis. A p-value of <0.05 was considered statistically significant. Data was presented as Mean ± S.D.

RESULTS: There was no significant difference among the groups with respect to age, weight, height, ASA status, gestational age, Apfel score, incidences of hypertension, hypotension, hypoxia, efficacy of sensory block, blood loss >700mL, nausea after eversion of uterus, nausea after replacement of uterus, nausea upon arrival to PACU, and overall satisfaction. There was a significant difference between the groups for vomiting and nausea during procedure and N/V satisfaction >7 (Table 1). Specifically in the procedure itself, there was a significant difference between the groups with respect to nausea after application of CSE (Table 1).

CONCLUSIONS: There was a significant difference in the incidence of nausea and vomiting when comparing control with median nerve stimulation during C/S with CSE. Furthermore, there was a significant difference in the incidence of nausea specifically during phase 1 of the procedure - after application of CSE. High satisfaction (>7/10) from N/V was significantly greater in the median nerve stimulation group as opposed to control. Therefore, this shows that the use of median nerve stimulation was effective in prophylactically treating N/V in our parturients undergoing C/S with CSE.

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Table 1: Control vs. Nerve Stimulation N/V and N/V Satisfaction

	Group I: Control n=76	Group II: Nerve Stimulation n=77	P-Value
Vomiting During Procedure	30/63 (47.6)	20/68 (29.4)	0.032
Nausea During Procedure	50/72 (69.4)	32/71 (45.1)	0.003
Phase 1 - Nausea After Application of CSE	39/75 (52.0)	21/76 (27.6)	0.002
Phase 2 - Nausea After Eversion of Uterus	11/71 (15.5)	13/75 (17.3)	0.764
Phase 3 - Nausea After Replacement of Uterus	13/71 (18.3)	12/74 (16.2)	0.739
Phase 4 - Nausea Upon Arrival to PACU	4/71 (5.6)	1/71 (1.4)	0.366
N/V Satisfaction >7	27/74 (36.5)	47/76 (61.8)	0.0019

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S-191.

INTRAUTERINE RESUSCITATION AUDIT AT A DISTRICT GENERAL HOSPITAL

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INTRODUCTION: The aim of this audit study was to assess the compliance with recognised intrauterine resuscitation measures in women undergoing category 1 & 2 emergency caesarean sections for fetal distress1. 'Intrapartum Care (Clinical Guideline 55, Sept 2007)' by National Institute of Clinical Excellence (UK) provides guidelines for the management of abnormal fetal heart rate during labour2. The Obstetric Anaesthesia Association (OAA) in UK has reviewed some local hospital guidelines and provided comment on its website3.

METHODS: In accordance with local practice for audit projects, after approval by the departmental lead for audit, relevant data were collected prospectively from 78 women undergoing category 1 or 2 emergency caesarean section for fetal distress. Data on the following intrauterine resuscitation measures were noted upon arrival of the woman in the operating theatre:

1. Was there an oxytocin infusion present and, if so, had it been stopped?
2. What was the position of patient - supine or lateral?
3. Had a tocolytic drug been given?
4. Was the mother receiving supplemental oxygen?
5. Was an intravenous fluid infusion present?
6. Had an intravenous fluid bolus been administered?
7. Had a vasopressor agent been given to treat hypotension?

This data was collected by the anesthesiologist involved with the case and recorded on a specific audit form. Out of these 78 women, 15 were excluded from analysis due to incomplete data collection. Data from the remaining 63 (81%) was examined.

RESULTS:

Table 1: Data analysis

	Category 1 LSCS	Category 2 LSCS
Number of patients	15/63 (24 %)	48/63 (76%)
Oxytocin infusion present	8/15 (53%)	32/48 (67%)
Oxytocin infusion discontinued	5/8 (62%)	28/32 (88%)
Position - tilted / lateral	11/15 (73%)	27/48 (56%)
IV fluid infusion present	7/15 (47%)	18/48 (38%)
IV fluid bolus administered	2/7 (28%)	8/18 (45%)
Supplemental oxygen	None	None
Tocolytic administered	None	None
Vasopressor administered	None	None

Table 2: Type of Anesthesia administered.

	GA	Spinal	Epidural Top-up
Category 1 LSCS (n=15)	10/15 (67%)	2/15 (13%)	3/15 (20%)
Category 2 LSCS (n=48)	None	30/48 (63%)	18/48 (37%)

CONCLUSION: Our data suggest that our compliance with intrauterine resuscitation measures can be improved. In particular, we found that 'easy' measures such as stopping an oxytocin infusion, positioning the woman in a lateral position and administering a fluid bolus to those with an infusion already present were not followed in all cases. This data was presented and discussed at a joint meet of the Anesthesia and Obstetric departments of our hospital. It was planned to review the local departmental guideline and to provide it as a laminated sheet in both the obstetric theatre and the delivery suit. Re-audit is planned after a further 6 months.

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S-192.

THROMBOMODULIN IMPROVES MATERNAL AND FETAL CONDITIONS IN AN EXPERIMENTAL PRE-ECLAMPSIA RAT MODEL.

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INTRODUCTION: Pregnancy-induced hypertension and pre-eclampsia (PIH/PE) complicates 2 to 8% of pregnancies. Since these syndromes are major contributors to mortality and morbidity in both the mother and the fetus, these syndomes are recognized as the important disease in not obstetrics but also in emergency / intensive care field. There is no universally established standard of fundamental treatment for PE. The aim of this study was to investigate whether the consecutive administration of recombinant thrombomodulin (r-TM), which acts as anti-disseminated intravascular coagulation drug, for four days improves maternal and fetal conditions and physiological outcomes in an N'-nitro-L-arginine-methyl ester hydrochloride (L-NAME) and low-dose endotoxin-induced pre-eclampsia.

METHODS: A total of 41 rats were randomly divided into four groups: the control group (C-group, n=12); the PE group (P-group, n=11); the control group administered r-TM (CT-group, n=9); and the PE-group administered r-TM, (PT-group, n=9).To establish experimental PE rats, a modified Sakawi's method1 was employed in the P and PT-group. L-NAME was administered orally by dissolving 3 mg/kg/day in drinking water from day 6 of pregnancy up to the day 21. 1 μg/kg of LPS was prepared in 0.3 mL of pyrogen-free normal saline and carefully injected intraperitoneally on the 14th day of pregnancy. r-TM or saline was administered intravenously to normal pregnant and experimental PE rats for four days. The maternal condition (body weight, arterial blood pressure), albuminuria, vascular endothelial growth factor receptor-1 (VEGFR-1), fetal conditions (fetal body weight, fetal brain weight, the percentage of fetal resorption), uteroplacental blood flow (UPBF) measured by laser-Doppler flow meter, and oxygenation measured with an needle-type polarographic oxygen electrode in the placenta and fetal brain, was evaluated on gestational day21.

RESULTS: Significant increases in the mean arterial blood pressure, albuminuria, VEGFR-1 values, and fetal death rate were observed in P-group compared with C-group, while maternal and fetal body weight and fetal brain weight were substantially lower. Hypoperfusion and hypooxygenation in both the placenta and fetal brain tissues occurred in P-group (Figure). Although r-TM failed to improve hypertension, albuminuria and did not affect the differences in maternal body weight between the groups, r-TM significantly improved hypoperfusion and fetal and maternal conditions, including VEGFR-1 values (6.5 ± 4.0 vs.2.2 ± 2.7 ng/mL, P vs. PT-group, respectively; $P < 0.05$). Although not significant, a decrease in the fetal death rate was observed in PT-group (36.1 ± 17.6 vs. 25.0 ± 23.8%, $P = 0.077$).

CONCLUSIONS: The severe reductions in the UPBF and the placental oxygenation imply that regional hypoperfusion occurs in dissociation with systemic mean arterial pressure. r-TM may be a candidate medical treatment for PE complications.

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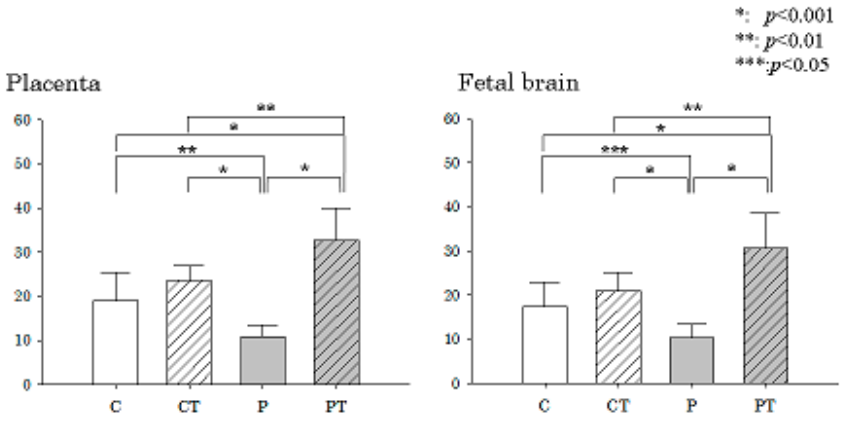

Figure. Tissue oxygenation in placenta and fetal brain

C: Control
CT: Contorol + rTM
P: PE
PT: PE + rTM

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S-193.

ARTIFICIAL NEURAL NETWORKS IN PREDICTION OF DELIVERY OUTCOME AND NEED FOR EPIDURAL ANALGESIA IN OBSTETRIC ANESTHESIA

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INTRODUCTION: Predictive analytical techniques are being increasingly applied in scientific, clinical and commercial applications. We have compared logistic regression and artificial neural network analyses (ANN) of several patient variables that are obtained relatively early in the patient encounter to predict whether that patient proceeds to normal vaginal delivery or to cesarean section. These early patient characteristics were also analyzed for their possible predictive contribution to whether a patient would require epidural analgesia for delivery.

METHODS: The data were collected with New York Medical College IRB approval by a retrospective chart review of 205 patients that received a combined spinal-epidural anesthesia technique. The Department of Anesthesia database is maintained by one of the authors (M.G.). In all cases, patients received 25 μg of fentanyl and 250 μg of preservative-free morphine (Duramorph) intrathecally. The epidural catheter was tested but only activated as indicated. For prediction of mode of delivery, the composite of contributions of the following variables were analyzed for strength of prediction of target outcome (normal vaginal delivery vs cesarean section): ASA grade, age, body mass index, comorbidities, gravidity, parity, cervical dilation, cervical effacement, and fetal station. In assessment of prediction of the second outcome event, i.e., non-use of epidural vs use of epidural analgesia, the visual analog pain score before administration of the intrathecal regional analgesics was added to the above variables. IBM-SPSS Amos 21 statistical software was used for both the logistic regression and ANN analyses.

RESULTS: A comparison of the predicted distribution of outcomes for mode of delivery by logistic regression and ANN are presented in Table 1. Prediction of normal vaginal delivery was 92.4% and 100% by logistic regression and ANN, respectively; cesarean section was predicted 57.1% and 90.5% by logistic regression and ANN, respectively. Predictions for the need to utilize epidural analgesia are presented in Table 2 (non-use of the epidural was predicted 67.5% and 86.7% by logistic regression and ANN, respectively; use of epidural was predicted 52 % and 92% by logistic regression and ANN, respectively).

TABLE 1 PREDICTION OF NORMAL VAGINAL DELIVERY (NVD) AND CESAREAN SECTION (C/S)

LOGISTIC REGRESSION ANALYSIS

	PREDICTED		
OBSERVED	NVD	C/S	PERCENTAGE CORRECT
NVD	110	9	92.4
C/S	18	24	57.1

ARTIFICIAL NEURAL NETWORK ANALYSIS

	PREDICTED		
OBSERVED	NVD	C/S	PERCENTAGE CORRECT
NVD	119	0	100
C/S	4	38	90.5

TABLE 2 PREDICTION OF USE OF EPIDURAL ANALGESIA

LOGISTIC REGRESSION ANALYSIS

	PREDICTED		
OBSERVED	Epi NO	Epi YES	PERCENTAGE CORRECT
Epidural - NO	56	27	67.5
Epidural - YES	36	39	52

ARTIFICIAL NEURAL NETWORK ANALYSIS

	PREDICTED		
OBSERVED	Epi NO	Epi YES	PERCENTAGE CORRECT
Epidural - NO	72	11	86.7
Epidural - YES	6	69	92

DISCUSSION: ANN modeling of the predictions of mode of delivery and need for epidural analgesia was superior to logistic regression in both outcomes that were analyzed. It would appear that ANN gains in predictive strength by virtue of its iterative attempts to evaluate all of the possible interactions among the patients' clinical variables, In comparison, logistic regression only considers the independent, linear contribution of each variable. ANN models may represent a valuable asset in the anticipation of potential risk factors or need for interventions in the obstetric setting. The present ANN models must be further evaluated for their prediction accuracies with data that are independent of the trained models.[1]

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S-194.

ONDANSETRON DOSE NOT ATTENUATES HYPOTENSION IN PATIENTS UNDERGOING ELECTIVE CESAREAN DELIVERY UNDER SPINAL ANESTHESIA: A DOUBLE-BLINDED, PLACEBO-CONTROLLED RANDOMIZED TRIAL

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INTRODUCTION: Elective Cesarean deliveries are commonly performed under spinal anesthesia. However, hypotension is a frequent complication[1]. Several strategies are used to attenuate hypotension due to spinal anesthesia with a variable success. Anti-serotonin drugs have been suggested to attenuate this complication[2]. We sought to determine whether prophylactically administered intravenous ondansetron, could attenuate hypotension in patients undergoing elective cesarean section performed under spinal anesthesia.

METHODS: Eighty-five patients undergoing elective cesarean section were recruited and randomly allocated to receive either 8 mg intravenous ondansetron (group A; N=44) or placebo (group B; N=41) in a prospective double blind design. Systolic blood pressure (SBP), mean arterial pressure (MAP), diastolic blood pressure (DBP) pressure and heart rate (HR) were measured at baseline and at 2-minute intervals after study drug injection until delivery and every 3 to 5 minutes thereafter. We defined hypotension as a 20% decrease from baseline. Differences in blood pressure and heart rate, the number episodes of hypotension, and phenylephrine consumption were analyzed.

RESULTS: We did not find a difference in the blood pressure (SBP, MAP, or DBP) (Figure 1) or HR between the groups. We also did not find a difference in the incidence of hypotension or bradycardia, nor in the amount of phynelephrine consumed (p = 0.48). The incidence of pruritus was similar (p = 0.67), and no difference in sensory or motor blockade was observed (p = 0.87, and 0.64).

CONCLUSION: Ondansetron premedication does not attenuate the blood pressure drop after subarachnoid anesthesia, the number of hypotension or bradycardia events, or the incidence of pruritus in parturients that underwent cesarean section under spinal anesthesia.

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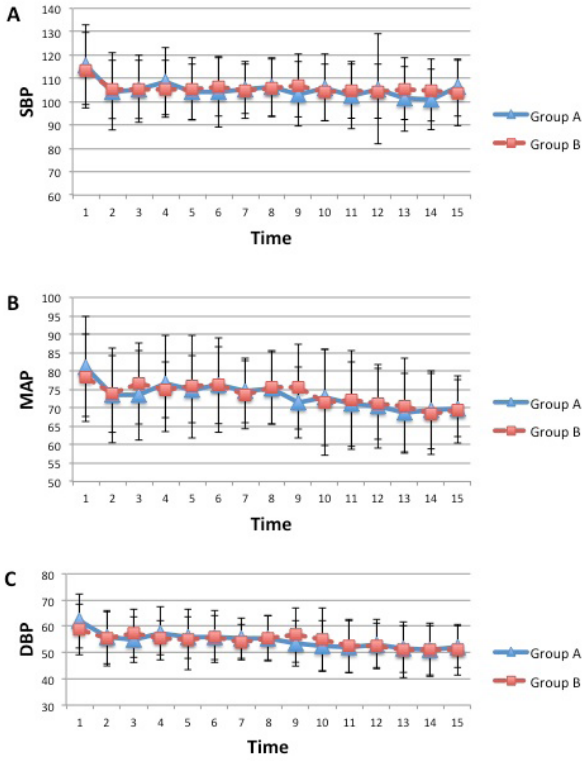
Figure 1: (A) Systolic blood pressure (SBP), (B) Mean arterial pressure (MAP), and (C) Diastolic blood pressure (DBP). No significant blood pressure differences were found between the two treatment groups.



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Pain Mechanisms

S-195.

THE THERAPEUTIC EFFECTS OF GABAPENTIN ON THE NEUROPATHIC PAIN AND ITS POSSIBLE MECHANISMS IN BILATERAL CCI RATS.

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AFFILIATION: Anesthesiology, Peking Union Medical College Hospital, Beijing, China

INTRODUCTION: The incidence of neuropathic pain in the general population exceeded 5%, has became one major problem of the global public health. However, effective management is still insufficient due to the complicated mechanism. In our previous study, we have found that miR-203 expression was significantly decreased in spinal dorsal horn of neuropathic pain rats. We also found protein phosphatese1, catalytic subunit, beta isozyme(PPP1CB) and other protein expression changed by the use of proteomics screening. As a neurological function related protein catalytic subunit, PPP1CB may play a role in neuropathic pain mechanisms.

OBJECT: In this study, bilateral chronic constrictive injury was used as a model and gabapentin as a treatment measure. This study aimed to clarify the effect of gabapentin on bCCI rats' behavior, as well as on PPP1CB expression in spinal cord dorsal horn and its relationship with miR-203.

METHOD: 48 female Sprague-Dawley rats(180-200g) were randomly divided into 4 groups: 1) Naïve(N=12); 2)SHAM (N=12); the bilateral sciatic nerves were exposed but not ligated, 3) bCCI (N=12); establish the bilateral constrictive injury model of rat, 4) bCCI+GBP (N=12); 100mg/Kg gabapentin were injected 15min before, 7 days after operation for 7 consecutive days, bid, ip. Series of tests were carried out including weight, MWT, heat hyperalgesia and cold allodynia. All rats were sacrificed at POD14. Spinal dorsal horn(L4-L6) were assayed for Real-time PCR, Western-blot to detect mRNA and protein level change and bioinformatics analysis was also involved.

RESULTS: 1. Body weight, MWT, heat hyperalgesia and cold allodynia of the bCCI neuropathic pain rats were decreased compared to Naïve and SHAM rats. However, MWT and heat hyperalgesia of the neuropathic pain rats were changed after gabapentin intervention, while body weight and cold allodynia were not.2. In the bCCI model, the PPP1CB protein expression level of spinal cord dorsal horn (L4-L6) significantly increased approximately 2-fold compared with normal control and sham group, while PPP1CB mRNA expression level was significantly decreased by about 0.8 times or so. After gabapentin intervention, PPP1CB protein level was changed while PPP1CB mRNA expression was back to normal compaired to bCCI+NS group.3. Verified PPP1CB is one of the target genes of miR-203 by using bioinformatics tools. This may explain the differential expression of PPP1CB in the spinal dorsal horn may be due to the negative regulatory role of miR-203, i.e. reduced expression level of miR-203 may result in increased expression level of PPP1CB.

CONCLUSION: 1. Gabapentin is able to relieve thermal and mechanical hyperalgesia of neuropathic pain rat, but not conducive to the cold allodynia or weight regain.2. Gabapentin is able to change the spinal dorsal horn expression level of PPP1CB protein and mRNA of the neuropathic pain rat.3. The increase expression of PPP1CB protein in the spinal dorsal horn may play a role in the mechanism of neuropathic pain, and might be regulated by miR-203.

S-196.

WITHDRAWN.

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S-197.

LOW-DOSE KETAMINE INFUSION REDUCES POSTOPERATIVE HYDROMORPHONE REQUIREMENTS AND PAIN SCORES IN OPIOID-TOLERANT PATIENTS AFTER SPINAL FUSION

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AFFILIATION: [1]Anesthesiology, NYU-HJD, New York, NY, [2]Anesthesiology, NYU Langone Medical Center, New York, NY, [3]NYU School of Medicine, New York, NY

INTRODUCTION: Patients presenting for major spine surgery are often tolerant to opioids, which makes controlling postoperative pain challenging. This has led to a search for adjuvant medications to reverse opioid tolerance, reducing postoperative opioid requirements and opioid-mediated side effects[1,2,3]. Mu opioid receptor activation by morphine has been implicated in the development of opioid tolerance via an increase in glutamate synaptic effect at NMDA receptors[4]. These receptors are also involved in central pain sensitization via a wind-up phenomenon and altered pain memory, a process that can be blocked by ketamine, a noncompetitive antagonist[5].

Our hypothesis was that ketamine would be of particular benefit in opioid tolerant patients because of NMDA antagonism and would allow decreasing opioid requirements without compromising the quality of pain control.

MATERIAL AND METHODS: This is a prospective, randomized, double-blinded, four-arm parallel, single-center study. In this preliminary report, we included 44 patients undergoing lumbar spinal fusion surgery. They were assigned either to the opioid tolerant (daily strong opioid medication during the two weeks preceding the surgery) or the opioid naïve group. Each group was then randomized to either ketamine or placebo infusion. The appropriate infusion and an IV PCA using hydromorphone were started immediately on arrival to the PACU. Ketamine was administered as an initial bolus of 0.2 mg/kg followed by a fixed-rate infusion of 0.12 mg/kg/hr for 24 hours. Numeric pain scales were recorded at arrival in PACU, then every 30 min during the first 2 hours, and then every 2 hours on the floor during the first 24 hours after surgery. Hydromorphone use via PCA and pain scores during the first 24 hours were recorded.

RESULTS: The hydromorphone requirements in the placebo/tolerant group were significantly higher than in the ketamine/tolerant group (p=0.016). Opioid requirements were not significantly different between the groups receiving ketamine regardless of opioid tolerance (p=0.746).

Pain scores over 4 ranges values were averaged and indexed by the middle of the range. The last two pain scores were combined as the equilibrated pain score. Using rank analysis enabled us to reject (p=0.028) the null hypothesis that all 4 groups had equal equilibrated pain scores and then show that ketamine was significant in modulating pain scores in the tolerant patients (p=0.021; rank comparison of opioid tolerant for placebo vs. ketamine).

CONCLUSIONS: Low-dose ketamine infusion is a useful adjunct to improve pain control and reduce opioid requirements in opioid-tolerant patients undergoing major spine surgery. It does not benefit opioid-naïve patients.

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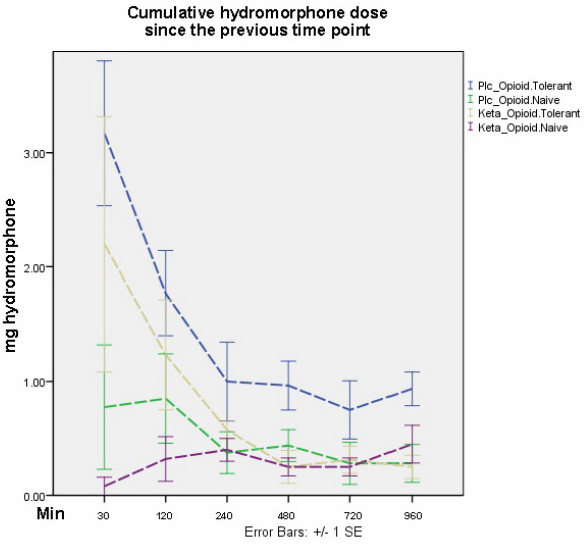

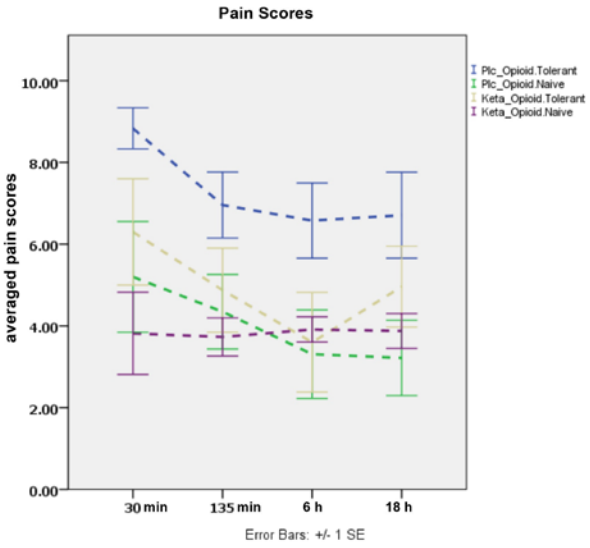

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S-198.

THE DYNAMIC PROGRESSION OF DIABETIC NEUROPATHY IN THE PERIPHERAL SENSORY LEVEL IN THE TYPE 1 DIABETIC MOUSE MODEL

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INTRODUCTION: Diabetic neuropathy (DN) is a secondary consequence of longstanding diabetes mellitus (DM). The progression of DN may represent a window through which the level of nerve injury can be diagnosed and the mechanisms of therapy can be understood. This study was designed to investigate the course of diabetes-induced abnormal sensation in a Type 1 diabetes mouse model. The involvement of toll like receptor 4 (TLR4) expression and dynamic neuropeptide calcitonin gene related peptide (CGRP) expression in dorsal root ganglia (DRG) and dorsal horn of spinal cord were investigated as was the function of the anti-oxidant Coenzyme Q10 (CoQ10).

METHODS: DM was induced in mice through the use of streptozotocin (STZ). Mechanical and thermal nociceptive behavioral assays were applied to evaluate diabetic neuropathic behavior. DRG and spinal cord tissue immunocytochemistry and reverse transcription and polymerase chain reaction (RT-PCR) were used to evaluate the molecular mechanisms that are responsible for the progression of DN.

RESULTS: DM mice developed both mechanical and thermal hypersensitivities 2-4 weeks post-DM. However, thermal sensitivity returned to a non-sensitive level 6 weeks post-DM, after which the mice gradually developed thermal hypoalgesia in the late stages of DM (from 10 weeks post-DM to 24 weeks post-DM). Mechanical allodynia remained for a longer period, from 2 weeks to 10 weeks post-DM, however, the mice eventually developed mechanical hypoalgesia in the late stages of DM (at 16 to 24 weeks of post-DM) (Figure 1). CGRP expression levels in DRG and the dorsal horn of the spinal cord corresponded to a transient increase 3 weeks post-DM, followed by a significant decrease in the last stages of DM (Figure 2). TLR4 expression increased in DRG -neurons and satellite cells, and dorsal horn of spinal cord post-DM -co-localized with microglia and astrocytes in the spinal cord in the early stage of DM. RT-PCR results indicated that CGRP and TLR4 both increased in the early stage of DM, but decreased in the later stage of DM. CoQ10 levels in DRG decreased gradually after DM.

CONCLUSIONS: Our results demonstrate that hyperglycemia-induced diabetic neuropathic behavior includes early-stage hypersensitivity and late-stage hyposensitivity. CGRP and TLR4 pathway may play a role in early-stage diabetic neuropathic pain. The molecular abnormalities underlying the degeneration of diabetic-induced neuropathy include coenzyme Q10 deficiency in the neurons.

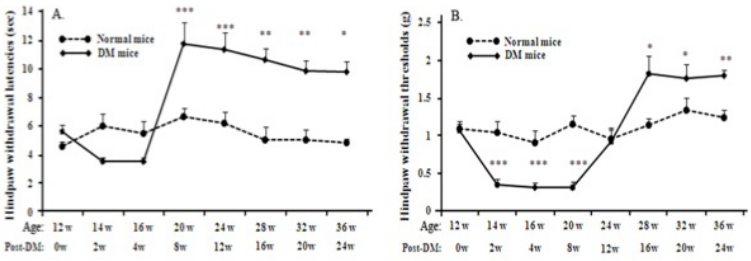

Figure 1. The progression of diabetic neuropathic behavior. Figure 1A, the thermal sensory test indicates that thermal hyperalgesia only appeared for a short time, Figure 1B, the mechanical sensory test reveals that DM induces significant mechanical hypersensitivity; but thermal and mechanical hyposensitivity developed gradually in the later stages of DM. The symbol * or ** indicates $p<0.05$ or $p<0.01$, comparing DM mice with age-matched normal controls.

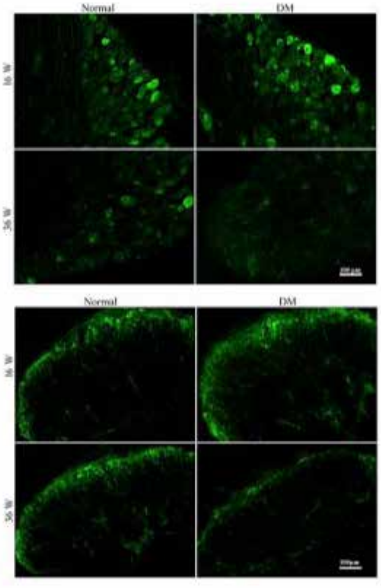

Figure 2. Immunohistological staining of CGRP in DRG and the spinal cord dorsal horn. The CGRP-positive neurons in DRG and the expression level in the dorsal horn of the spinal cord increased 4 weeks post-DM and then decreased significantly in the later stages of DM (36 weeks post-DM). Bar=100 μm.

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S-198 • continued

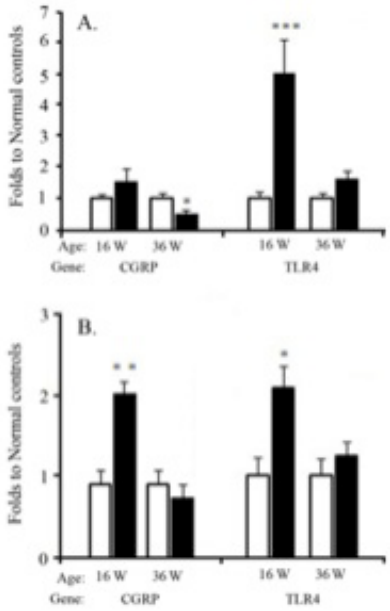

Figure 3. CGRP and TLR mRNA expression in DRG and spinal cord. Tissue from normal and DM mice with 4 (age 16 weeks) or 24 weeks (age 36 weeks) post-DM. Figure 3A shows in DRG; Figure 3B shows in spinal cord tissue. The symbol * or ** denotes $P <$ 0.05 or $P < 0.01$ compared to corresponding samples of normal controls.

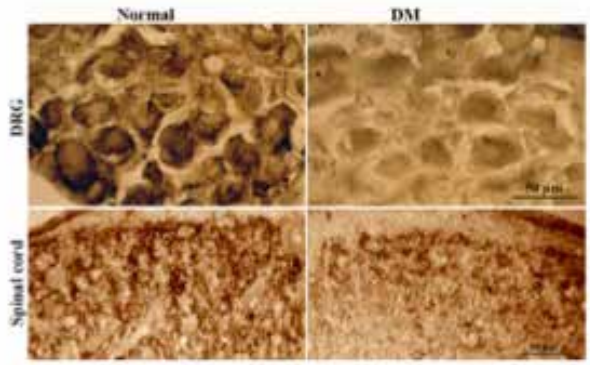

Figure 4. CoQ10 immunohistological staining in DRG and spinal cord. Images showed that CoQ10 staining intensity decreased after DM. DM tissue were from 24 weeks post-DM. Control tissue were from age-matched normal animals.

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S-199.

COMPUTATIONAL ANALYSIS OF THE PF2-LIKE DOMAIN OF WNK4

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BACKGROUND: The Na(+)-K(+)-2Cl(-) cotransporter NKCC1 is expressed in sensory neurons where it accumulates intracellular Cl(-) and facilitates primary afferent depolarization[1]. WNK4 regulates the activity of NKCC1 through the phosphorylation of key residues within SPAK/OSR1 leading to kinase activation[2]. This ultimately results in phosphorylation and stimulation of NKCC1 activity[2]. In this study, we computationally show that WNK4 possesses a domain (PF2-like) whose structure resembles the NKCC1 binding domain of SPAK and OSR1 (PF2), possibly leading to direct binding and activation of NKCC1.

METHODS: The primary sequence of the PF2-like domain of WNK4 was aligned with the PF2 domain of OSR1 and then threaded over a template based on the crystal structure of the PF2 domain of OSR1 (2v3s) utilizing a python script supplied in the Rosetta software suite[3,4]. After creation of the appropriate files, 10,000 comparative models of the PF2-like domain were generated using the Rosetta loop modeling modality. The top 500 scoring models were then clustered based on root-mean-square deviation to 2.0 Å and the top ten comparative models based on Rosetta energy and clustering were selected for peptide docking. For each of the models, the Gly-Arg-Phe-Gln-Val-Thr hexapeptide of 2v3s was manually placed into the PF2-like domain that corresponded to the CCT binding pocket of OSR1 using PyMOL. The peptide was then docked into the binding pocket through the use of the FlexPepDock application of Rosetta and a Rosetta binding energy (ddG) was calculated. Lastly, the Gly-Arg-Phe-Gln-Val-Thr hexapeptide was also computationally docked using FlexPepDock as previously stated into the crystal structure of the PF2 domain of OSR1 in order to determine relative energies.

RESULTS: Through the use of various modalities of the Rosetta modeling suite, it was shown that only a room-mean-square deviation (RMSD) of 0.603 Å separated the three-dimensional conformation of the binding pockets of the two domains (PF2 and PF2-like). The hexapeptide interacted with the PF2-like domain with slightly less affinity (more positive ddG) compared to the native CCT domain (Table 1). However, the individual binding energies of the RFxV portion of the two motifs were extremely similar, varying from one another by less than 0.03 Rosetta energy units.

CONCLUSIONS: In previous experiments, we noticed sequence homology between 58 residues of the CCT/PF2 domain in SPAK/OSR1 and a region of WNK4, which is located downstream of the catalytic domain. Rosetta modeling revealed structural homology between this WNK4 domain and the hydrophobic pocket of the CCT/PF2 domain. In addition, the docking portion of this analysis indicates that the RFxV peptide is highly likely to bind to this region of WNK4. Due to these preliminary results, we are continuing to examine the possibility that WNK4 directly interacts and activates NKCC1 through the use of Xenopus laevis oocytes.

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Table 1. Binding energies (ddGs) of CCT and CCT-like domains.

	Hexamer(or Total)	Glycine(-1)	Arginine(+1)	Phenylalanine(+2)	Glutamine(+3)	Valine(+4)	Threonine(+5)
PF2 (OSR1)	-17.59	0.002	-1.504	-2.356	-2.553	-0.831	-0.523
PF2-like (WNK4)	-16.62	-0.01	-1.765	-2.323	-2.288	-0.895	-0.461

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S-200.

LONG-LASTING SCIATIC NERVE BLOCK REDUCES ACUTE HYPERALGESIA, NEURONAL HYPEREXCITABILITY AND OPPOSES PAIN VULNERABILITY DEVELOPMENT AFTER SURGERY IN RATS

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INTRODUCTION: Long-lasting regional anesthesia (RA) has been shown to better reduce pain vulnerability long-term after surgery[1].The present study aims at evaluating the effect of RA based on long-lasting bupivacaine administration on hyperalgesia and neuronal excitability occurring one day after the initial ipsilateral surgery (POD1), and on central sensitization after a contralateral surgery 15 days (POD15) after the first one.

MATERIAL AND METHODS: All Plantar Incisions[2] (PI) were performed under general anesthesia (isoflurane) +/- Sciatic Nerve Block (SNB) on D0 (left hind paw, also called ipsilateral PI) and on POD15 only under isoflurane (right hind paw, also called contralateral PI). Three groups of rats were included: G0: ipsilateral SNB with single shot salin prior to PI on D0; G1: ipsilateral SNB with single shot 0.375% bupivacaine prior to PI on D0; G3: ipsilateral SNB with several shots of 0.375% bupivacaine prior to PI on D0 and every 4hs until H20 after PI. Rats' nociceptive threshold was evaluated with mechanical stimulation (g) (Randall Selitto) every 4 hours the days of surgery and once daily for the other days until POD26. The variation of nociceptive threshold after the second surgery performed at POD15 evaluated the development of long-term pain vulnerability after the first surgery done at D0[3]. In each group, 5 more rats were exposed to the same protocol, but on POD1 after PI in vivo electrophysiology recording of dorsal horn Wide Dynamic Range Neurons (WDR) coming from the surgical area was performed to assess the effect of the 3 different regimen of SNB on the development of central sensitization and neuronal excitability.

RESULTS: On D0, hyperalgesia occurred right after awakening from anesthesia for G0 rats (salin group). The SNB-induced analgesia lasted 4hs in G1 and 20hs in G2 before hyperalgesia occured. Area under the curve (AUC) of hyperalgesia after D0 was significantly reduced ($p < 0.05$) in G2 compared to both G1 and G0. After the second and contralateral PI done on POD15, AUC of hyperalgesia was drastically decreased ($p < 0.05$) in G2 versus both G0 and G1. G1 did not differ from the control group (G0) after POD15. In vivo electrophysiological recording showed on POD1 that rats protected by a long-lasting SNB (G2) had very small excitability of WDR neurons in their dorsal horns (p 0.05 for comparison between G0 and G1). Hyperexcitability of WDR neurons assessed by post-discharges of these WDRs after 300g stimulus next to the surgical area reported a significant difference between G2 and both G0 and G1 ($p < 0.05$). Again, G0 and G1 did not differ in terms of WDRs post-discharges on POD1 ($p > 0.05$).

CONCLUSION: Single shot SNB does not protect against the development of acute hyperalgesia and WDRs hyperexcitability one day after surgery, nor does it prevent well the development of long-term central sensitization and vulnerability to a new painful stimulus. A long-lasting regional anesthesia around the first surgical event allows for a better protection against postoperative pain sensitization.

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S-201.

OPIOID SIGNALING IN MOUSE GLIAL CELLS: IMPLICATIONS FOR OPIOID ANALGESIA AND TOLERANCE

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INTRODUCTION: Chronic pain is a widespread disease that anesthesiologists are uniquely positioned to treat. Opioids are the mainstay of therapy for persistent pain states; however, their use is fraught with side effects. While aberrant neuronal signaling is the ultimate cause of pain, CNS glial cells (astrocytes and microglia) are now known to actively modulate neurotransmission. It has previously been shown that morphine treatment induces glial activation, which might contribute to opioid tolerance. The expression of all three opioid receptors (mu, delta and kappa) by glia has been shown in in vitro studies, but data from in vivo studies is lacking. The goal of this work was therefore twofold:(1) To determine if spinal cord astrocytes and microglia express opioid receptors and (2) To determine if the mu opioid receptor (MOR) is required for glial cell activation in opioid tolerance.

METHODS: All studies were performed in mice in accordance with policies set forth by the Stanford University IACUC. For the first part of the study, we took advantage of mice expressing the delta opioid receptor (DOR) as a fusion protein coupled to the reporter green fluorescent protein, to visualize the delta opioid receptor (DOR-eGFP). Mice were deeply anesthetized, transcardially perfused and spinal cord tissue was removed and stained for neuronal markers (NeuN), microglial markers (Iba1, CD11b) and/or astrocyte markers (GLT1, GFAP). Confocal images were acquired using the Leica TCS SPE microscope. For the second part of the study, MOR knockout mice (Oprm1 -/-) and littermate controls (Oprm1 +/+), were treated twice daily with morphine 10 mg/kg subcutaneously for 5 days. Measuring the tail flick latency after morphine treatment monitored the development of analgesic tolerance. Spinal cord tissue was then collected as described above to assess for changes in glial markers.

RESULTS: (1) Using DOR-eGFP reporter mice, we found that the vast majority of spinal cord cells that were DOR-eGFP positive co-expressed the neuronal marker, NeuN. In contrast, there was no overlap between DOR-eGFP and the astrocyte marker, GLT1, which labels the entire cell body, or GFAP, which labels the astrocyte cytoskeleton. In addition, we did not observe any co-localization of DOR-eGFP with the microglial markers Iba1 or CD11b. (2) As expected, Oprm1 -/- mice did not exhibit any analgesic effect of morphine. In contrast, Oprm1 +/+ littermate controls demonstrated an increased tail flick latency, which decreased as tolerance developed. Chronic morphine treatment changed the morphology of microglia and astrocyte towards an activated state in Oprm1 +/+ mice and is currently being assessed in Oprm1 -/- mice.

CONCLUSIONS: Our preliminary results suggest that glial cells in vivo do not express the DOR, with similar studies underway for the mu and kappa opioid receptors. In addition, we confirm that morphine tolerance leads to glial activation, which may be MOR-dependent. Our ongoing work will answer the fundamental question of whether it is the direct activation of glial opioid receptors that generates opioid tolerance, which may lead to novel therapies to treat persistent pain.

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S-202.

THE POSTERIOR INSULA REVEALS PAIN VS REST FUNCTIONAL CONNECTIVITY DIFFERENCES NOT PRESENT WITH THE ANTERIOR INSULA

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AFFILIATION:[1]Department of Anesthesiology, University of Pittsburgh Medical Center, Pittsburgh, PA, [2]Pittsburgh Center for Pain Research, University of Pittsburgh, Pittsburgh, PA

INTRODUCTION: Multiple studies across imaging modalities suggest the insula has a key role in pain processing[1]. Recent work using functional connectivity MRI (fcMRI) during painful and innocuous thermal stimulation demonstrated anatomically different connectivity: the anterior insula (aIns) was more strongly correlated to the anterior cingulate cortex (ACC), while the posterior insula (pIns) better correlated to the primary somatosensory (S1) and motor (M1) cortices[2]. Our prior work on optimizing the fcMRI analysis methodology showed increased connectivity of the pIns to the ACC during pain versus rest3. This present study compares resting fcMRI maps to those during painful electric nerve stimulation (ENS), examining both correlations and anti-correlations to seed regions in the contralateral aIns and pIns. We hypothesized that insula-ACC connectivity would increase during pain processing, with an even greater change seen in the aIns compared to the pIns results presented previously.

METHODS: 3 T BOLD data was acquired in 14 healthy adults during REST and while painful ENS (PAIN), self-rated at 7/10, was delivered to the right index finger. Seed time courses for the contralateral aIns and pIns were extracted from the anatomic locations shown in Fig. 1, and functional connectivity was determined for both seed regions in both data sets using FSL 5.0. An optimized analysis pipeline was used3, including low pass filtering, spatial smoothing, and regression of the global signal, motion correction parameters, and the pain stimulation model as effects of no interest. Group average and PAIN vs. REST difference maps were generated with cluster thresholds of $Z > 4$ and $p < 0.0001$.

RESULTS: Group average functional connectivity (Fig. 2) between the aIns and ACC was present in REST and PAIN, while only present for the pIns and ACC in REST. Both aIns and pIns were positively correlated to the ipsilateral insula and to S1 and M1 bilaterally in both PAIN and REST. Notably the difference maps (Fig. 3) show almost no statistically significant PAIN versus REST differences in aIns connectivity. In contrast, the pIns showed stronger correlation to the ACC in REST compared to PAIN. Further, the pIns shows strong anti-correlation to the posterior cingulate cortex during REST, making the PAIN>REST difference significant.

CONCLUSIONS: Our results clearly demonstrate the impact that the selection of seed region can have on functional connectivity maps. Our data suggests that aIns connectivity is similar between PAIN and REST. In contrast, the pIns had more dynamic changes in connectivity with PAIN as evidenced by multiple areas of significance in the PAIN vs. REST difference maps; most notably the ACC, which may provide a means of differentiating between the two states.

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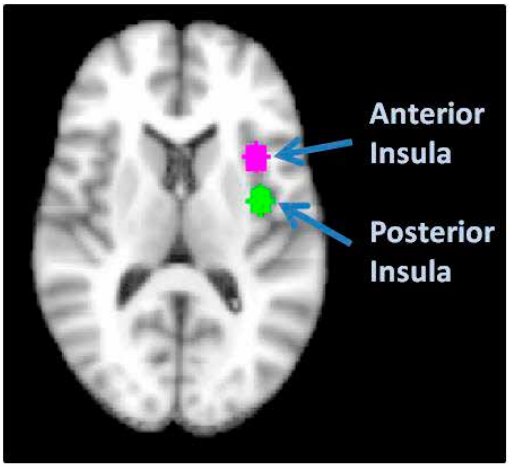

Fig 1. Oblique slice through the insula showing the locations for the functional connectivity analysis.

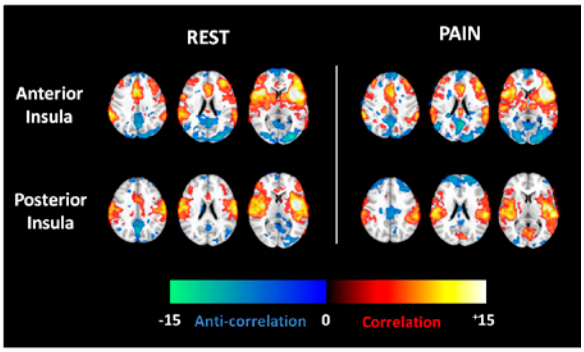

Fig 2. Group average functional connectivity maps with color bar showing Z-score of significant correlations to the left insula seed regions.

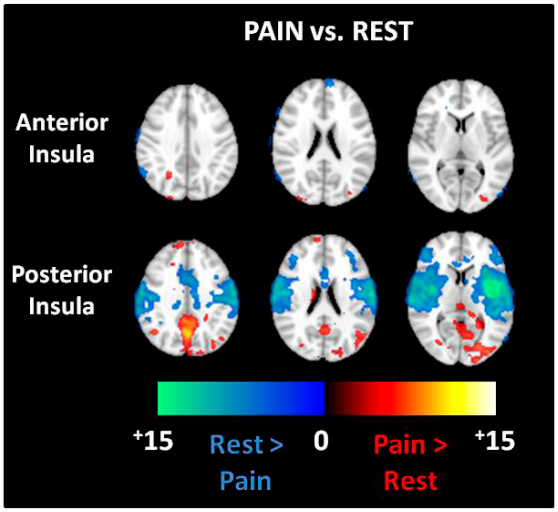

Fig 3. Maps of significant connectivity differences for the Pain > Rest (red-yellow) and Rest > Pain (blue-green) comparisons, with Z-scores as shown on the two color bars.

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Pain Medicine

S-203.

MULTIMODAL ANALGESIA WITH LIDOCAINE FOR ACUTE PAIN- A RETROSPECTIVE STUDY

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INTRODUCTION: Lidocaine is an amide local anesthetic with a significant analgesic, anti-hyperalgesic and anti-inflammatory properties when used intravenously. In 2009, the Acute Pain Service of a tertiary level university hospital implemented a protocol for the use of lidocaine infusions for perioperative pain management. The aim of this study was to review this use of intravenous lidocaine over a three year period.

METHODS: After approval from Research and Ethics Board, this retrospective study was completed. A list of patients for whom lidocaine was dispensed from the pharmacy was obtained from September 2009 to August 2012. This inpatient study included only those patients who received lidocaine infusion for pain. Patients receiving lidocaine only as a bolus, for other indications and in the ICU while on ventilatory or inotropic support were excluded. The data from anesthesia charts, acute pain service order sheets, pain assessments and acute pain medications administration records were reviewed. Indications, demographics, impact and side- effects for the patients receiving lidocaine were collected.

RESULTS: In the study period, 169 patients were identified as having received lidocaine. After exclusions, 102 patients were included in this study. The patients were 52% male with mean age 53 years (±36). The mean weight was 75 kg (range 40-80 kg) .The indications for intravenous lidocaine were laparotomy (49%),spine surgery (16.7%), polytrauma (12.7%), amputations (6.9%), hysterectomy (5.9%), orthopedics (3.4%) and others (4.9%). History of chronic pain was present in 50%, while only 35.3% of whole patients were chronic opioid users. Bolus dose was used 95% of our patients, with a mean dose of 1.34 mg/Kg (range 0.75- 2.5). The infusion dose was ranging between 0.5-2 mg/kg/hour. Lidocaine infusion was started as a part of intraoperative care and continued postoperatively in 61 patients (60%). Regarding the other 41 patients (40%), it was started as adjuvant after failure of the initial plan in controlling pain. Table 1 is showing the duration of lidocaine infusion. Mild side effects and/or signs of toxicity were reported in 10 patients (9.8%) and the infusion was stopped for 8 of them. No serious side effects or toxicity was reported.

DISCUSSION: This quality assurance study reports the safety and efficacy of intravenous lidocaine by an Acute Pain Service. The use of lidocaine for acute pain outside the anesthesia and critical care environment has not been previously reported and requires further investigation.

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S-204.

INTRATHECAL MULTIDRUG INFUSION FOR PAIN CONTROL IN ELDERLY PATIENTS AND END-STAGE MALIGNANCIES- 3 CASE REPORT SERIE

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INTRODUCTION: Achieving effective, durable, and safe pain relief, especially in old age patients and end stage malignancies, can be a clinical challenge[1]. We present an alternative method, based on time-limited intrathecal infusion of an analgesic mixture.

METHOD: Three old patients (64-94 y/o), admitted in hospital for intractable pain due to metastatic malignancy or fracture, became candidate. An intrathecal catheter 20G was placed by percutaneous approach while tunneled subcutaneously and fixed to skin. A preservative-free mixture of bupivacaine 1mg/ml, naloxone 0.02 ng/ml, ketamine 100 microg/ml, morphine 0.01 mg/ml and clonidine 0.75 microgram/ml was infused by an external pomp with a rate of 1-2 ml/h that was decreased during the following days due to patients' requirement. Mixture stability was assessed during five days and still continues(Fig-1).

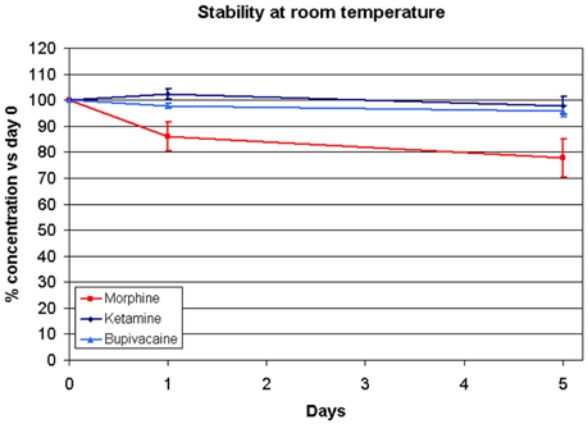
RESULTS: In all patients, pain was successfully controlled without any major complication such as lower limb muscles weakness, sphincter dysfunction, constipation and cognitive or mood dysfunction. In two patients, catheter was removed after four weeks before leaving hospital. (In one of them, catheter was infected on the fourth week following an urinary infection so it was removed. Infection was treated and cured completely. In the second patient, it was removed following complete pain control). The third one with cancer still benefices from the treatment after six months at home.

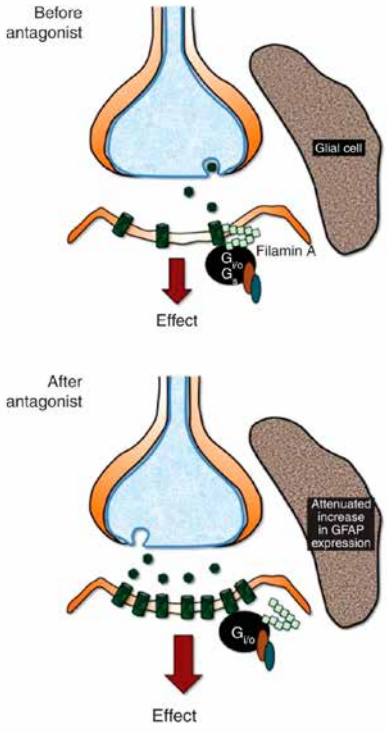
DISCUSSION: The evidences show better result for intrathecal approach in comparison to epidural (2B+ and 2C+ respectively[2]. Morphine, clonidine and bupivacaine have been widely used by intrathecal way[3]. Naloxone in ultra low-dose helps controlling pain and prevents from hyperalgesia by multiple mechanisms[4,5](Fig-2). Ketamine has an analgesic and anti-hyperalgesic effects via NDMA receptors. It could be used as intrathecal approach in end-stage cancer related pain. But the main concern is possible neurotoxic effect on long term intrathecal use (even with preservative-free S(+)). In an animal study, intrarhecal injection of a large dose of 1mg/kg in dogs had no histological effect[6]. Besides, our doses are much less than what have been already recommended[3] (Table-1). Regarding to very low concentration of drugs, absorption and systemic effect could not explain analgesic effect of the mixture. Synergic effect and different mechanisms of action by spreading in cerebrospinal fluid could explain sufficient analgesic effect of the mixture. The other advantage of our mixture is lower risk of neurotoxicity.

CONCLUSION: Infusion of multiple drugs in a mixture lets to control perfectly the pain, and decreases the needed dose of everyone, so, the possibility of systemic side effects. We succeeded to control severe pain with a very low daily intrathecal dose without major complication.

Table 1: Comparison of recommended daily drugs' doses and our doses

Product	Recommended dose3	Our dose
Morphine	1-20mg	0.08-0.25mg
Bupivacaine	4-30 mg	8-24mg
Clonidine	30-1000 micrgram	8-25 microgram
Naloxone	no data available	0.2-0.5 ng
Ketamine	1-50 mg	1-2.5 mg
Naloxone	no data available	0.2-0.5 ng
Ketamine	1-50 mg	1-2.5 mg





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S-205.

IMPROVING THE UTILIZATION OF AN INPATIENT PAIN SERVICE AT A COMMUNITY HOSPITAL

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INTRODUCTION: With the necessity for adequate pain management in inpatients well documented, the creation of an inpatient pain management service is a logical extension to improving care. The institution of such a service is shown to have improved outcomes, provide better pain control and patient satisfaction; a reduction in both cost and length-of-stay has also been suggested. However, the structure of inpatient pain management services varies greatly in different institutions, from a full department with dedicated personnel and structured policies to a single individual with other unrelated clinical responsibilities. In an environment with limited resources, improving utilization of such services can allow for the appropriate allocation of resources to patients with the greatest need.

METHODS: A survey was created to determine what steps were taken by the primary service to address patients' pain prior to a pain management consult. The pain management consultants were asked to complete this survey for all consults and judge the appropriateness of the consult.

RESULTS: 103 surveys were received and analyzed. The data was divided into those deemed appropriate (n=49) and inappropriate (n=52). Within these categories, the remaining questions were analyzed via contingency tables.

Consults were more likely to be deemed appropriate in the following scenarios: acute pain over chronic pain (p=0.01); the patient was started on any pain medication (p=0.027); home pain medications were continued (p=0.001). While not statistically significant, consults communicated physician-to-physician showed a trend toward increased appropriateness (p=0.07). No differences were seen between admitting services, timing of consult or prior work-up.

Of 52 consults deemed inappropriate, the most common reason was "Straightforward case that primary team should have been able to handle" (27 cases), followed by "Only needed to restart home medications" (18).

CONCLUSIONS: The results of this study indicate there is significant difference of perception between members of the admitting team and those on the pain service as to what criteria warrant an inpatient consultation. To encourage efficient utilization of the pain service, we suggest that the following criteria be met prior to obtaining a consult: ensure that the patient is experiencing an acute change in their pain, restart/continue all home pain medications and order additional pain medications to address the patient's pain. If these measures are inadequate, a consultation may be indicated. Additionally, it is preferable that the consult be communicated physician-to-physician, providing a higher quality of care.

The limitation of this study is the data is self-reported; consults perceived negatively are more likely to be reported than those deemed appropriate. Additionally, this study suggests what problems exist; however, it does not explore why these obstacles exist. Further areas of study may include evaluation of the opinions and attitudes of primary services on their knowledge and comfort in approaching and managing pain.

S-206.

PERIOPERATIVE DEXAMETHASONE AND THE DEVELOPMENT OF CHRONIC POST-MASTECTOMY PAIN: A PROPENSITY MATCHED ANALYSIS

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AFFILIATION: Anesthesiology, Northwestern University, Chicago, IL

INTRODUCTION: Chronic pain after breast cancer surgery can occur in approximately forty percent of patients but effective strategies to prevent its development are largely understudied. Perioperative modulation of surgical inflammatory response has been repeatedly hypothesized as a viable pharmacological preventive target. The main objective of the current investigation was to evaluate an association between the use of a potent anti-inflammatory drug (dexamethasone) and the development of chronic pain after mastectomy.

METHODS: The study was a retrospective cohort investigation. Subjects who have undergone mastectomy surgery were evaluated at least 3 months after the surgical procedure for the presence of chronic post-surgical pain using validated pain questionnaires. Propensity matched analyses to control for confounding covariates were performed in subjects who received and did not receive perioperative dexamethasone.

RESULTS: 310 patients were included in the study. 132 patients (43%) reported the presence of chronic pain in the breast and/or axillary region. 211 out of 310 (68%) subjects received perioperative dexamethasone on doses varying from 4-10 mg. After propensity matching, the incidence of chronic pain in the mastectomy group who received perioperative dexamethasone was not different, 33 out 87 (38%) compared to 41 out 87 (41%) in the group who did not receive perioperative dexamethasone, P= 0.76. Pain intensity was also similar between the groups.

CONCLUSIONS: Perioperative dexamethasone is not associated with a reduction in the incidence and/or severity of chronic post-mastectomy pain. Our results do not support the current concept that short perioperative interventions are effective to prevent chronic postsurgical pain.

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S-207.

WITHDRAWN.

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S-208.

EFFECT OF INTRAVENOUS LIDOCAINE ON POSTOPERATIVE RECOVERY IN PATIENTS UNDERGOING BREAST SURGERY: A DOUBLE-BLINDED, PLACEBO RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Pain after breast surgery is usually treated with narcotics; however, these are associated with a high incidence of side effects such as itching, nausea and vomiting (PONV), constipation, urinary retention and dizziness[1]. Intravenous lidocaine has been shown to reduce opioid consumption and improve postoperative outcomes overall in abdominal surgery[2]. In this study, we tested the effect of intraoperative intravenous lidocaine infusion on the quality of postoperative recovery after breast surgery.

METHODS: Seventy-one patients undergoing breast surgery were randomly allocated to receive either placebo (Group A; n=34) or intracenous lidocaine (Group B; n=37, bolus 1.5 mg/kg at induction, then infusion at 2 mg/kg/hr, stopped at procedure end) in a prospective double blind design. Intraoperative and postoperative morphine consumption was calculated. Postoperative pain scores, PONV, as well as fatigue were assessed at 2, 24 and 48 hours after surgery. Duration of postoperative hospital stay was recorded.

RESULTS: Demographics were the same between the groups. There was no difference in intraoperative or postoperative (Figure 1) morphine consumption (p= 0.188, and p=0.758), pain scores either at rest or activity (p=0.348, and p= 0.810, respectively), PONV (p=0.350) and fatigue (p=0.758). Discharge times were similar (p=0.218).

CONCLUSION: Our findings did not show a significant effect of intravenous lidocaine during breast surgery on opioid consumption, pain score, PONV or fatigue, indicating that benefit of this approach is not seen after all types of surgery.

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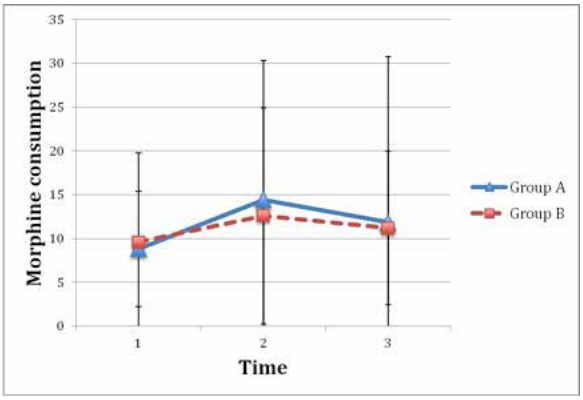
Figure 1: Postoperative morphine consumption



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S-209.

HUMAN FACTORS RESULTS FOR IONSYS (FENTANYL TRANSDERMAL SYSTEM) FOR POSTOPERATIVE PAIN MANAGEMENT

AUTHORS: H. Minkowitz[1], N. Joshi[2], B. Phipps[3], S. B. Wilcox[4], P. Sneeringer[4]

AFFILIATION: [1]Anesthesiology, Memorial Hermann Memorial City Hospital, Bellaire, TX, [2]Global Product Development, The Medicines Company, Redwood City, CA, [3]Chief Science Officer, The Medicines Company, Redwood City, CA, [4]Consultant, Design Science Consulting, Inc., Philadelphia, PA

INTRODUCTION: IONSYS is a convenient means to deliver patient-controlled analgesia for management of acute post-operative pain. The system is applied by a nurse to the arm or chest and fentanyl is delivered through the skin when the patient presses a button on the device. Usability of the system was tested in 2 studies with patients, nurses, & pharmacists.

MATERIALS AND METHODS: The product design (Figures 1 & 2), in particular the user interface, was refined based on findings from formative studies conducted during device development. Two simulated-use studies were completed with the product to validate usability. In the 1st study, 30 adult patients undergoing treatment for post-operative pain were randomized to receive placebo IONSYS on their arm or chest. The ability of patients to administer treatment and respond appropriately to various system alerts was evaluated. The 2nd study with 31 pharmacists & nurses evaluated the participants' ability to assemble and apply IONSYS to a mannequin; comprehend and respond to normal operation and alert states; and remove and dispose of IONSYS.

RESULTS: Patient Study: 30/30 patients were able to successfully administer a simulated treatment using IONSYS. One participant had difficulty pressing the dosing button on the 1st attempt, but was successful in initiating a dose on the next attempt. All participants responded appropriately to a simulated system alert by indicating they would call the nurse. Overall, patients found the system convenient and very easy to use at both application sites. They liked the size and discreteness of the device and the ability to do other necessary activities while wearing the device. Patients made no errors and had no near misses that could lead to potential unsafe situations. Therefore, this study validated that patients were able to easily use IONSYS safely.

Healthcare Professional (HCP) Study: No training was provided to the nurses or pharmacists; however, they had access to the Quick Guide that is provided with IONSYS. A majority of participants were able to assemble IONSYS in less than 1 minute. After assembling and applying to a mannequin, participants were able to correctly determine all operational states (ready state, dosing state, end of use) and comprehend system feedback (light, beeps, display). Though some had minor difficulty comprehending alerts, all participants were able to respond appropriately to system alerts. Many participants noted that IONSYS would become even easier to use upon repeated use. All participants were able to remove IONSYS from the mannequin and properly dispose. Overall, HCPs found IONSYS convenient and very easy to use. They liked the size of the product, benefits of a prefilled and preprogrammed product, and the perceived ease of use by patients. A few noted the fixed dose may be a limitation for use with some patients.

DISCUSSION: Patients, nurses, and pharmacists were able to use IONSYS with ease. There were no errors or near misses that could have led to potential unsafe use.

Figure 1: Illustration of the Controller and Drug Unit of IONSYS

Figure 2: Illustration of IONSYS Use by Patient

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S-210.

EFFICACY OF SPINAL CORD STIMULATION FOR RELIEF OF NON-MALIGNANT CHRONIC PAIN AND THE IMPORTANCE OF PROPER PATIENT SELECTION

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AFFILIATION: Anesthesiology, Advocate Illinois Masonic Medical Center, Chicago, IL

INTRODUCTION: Spinal Cord Stimulator (SCS) technology has improved in recent years and these devices been implanted in increasing numbers of chronic pain patients. A trial period of 5-7 days is commonly recommended by most clinicians before permanently implanting the devices and the decision for permanent SCS is made based on a minimum of 50% improvement during the trial.[1] The importance of patient selection is emphasized by many studies and clinicians to improve outcome and reduce application in non-responders.

METHOD: The aim of this study was to demonstrate the efficacy of SCS in reducing pain and improving quality of life. After obtaining IRB approval, we included all patients that received trial SCS treatment at our hospital between January 2012 and March 2013. Patient selection criteria for SCS treatment were chronic pain with poor response to the conventional treatments for a minimum of six months, low chance of success of any surgery, no malignancy, no active drug abuse and completion of psychological evaluation.[2]

RESULTS: Twenty six patients were eligible for inclusion. Demographic information is shown in the Table-1. 23% of patients were employed, 15% retired and the rest were on disability before SCS treatment. More than 76% of patients had lower extremity pain and 54% of patients had a diagnosis of Failed Back Surgery Syndrome before the SCS trial. Other indications for SCS were Complex Pain Regional Syndrome (27%), Chronic Sacroiliac Pain, and chronic hip pain. Almost all patients had undergone multiple steroid injections, >50% had failed physical therapy and >85% were using opioids prior to the SCS trial.

All patients had a positive response to the trial defined as 50% to 100% improvement in pain (average 78%) during 3 to 9 days of trial (average 6 days). The average NRS pain rating before trial was 7.9/10 and was reduced to 3.0/10 by the end of trial period. All patients proceeded to a permanent SCS implantation.

The average daily pain after receiving permanent SCS decreased from 7.7/10 to 4.0/10 on the NRS. Interference of pain with general daily activity was reduced from 8.2 to 4.9, Sleep difficulties improved from 8.8 to 5.6 and interference with walking reduced from 6.6 to 4.4 on a scale of one-to-ten. (Shown in the Diagram-1)

No meaningful correlation was seen between degree of response and race, age, employment condition or diagnosis before trial SCS. There was no statistically significant difference between results attained using SCS from three different vendors.

CONCLUSION: Results of this retrospective study showed that SCS therapy could be an effective treatment option for many patients with strict selection criteria. Besides the aforementioned recommended indications and benefits for SCS treatment; this treatment is still underutilized and further studies are recommended to measure benefits and possible new indications.

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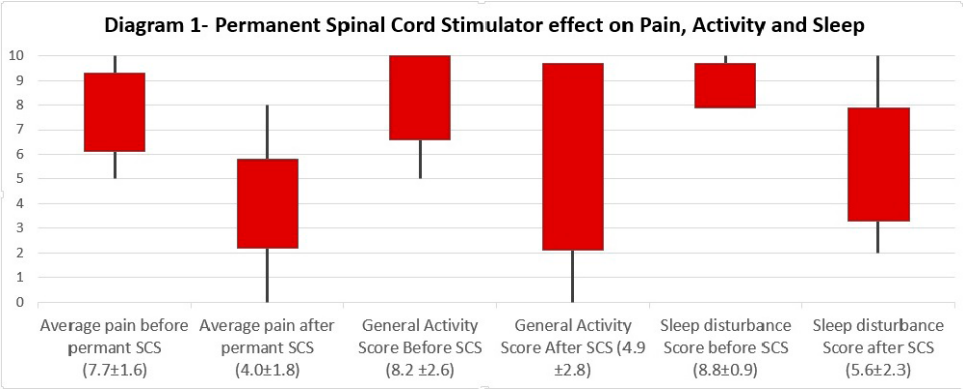

Index	Range (mean ±SD)
Age (years)	50±11
Gender (F/M)	58%/42%
Race (W/H/B)	58%/31%/4%
Height (inches)	65.6±5.0
Weight (lbs)	163±37

Table-1 Demographic Information

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S-212.

PHARMACOKINETIC CHARACTERISTICS OF THE IONSYS® (FENTANYL) SEPARATED SYSTEM WITH ENHANCED CONTROLLER

AUTHORS: R. S. Sinatra[1], B. Phipps[2], N. Joshi[3]

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INTRODUCTION: IONSYS Separated System with Enhanced Controller is being developed for the short-term (in hospital) management of postoperative pain in adult patients requiring opioid analgesia. This study evaluated the pharmacokinetic (PK) characteristics of a new version of IONSYS referred to as the Separated System with Enhanced Controller (SSEC). The primary objective of this study was to measure five key PK parameters as a function of applied current. A key secondary objective of this study was to evaluate the bioequivalence of the SSEC to an earlier integrated version of IONSYS.

METHODS: This was a single-center, randomized, open-label, 3-period, 5 treatment, 6-sequence design. A total of 52 subjects received three total treatments. All subjects received oral naltrexone (b.i.d) to block opioid effects. Each subject was randomly assigned to receive a treatment sequence consisting of IV fentanyl citrate (hourly infusions of 80 µg fentanyl over 20 minutes) and the SSEC at 170 µA (2 consecutive 10 minute doses per hour), and then one of three additional hourly treatments with SSEC at 140, 200, or 30 µA. All hourly treatments were administered for 23.33 hours with blood samples drawn frequently from 23 to 25 hours and then periodically through 48 hours. At least 6 days separated each of the treatment periods. The following PK parameters were determined: Cmax, tmax, t½, AUC, and amount of fentanyl absorbed. The calculated PK parameters were derived using a non-compartmental analysis of the serum concentration-versus-time data. The amount of fentanyl absorbed for each subject was calculated from the ratio of the area under the serum fentanyl concentration profile (AUC) for the 23rd and 24th hours for the SSEC treatments to the AUC for the IV infusion, multiplied by the IV dose of 80 µg. Bioequivalence criteria were applied to the comparison of geometric mean Dose Absorbed from the SSEC (170 µA) to the mean Dose Absorbed from the historical IONSYS Integrated System.

RESULTS: In general, the fentanyl concentration profiles were similar in shape for each of the SSEC treatments, demonstrating increasing concentrations at increased current. The key PK parameters for each treatment are presented in Table 1 with the historical IONSYS values.

Statistical comparison of the Dose Absorbed from the SSEC (170 µA) (test) relative to the historical Integrated System (reference) indicated that the ratio of the geometric means (104.10%) as well as the 90% CIs (92.35%, 117.35%) were fully contained within the bioequivalence limits of 80% - 125%. Therefore, these data establish that the SSEC is bioequivalent to the historical comparator.

DISCUSSION: Overall, exposure of fentanyl administered transdermally with an iontophoretic system increased with the magnitude of the applied current, and bioequivalence criteria were met for the Dose Absorbed for the SSEC (170 µA) when compared with historical IONSYS Integrated system.

Table 1: PK Parameters for IONSYS (Historical Data), IV Fentanyl Infusion (80 µg) and the SSEC

Parameter (units)	**IONSYS 170 µA N=35**	**IV Infusion N=43**	**SSEC 140 µA N=9**	**SSEC 170 µA N=41**	**SSEC 200 µA N=13**	**SSEC 230 µA N=12**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
AUC_{23-24} (hr*/ng/mL)	2.41(0.56)	2.21 (0.50)	1.47(0.43)	1.96(0.50)	2.46(0.46)	3.42(1.25)
C_{max} (ng/mL)	1.37(0.30)	1.52 (0.40)	0.87(0.23)	1.25(0.43)	1.51(0.28)	2.06(0.71)
t_{max} (hr)	23.65(0.25)	23.48 (0.78)	23.75(1.6)	23.29(0.60)	23.19(0.28)	23.24(0.39)
$t_{1/2}$ (hr)	11.0(2.4)	13.0 (7.4)	11.5(3.1)	11.0(4.4)	11.9(5.9)	11.1(3.1)
Fentanyl absorbed (µg)	74.8(11.5)	80 (reference)	56.0(14.0)	69.9(13.2)	86.5(16.0)	117.8(21.3)

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S-213.

THE EFFECTS OF A NEW ORAL FORMULATION OF METHYLNALTREXONE ON BIOAVAILABILITY AND MORPHINE-INDUCED GI TRANSIT CHANGES IN RATS

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INTRODUCTION: Methylnaltrexone (MNTX), a peripherally restricted opioid antagonist with mu-opioid receptor selectivity, can reduce opioid activity in the gastrointestinal (GI) tract without affecting the pain relief afforded by opioids[1]. A subcutaneous injectable form of MNTX is currently approved for the treatment of opioid-induced constipation in patients with advanced illness. Compared to injection, however, oral administration is more convenient and safer for drug delivery. Since the bioavailability of oral MNTX is low[2], in this study we prepared a new oral formulation of MNTX to observe if its bioavailability could be increased. Then, the reversal of morphine-induced GI transit changes were compared between the new MNTX-PC formulation and unformulated MNTX.

METHODS: The MNTX-phosphatidylcholine complex (MNTX-PC) was prepared, and the physicochemical properties of this formulation were analyzed[3] and compared with those of the unformulated MNTX. After 250 mg/kg of oral MNTX-PC or MNTX, rat plasma samples were collected for up to 9 hr. The plasma MNTX concentrations were quantified using LC/MS/MS for bioavailability comparison (n=5/group). Gut motility was determined by measuring GI transit with a charcoal marker expressed as percent total distance in the small intestine the marker traveled[4] in animals given IP 3-10 mg/kg of morphine, oral 10-30 mg/kg MNTX or MNTX-PC (n=8/group). Data were analyzed using a two-way analysis of variance (ANOVA).

RESULTS: In both MNTX and MNTX-PC groups, two peaks in MNTX plasma concentration were observed at 120 and 180 min. The AUC (0-540 min) for MNTX and MNTX-PC groups were 1405.9 ± 447.8 and 5758.2 ± 1474.2 ng•h/mL, respectively (Figure 1, left panel). The relative bioavailability after oral MNTX-PC administration was increased 410% compared to that with unformulated MNTX. In a separate experiment, GI transit was 59.2 ± 2.5% after vehicle (control). Morphine 10 mg/kg significantly reduced transit to 41.9 ± 3.9%. The effects of morphine on transit were significantly revered by MNTX-PC complex (55.3 ± 3.2%) compared to unformulated MNTX (46.3 ± 4.0%) (Figure 1, right panel; $P < 0.05$).

CONCLUSIONS: The MNTX-PC complex formulation significantly increased oral bioavailability of MNTX and enhanced the reversal of morphine-induced GI transit changes. Our data suggest that the PC-based oral MNTX formulation may have clinical utility for opioid-induced bowel dysfunction.

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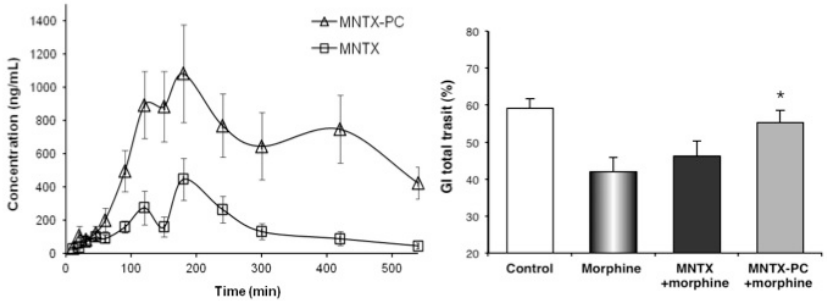

Figure 1. Left panel: MNTX plasma concentration-time profile after oral administration of MNTX-PC complex formulation and unformulated MNTX. Right panel: Effects of MNTX or MNTX-PC on morphine-induced GI transit changes.

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S-214.

MORPHINE 6-O-SULFATE SODIUM: A NOVEL OPIOID ANALGESIC ALTERNATIVE EVALUATED IN A RAT MODEL OF DIABETIC NEUROPATHY

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INTRODUCTION: Treatment of diabetic neuropathic pain still remains a vexing problem. Various drugs, including opioids, have limited efficacy and undesirable side effects. Hence further enhancement of this drug class is required to develop compounds, which are effective for neuropathic pain while lacking opioid side effects, including tolerance. Morphine 6-O-sulfate (M6S) appears to be one such promising agent. This study was designed to compare the analgesic efficacy of morphine and M6S in a rat model of diabetic neuropathy.

METHODS: Protocol was approved by the Institutional Animal Care and Use Committee. Diabetes was induced in male Sprague Dawley rats with Streptozotocin 65mg/kg (i.p.). Rat hind limb paw withdrawal and deep pressure pain threshold (PPT), pinprick sensitivity threshold (PST) and heat pain threshold (HPT) were measured using an Ugo Basile Analgesy Meter (Stoelting), a gradient hot plate instrument (Life Science) and a sharp needle attached to a force transducer (World Precision Instruments). Thresholds were measured before and 1-3 weeks after induction of diabetes and before and at 1-4 hours after drug injection (i.p.0.25mg/kg-3mg/kg). In tolerance studies, the test drug was injected daily with thresholds measured on the1st, 3rd and 7th days of treatment.

RESULTS: In naive animals, morphine and M6S produced a dose-dependent increase in HPT, with maximum analgesic effect at 1.5mg/kg dose. However, compared to morphine, a half-maximum effect of M6S on HPT was observed at a 3 times lower dose (i.e. 0.25±0.04 mg/kg). With a 1.5mg/kg dose both drugs produced a weak, temporary increase in PPT and neither drug affected PST. Experimental diabetes caused deep tissue hyperalgesia (decrease of PPT from 103±4g to 73±2 g; $p<0.01$), pinprick hypoalgesia (increase in PST from 9.7±0.7 g to 71±6 g; $p<0.01$) but no changes in HPT. Also, 50% of diabetic rats (but no control animals) demonstrated paw licking and guarding behavior in the pinprick test. Morphine and M6S (1.5mg/kg) relieved deep pressure hyperalgesia and almost eliminated licking behavior in the pinprick test in diabetic animals (without significant effect on PST). Licking behavior remained suppressed during a week of repeated drug injections showing no tolerance to M6S or morphine. Tolerance to morphine's action on deep pressure pain developed in sharp contrast to the lack of tolerance observed with M6S. The analgesic efficacy of M6S on heat pain was increased in diabetic rats (compared to control rats) while that of morphine was suppressed.

CONCLUSIONS: This study suggests that M6S is an efficacious alternative to morphine in treating superficial heat and deep pressure pain in diabetic neuropathy. Compared to morphine, the analgesic effect of M6S on HPT is retained during diabetes while requiring about 3 times lower drug concentration. Furthermore, even though both morphine and M6S relieved deep pressure hyperalgesia in diabetic rats, tolerance developed only to morphine. Further studies are needed to determine if M6S is also superior to morphine in the treatment of licking behavior (a putative sign of central nociceptive sensitization) in the pinprick test.

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S-215.

MARKOV CHAIN MODELING OF POSTOPERATIVE PAIN STATE TRANSITIONS

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INTRODUCTION: Over 60% of surgical patients suffer from moderate to severe acute postoperative pain.[1] Recent efforts to predict postoperative pain have begun to examine the dynamic nature of postoperative pain, rather than focus on whether or not a patient suffers from pain within a fixed interval of time.[2] Here, we investigate how patients transition from one pain score to the next by deriving a Markov chain for each of over 8,000 surgical patients.

METHODS: This retrospective cohort study was approved by the University of Florida IRB. We examined 476,613 postoperative pain score observations recorded between the end of surgery and postoperative day seven from a mixed surgical cohort of 8,346 subjects. Each pain scores was classified 0-10 using the numerical rating scale, with an additional state of 'asleep', with each of these classifications considered a pain state. We then calculated a transition matrix to demonstrate the probability that a patient would move from the current pain state i to the subsequent pain state j. For the purposes of this experiment, and given the extremely large number of factors directly influencing the dynamicity of postoperative pain, we presumed the Markov property such that the conditional probability distribution of a future pain state depends only on the present state. Finally, we report the overall Markov Chain transition matrix, as well as the steady state probability vector.

RESULTS: We found the transition matrix to be irreducible and aperiodic, where all states can be obtained during a random walk and no state was absorbing. In general, patients transitioned to a similar pain score, with the highest probabilities centered on the current pain score, but skewed toward decreased pain scores. (Figure 1) Patients with moderate to high pain scores (scores of 5-8) frequently transitioned to asleep and 0 (range of 19.8 - 23.8% probability) and patients with a score of 10 transitioned to 0 or asleep (17.3% probability). Next, we computed the steady state distribution vector that demonstrates the amount of time a patient spends in each pain score and describes the long-term nature of the pain trajectory. (Figure 2) Pain states of 0 (23.6%) and asleep (23.3%) had the highest probability in the steady state distribution followed by pain score states of 5 (7.4%) and 8 (6.2%).

CONCLUSION: Our work provides a new framework, based on the assumption of the Markov property, to predict post-operative pain trajectories. The transition matrix provides insight into how patients transition from one pain score to the next and can be used to simulate patient's pain trajectories and steady state probabilities.

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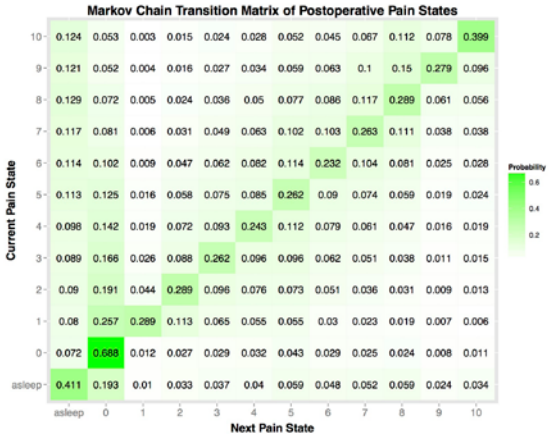

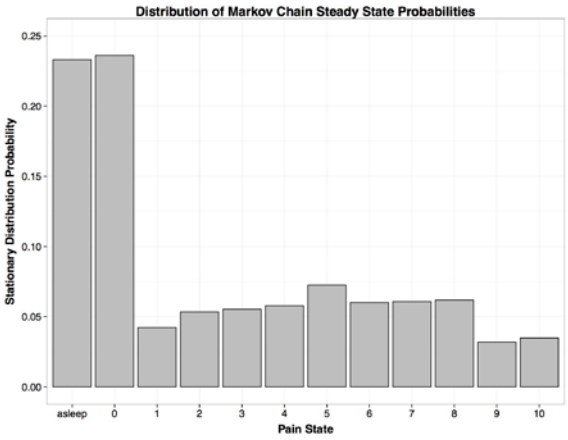

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Patient Safety

S-216.

AN AUDIT TO DETERMINE THE SAFETY OF THE NOVEL ORAL ANTICOAGULANTS, DABIGATRAN AND RIVAROXABAN, FOR PATIENTS INITIATED ON ANTICOAGULANT THERAPY

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INTRODUCTION: In the UK, dabigatran and rivaroxaban are licensed and approved by National Institute for Health and Care Excellence (NICE) for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AF) and rivaroxaban is also licensed for treatment and secondary prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE), approved by NICE in 2012. However, experience amongst clinicians in the UK using novel oral anticoagulants (NOACs) agents remains fairly limited.

Until the introduction of these agents, warfarin therapy was considered the first line option for these indications where the experience and knowledge of warfarin use is substantially greater including management strategies for underanticoagulation and overanticoagulation, which is not as clear with NOACs as there is no specific antidote. However, the advantages of the novel agents are: no routine anticoagulant monitoring, fixed dosing and no lifestyle/food interference, offering convenience to patients.

At our hospital, NOACs were prescribed from December 2011 for stroke prevention in AF and VTE treatment where warfarin therapy was ineffective and prescribing was restricted.

The aim of this audit is to determine the safety of dabigatran and rivaroxaban in clinical practice, specifically with a focus on adverse effects, bleeding outcomes, and management.

METHODS:

1. The audit team agreed the aims and standards and reviewed the literature
2. A pharmacy report identified patients prescribed NOACs from December 2011 to April 2013
3. Clinical information was accessed using patient medical notes and electronic records
4. A data template spreadsheet was developed to record audit data

RESULTS:

165 patients were initiated on NOAC therapy; 33 patients excluded. 132 patients were included in the audit. The majority of patients on rivaroxaban (n=50) were aged 71 to 90years old and on dabigatran (n=43) were aged 61 to 80years old.

Management of the major gastrointestinal bleeding events involved a 7 unit blood transfusion and Novoseven (coagulation factor VIIa recombinant) for a patient on rivaroxaban and a 4 unit blood transfusion for the patient on dabigatran. Both patients survived.

CONCLUSIONS: The NOACs have many advantages, generally well tolerated with a good adverse effect profile and are convenient for patients. However, patients did experience bleeding events and the management is challenging with no specific antidote currently available.

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132 patients		
	Rivaroxaban (n=79)	**Dabigatran (n=53)**
Number of patients	79	53
Indication for NOAC DVT		
Proximal	10	
Distal	6	
Proximal and Distal	3	
Unknown description	4	
PE		
Asymptomatic	2	
Symptomatic	11	
Unknown description	2	
DVT and PE	7	
Stroke		
Secondary to new AF	4	1
Secondary to Paroxymal AF	2	7
Secondary to Persistent AF	7	10
Prophylaxis for new AF	3	6
Prophylaxis for Paroxymal AF	3	6
Prophylaxis for Persistent AF	15	23
Adverse Effects		
Dyspepsia	1	3
Dizziness	0	0
Back Pain	1	0
Chest Pain	2	0
Fatigue	1	0
Diarrhoea	0	1
Arthralgia	1	0
Bleeding Events		
Non-Major Bleeding Event		
Epistaxis	2	0
Haemoptysis	0	1
Uterine	0	0
Tooth Extraction	0	0
Haematuria	1	3
Ear	0	0
Skin	1	0
Gastrointestinal related	3	2
Major Bleeding Event		
Decreased in Hamoglobin >4.0 g/dL	1	1
Transfusion of ≥3 units of red blood cells within a 24 hour period	0	0
Requiring intervention e.g. embolisation, superficial vascular repair, nasal packing	0	0
Intraspinal or intramusclar bleed wit compartment syndrome	0	0
Retroperitoneal, pericardial or intraocular bleed	0	0
Sex		
Male	28	31
Female	51	22

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S-217.

VENOUS AIR EMBOLISM DURING ADVANCED ENDOSCOPIC PANCREATICO-BILIARY PROCEDURES (AEPBP): THE SOUND OF CATASTROPHE

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INTRODUCTION: Exposure of vasculature to gas under pressure is the sine qua non of venous air embolism (VAE). Specific procedural events, historical features, and coexisting disease are risk factors for VAE.[1-2] This preliminary report determined the incidence of VAE in patients undergoing low and high risk AEPBP.

METHODS: After IRB approval and informed consent, 528 of a planned 1,000 patients undergoing AEPBP were monitored with precordial Doppler ultrasound (PDU) for evidence of VAE. Anesthetic management was at the discretion of the anesthesia care team. High risk procedures included sphincterotomy, use of metal stents, biopsy, necrosectomy and cholangioscopy. PDU sounds were digitally recorded and analyzed retrospectively to confirm suspected VAE. Comparisons of the incidence of VAE between low and high risk procedures were made by Chi-squared analysis; a value of $p < 0.05$ was considered statistically significant.

RESULTS: Of the 528 patients studied, 346 and 182 had low and high risk procedures, respectively. No patients in the low risk group had VAE; whereas 3 patients in the high risk group (1.6%) had VAE (odds ratio 13.5, $p = 0.086$, 95% CI of 0.7-263).

In case 1, a 24 year old male with necrotizing pancreatitis underwent necrosectomy under general anesthesia (GA). After stent removal and dilation of the transmural entrance, cyst contents were expressed into the stomach. PDU indicated VAE; the endoscopist was notified, and the procedure was aborted. A “mill-wheel” murmur evolved, followed by hypotension, hypoxemia and fall in EtCO2. Vital signs stabilized after supportive treatment and he was later extubated.

In case 2, a 36 year old female with cholangiocarcinoma underwent ERCP under GA due to a malpositioned metal biliary stent in the setting of cholangitis. During cannulation of the bile duct (7F plastic stent), PDU changes were detected and the EtCO2 declined to zero. Despite aborting the procedure and supportive treatment, she went into PEA arrest. Air was unsuccessfully aspirated from an indwelling central catheter. Spontaneous circulation and ventilation was restored after ACLS. The postoperative course was complicated by aspiration pneumonia and Takotsubo cardiomyopathy. She was discharged home 10 days later.

In case 3, a 72 year old female with recurrent acute pancreatitis presented for ERCP. Biliary sphincterotomy was performed under MAC anesthesia. VAE was detected by PDU. The endoscopist aborted the procedure and the patient remained asymptomatic.

DISCUSSION: Whereas the incidence of VAE in patients undergoing AEPBP is not fully known, there are a growing number of case reports describing severe morbidity and mortality from VAE in these patients. Our preliminary data suggest that VAE occurs most often in patients undergoing high-risk procedures at an incidence of 1.6% and can lead to profound cardiovascular instability and morbidity. Given the low cost and safety of PDU, it would seem reasonable to utilize this non-invasive device to monitor for VAE in all patients undergoing high risk AEPBP.

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S-218.

USING AN ADVERSE EVENT REPORTING TOOL TO ANALYSE THE SAFETY OF SEDATIONS BY NON-ANESTHESIOLOGISTS

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INTRODUCTION: Propofol has a rapid onset and short effect of duration, but also a small therapeutic range associated with the risk of hemodynamic and respiratory side effects. Nevertheless, it is frequently used for deep sedation outside the operating room. In The Netherlands, qualified sedation practitioners (specialized anaesthesia nurses, non-physicians) perform moderate to deep sedation using propofol and opioids. Using the Adverse Event Reporting Tool (AERT) designed by the World Society of Intravenous Anesthesia (SIVA) Sedation Task Force[1], we analyzed the safety and quality of these nurse-administered sedations.

METHODS: An Adverse Event Reporting Tool (AERT) was modified to local circumstances, and was introduced for deep sedations. Sedation practitioners were asked to fill in one form for each deep sedation performed. Data of 1615 cases were collected during the first eight months of registration (October 1st 2012 - May 31st 2013), and 811 cases not involving an anesthesiologist at the scene were analysed for incidence of sedation related adverse events (e.g., drop or increase in heart rate or blood pressure ± 25% of baseline, airway obstruction, decline of oxygen saturation). Analysis whether an AERT was made for every sedation and whether these AERT were filled in completely and correctly was used to draw conclusions about quality of registration.

RESULTS: One or more adverse events occurred in 26.6% of all sedations, with most frequently oxygen desaturation present. Event rates were higher in patients with higher ASA classes, although not significantly. An adverse outcome was only determined in two cases.

An AERT was used in 92.4% of all sedations, however, only 48.1 of all AERT were filled in completely. According to the electronic registration system, adverse events were reported correctly only on 60.4% of all completed AERT.

CONCLUSION: Quality of registration in the first eight months was poor and health professionals should keep in mind that proper evaluation of sedation quality can only be done when quality of registration is improved. Serious injury caused by sedation related adverse events was extremely rare, suggesting that deep sedations performed by sedation practitioners is safe under the local circumstances, although the number of non-serious adverse events shows that there is still room for quality improvement. Sedations in patients with higher ASA classes go along with higher complications rates.

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S-219.

PRE-PRINTED SYRINGE LABEL PROJECT: A PILOT STUDY

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AFFILIATION: Department of Anesthesiology, Stony Brook Medicine, Stony Brook, NY

INTRODUCTION: Anesthesiologists are in a unique and challenging position of preparing their own medications, often in non-standard concentrations and volumes[1]. They must also frequently give hand-offs; medications used during a case are an essential part of this hand-off. Properly labeled syringes are important for patient safety and also a Joint Commission requirement. However, compliance is not always guaranteed. Improper labeling can lead to medication errors resulting in adverse outcomes as well as increased healthcare costs[2]. Existing system of syringe labeling at our institution consists of rolls of color coded[3] adhesive tape which contain only the drug name. This requires providers to manually write the drug concentration, provider initials, date and time. Moreover, the choice of labels is limited requiring the use of blank/white adhesive tape for many medications. With approval from our departmental Quality Improvement Committee, we developed pre-printed syringe labels customized for each resident in order to improve the process. We also wanted to obtain feedback from the residents who were willing to use the new syringe labeling system.

METHODS: A standardized template of pre-printed syringe labels (with drug name/concentration, initials, date/time) was created using Microsoft Excel and a macros was developed which allowed quick printing of customized labels for each resident interested in the project. The labels were printed one day prior to its intended use and were available for pick up at the operating room pharmacy window on the morning of its intended use. The pilot study was conducted from 9/2/2013 to 10/4/2013. Pre-project and post-project surveys were also distributed to gather data.

RESULTS:

- 22 residents and 15 residents participated in the pre- and post-project survey, respectively
- 100% of residents reported medication syringe labeling is important for patient safety
- 32% of residents reported they always label medication syringes
- 85% of residents preferred pre-printed syringe labels over existing labels
- 78% of residents reported pre-printed syringe labels decrease turnover time compared to existing labels
-5 3% of residents reported that the pre-printed syringe labels did not stick well enough
- 100% of residents reported pre-printed syringe labels should be permanently implemented

CONCLUSIONS:

1. There was an overwhelmingly favorable response toward the pre-printed syringe labels, largely due to its convenience and the efficiency it provides
2. The biggest complaint with the pre-printed syringe labels was that it did not stick well enough to the syringes. As a result, a different label sheet with improved adhesive was used which eliminated the problem.
3. This new system of labeling offers flexibility and expanded options for various medications. More importantly, these labels greatly improve legibility of medication information. Our department is in the process of expanding its use.

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S-220.

EVALUATION OF RISK FACTORS FOR ARYTENOID DISLOCATION AFTER ENDOTRACHEAL INTUBATION A RETROSPECTIVE CASE-CONTROL STUDY

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INTRODUCTION: Arytenoid dislocation is a rare clinical entity. Common presenting symptoms include hoarseness, breathy voice, and dysphagia. The etiology is most commonly intubation, direct laryngoscopy, or blunt laryngeal trauma, while it has also been reported to be caused by laryngeal mask airway use and esophageal probe placement[1]. Few studies have showed some definite or possible confounding factors correlated with arytenoid dislocation. This matched case-control study investigated the relation between anesthesia procedures and arytenoid dislocation, taking into account possible confounders, such as patients' demographic characteristics, preoperative conditions and surgical procedures.

METHODS: To evaluate potential risk factors for postoperative arytenoid dislocation, we used a case-control strategy. For each case of postoperative arytenoid dislocation, one patient matched for date of procedure and type of procedures was chosen as the control. From Sep, 2003 to Aug, 2013, altogether sixteen patients with a history of postoperative arytenoid dislocation were recruited. Medical records for all patients and controls were reviewed. Recorded for all patients were demographics, smoking status, alcoholic status, preoperative physical status, airway evaluation, intubation procedures, preoperative laboratory values, anesthetic consumption and intensive care unit (ICU) stay. For arytenoid dislocation cases, we further recorded the left vs right arytenoid dislocation and surgical repair vs conservative treatment.

Categorical variables were compared using the Chi-squared test and continuous variables were compared using the Student unpaired t-test. To determine the predictors of arytenoid dislocation, a Binary logistic regression model was used for multivariable analysis. All reported p-values were two-sided, and p-values <0.05 were considered to indicate statistical significance.

RESULTS: We included sixteen patients of postoperative arytenoid dislocation (eight women and eight men) with a median age of 52 years; ten patients (62.50%) were left side arytenoid dislocation and six (37.50%) were right (Table 1, Table 2). Most postoperative arytenoid dislocation patients (fifteen, 93.75%) received surgical repair, except one patient recovered after conservative treatment. Interestingly, when compared arytenoid dislocation cases with controls, none of postoperative arytenoid dislocation patients were smokers, with five smokers in control group (p=0.017) (Table 1). Red blood cell (p=0.044) and hemoglobin (p=0.031) levels were significantly lower among arytenoid dislocation cases than control patients (Table 3). Either intubation procedure or ICU stay had no influence on the morbidity of postoperative arytenoid dislocation.

CONCLUSIONS: Non-smoking and anemic patients may be susceptible to postoperative arytenoid dislocation. However, neither of them was the independent risk factor for postoperative arytenoid dislocation.

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Demographics of Arytenoid Dislocation Cases vs Controls			
Variable	Cases(n = 16)	Controls(n = 16)	PValue
Age	51.69±19.84	58.63±9.01	0.217
GenderFemaleMale	8 (50.00%)8 (50.00%)	6 (37.50%)10 (62.50%)	0.483
Height (cm)	164.75±7.21	167.75±6.40	0.223
Body weight (kg)	61.34±11.84	69.00±12.93	0.091
BMI (kg/m2)	22.53±3.65	24.38±3.51	0.155
Smoking statusSmokerNon-smoker	0 (0.00%)16 (100.00%)	5 (31.25%)11 (68.75%)	0.017
Alcoholic statusDrinkerNon-drinker	1 (6.25%)15 (93.75%)	2 (12.50%)14 (87.50%)	0.551
ASA gradeI-IIIII-IV	12 (75.00%)4 (25.00%)	12 (75.00%)4 (25.00%)	1
NYHA gradeIIIIII	13 (81.25%)1 (6.25%)2 (12.50%)	7 (43.75%)9 (56.25%)0 (0.00%)	0.084

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S-220 • continued

Surgical and anesthesia procedures of Arytenoid Dislocation Cases vs Controls			
Variable	Cases(n = 16)	Controls(n = 16)	PValue
Surgical proceduresAbdominal or general surgeryNeurosurgeryOrthopedics surgeryCardiovascular surgery	11 (68.75%)1 (6.25%)1 (6.25%)3 (18.75%)	11 (68.75%)1 (6.25%)1 (6.25%)3 (18.75%)	1
Mallampatti gradeI-IIIII-IV	15 (93.75%)1 (6.25%)	16 (100.00%)0 (0.00%)	0.317
Intubation timesOnce≥2 times	13 (81.25%)3 (18.75%)	15 (93.75%)1 (6.25%)	0.293
Intubation styletWithWithout	11 (68.75%)5 (31.25%)	8 (50.00%)8 (50.00%)	0.288
Postoperative ICU stayYesNo	5 (31.25%)11 (68.75%)	5 (31.25%)11 (68.75%)	1
Arytenoid dislocation sideLeftRightBoth	10 (62.50%)6 (37.50%)0 (0.00%)	N/AN/AN/A	N/A
Arytenoid dislocation treatmentSurgical repairConservative treatment	15 (93.75%)1 (6.25%)	N/AN/A	N/A

Laboratory Data of Arytenoid Dislocation Cases vs Controls			
Variable	Cases(n = 16)	Controls(n = 16)	PValue
Red blood cell (×10E12/L)	3.80±0.76	4.30±0.51	0.044
White blood cell (×10E9/L)	8.17±3.11	7.41±2.41	0.447
Hemoglobin (G/L)	114.38±22.27	129.44±14.71	0.031
Platelet (×10E9/L)	217.00±90.52	232.50±78.36	0.608
Albumin (G/L)	35.69±4.99	37.63±5.93	0.325
Alanine aminotransferase (U/L)	18.71±10.34	28.88±25.55	0.176
Prothrombin time (sec)	13.66±4.58	12.22±1.56	0.244
activated partial thromboplastin time (sec)	32.82±13.96	28.63±8.77	0.317

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S-221.

KEEP UP OR ELSE! NATIONWIDE TRENDS IN SCIP PERFORMANCE FROM 2008 TO 2012

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INTRODUCTION: The Surgical Care Improvement Project (SCIP) is a national quality initiative dedicated to reducing the rate of surgical complications. The program consists of process of care measures intended to decrease the risk of undesired postoperative outcomes[1-3]. Hospital reporting of performance on these measures is linked to reimbursement from the Centers for Medicare & Medicaid Services. The purpose of this study was to examine the trend of nationwide performance on 6 SCIP core measures over the past 5 years (2008-2012) among hospitals performing heart valve surgery. The included measures have been reported annually over this 5 year period and are related to the prevention of postoperative infection and venous thromboembolism (VTE).

METHODS: Publicly available data was accessed from the Hospital Compare website for U.S. hospitals who reported performance on core SCIP measures in each year from 2008-2012. The 6 SCIP core measures included in this study were: INF-1 (received prophylactic antibiotics within 1 hour prior to surgical incision), INF-2 (received appropriate prophylactic antibiotics), INF-3 (prophylactic antibiotics were discontinued within 24 hours after surgery end time), INF-4 (cardiac surgery patients with controlled 6 AM postoperative blood glucose level), VTE-1 (treatment ordered to prevent VTE), and VTE-2 (treatment received to prevent VTE within 24 hours before or after surgery). The included 6 core measures were selected because they were consistently reported in every year during this period. Only hospitals performing heart valve surgery were included in this analysis (N=726 in 2008, N=600 in 2009, N=527 in 2010, N=525 in 2011, N=568 in 2012). The average performances for individual measures and all measures in aggregate were calculated for each year.

RESULTS: Over the last 5 years, the average nationwide performances for each of the individual SCIP measures and for all 6 measures in aggregate have improved annually (see Figure 1). The overall average adherence rate for all included measures increased from 91.02% in 2008 to 97.97% in 2012 among all hospitals performing heart valve surgeries.

CONCLUSIONS: Adherence rates have improved annually from 2008-2012 for all 6 SCIP core measures that were consistently reported during this time period by hospitals performing heart valve surgery. This finding indicates that hospitals will need to continually improve their compliance to SCIP measures in order to maintain their performance relative to other hospitals in the country. In addition, the progressive decline in the number of hospitals performing heart valve surgery who reported SCIP measure performance over this time period may indicate the presence of survivor bias, in which the overall average performance has risen secondary to low performers being culled from the herd. Future work could include looking for a similar pattern with other surgical procedures.

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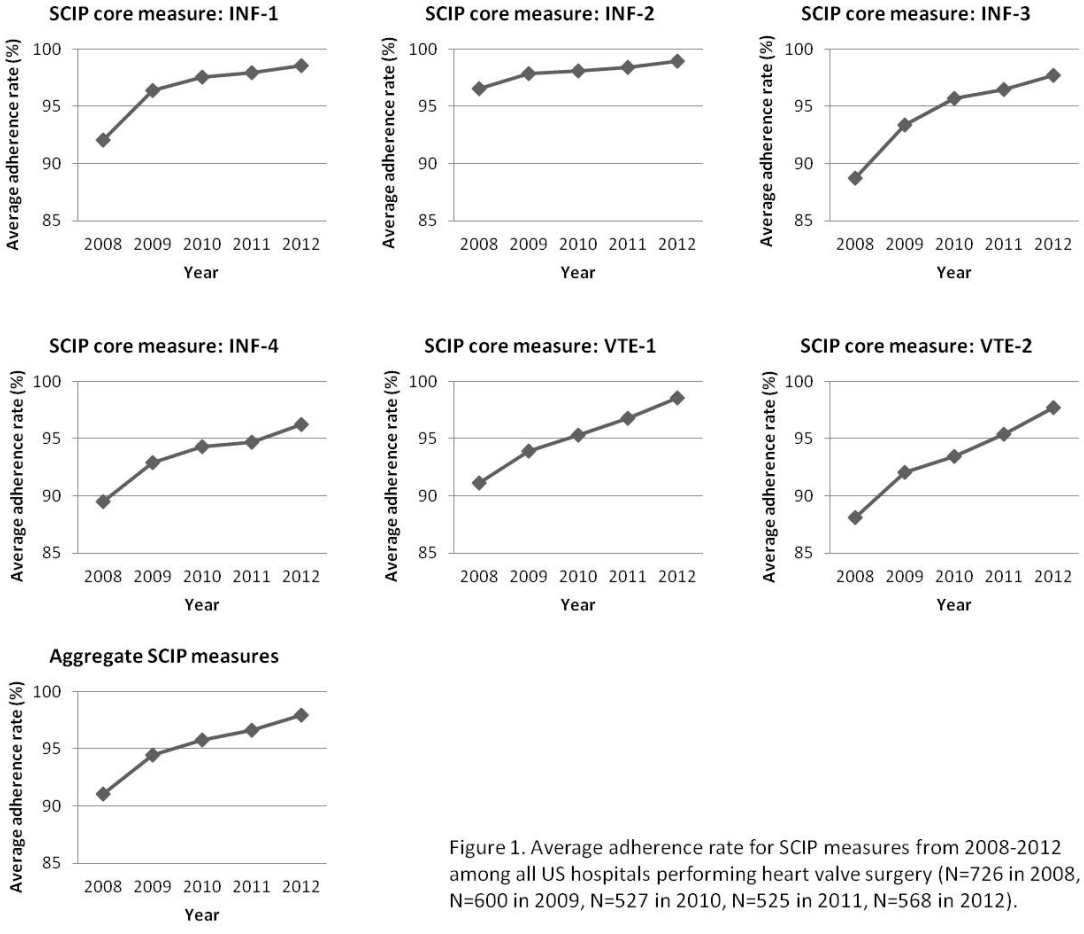

Figure 1. Average adherence rate for SCIP measures from 2008-2012 among all US hospitals performing heart valve surgery (N=726 in 2008, N=600 in 2009, N=527 in 2010, N=525 in 2011, N=568 in 2012).

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S-222.

RISK FACTORS ASSOCIATED WITH SEVERE ARTERIAL LINE COMPLICATIONS

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: Complications associated with arterial cannulation include; temporary vascular occlusion, thrombosis, ischemia, hematoma formation, local and catheter related infection and sepsis.[1-3] The goal of our study was to define the epidemiology of these complications in a large surgical cohort.

METHODS: All patients requiring arterial line placement with documentation available in the Charts+ data system at Mayo Clinic in Rochester, MN were included in this retrospective study between January 1, 2006 and December 31, 2012. The timeframe of data collection began at the time of arterial line insertion and ended at 30 days post line removal. Following IRB approval, we utilized our innovative informatics resources to identify all patients with an arterial catheter placed in the operating room environment during the study interval. We than queried our validated databases for documented vascular and/or neurologic consults. We also evaluated for returns to surgery within 30 days of catheter placement in order to identify potential catheter-associated complications.

RESULTS: A total of 62,626 arterial lines were placed in 57,787 patients. The vast majority, 90.1%, of the catheters placed were 20 gauge catheters. The radial artery was cannulated in 94.5% of patients. The majority of femoral catheters were either 15 cm 5 french catheters, 44.7%, or 10 cm 18 gauge catheters, 44.8%. A total of 21 patients were identified as having experienced vascular complications or nerve injuries. Complication rate 3.4/10,000 (95% C.I. = 2.1, 5.1). Cardiac surgery had the largest number of catheters placed, n = 15,419 with 12 complications. Complication rate 7.8/10,000 (95% C.I. = 4.0, 13.6). General surgery had a similar number of catheters placed, n= 14,961 with 4 complications. Complication rate 2.7/10,000 (95% C.I = .0.7, 6.8). Female gender (p=0.46) and preoperative use clopidogrel (p = 0.033) were associated with increased risk of catheter-associated complications.

CONCLUSIONS: In this large observational study, we characterized the rate of arterial catheter-related complications in a heterogenous surgical population. Further, we found that female gender and preoperative use of Plavix were associated with greater risk of arterial line complications.

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S-223.

ACCURACY OF MALIGNANT HYPERTHERMIA DIAGNOSES IN HOSPITAL DISCHARGE RECORDS

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AFFILIATION: [1]Anesthesiology, Columbia University, New York, NY, [2]Medical Education and Clinical Research, Saint Barnabas Medical Center, Livingston, NJ, [3]Anesthesiology, Northwestern University, Chicago, IL, [4]Anesthesiology, Toronto General Hospital, Toronto, ON, Canada

BACKGROUND: In 1997, the International Classification of Diseases, 9th Revision Clinical Modification (ICD-9CM) coding system introduced the code for malignant hyperthermia (MH) (995.86). The aim of this study was to estimate the accuracy of coding for MH in hospital discharge records.

METHODS: An expert panel of anesthesiologists reviewed medical records for patients with a discharge diagnosis of MH based on ICD-9 or ICD-10 codes from January 1, 2006 to December 31, 2008 at six tertiary care medical centers in North America. All cases were categorized as possible, probable, or fulminant MH, history of MH (family or personal) or other.

RESULTS: A total of 47 medical records were reviewed. The mean age was 40 years and 49% were male. A surgical procedure and general anesthesia were documented in 68% and 23.4% had a possible, probable, or fulminant MH event. Dantrolene was given in 81% of MH cases. All patients judged to have an incident MH event survived to discharge. Family and personal history of MH accounted for 46.8% of cases. High fever without evidence of MH during admission accounted for 23.4%, and in 6.4% cases there was an unclear reason for coding.

CONCLUSIONS: About 70% of ICD-9 or ICD-10 coded MH diagnoses in hospital discharge records refer to incident MH episodes or MH susceptibility. Additional information such as surgical procedure, anesthesia billing data, and dantrolene administration may aid in identifying incident MH cases in administrative databases.

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S-224.

TSE "MASK" IMPROVES OXYGENATION AND DECREASES SEVERE DESATURATION IN PROPOFOL-SEDATED PATIENTS DURING ERCP

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INTRODUCTION: Patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) often receive IV sedation and nasal cannula (NC) O_2. NC O_2 reservoir is lost when the mouth is kept open with a bite-block. Over-sedation and/or airway obstruction may cause severe desaturation (Desat) and require assisted ventilation and oxygenation. A simple plastic sheet has been shown to improve oxygenation by transforming an ineffective NC to an effective face tent (TSE "Mask") in deeply sedated patients during upper GI endoscopy in a prospective study[1]. We have used this technique in the Endoscopy Suite and wish to confirm its effectiveness in improving oxygenation in propofol-sedated patients during ERCP.

METHODS: This retrospective review of 90 patients who underwent ERCP identified 2 groups. NC (n=7) received only NC O_2. TM (n=83) received NC O_2 and a TSE "Mask" using a clean, clear plastic sheet to cover patient's eyes, nose and mouth as previously described (Photo)[1-3].Standard ASA monitors were applied including capnography. All procedures were performed with the patients in left lateral decubitus position. Patients received NC O_2 (3-5 L/min or higher as needed) and only IV propofol for sedation. Student t-test and Chi Square test were used for analysis. A p value <0.05 was considered as significant. Data are presented as Mean±S.D.

RESULTS: There were no differences in age (NC: 68±17 yrs; TM: 56±15), Body Mass Index (NC: 28±5 kg/m2; TM: 26±6), ASA Physical Status (NC: 2.3±0.5; TM: 2.3±0.6), baseline O2 saturation (Sat) (NC: 96±3%; TM: 97±2%), overall propofol dosage (NC: 196±43 mcg/kg/min; TM: 193±61) and procedure duration (NC: 47±24 min; TM: 50±30). There were significant differences in the highest NC O_2 flow (NC: 5.7±1.3 L/min; TM: 4.5±0.9, p<0.002), FiO2 (NC: 0.27±0.06; TM: 0.57±0.16, p<0.0002), O_2 Sat after 5 min pre-oxygenation (NC: 98±2%; TM: 100±1%, p<0.003), the lowest O_2 Sat (NC: 87±7%; TM: 98±3%, p<0.0001) (Fig. 1), severe Desat (O_2 Sat<85%) (NC: 5/7; TM: 0/83, p<0.001) (Fig. 2) and assisted bag-mask ventilation (NC: 1/7; TM: 0/83, p<0.001). Five NC patients had severe Desat (O_2 Sat: 83±1%). One of these NC patient received assisted bag-mask ventilation. Four others' NCs were converted to TMs and their O_2 Sat was improved from 83±2% to 97±4%, 99±2% and 99±2% at 5 min intervals (p<0.0001).

CONCLUSION: These data show that this simple face tent improves oxygenation and reduces severe desaturation and the need for bag-mask ventilation in patients under deep propofol sedation during ERCP. It increases O_2 delivery without raising NCO_2 flow. When ERCP is performed under monitored anesthesia care in our Endoscopy Suite, it is usually done with this simple face tent. Although it can also be used as a rescue device when patient's oxygenation deteriorates, this face tent should be routinely used prior to sedation during ERCP. It takes only a few seconds to prepare and may improve patient safety at no extra cost.

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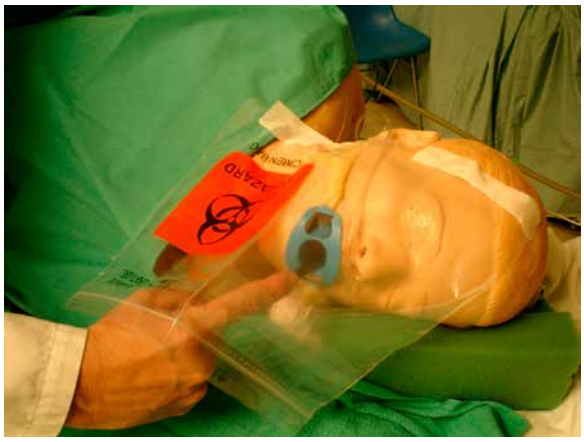
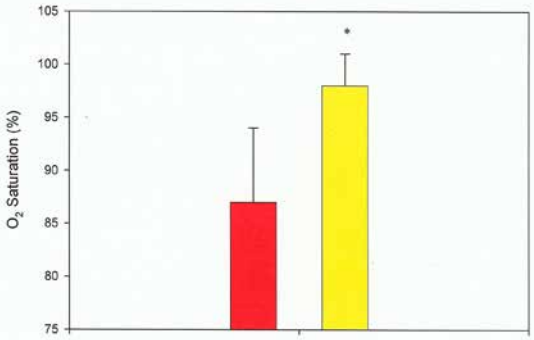
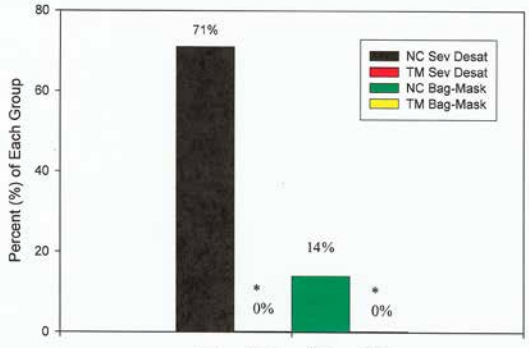


Fig 1. Effects of TSE "Mask" on the Lowest O_2 Saturation in Propofol-Sedated Patients during ERCP



NC: Nasal cannula group; TM: TSE "Mask" group
*Significantly different from Nasal Cannula Group, p<0.0001.

Fig 2. Effects of TSE "Mask" on Severe Desaturation (O_2 Sat <85%) and the Need of Bag-Mask Ventilation in Propofol-Sedated Patients during ERCP



NC: Nasal Cannula group; TM: TSE "Mask" group
*Significantly different from Nasal Cannula group, p<0.001.

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S-225.

EXTINGUISHING THE FLAMES OF HARM: CHANGING THE STAFFING MODULE

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AFFILIATION: [1]Anesthesiology, University of Florida, Gainesville, FL, [2]Surgery, University of Florida, Gainesville, FL, [3]University of Florida, Gainesville, FL

INTRODUCTION: The care of burn patients, especially those with critical illness, can be challenging in the operating room as well as the Intensive Care Unit (ICU). To optimize perioperative care of this specific patient population, a new staffing model was instituted and the impact of this staffing model examined.

METHODS: A new model was instituted in which in the burn operating room and intensive care unit in which a core group of critical care anesthesiologists and anesthesiology residents provided anesthesia services for the burn operating room as well as the intensive care unit. This dedicated team provided anesthesiology services to the burn OR as well as critical care services for the burn intensive care unit. The anesthesiology residents rotated in 2 week blocks dedicated every day to this area during that time. This replaced the previous model, which involved general anesthesiologists and other anesthesiology providers including anesthesiology residents, certified registered nurse anesthetists, and anesthesiology assistants provided anesthesia services to the burn operating room. In this previous model, separate group of critical care anesthesiologists provided intensive care unit patient care that were different than the Burn OR anesthesiologist. The surgeons providing care for the majority of these patients remained unchanged. To assess the impact of this model, the number of patient safety reports (PSR) was examined for the burn operating and burn ICU. A 12 month time period before implementation (Jan 1-Dec 31, 2010) of the new model was compared to a 12 month time period following implementation (Jan 1-Dec 31, 2012). The new model involved a small number of attending critical care anesthesiologists providing care.

RESULTS: A total of 534 burn operative cases were performed for the 12 month period of 2010 compared to a total of 438 following implementation of the new staffing model. The total number of PSR events for the OR was 116 in 2010 compared to 63 in 2012. In addition PSRs filed for treatment, test, or procedure variances decreased from 32 in 2010 to 10 in 2012.

DISCUSSION: The new staffing model as examined by PSR shows an improvement in quality following its implementation. In this critically ill patient population, the small number of faculty providers improved care of these patients probably for several reasons. These attending providers had often provided ICU consultation for these patients on admission and thus were familiar with the patients who were critically ill. For patients who required numerous procedures the knowledge of having previously performed anesthetic management may have led to improved care however further analysis would be required.

CONCLUSIONS: The new model resulted in fewer major adverse events specifically in the critically ill burn patients intra-operatively and for treatment, test, or procedural variances. This may have resulted from the additional background from the ICU care of these patients. This new model has anecdotally resulted in an increase in satisfaction for the burn surgeons and the critical care nurses in the Burn ICU (Figure 2).

Figure 1

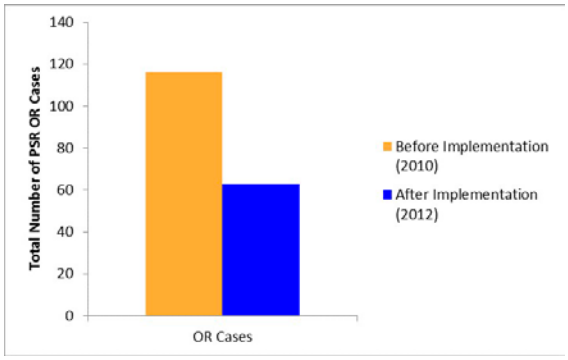
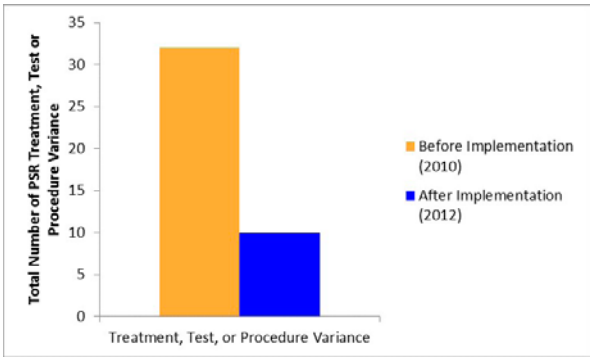


Figure 2



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S-226.

TEAMSTEPPS IMPLEMENTATION IN CRITICAL CARE: A MULTIDISCIPLINARY AND MULTIPROFESSIONAL APPROACH

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AFFILIATION: Anesthesiology, Ochsner Clinic Foundation, New Orleans, LA

INTRODUCTION: TeamSTEPPS is an evidence based curriculum designed by Agency for Healthcare Research & Quality (AHRQ) and the Department of Defense (DoD) to provide strategies and tools to improve patient safety and team based care. The program aims to improve knowledge, skills, and attitudes of all providers, by presenting four modules, 1) leadership, 2) mutual support, 3) situation monitoring, 4) communication. We present our implementation approach and methodology using a metric developed by AHRQ and published on their website. (www.ahrq.org)

METHODS: We presented the TeamSTEPPS curriculum to 290 providers in 9 sessions, 4 hours duration. Prior to the sessions participants completed the Team Attitudinal Questionairre (T-TAC). Post course work, 145 rendomly selected participants were asked to again complete the T-TAC survey. We abstracted seven domains of particular interest to our organization for analysis. Participants included physicians, nurses, medical students and residents, RT, PT, OT, palliative care, eICU pesonnel, and administrative personnel

RESULTS: 92 participants provided before and after T-TAC surveys for a response rate >70%. For purposes of analysis we adopted a yes/no binary methodology from the Likert scale (agree, strongly agree = yes, all other responses = no). The standard error for responders: +/- 10%, 95% confidence level. Responses for the 7 domains were compared.showing no overlap for +/- 1 SE.

CONCLUSION: With substantial support from the Executive Oversight Committee, this curriculum was conceived and delivered by 5 TeamSTEPPS Master Trainers; 4 within the department of anesthesiology (2 staff physicians, 1 resident physician, 1 CRNA) and 1 critical care nurse specialist. Currently RVU accumulation dominates physician activities, but physician leadership is critical to success. Our model is based on 3 principles: 1. EVERYONE is a provider, 2. dedicated time is necessary to show leadership support, 3. employees must be off site and "on the clock". We generated a "short term win". [1] and expanded our efforts to include all resident physicians [2] and medical students.

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T-TAC Pre and Post Curricular Intervention: +/-10%				
Overall perception of patient safety	40%	30-50%	94%	84-100%
Non-punitive responses to error	45%	35-55%	77%	67-87%
Leadership promotes pt safety	35%	25-45%	85%	75-95%
Feedback/communication re:error	49%	39-59%	83%	73-93%
Teamwork across units	53	43-63%	92%	82-100%
Hand-offs and transitions of care	23%	13-33%	74%	64-84%
Corganizationa learning, continuous improvement	51%	41-61%	84%	74-94%

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S-227.

ULTRASOUND GUIDED CVC TIP POSITIONING AND LUNG ULTRASOUND COMPARED WITH CHEST RADIOGRAPH

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INTRODUCTION: Ultrasound-guided central venous catheter (CVC) placement has been shown to be safer than the landmark technique.[1] Penetration depth of common linear ultrasound probes limits the visualization of the intravenous guidewire. Thus, correct position of the CVC tip in the distal superior vena cava (SVC) and exclusion of pneumothorax have to be confirmed with chest radiograph exposing patients to radiation. We hypothesize that CVC tip positioning and exclusion of pneumothorax can be performed with ultrasound.

METHODS: This observational study was approved by the IRB and abides the Declaration of Helsinki. Following written informed consent, perioperative patients scheduled for elective surgery and patients with an indication for a CVC for therapeutic infusion were included. Venopuncture was performed under ultrasound-guidance with a microconvex probe placed in short-axis view of the vein (Internal jugular vein, Subclavian vein). Guide wire was introduced into the vein and advanced to the distal SVC following visualization of the SVC and crossing of the right pulmonary artery. Insertion depth was read from the markings of the guidewire and CVC was placed after venodilation. In patients with a p-wave sinus rhythm, intracardiac ECG was used for additional insertion depth confirmation. After surgery and extubation or sole CVC placement, respectively, bedside lung ultrasound with B-Mode for lung sliding and M-Mode for seashore sign were performed in the postanesthesia care unit to exclude pneumothorax. Radiology technicians were called immediately after arrival of the patient in the postanesthesia care unit or after completion of CVC placement, respectively. Chest radiograph in supine position was performed following standard hospital protocol and reviewed by consultant radiologists who were unaware of the study.

RESULTS: No complications occurred including arterial puncture, pneumo- or hemothorax, cardiac tamponade, cardiac arrhythmias or misplaced CVC. Mean time from ultrasound prescan to guidewire final position was 10 min 30 s ± 4 min 45 s standard deviation (n = 9). Bedside lung ultrasound was performed within a median of 220 s (interquartile range = 147 - 242 s) whereas chest radiograph was delayed by a median of 82 min (interquartile range = 36.5 - 324 min; n = 9). Lung sliding and seashore sign were detected in all bilateral chest quadrants in each patient. Bland-Altman analysis showed a difference between the means of -0.5 cm for ultrasound versus intracardiac ECG (95% limit of agreement - 3.8 - 2.7 cm).

CONCLUSION: CVC placement and tip positioning is safe using a microconvex probe. Chest radiograph is redundant if an additional lung ultrasound to exclude pneumothorax is performed. Exposure to radiation, patient discomfort and costs can be limited to a minimum.

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S-228.

IN VIVO IMMUNE PRIMING TO REDUCE BACTERIAL LOAD IN A MOUSE MODEL OF SURGICAL SITE INFECTION

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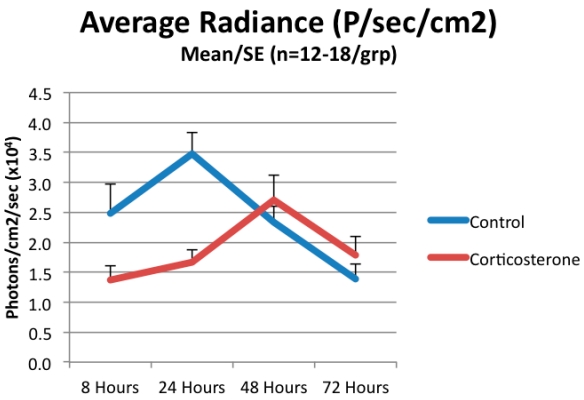
INTRODUCTION: Surgical site infections (SSI) remain a significant clinical problem that affect 3-5% of surgical patients with substantial associated morbidity[1]. There are currently no widely available non-toxic techniques to enhance host resistance to the bacteria that contaminate almost all wounds and that, when not eliminated, are the cause of SSIs. We applied the emerging concept of glucocorticoid (GC) priming of the innate immune system[2] to test the hypothesis that enhancement of innate immune responses to bacterial pathogens would reduce the bacterial load in an *in vivo* model of SSI during the critical first 24 hours after surgery.

METHODS: Male C57/Bl6 mice were inoculated on Day 1 with a single subcutaneous injection of the rodent GC, corticosterone, at a dose of 5mg/kg (total volume 25ul) or vehicle. On Day 2 animals were anesthetized with isoflurane and a 1cm full thickness skin incision was made in the nape of the neck into the subcutaneous tissue. With the wound open, 1x107 colony-forming units of a bioluminescent Staphylococcus aureus (strain SH1000 [3]) in a volume of 5ul were injected into the subcutaneous tissue. Three injections were made through the open wound on either side of the incision and into the base of the wound. The wound was closed with a single mattress suture. Wounds were subsequently imaged for bioluminescence using a commercially available device (Xenogen IVIS; Caliper Life Sciences, Hopkinton, MA) at 8, 24, 48 and 72 hours after surgery. Results: The measured bioluminescence has been shown to accurately represent bacterial burden *in vivo*[3]. Bioluminescence was readily observed at all time points and was declining at 72 hours in all animals. No animals had overt evidence of wound infection or abscess formation. At 8 and 24 hours after bacterial inoculation, bioluminescence (photons/sec/CM_2) was significantly ($p<0.05$) reduced in animals that had been pretreated with corticosterone ((Figure 1).



CONCLUSIONS: Previous work has shown that transient exposure to stress-associated concentration of GCs can robustly enhance innate immune responses to both Gram+ and Gram- bacteria, probably through a toll-like receptor mediated mechanism[4]. The results presented here are consistent with this *in vivo* priming effect of GCs on innate immune responses to bacterial contamination. Furthermore, the effect is observed during the critical first 24 hours after bacterial inoculation when surgical wound infections are most likely to evolve into a SSI.

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S-229.

IS NO-COST TSE "MASK" MORE EFFICIENT THAN HIGH NASAL CANNULA OXYGEN FLOW IN REDUCING SEVERE DESATURATION IN PATIENTS UNDER DEEP PRPOFOL SEDATION DURING VARIOUS MINOR SURGICAL PROCEDURES?

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INTRODUCTION: Patients under monitored anesthesia care (MAC) routinely receive intravenous (IV) sedation and nasal cannula (NC) O_2 at a flow rate of 3-5 L/min. Over-sedation and/or airway obstruction may cause respiratory depression and severe desaturation (Desat). Raising NC O_2 flow in an attempt to improve oxygenation may increase the risk of fire hazard, especially during upper body procedures. A simple plastic sheet was shown to improve oxygenation without raising NC O_2 flow by transforming an ineffective NC to a face tent (TSE "Mask") in deeply sedated patients[1-3]. We compared it with high NC O_2 flow in reducing severe Desat in patients under MAC.

METHODS: Retrospective review of patients who underwent various minor surgical procedures (breast biopsy, a-v fistula, cystoscopy, melanoma excision, etc.) identified 2 groups. Group 1 (NC, n=43) received only NC O_2. Group 2 (TM, n=101) received NC O_2 and a TSE "Mask" using a clean plastic sheet or a fluid-shield surgical mask to cover patient's mouth and nose (Photo)[1-3]. Patients received NC O_2 (3-5 L/min or higher as needed) and only IV propofol for sedation. NC patients were separated according to NC O_2 flow into NC1 (3-5 L/min, n=23) and NC2 (6-10 L/min, n=20). Student t-test and Chi Square test were used for analysis. A p value <0.05 was considered as significant. (Mean±S.D.)

RESULTS: There were no differences in age (NC1: 50±18 yrs; NC2: 56±11 yrs; TM: 56±17), propofol dose (NC1: 154±88 mcg/kg/min; NC2: 139±72; TM: 160±73) and ASA Physical Status (ASA III/ASA I-II: NC1: 3/20 & NC2: 9/9 vs. TM: 32/66). However, CN1 had less ASA III patients than CN2 ($p<0.01$). There were significant differences in BMI (NC1: 25±4 kg/m2 vs. NC2: 29±7 & TM: 29±6, $p<0.02$), the highest NC O_2 flow (NC1: 4.1±0.5 L/min & TM: 4.4±1.0 vs. NC2: 7.2±1.8, $p<0.005$), room air O_2 Sat (NC1: 99±1% vs. NC2: 98±2% & TM:98±2%, $p<0.003$), procedure duration (NC1: 32±17 min vs. NC2: 49±27 & TM: 48±28, $p<0.05$), the lowest O_2 Sat (NC1: 95±6% & NC2: 91±8% vs. TM: 97±3%, $p<0.01$) (Fig. 1), severe Desat (O_2 Sat≤85%) (NC1: 2/23 & NC2: 4/20 vs. TM: 1/101), bag-mask ventilation (NC1: 1/23 & NC2: 2/20 vs. TM: 0/101, $p<0.05$) (Fig. 2), FiO_2 (NC1: 0.29±0.07 & NC2: 0.35±0.10% vs. TM: 0.59±0.18, $p<0.0001$) and O2 level under the surgical drapes near surgical field (NC1: 44±16% & NC2: 42±11% vs. TM:22±1%, $p<0.0001$). Five NC patients had severe Desat (O_2 Sat: 87±4%) and one of these required assisted mask ventilation and oxygenation. The other four patients' NCs were converted to TMs and their O_2 Sat was improved to 95±5%, 96±2% and 99±1% at 5 min intervals ($p<0.02$).

CONCLUSION: Data show that TSE "Mask" is more efficient than high NC O_2 flow in reducing severe desaturation and bag-mask ventilation in patients under deep propofol sedation during various minor surgical procedures. It also reduces the risk of fire hazard by preventing O_2 from pooling under the surgical drapes. Although it can be used as a rescue device when patient's oxygenation deteriorates, it should be routinely used prior to sedation. This face tent takes a few seconds to prepare and may improve patient safety at no extra cost.

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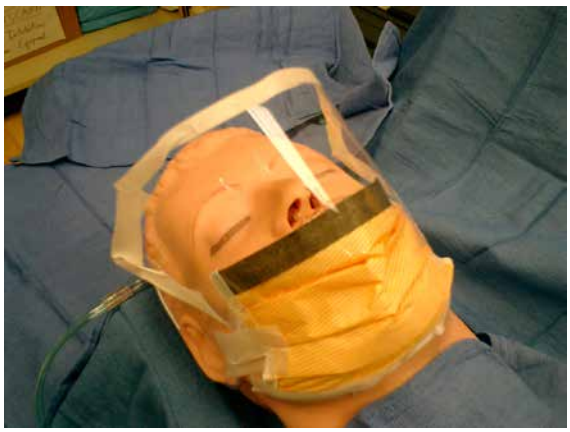

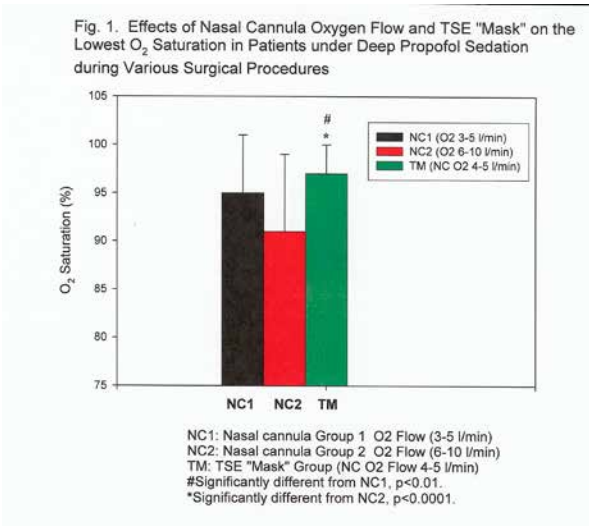

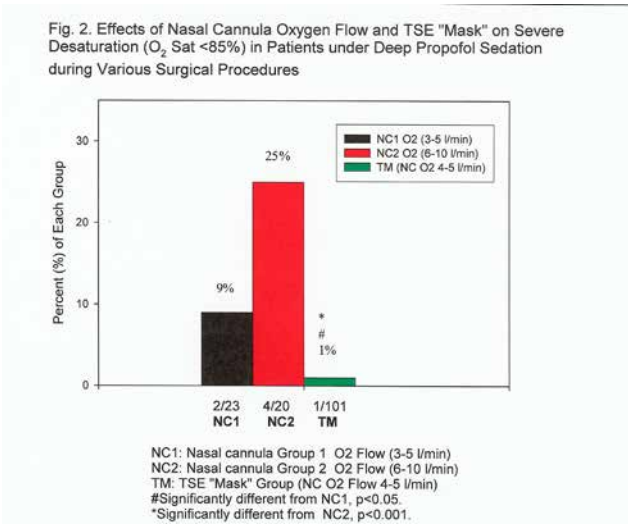

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S-230.

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S-231.

COMPARISON OF HOSPITAL LENGTH OF STAY, PERIOPERATIVE RESOURCES AND HYPOXEMIC EVENTS BY SURGICAL PATIENTS WITH AND WITHOUT THE DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA

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INTRODUCTION: There is an estimated 70 million people in the United States who have obstructive sleep apnea (OSA) and it is estimated that up to 75% of OSA patients (OSApt) arrive for surgery without a definitive diagnosis or therapy. It is established that the chronic physiologic stress associated with OSA contributes to long-term cardiovascular and respiratory disease. OSA is associated with difficult airway management and hypoxemia. It has been assumed, but not established, that OSA leads to longer hospitalizations (LOS) due to a greater frequency of surgical (eg, infection), pulmonary and cardiac complications. We previously reported that OSApt had significantly more perioperative airway management and hypoxemic events than patients without OSA (noOSApts)[1]. Using the same patient cohort we hypothesized that OSApts would have increased postoperative complications. The primary outcome indicator was hospital length of stay (LOS) and secondary outcomes were admission to ICU, postoperative ventilation, oxygen therapy and hypoxemic episodes.

METHODS: The Epic Clarity database was queried for all inpatient surgeries (LOS≥1day) performed at the University of Colorado Hospital between 1/2012 and 1/2013. The anesthesia preoperative assessment was used to determine OSA classification: OSApts had a formal or bedside diagnosis (≥3 STOPBANG criteria (Snoring, Tired, Observed apnea, hyPertension, BMI > 35 kg/m2, Age>50yr, Neck>16in, Gender male): noOSApts did not meet OSA criteria. All extracted data was entered by clinicians during routine perioperative care, by vital signs monitors at the location of care, PACU, ICU, floor. The Epic extraction was : demographics, STOPBANG elements, surgical service, PACU/floor SPO2<90% or <80%, O2 use (am, pm), postoperative mechanical ventilation need, ICU admission, and LOS. Patients with missing data were excluded. Significance was determined by Chi Square or t-test analyses, $p<0.05$.

RESULTS: Of 18,351 patients, 7,779 were excluded, leaving 1,594 OSApts and 8,978 noOSApts. OSApts were more likely to be male, older, and have a greater BMI than noOSApts (Table 1). noOSApts had a significantly more ICU admissions, more ventilation and less use of O2 therapy than OSApts. Within the first 5 days noOSApts had a trend to a longer LOS than OSApts. LOS 6-30 days was more likely to occur in the OSApts with the LOS>30 days being 1.5X greater in the noOSApts (Table 2).

Table 1: Comparison in between OSA and noOSA in postoperative period.

	OSA	noOSA
	N=1,594	N=8,978
Age (years)	56.6 ±10.7	40 ±17.8
Male (%, N)	61.1% (942)	40.5% (3640)
BMI (kg/m^2)	35.3±6.5	27.3±5.9
ICU admission (%, N)	23.2% (417)	27.3% (2452)*
Ventilated (%, N)	6.2% (99)	8.7% (778)*
PACU SPO2 <90%	7.4% (118)	5.6% (504)*
Postop unit SPO2 <90%	55.1% (877)	46.1% (4140)*
On O2 during desaturation	100% (877)	45.1%(4043)*
O2 administered am or pm	100%	92.2% (8278)
O2 NOT used pm	7.3% (115)	23.7 (2128)*
LOS Mean (days)	6.6 ±13.2	7.3 ±12.1*
Mode	1	1
Range	1-150	1-152

CONCLUSIONS: In our study OSApts had fewer complications and and shorter LOS that noOSApts. noOSApt had clinically and statistically greater ICU admissions and need for ventilation. LOS and similar frequency of SPO2<90%. OSApts all received O2 therapy. Further analysis and data regarding outcomes based on complexity of surgery comorbidities and medical interventions may improve our understanding of the perioperative risks conferred by OSA.

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S-232.

INAPPROPRIATE IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR THERAPY DURING SURGERY: AN IMPORTANT AND PREVENTABLE COMPLICATION

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INTRODUCTION: Mounting evidence suggests that inappropriate implantable cardioverter-defibrillator (ICD) therapy, whether shock or antitachycardia pacing, causes myocardial injury and increases mortality. ICD patients undergoing surgery often experience electromagnetic interference (EMI) placing them at risk for inappropriate ICD therapy unless mitigating steps are taken. We present 3 cases in which failure to take necessary precautions resulted in inappropriate ICD therapy.

CASE REPORT: Case 1) A 84 year-old man with nasopharyngeal carcinoma and a Boston Scientific ICD presented to the device clinic for pre-radiation assessment. ICD interrogation revealed delivery of inappropriate anti-tachycardia pacing during his endoscopic sinus surgery at a community hospital. Although preoperative notes from both the surgeon and anesthesiologist acknowledge presence of an ICD, there appears to be no discussion in the record of device parameters, plans to mitigate EMI, or recognition that EMI occurred. There was no mention of device reprogramming or magnet application. The date of the prior interrogation stored in the ICD memory documents the lack of preoperative or postoperative evaluation of the ICD. The patient was unaware of any issues and suffered no overt injury.

Case 2) A 91 year-old man with tongue cancer and St. Jude ICD presented to device clinic for evaluation and treatment planning. ICD interrogation showed an inappropriate shock resulting from EMI during his operative biopsy at a community hospital. Although the anesthesia record shows “magnet on ICD” there was no documentation of device parameters or plans to mitigate EMI (this ICD has no method to confirm appropriate magnet placement). The ICD discharge during the procedure was not documented.

Case 3) A 62 year-old man with a Medtronic biventricular ICD and suspected ICD pocket infection presented for pocket exploration, debridement, and repositioning of the ICD to a sub-pectoral location. The ICD was not interrogated or reprogrammed preoperatively; short bursts of monopolar electrosurgery were planned to prevent unwanted pacing inhibition and ICD firing due to EMI. Soon after surgical incision, the ICD discharged. The patient remained hemodynamically stable in an A-V sequentially paced rhythm. The operative care team then disabled antitachycardia therapy using a device programmer. At the conclusion of the procedure ICD therapy was restored, the patient was extubated and then taken to the recovery room in stable condition.

CONCLUSION: In-hospital EMI appears to offer significant risk to patients with ICDs, and we believe that these events frequently remain undetected and unreported. We present cases from 3 different institutions in which failure to adhere to appropriate precautions resulted in inappropriate intraoperative ICD therapy. Since inappropriate ICD therapy causes myocardial injury and increased mortality, these cases reinforce the need for adherence to published perioperative management recommendations from the American Society of Anesthesiologists and Heart Rhythm Society for patients with cardiac implantable electronic devices.

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S-233.

IS AXILLARY VEIN SIZE SYMMETRIC AND HOW MUCH DOES PATIENT POSITION MATTER?

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BACKGROUND: Anesthesiologists choose the right internal jugular vein for central venous placement because of its size and ease of access. The right internal jugular vein is larger in 73% of people[1] and expands up to 40% in the Trendelenburg (T-burg) position[2]. An alternative is the axillary vein (AxV), which, unlike the subclavian, is easily visualized with ultrasound. We hypothesized that patient position and hand dominance will affect the diameter of the AxVand therefore merit consideration.

METHODS: Following IRB approval and informed consent from 50 volunteers, transcutaneous ultrasound (CX50, Phillips, Andover, MA) was used to measure the diameter of the AxV 2 and 4cm lateral from each clavicle in T-burg, flat, and sitting up positions. Measurements were taken when the vein was at its largest during normal respiration. Data were analyzed by paired sample t-tests.

RESULTS: In comparison to the left AxV, the right AxV diameter in T-burg 2cm from the clavicle was larger by almost 10% (0.90-0.98cm; p= 0.024). In the majority (60%) of volunteers, the AxV was slightly larger on the dominant hand side Ax diameter (2cm) was largest in the T-burg position (Figure2) and progressively decreased in size with change of position: T-burg (0.98cm) >flat (0.93cm)> sitting (0.53cm).

CONCLUSION: The AxVsize is relatively symmetric, becomes 5% larger inT-burgposition, and is likely to be larger on the side of the dominant hand. The average AxV diameter of >0.9cm is large enough to accept a 9 French. Its ready visibility with ultrasound makes the AxV another attractive alternative for central vascular access.

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Figure 1

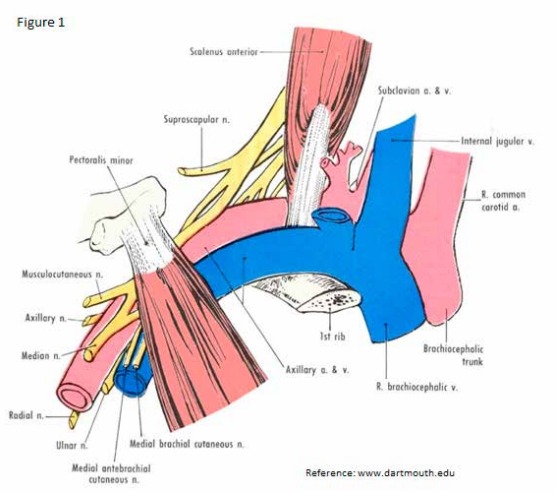
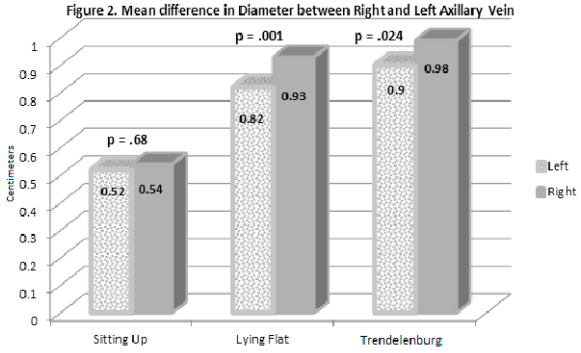


Figure 2. Mean difference in Diameter between Right and Left Axillary Vein



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S-234.

OBJECTIVE POSTOPERATIVE VENTILATORY ASSESSMENT ALGORITHMS IN OBESE PATIENTS FOR PACU MONITORING

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INTRODUCTION: Identifying patients at risk for post-operative apnea (POA) and opioid-induced respiratory depression (OIRD) is challenging with current monitoring and clinical assessment. A non-invasive respiratory volume monitor (RVM) that provides accurate measurements of minute ventilation (MV), tidal volume and respiratory rate in non-intubated patients is available[1]. Recent studies have shown that a majority of patients with > 80% of expected MV prior to PACU opioid administration rarely declined to below 40% of expected after opioid. A pre-opioid MV < 80% had a good sensitivity (93%) and specificity (86%) for predicting a MV < 40% of expected following PACU opioid[2]. These results were obtained in a normal weight population (BMI <30 kg/m2). We examined whether this 80/40 algorithm performed equally in an obese population or if it may require changes.

METHODS: In this multi-center study, following IRB approval and informed consent, respiratory traces were recorded with an impedance-based RVM system (ExSpiron, Respiratory Motion, Inc. Waltham, MA) from 37 obese patients (Age 20-75, mean 49; BMI 35-65, mean 44) undergoing elective surgery with general anesthesia and mechanical ventilation. The RVM was synchronized to the ventilator MV intra-operatively which served as the individual baseline ($MV_{BASELINE}$). The post-operative MV values within 15 minutes prior to and following PACU opioid administration were compared. The previously derived 80/40 MV stratification was applied to this cohort and compared to a 75/40 algorithm using sensitivity and specificity analyses.

RESULTS: Using the 80/40 model, 8/18 (44.4%) patients with an MV <80% of $MV_{BASELINE}$ before opioid administration had an MV decrease to <40% of $MV_{BASELINE}$. Only 1/19 (5.2%) patient with an MVEXP >80% experienced the same. This stratification was 89% sensitive, 64% specific, with a positive predictive value (PPV) of 44%, and a negative predictive value (NPV) of 95% (Figs. 1,3). In the 75/40 algorithm, 8/16 (50%) patients with a $MV_{BASELINE}$ <75% before opioid administration decreased to <40% of $MV_{BASELINE}$, while 1/21(4.8%) patient with an MVBASELINE >75% prior to opioid declined <40% (Fig. 2). This stratification had a sensitivity of 89%, specificity of 71%, a PPV of 50%, and a NPV of 95% (Fig. 3).

CONCLUSIONS: A dramatic reduction in MV from baseline occurs in a subset of post-operative obese patients in the PACU following opioid administration to values < 40% of $MV_{BASELINE}$. The RVM allows real time identification of such patients and further study will determine whether this is associated with a risk for increased post-operative complications. The data suggests that a 75/40 stratification algorithm may be better suited in the obese population than the 80/40 stratification. Further refinement of stratification algorithms are needed to facilitate focused post-operative care and protocols aimed at reducing post-operative respiratory complications and improving patient safety.

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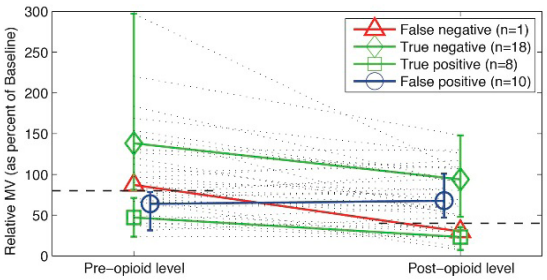

Figure 1: 80/40 stratification model. Patients stratified based on individual % $MV_{BASELINE}$ values before PACU opioid administration. Circle and square = pts with < 80% $MV_{BASELINE}$ before opioid. Diamond and triangle = pts with $MV_{BASELINE}$ >80% before opioid.

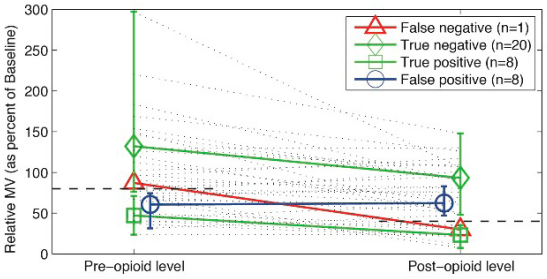

Figure 2: 75/40 stratification protocol. Patients stratified based on individual % $MV_{BASELINE}$ values before PACU opioid administration. Circle and square = pts with < 80% $MV_{BASELINE}$ before opioid. Diamond and triangle = pts with $MV_{BASELINE}$ >80% before opioid.

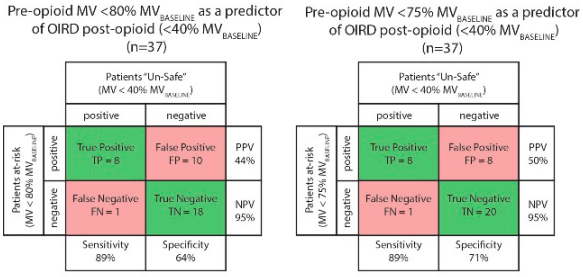

Figure 3: Left: Pre-opioid MV as a predictor of opioid-induced minute ventilation changes in obese patients; 80/40 stratification protocol. Right: Pre-opioid MV as a predictor of opioid-induced minute ventilation changes in obese patients; 75/40 stratification protocol

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S-235.

REMOTE VIDEO AUDITS OF OPERATING ROOM PRACTICES SUSTAINABLY IMPROVE PATIENT SAFETY PROCESSES AND OPERATING ROOM THROUGHPUT

AUTHORS: F. Overdyk[1], O. Dowling[1], J. F. Di Capua[2], D. Armellino[1], J. Iammatteo[1], R. Mercieca[1]

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BACKGROUND: Objective performance data for processes essential to patient safety and OR efficiency, such as surgical time out (STO), OR cleaning, and OR throughput, are challenging to obtain. When collected by OR stakeholders, these metrics are often biased and time consuming to collect[1]. Video auditing has been described in the OR and beyond to improve the quality of care by influencing behavior, analyzing adverse events, and encouraging best practice[2,3]. This quality improvement initiative uses an off-site, third party video audit service to provide objective data on compliance with STO and OR cleaning, as well as OR efficiency metrics, integrating real time feedback to optimize team performance.

METHODS: Video only feeds from the eight OR's at Forest Hills Hospital, NY are analyzed in real time by Arrowsight Inc. After a baseline data collection period, OR staff were educated on the 'best practice' for STO and OR terminal/overnight cleaning (TC). Feedback on compliance with best practices, as well as OR throughput metrics, are displayed electronically throughout the OR suite (Fig 1,2) and distributed in daily and weekly reports. In addition, text messages alert practitioners and OR staff to changes in OR status. The video, intentionally 'blurred' to limit facial recognition, is erased after review, and only data on team performance is retained. Inter-rater variability of audit staff was calculated.

RESULTS: With IRB approval, data from the first 4 weeks of video auditing were compared to 4 weeks of recent data for STO/TC compliance and 2 weeks of data for throughput performance (Table 1). Use of an STO 'check list', an adequate duration of STO, and attention to STO by the OR team improved to near 100%. Compliant TC consistent with guidelines improved from 12% to 99%. Average first case starts improved by 19 minutes, and 4.8/23.6 min of non-surgical time was saved per case before/after noon, which equates to 52 min per OR (3 sched cases/OR/day). The intra-class correlation coefficient for agreement of time segments among 3 video auditors assigning timestamps was 1, and similarly high for pass/fail criteria of required elements of the STO/terminal cleaning (Fleiss Kappa statistic =1.00).

CONCLUSION: Initial results suggest remote video performance feedback produces meaningful improvements in compliance with safety processes and OR efficiency, especially after noon, due to more effective communication/team dynamics. We anticipate efficiency gains may be improved with further refinement. The impact of video auditing on reducing preventable patient harm (ie. wrong patient/site surgery, surgical site infections) and provider and patient satisfaction remains to be studied.

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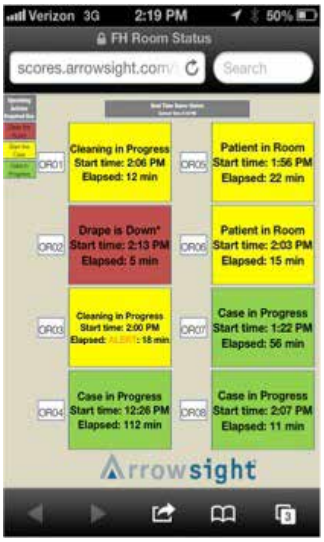
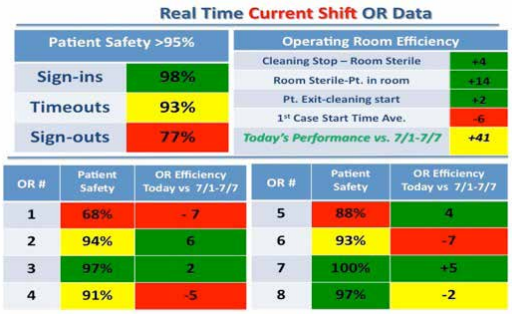


Disclosure: Material support provided by Arrowsight Inc.



Safety Metrics Before/After Remote Video Audit + Feedback		
Surgical Time Out (STO) % Compliance	Baseline	After Feedback
Each team member is attentive to STO	88%	100%
STO performed after surgical drape is up	97%	100%
STO minimum duration of 60 seconds	83%	99%
Terminal OR Cleaning % Compliance		
Minimum cleaning time (60min - 1 cleaner;	9%	97%
(40min - 2 cleaners)		
% of tasks completed:PPE; wipe equipment, scrub/dry floor, repo equip, clean walls/waste	12%	99%

OR Thruput Metrics pre/post Remote Video Audit & Feedback				
ALL DATA in minutes	Baseline n=243	After Feedback n=150	Baseline n=168	After Feedback n=90
	Before 12 noon	Before 12 noon	After 12 noon	After 12 noon
First Case Start Delay	18.9	0.6	N/A	N/A
Room ready -> Pt in Room	19.5	13.8	32.1	18.6
Pt in Room -> Start Surgery	21.2	25.3	25.6	26.1
Drape down --> Pt exit	13.3	13.2	15.9	14.1
Pt out of room -> Room cleanup start	3	-0.1	2.5	0.7
Room clean up (start-stop)	16.5	16.9	17.6	16
Non surgical time	73.5	69.2	93.7	75.5

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AGREEMENT BETWEEN PATIENT-REPORTED IN-HOSPITAL POSTOPERATIVE COMPLICATIONS AND COMPLICATIONS FOUND BY CHART REVIEW

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INTRODUCTION: Increasing emphasis has been placed on patient-reported outcomes (PROs) in recent years, yet their validity in regard to specific medical complications, such as postoperative myocardial infarction, has not been characterized. Non-surgical patients report elements of their medical history with excellent negative agreement and poor/moderate positive agreement compared to medical records.[1-4] The goal of this study was to quantify agreement between PROs of in-hospital postoperative complications and the medical record.

METHODS: With IRB approval and written informed consent, a survey including a question about 18 complications is being sent to patients 30 days after a variety of surgeries at one academic medical center. From the 1578 responses received by June 2013 (representing a response rate of about 66%), a sample of 750 was taken. The sample was enriched with all 470 patients who reported a complication. The remaining 280 patients were randomly selected: 129 reported no complication, 140 preferred not to answer, and 11 left the question blank. Medical records of these 750 patients were reviewed independently by two researchers in consultation with a clinical researcher. Discrepancies were resolved by another clinical researcher. Agreement between PROs and chart review was quantified using positive and negative agreement, as well as the kappa statistic. To investigate discrepancies, 70 patients with discordance between PROs and chart review were phoned.

RESULTS: Of 1578, 470 patients (30%) reported at least one complication, 742 (47%) reported no complication, 249 (16%) preferred not to answer, and 117 (7%) left the question blank. The most common PROs were severe pain (n = 188), abnormal heart rhythm (n = 86), and severe nausea/vomiting (n = 63). In the 750 selected for chart review, negative agreement was excellent for most complications, while positive agreement and kappa were in the low-moderate range (Table). Reporting no complication and preferring not to answer both predicted absence of complications on chart review (predictive value [95% CI] 98.4% [96.3%, 100%] and 98.6% [96.6%, 100%] respectively). By phone, 42 patients were reached, representing 54 discordant complication reports. Twenty-four had reported events that occurred before surgery, while nine reported post-discharge events. Two in-hospital complications were not detected by chart review, and three patients misinterpreted routine in-hospital events as complications.

TABLE – AGREEMENT BETWEEN PATIENT REPORT AND CHART REVIEW AMONG PATIENTS WHO REPORTED (N = 470) OR DENIED (N = 129) COMPLICATIONS ON SURVEY

Complication	Reported on Survey – n (%)	Found on Chart Review – n (%)	Positive Agreement	Negative Agreement	Kappa (95% CI)
Myocardial infarction	7 (1.2%)	0 (0%)	0%	99%	N/A
Cardiac arrest	5 (0.8%)	0 (0%)	0%	100%	N/A
Congestive heart failure	23 (3.8%)	2 (0.3%)	8%	98%	0.07 (-0.07,0.22)
Arrhythmia	86 (14.4%)	42 (7.0%)	47%	94%	0.41 (0.30,0.52)
Angina	8 (1.3%)	3 (0.5%)	18%	99%	0.18 (-0.13,0.48)
Stroke	11 (1.8%)	4 (0.7%)	53%	99%	0.53 (0.22,0.83)
Deep venous thrombosis	20 (3.3%)	7 (1.2%)	37%	99%	0.36 (0.13,0.59)
Pulmonary embolism	8 (1.3%)	3 (0.5%)	55%	100%	0.54 (0.19,0.90)
Wound infection	36 (6.0%)	8 (1.3%)	5%	96%	0.02 (-0.06,0.11)
Respiratory arrest	7 (1.2%)	0 (0%)	0%	99%	N/A
Respiratory failure	22 (3.7%)	2 (0.3%)	17%	98%	0.16 (-0.04,0.36)
Pneumonia	21 (3.5%)	4 (0.7%)	32%	99%	0.31 (0.08,0.55)
Kidney failure requiring dialysis	16 (2.7%)	2 (0.3%)	22%	99%	0.22 (-0.03,0.47)
Nerve injury	38 (6.3%)	11 (1.8%)	24%	97%	0.22 (0.06,0.38)
Gastrointestinal bleed	10 (1.7%)	2 (0.3%)	17%	99%	0.16 (-0.12,0.45)
Gastric or duodenal ulcer	7 (1.2%)	1 (0.2%)	0%	99%	0.00 (-0.01,0.00)
Severe pain lasting >1 day	188 (31.4%)	189 (31.6%)	49%	76%	0.25 (0.17,0.33)
Severe nausea/vomiting lasting >1 day	63 (10.5%)	185 (30.9%)	34%	83%	0.22 (0.14,0.29)

CONCLUSION: Our findings of high negative agreement and low positive agreement are consistent with studies of non-surgical patients. Possible explanations include inaccurate chart review, in-hospital miscommunication with patients, inaccurate recall, or misunderstanding of the survey question. While PROs are often reliable, they might have some limitations in relation to certain medical diagnoses and complications, especially those based on clinician judgment and special investigations.

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S-237.

PREOPERATIVE FACTORS FOR PREDICTING POSTOPERATIVE HYPOTHERMIA AND TEMPERATURE CHANGE FOLLOWING ABDOMINAL SURGERIES

AUTHORS: O. Visnjevac[1], R. Kocz[1], P. Kim[1], M. E. Hsia[1], C. G. Samuelson[2], J. Grande[1], N. D. Nader[1]

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INTRODUCTION: Perioperative hypothermia is an important patient safety issue, and often leads directly to significant perioperative morbidity. Greater body fat percentage and body mass index (BMI) have been considered protective and have been shown to be associated with reduced perioperative heat loss[1]. Body surface area (BSA) was also found to be inversely related to the rate of patient rewarming[2], but these studies both had small sample sizes. Hence, a large retrospective review of perioperative temperature change was undertaken to assess the relationship between BMI and BSA for abdominal with the hypothesis that a BMI:BSA ratio would be a useful predictive index for postoperative hypothermia.

METHODS: Data for 5168 consecutive adult abdominal procedures, collected from 3 hospitals over two years, were separated into laparoscopic, intracavitary, or peripheral surgeries. Multivariate analyses were utilized to identify significant variables contributing to decreases in perioperative temperature. All patients under general anesthesia received forced-air warming blankets.

RESULTS: Using logistic regression: age, total operating room time, laparoscopic and peripheral procedures, BMI, and BMI:BSA ratio were not found to significantly correlate with decreased perioperative temperature. In contrast, BSA (OR 0.39, 95% CI 0.18-0.84, P=0.016), intracavitary procedures (OR 1.95, 95% CI 1.12-3.39, P=0.017) and patients' preoperative temperature (OR 34.69, 95% CI 18.90-63.67, P<0.00001) were found to be significant predictors of decreases in perioperative temperature. Linear regression identified each °C increase in patients' preoperative temperature ratio to reliably predict a 0.65°C reduction in the total perioperative temperature change (b = -0.65, 95% CI -0.68 - -0.62, P<0.0001).

CONCLUSIONS: BMI:BSA was shown to be an inferior index than BSA alone for predicting postoperative hypothermia. This positive correlation between BSA and perioperative temperature may be explained by effective intraoperative warming, with consideration that patients with greater BSA have more contact points with forced-air warming blankets than those with lesser BSA. Preoperative hypothermia was the most significant factor contributing to postoperative hypothermia, suggesting that preoperative patient warming may be an important intervention for the prevention of postoperative hypothermia.

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S-238.

BARRIERS TO THE IMPLEMENTATION OF CHECKLISTS IN THE OFFICE-BASED SETTING

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INTRODUCTION: The number of procedures performed in the office-based setting continues to increase, yet these types of practices are subject to very few state and federal regulations. Patient safety is critical for the patients, providers and risk managers, and the same standard of care should be maintained regardless of the healthcare setting. The use of a checklist may improve patient safety and potentially help minimize risk. Currently, there are no mandatory requirements to use checklists in the office-based setting, unlike inpatient and ambulatory surgical care facilities. This study was designed to ascertain whether checklists were being utilized in the office-based setting and the potential barriers to their implementation.

METHODS: This study was approved by the institutional review board. A cross-sectional prospective study was performed by using a 19-question anonymous survey designed with RedCap®. A total of 103 medical providers that included physicians and nurses from 25 different offices that performed medical and/or surgical procedures were identified and asked to participate. There were 43 responses and 38 were included in the study.

RESULTS: Only 50% of offices surveyed use safety checklists in their practice. Only 34% had checklists or equivalent protocol for emergencies such as anaphylaxis or failed airway. As many as 23.7% of respondents indicated that they encountered barriers to implementing checklists. The top barriers identified in the study were no incentive to use a checklist (77.8%), no mandate from a local or federal regulatory agency (44.4%), being too time consuming (33.3%), and lack of training (33.3%). When asked to pick a reason that would encourage providers to use checklists, the most common responses were a clear mandate (36.8%) and if research showed improved benefit to the patient (26.3%). Table 1 summarizes our results.

CONCLUSIONS: Checklists are not being universally utilized in the office-based setting, unlike inpatient procedural facilities where their use has been shown to potentially decrease patient morbidity and costs of care. Furthermore, there appear to be barriers preventing their successful implementation. The perioperative team and risk managers may be able to improve patient safety and minimize risk by encouraging the use of customizable safety checklists and providing incentive to the practitioners by working with a diverse group of stakeholders.

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Table 1: Office survey results

Survey Item	Survey Result
Offices with accreditation	61%
Offices using checklists	50.0%
Most common time when checklist is used	Initial encounter (47.4%) Immediately pre-procedure (89.5%)
Most common type of checklist used	Facility-generated (57.9%) Professional society/specialty generated (21.1%) W.H.O. (15.8%)
Offices using checklists for emergencies	34.2%
Responders who identified barriers to checklist use (from the group who are not currently using checklists)	23.7%
Top barriers to checklist use	No incentive to use (77.8%) No mandate from a local or federal regulatory agency (44.4%) Too time-consuming (33.3%) Lack of training (33.3%) Not familiar with the concept (11.1%) Lack of educational resources (11.1%)
Factors that would encourage the use of checklists	Clear mandate (36.8%) If research showed improved benefit to the patient (26.3%) If encouraged to use by professional agency/regulatory society (13.2%) Additional training (13.2%)

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S-239.

DEVELOPMENT OF A COLORECTAL SURGERY REPORTING TOOL: THE NO BUGS DASHBOARD

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INTRODUCTION: Despite advances in surgical techniques and perioperative care, colorectal surgery has one of the highest rates of surgical site infections (SSI).[1] However, evidence suggests that a number of perioperative interventions may help modulate SSI rates, including maintenance of normothermia, management of blood glucose levels, achievement of mild hypercapnea, appropriate utilization of prophylactic antibiotics, and provision of a high concentration of inspired oxygen.[2,3,4,5,6] In order to help our clinicians improve their performance in these areas, we developed the NO BUGS Reporting Dashboard.

METHODS: We began by reviewing the literature and engaged in a multi-disciplinary consensus driven process to determine what represents the optimal perioperative care of colorectal patients. A NO BUGS protocol7 was developed (see Figure 1a and 1b) and we then developed a list of metrics mapped to the protocol which could be automatically obtained from our routine clinical documentation. We are now in the process of validating six of the proposed performance metrics. Each metric is scored in a pass/fail system, and if any applicable metric for a case is failed, then the case is flagged as a 'fail.' These failed case then appear in the NO BUGS dashboard and can be selected in order to load the electronic perioperative care record for review.

RESULTS: We developed six performance metrics mapped to the NO BUGS Protocol shown in Figure 1 which are a) maintenance of normothemia, b) high inspired oxygen content, c) proper antibiotic administration and redosing, d) mild underventilation, e) glucose monitoring & control, and f) appropriate skin preparation prior to incision and line placement. Faculty performance on 2,847 completed colorectal surgery cases has been incorporated into our automated dashboard as shown in Figure 2.

CONCLUSIONS: We demonstrate the development of a perioperative colorectal surgery process dashboard and six potential clinical performance metrics. These metrics have been implemented in an online dashboard that will soon provide near real-time feedback to our faculty. These data are reviewed bi-monthly by a multi-disciplinary team. Educational interventions have been undertaken for anesthesia, surgery, and nursing personnel involved with these patients. Longitudinal assessment will involve evaluation of both patient outcomes and effectiveness of educational and organizational methods for consistent implementation.

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Figure 1a

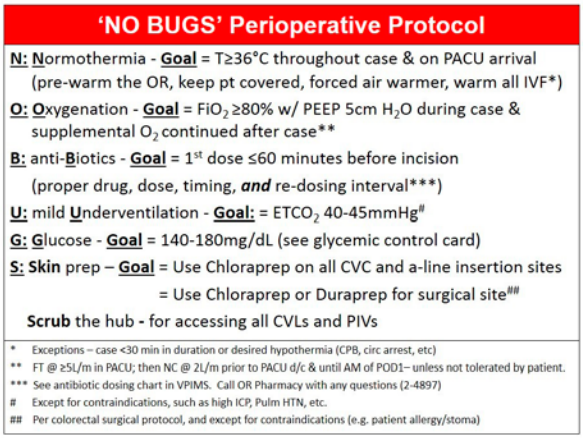

Figure 1b

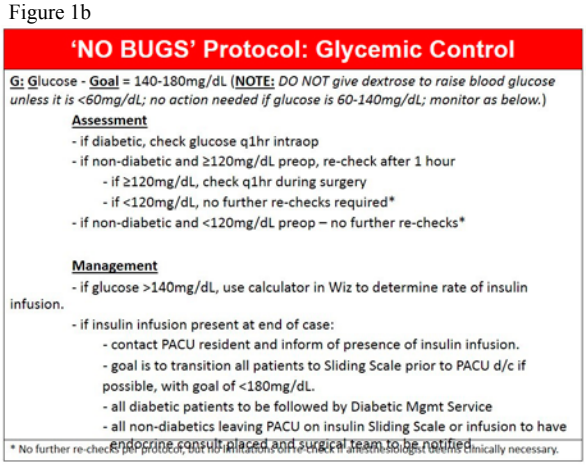

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Figure 2: This figure displays the NO BUGS dashboard view which is accessed through a password-protected website.

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S-240.

PREVENTING IATROGENIC HYPERKALEMIA: A PATIENT SAFETY CASE REPORT

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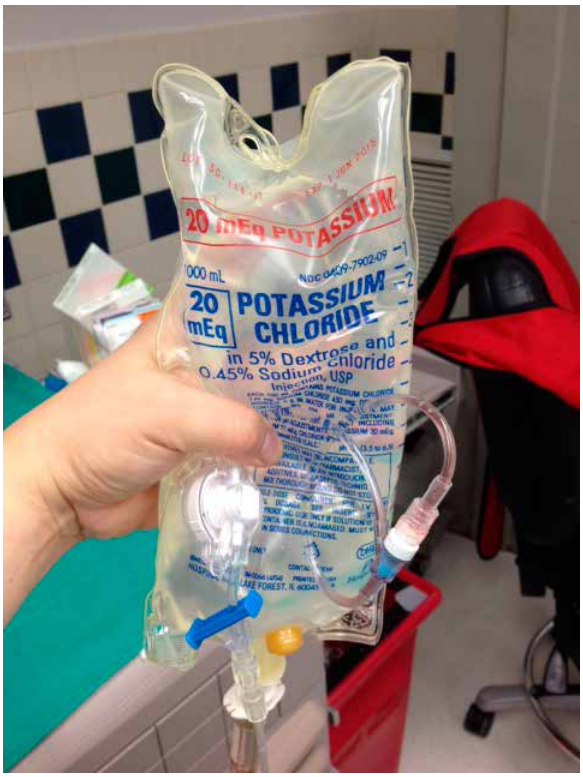
INTRODUCTION: Iatrogenic hyperkalemia is a serious and life-threatening circumstance that must be avoided at all costs. Resuscitation from hyperkalemic cardiac arrest requires aggressive therapy that is not always successful.[1] In 2006, JCAHO targeted potassium chloride as a "high-alert medication," [2] This was echoed again in 2012, when it was listed as a goal for the improvement of patient safety[3] It is for these reasons that we began a hospital-wide protocol for the management of patients receiving potassium intravenously. The impetus for our initiative is presented in the following near-miss case report and then addressed in the subsequent protocol.

CASE REPORT: A 37-year-old mother of two presented to the emergency department with symptomatic cholelithiasis two days prior to Thanksgiving Day 2013. She was then scheduled for a cholecystectomy under general anesthesia. On leaving the ED for the operating room, her peripheral IV access was directly attached to a crystalloid solution containing 20mEq/L of Potassium Chloride in 1000mL without a pump to regulate the infusion rate. When the patient arrived to the pre-op holding area, fortunately, the mostly full IV bag containing 20mEq/L KCL was soon noticed by the anesthesiologist and immediately removed. Failure to recognize the KCL could have potentially led to the patient suffering iatrogenic hyperkalemic cardiac arrest if the solution was rapidly infused. The patient's operation proceeded smoothly and successfully. She was then discharged from the hospital.



CONCLUSION: After this case we began a hospital-wide protocol that mandates the use of pumps for the infusion of potassium and limited the rate to 10mEq/hr.[4] An incident of iatrogenic hyperkalemic cardiac arrest would have been a tragedy for the patient's family and for the health care providers involved. Our goal for this poster presentation is to educate and remind anesthesiologists to always be vigilant and check what IV solutions are attached to a patient's IV prior to proceeding with an anesthetic.

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RATES AND PREDICTORS OF PERIOPERATIVE MORTALITY: PRELIMINARY DATA FROM THE NATIONAL ANESTHESIA CLINICAL OUTCOMES REGISTRY

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INTRODUCTION: The National Anesthesia Clinical Outcomes Registry (NACOR) was created in 2010 as a quality improvement data warehouse and has accumulated over twelve million cases. We present a preliminary analysis of the NACOR database focusing on rates of and associations with perioperative death.

METHODS: We conducted a retrospective analysis of 12,751,712 cases in NACOR performed between 1/1/2010 and 11/6/2013. Cases from practices not reporting outcomes data (10,534,952 cases), cases with no procedure information (77,513 cases), non-surgical obstetric procedures including vaginal delivery (41,366 cases), and patients with ASA physical status (ASAPS) 6 and/or undergoing organ procurement (432 cases) were excluded. Mortality was reported by the anesthesia provider and varied by practice, with some including deaths prior to PACU discharge and others reporting deaths up to 48 hours after induction of anesthesia. Logistic regression was performed on cases that had complete information for the variables of interest (1,498,660) cases). Facility type, region, and primary anesthesia type were not included in the final model because of concerns of incomplete data.

RESULTS: The final analysis included 2,099,392 cases and 594 deaths (crude death rate 28/100,000). Comparison between included and excluded cases and proportion of missing data by variable are in Table 1. Logistic regression adjusting for patient age group, sex, ASAPS, emergency case status, time of day, and body region of procedure demonstrated that increasing ASAPS, emergency cases, cases performed outside regular daytime hours, and age <1 year were independently associated with increased perioperative mortality (Table 2). A subgroup analysis of 229,746 patients limited to 22 elective case types confirmed the association with time of day. The most common outcomes concurrently documented in patients who died were major or minor hemodynamic instability, major or minor respiratory complications including airway/intubation complications, upgrade of care, and resuscitation.

CONCLUSIONS: Several factors were associated with increased perioperative mortality. Of the modifiable factors, a case start time after 6pm was associated with an adjusted odds ratio of at least 1.74 for perioperative death, which is higher than previously reported. Limitations of this study include non-standardized mortality reporting and the large proportion of cases that had to be excluded for missing data. The NACOR database is nonetheless a powerful tool for exploring rare perioperative events. Improvements in practice reporting will maximize data completeness and generalizability and will allow further investigation of regional and national contributors to morbidity and mortality.

ACKNOWLEDGMENT: We thank the Anesthesia Quality Institute and NACOR for collecting and sharing the data that made the preparation of this abstract possible.

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Table 1. Comparison between included and excluded patients. Patient ages were compared with a t-test; all other comparisons were performed with chi square.

	Variable	Included, n (% of included)	Excluded, n (% of excluded)	P-value
Patient age	Mean ± standard deviation	49.8 ± 21.9	48.8 ± 22.5	**<0.001**
	Missing	18,158 (0.9%)	243,864 (2.3%)	
Patient sex	Male	874,134 (41.6%)	4,127,191 (41.7%)	**<0.001**
	Female	1,214,119 (57.8%)	6,224,430 (57.7%)	
	Missing	11,139 (0.5%)	300,699 (3.0%)	
ASA physical status	1 or 2	1,368,567 (65.2%)	5,501,515 (51.7%)	**<0.001**
	3	576,683 (27.5%)	2,175,490 (20.4%)	
	4	128,375 (6.1%)	404,842 (3.8%)	
	5	3,441 (0.2%)	10,724 (0.1%)	
	6	0	3,729 (<0.1%)	
	Missing	22,326 (1.1%)	2,556,020 (24.0%)	
Procedure urgency	Emergent	44,241 (2.1%)	428,932 (4.0%)	**<0.001**
	Nonemergent	68,225 (3.3%)	155,598 (1.6%)	
	Assumed nonemergent*	1,964,611 (93.6%)	7,519,303 (70.6%)	
	Missing	22,315 (1.1%)	2,548,487 (23.9%)	
Primary anesthesia technique	General	1,393,488 (66.4%)	5,130,345 (48.2%)	**<0.001**
	Neuraxial	162,367 (7.7%)	684,626 (6.4%)	
	Regional	28,961 (1.4%)	161,851 (1.5%)	
	Monitored anesthesia care	389,499 (18.6%)	1,137,050 (10.7%)	
	Sedation	0	108,429 (1.0%)	
	Local	10 (<0.1%)	9,899 (0.1%)	
	Other	1,732 (0.1%)	94,820 (0.9%)	
	Missing	123,335 (5.9%)	3,325,300 (31.2%)	
Body region of procedure	Extremity	411,499 (19.6%)	2,049,098 (19.2%)	**<0.001**
	Head/spine	329,442 (15.7%)	1,925,724 (18.1%)	
	Neck/thorax	244,735 (11.7%)	1,305,282 (12.3%)	
	Abdomen/pelvis	679,988 (32.4%)	3,509,905 (33.0%)	
	Obstetric	114,884 (5.5%)	946,621 (8.9%)	
	Radiological	47,152 (2.3%)	249,220 (2.3%)	
	Other	8,136 (0.4%)	53,991 (0.5%)	
	Missing	263,556 (12.6%)	612,479 (5.8%)	
Case start time	07:00 – 15:59	1,566,373 (74.6%)	9,026,631 (84.7%)	**<0.001**
	16:00-17:59	82,332 (3.9%)	426,604 (4.0%)	
	18:00-22:59	59,087 (2.8%)	370,803 (3.5%)	
	23:00-06:59	48,387 (2.3%)	423,073 (4.0%)	
	Missing	343,213 (16.4%)	405,209 (3.8%)	
Region	Northeast	584,322 (27.8%)	985,427 (9.3%)	**<0.001**
	Midwest	640,153 (30.5%)	2,980,312 (28.0%)	
	South	709,869 (33.8%)	4,288,572 (40.3%)	
	West	150,954 (7.2%)	2,070,992 (19.4%)	
	Missing	14,094 (0.7%)	327,017 (3.1%)	
Facility type	University hospital	313,004 (14.9%)	875,804 (8.2%)	**<0.001**
	Community hospital, >500 beds	301,518 (14.4%)	1,922,938 (18.1%)	
	Community hospital, 100-500 beds	945,774 (45.1%)	3,872,611 (36.4%)	
	Community hospital, <100 beds	55,313 (2.6%)	304,903 (2.9%)	
	Specialty hospital	29,374 (1.4%)	144,397 (1.4%)	
	Attached surgical center	64,991 (3.1%)	546,171 (5.1%)	
	Freestanding surgical center	79,620 (3.8%)	1,282,867 (12.0%)	
	Pain clinic	41,714 (2.0%)	19,382 (0.2%)	
	Surgeon office	1,790 (0.1%)	62,389 (0.6%)	
	Unknown/other	252,200 (12.0%)	1,341,466 (12.6%)	
	Missing	14,094 (0.7%)	279,392 (2.6%)	
Mortality	Yes	594 (0.03%)	25 (<0.001%)	**<0.001**
	No	273,583 (13.0%)	50,405 (0.5%)	
	Missing	1,825,215 (87.0%)	10,601,890 (99.5%)	
Total		2,099,392	10,652,320	

* These cases had a documented ASA with a missing value for the emergency case modifier. They were assumed to be elective cases.

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Table 2. Crude and adjusted odds for mortality. Adjusted odds ratio reflects binary logistic regression for mortality with patient age group, sex, ASA physical status, emergency case status, time of day, and procedure region. Statistically significant comparisons are indicated in bold text.

	Variable	Deaths/total	Crude rate per 100,000 cases	Unadjusted OR (95% CI)	Adjusted OR (95% CI) (n=1,498,660)
Patient age group (years)	<1	31/13,448	231	**15.3 (10.2-22.8)**	**4.02 (2.13-7.60)**
	1-18	28/197,117	14	0.94 (0.62-1.42)	0.82 (0.40-1.68)
	19-49	107/707,291	15	(ref)	(ref)
	50-64	142/567,448	25	**1.65 (1.29-2.13)**	0.97 (0.68-1.40)
	65-79	181/451,991	40	**2.65(2.08-3.36)**	1.34 (0.95-1.90)
	≥ 80	84/143,891	58	**3.86 (2.90-5.13)**	1.32 (0.88-1.99)
Patient sex	Female	243/1,214,119	20	(ref)	(ref)
	Male	351/874,134	40	**2.01 (1.70-2.36)**	1.08 (0.86-1.37)
ASA physical status	1 or 2	45/1,368,567	3.3	(ref)	(ref)
	3	111/576,683	19	**5.85 (4.14-8.28)**	**3.97 (2.65-5.94)**
	4	242/128,375	189	**57.4 (41.8-79.0)**	**19.0 (12.6-28.6)**
	5	180/3,441	5230	**1680 (1200-2350)**	**256 (160-409)**
Procedure urgency	Nonemergent	459/2,032,836	23	(ref)	(ref)
	Emergent	120/44,241	271	**12.0 (9.85-14.7)**	**4.69 (3.44-6.40)**
Case start time	07:00 – 15:59	214/1,566,373	14	(ref)	(ref)
	16:00 – 17:59	33/82,332	40	**2.93 (2.03-4.23)**	1.29 (0.85-1.94)
	18:00 – 22:59	50/59,087	85	**6.20 (4.56-8.43)**	**1.74 (1.21-2.50)**
	23:00 – 06:59	39/48,387	81	**5.90 (4.20-8.31)**	**2.15 (1.43-3.24)**
Body region of procedure	Extremity	63/411,499	15	(ref)	(ref)
	Head/spine/eye	44/329,442	13	0.87 (0.59-1.28)	0.86 (0.54-1.35)
	Thorax/neck	98/244,735	40	**2.62 (1.91-3.59)**	0.91 (0.62-1.33)
	Abdomen/pelvis	229/679,988	34	**2.20 (1.66-2.91)**	1.17 (0.83-1.65)
	Obstetric	1/114,884	0.87	**0.06 (0.008-0.41)**	*
	Radiological	23/47,152	49	**3.19 (1.98-5.14)**	1.08 (0.60-1.93)
	Other	1/8,136	12	0.80 (0.11-5.79)	2.26 (0.31-16.6)
Primary anesthesia technique	General	554/1,392,934	40		
	Neuraxial	11/162,356	6.8		
	Regional	0/28,961	0		
	Monitored anesthesia care	21/389,478	5.4		
	Local	0/10	0		
	Other	0/1,732	0		
Facility type	University hospital	53/312,951	17		
	Community hospital, >500 beds	242/301,276	80		
	Community hospital, 100-500 beds	240/945,534	36		
	Community hospital, <100 beds	20/55,293	36		
	Specialty hospital	0/29,374	0		
	Attached surgical center	0/64,991	0		
	Freestanding surgical center	0/79,620	0		
	Pain clinic	0/41,714	0		
	Surgeon office	0/1,790	0		
	Unknown/other	39/252,161	15		
Total		594/2,099,392	28		

* Adjusted odds ratio for obstetric cases could not be calculated because of missing data in the single obstetric death. Abbreviations: OR, odds ratio. CI, confidence interval. Ref, reference category.

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S-242.

ASSOCIATION OF STOP-BANG SCORES OR OSA DIAGNOSIS WITH POSTOPERATIVE APNEA AND MINUTE VENTILATION IN AN OBESE SURGICAL POPULATION USING RESPIRATORY VOLUME MONITORING IN THE PACU

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INTRODUCTION: Sleep disordered breathing including obstructive sleep apnea (OSA) has a high prevalence in obese patients and is a risk factor for postoperative complications [1]. Tools such as the STOP-Bang (SB) questionnaire can identify patients at risk for OSA and offer stratification into risk categories. Post-operative care protocols have been developed for such patients, and may require prolonged PACU stays, CPAP or additional monitoring after PACU discharge. A non-invasive, impedance-based respiratory volume monitor (RVM) that provides, accurate, continuous, real-time, quantitative measurements of minute ventilation (MV), tidal volume (TV) & respiratory rate (RR) is now available. This study examines the association of SB scores or pre-operative OSA diagnosis with MV in the PACU as determined by this novel technology.

METHODS: Following IRB approval and informed consent, continuous respiratory traces were obtained from the RVM system (ExSpiron, Respiratory Motion, Inc. Waltham, MA) in obese patients undergoing elective surgery with general anesthesia. Demographics, prior OSA diagnosis and SB scores with patients stratified into low (0-2), intermediate (3-4) and high (5-8) were recorded. An apneic event (AE) was defined as no detected breaths for >10 sec. Postoperative apnea (POA) was defined as >5 AE/hr. The lowest MV (LMV) in the PACU (5 min avg) was identified for each patient, and an LMV of <40% predicted (based on IBW) was defined as a surrogate indicator of postoperative respiratory depression (PORD). The 2-tailed Fisher's exact test was used for statistical analysis with a $p < 0.05$ considered significant.

RESULTS: 80 patients (25 female) aged 47 ± 12 years with a BMI of 43 ± 7 kg/m2 completed the study. Table 1 summarizes the association of SB risk categories and preoperative OSA diagnosis with POA and PORD. No significant association could be demonstrated. Categorical differentiation based on SB scores and OSA diagnosis show that with increasing specificity, the model becomes less sensitive with no optimal pattern present (Table 2). POA was a poor predictor of LMV as an indicator of PORD due to rescue breath variability (Fig. 1). Correlation of SB scores with POA and PORD as continuous variables was not significant, and POA did not correlate well with PORD (Fig. 2).

CONCLUSIONS: Although the SB score is a useful tool for preoperative OSA risk stratification, it did not correlate well with objective measures of postoperative apnea and minute ventilation as determined by the RVM in obese patients recovering from general anesthesia. Furthermore, identifying patients with apneic events (POA) is not sufficient to identify patients with low minute ventilation in the PACU. This study demonstrates the potential utility of objective post-operative respiratory volume monitoring to better identify patients at risk for respiratory depression and individualize post-operative management protocols. Further study is needed to identify patients that can most benefit from this monitoring to optimize safety and streamline care.

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1. Br J Anaesth; 108; 2012: 768-775 Anesthesiology. 2009; 110(5): 1077-1085.

Table 1: Association of STOP-Bang score category and OSA diagnosis with postoperative apnea and postoperative respiratory depression.

	STOP-Bang				OSA Diagnosis		
	Low (0-2)	Intermediate (3-4)	High (5-8)		- OSA	+ OSA	
	n = 12	n = 25	n = 43	*p Value*	n = 51	n = 29	*p Value*
+ POA n (%)	3 (25)	5 (20)	17 (40)	0.24	16 (31)	9 (31)	1.00
+ PORD n (%)	2 (8)	3 (12)	8 (19)	0.91	7 (14)	6 (20)	0.53

Table 2:

SB score as a predictor of postoperative apnea and postoperative respiratory depression respectively.

	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
STOP-Bang score cut-offs as predictors for POA:								
3 (0-2 vs. 3-8, Low vs. Intermediate + High)	22	46	3	9	88.0	16.4	32.4	75.0
5 (0-4 vs. 5-8, Low + Intermediate vs. High)	17	26	8	29	68.0	52.7	39.5	78.4
OSA as a predictor of POA	9	20	16	35	36.0	63.6	31.0	68.6
STOP-Bang score cut-offs as predictors for PORD:								
3 (0-2 vs. 3-8)	11	57	2	10	84.6	14.9	16.2	83.3
5 (0-4 vs. 5-8)	7	36	6	31	53.8	46.3	16.3	83.8
OSA as a predictor of PORD	6	25	7	44	46.2	63.8	19.4	86.3

TP - True Positive; FP - False Positive; FN - False Negative; TN – True Negative; PPV – Positive Predictive Value; NPV – Negative Predictive Value. A predictive model, identifying patients with POA, based on just the SB score is not able to minimize Type I (FP) and Type II (FN) errors simultaneously. Similarly, SB score appears to be a poor predictor for PORD as various cut-off values yield either high sensitivity with low specificity or vise-versa.

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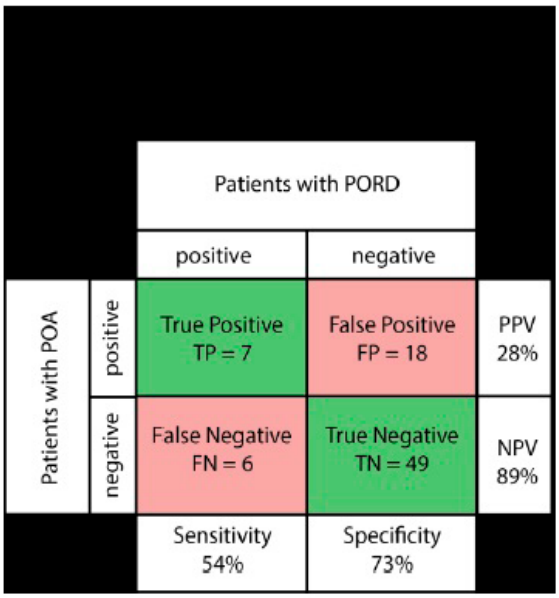

Figure 1: Post-operative apnea (POA) as a predictor of post-operative respiratory depression (PORD). N = 80

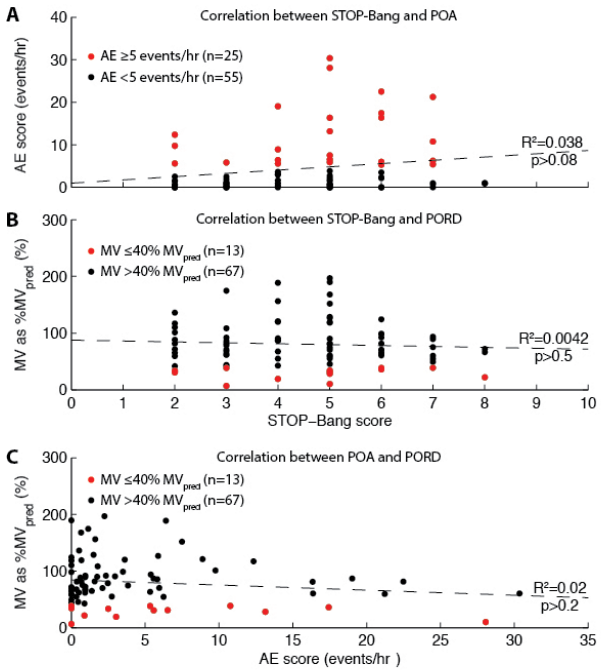

Figure 2: Correlations between POA, PORD, and STOP-Bang scored as continuous, rather than categorical variables. A) Trend (ns) between STOP-Bang scores and POA. B) No apparent correlation between STOP-Bang score and PORD. C) Combination of (A) and (B): poor correlation between the AEs (POA) and MVs (PORD).

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S-243.

COMPARISON OF TWO RISK SCALING SCORES FOR POSTOPERATIVE PULMONARY COMPLICATIONS

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INTRODUCTION: Postoperative pulmonary complications (PPC) depend on patients' co-morbidity, anesthetics and surgical factors and affect the morbidity and mortality in postoperative period. Recently many studies about PPC were published. For example, Pneumonia risk index (PRI) [1] and ARISCAT PPC score [2] are famous risk scaling systems. In this study, we measured the incidence of PPC and calculated these two risk scores for PPC. And we analyzed which scaling system is better in this population.

METHODS: All patients undergoing surgical procedures given general and/or neuraxial anesthesia in June 2013 were investigate retrospectively. Patients' perioperative data and incidence of PPC (defined as pneumonia, sepsis, respiratory failure, atelectasis, and pleural effusion) were collected from our electronic medical records. We measured PRI and ARISCAT PPC score in all patients.

RESULTS: Of the 200 postoperative patients, 17 patients (8.5%) had PPC. Mean age (± SD) was 65.5 ± 15.1 years in patients with PPC and 57.2 ± 17.2 in those without PPC ($P < 0.05$). Postoperative pneumonia developed in 4 patients, sepsis in 3, respiratory failure in 2, atelectasis in 10, and pleural effusion in 7. The patients with PPC had significant higher PRI (28.6 ± 9.2) than those without PPC (16.2 ± 10.0, $P<0.001$), and higher ARISCAT PPC score (46.3 ± 21.2 and 20.2 ±15.3, $P<0.001$). PRI had an odds ratio of 1.07 (95% CI, 1.08 to 1.20), and ARISCAT PPC score had an odds ratio of 1.09 (CI, 1.06 to 1.14) for developing PPC. We validated sensitivity and specificity. The area under the receiver operating characteristic (ROC) curve in PRI was 0.81 and those in ARISCAT PPC score was 0.85. It was easier to measure ARISCAT PPC score than PRI.

CONCLUSIONS: The incidence of PPC was 8.5% in general surgical population, which was similar to the numbers of previous studies. PRI and ARISCAT PPC score had a comparable level of accuracy, although ARISCAT PPC score was easier to obtain.

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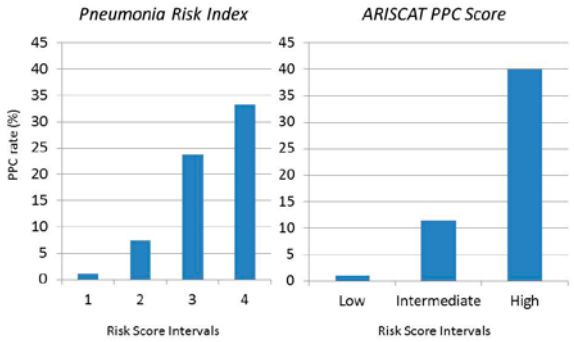
1. Ann Intern Med 2001; 135: 847-857.
2. Anesthesiology 2010; 113: 1338-50.

Figure 1. Comparison of frequency of each risk class by Pneumonia risk index and ARISCAT PPC score



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S-244.

INSERTION OF AN OROGASTRIC TUBE UNDER VISUAL GUIDANCE IN ANESTHETIZED PATIENTS. A PILOT STUDY

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INTRODUCTION: Orogastric tubes (OG) are inserted after induction of general anesthesia & after tracheal intubation, as standard of care, in patients undergoing abdominal surgery. Insertion of OG tubes in anesthetized patients can be difficult at times. While several techniques are described in the literature to facilitate OG tube insertion when routine insertion methods fail, direct visual guidance as a primary method has not been reported. We hypothesized that, when compared to the conventional blind method of inserting an OG tube, insertion of the OG tube immediately following tracheal intubation while continuing to visualize the hypopharynx with the direct laryngoscope would lead to fewer attempts required for its placement & perhaps lead to a reduction in the incidence of postoperative sore throat.

METHODS: Following IRB approval, consenting adult patients, undergoing elective laparoscopic abdominal surgery were randomized to the conventional method or OG tube insertion under visual guidance. In this pilot study we compared time required for tracheal intubation & OG tube insertion, & rate of successful insertion on the first attempt. As laryngoscopy would be prolonged to allow insertion of the OG tube we recorded the hemodynamic response (heart rate & Blood Pressure) following intubation.

All patients were positioned for tracheal intubation by the same anesthesiologist (the author) who also induced anesthesia these patients; while tracheal & OG tube insertions were performed by others (residents & CRNAs). Standard IV induction (using midazolam, fentanyl, propofol and rocuronium) & tracheal intubation techniques (Macintosh Laryngoscope, 18 Fr OG tube at room temperature) were used. The time from the start of laryngoscopy to tracheal intubation as confirmed by end-tidal CO2 detection was time to tracheal intubation. Time from the start of OG tube insertion to the suctioning of gastric contents was OG tube insertion time. The number of attempts required to insert both tubes & quality of laryngeal exposure were noted. All patients were interviewed postoperatively within 24 hours or before discharge from the hospital about a sore throat or a hoarse voice (rated mild, moderate or severe as reported by the patients).

RESULTS: A total of 60 subjects, 30 in each group were studied. While the total time taken for insertion of the tracheal & OG tubes are similar (125 seconds vs. 82 seconds); the success rate on first attempt was substantially different. The OG tube was inserted on the first attempt in 21 out of 30 subjects in the conventional group &in 30 of 30 subjects in the visual group. The incidence of sore throat was greater in the conventional group.

CONCLUSIONS: In anesthetized patients, insertion of an orogastric tube is sometimes difficult & can require multiple attempts. Inserting this OG tube under visual guidance using the same direct laryngoscope immediately following tracheal intubation is feasible. The process adds a few seconds to conventional laryngoscopy with tracheal intubation, but without significant hemodynamic perturbations.

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1.Anesthesiology 1999;91:137-43

2.Anesth Analg 2010; 110:115-8.

Table 1 Patient Characteristics

	OG tube inserted using Conventional Method	OG tube inserted under visual guidance	p-value
Number of patients	30	30	
Age in years, mean (SD)	40.6 (11.2)	43.4 (9.0)	0.28
Height in cm, mean (SD)	161 (5.8)	164 (7.4)	0.03
Weight in kg, mean (SD)	74.3 (15.8)	75.8 (17.4)	0.71
Propofol in mg, mean (SD)	170 (30.6)	175 (30.9)	0.55
Rocuronium in mg, mean (SD)	38 (11.5)	35 (10.8)	0.33
Laryngoscopic View during Intubation, Modified Lehane & Cormack Class			
Grade I view	21	16	
Grade II & III view	9	14	

Time taken for Tracheal Intubation & OG tube insertion

	Conventional Method	Visual Guidance	p-value
Number of patients	30	30	
Time to tracheal intubation in seconds, mean (SD)	64.2 (40.5)	56.9 (20.4)	0.39
Time to OG tube insertion in seconds, mean (SD)	61.4 (38.1)	26 (14.3)	<0.001
Total time taken for both in seconds, mean (SD)	125.6 (57.1)	82.9 (19.4)	0.0004
Number of patients in whom OG tube was successfully inserted on first attempt	21	30	
Number of patients with postoperative hoarse voice	3	4	
Number of patients with postoperative sore throat	9	4	

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S-245.

DEVELOPMENT OF A COGNITIVE AID TO IMPROVE THE QUALITY OF TRANSITION OF CARE IN CRISIS SITUATIONS

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BACKGROUND: Effective communication during transition of care (ToC) situations is essential since any loss of important information during the process can compromise patient care.[1,2] Our previous research has documented a significant loss of important patient information during the ToC process.[3] To facilitate the acquisition and transfer of important patient information during crisis situations, we hypothesize that the use of a cognitive aid will improve the quality and safety of the ToC process. This study describes the development and assessment of the ToC cognitive aid.

METHODS: Faculty members were asked to participate in the project (n=5). We developed 4 different cognitive aids by expert opinion and faculty group consensus. Aid 1 provided a minimal sketch of medical history headings, while the other aids offered advancing assistance to structure the information received during the report. Each participant tested every cognitive aid in a randomized sequence during a crisis simulated scenario.

SCENARIO: Rapid response patient simulation (PS) scenarios were developed by the authors. The study participant leads a rapid response team arriving at an unstable patient scenario. A cognitive aid is handed to the participant to be used during the scenario. The bedside nurse gives essential information and the participant has the opportunity to ask for further information. Before proceeding, a verbal statement by the confederate ensures that all essential information has been transferred. Following the report, the patient deteriorates and requires some additional patient intervention. Following stabilization, the participant transports the patient to the ICU and then gives a verbal report to the next provider.

After each scenario, the participant assessed the cognitive aids using a Likert scale (1=poor; 5=excellent). Study participants rated (mean ± SD) each cognitive aid for ease of use and effectiveness of data capture, as well as overall best cognitive aid.

RESULTS:

Cognitive aid #3 received the highest scores (Table 1) for ease of use, information organization and quality of receiving and transferring patient information. Aid #3 was rated as the overall best format for use in ToC in crisis management situations.Conclusions:

1)Four different cognitive aids for use in ToC crisis situations were developed by faculty consensus. 2) The cognitive aids were rated quite differently by faculty during a simulation ToC scenario, with Aid #3 (form giving most medical history information headings) being the best performer for aiding ToC. 3) Future research using simulation scenarios will assess whether use of cognitive aid #3 during a crisis simulation will reduce loss of patient information during ToC.

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1) Rebel A et al. Development of a Patient Simulation Experience to evaluate the transition of care Process in Crisis Situations. IMSH 2014.

2) Landrigan CP et al. Temporal Trends in Rates of Patient Harm resulting from Medical Care. N Engl J Med 2010;336:2124-34.

3) Rebel A et al Loss of Information during transfer of Care: preliminary results of a simulation project. PGA NY 2013. Funded in part by SGEA grant

Ratings of the cognitive aids				
Question	Aid 1	Aid 2	Aid 3	Aid 4
Ease to use	3.1±1.7	3.1±1.4	4.4±0.6	3.6±0.6
Information organization	3.2±1.6	2.7±0.8	4.0±0.0	2.8±0.5
Quality to receive complete information	2.6±1.5	2.9±1.0	4.0±0.7	3.4±0.9
Quality to transfer complete information	3.4±1.7	3.4±1.1	4.4±0.6	3.5±0.7

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S-246.

MONITORING MINUTE VENTILATION VERSUS RESPIRATORY RATE TO MEASURE THE ADEQUACY OF VENTILATION IN PATIENTS UNDERGOING UPPER ENDOSCOPIC PROCEDURES

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INTRODUCTION: Endoscopic procedures are generally performed under conscious sedation and require careful monitoring of respiratory status to prevent adverse outcomes. While oximetry is capable of detecting severe adverse events, it is not sensitive enough to detect early signs of hypoventilation. EtCo2, while useful, is most accurate in stable intubated patients and debate continues about the utility of capnography based respiratory rate monitoring for endoscopic procedures[1]. This study utilizes the RMV's continuous, accurate[2], real-time measurements of minute ventilation (MV), tidal volume (TV) and respiratory rate (RR) to assess the adequacy of ventilation during endoscopy.

METHODS: Digital respiratory traces were collected from 51 patients (age: 54 ± 5 yrs, BMI: 28 ± 2 kg/m^2) undergoing upper endoscopy using an impedance-based RVM (ExSpiron, Respiratory Motion, Inc., Waltham, MA). Baseline MV for each patient was derived from a 30 second period of quiet breathing prior to sedation ($MV_{BASELINE}$). MV, TV & RR were calculated from 30-second segments over the entire stay. All patients were sedated with propofol. Capnography data (Smart CapnoLine, Philips, Andover, MA) were collected. Because RR from capnography was infrequently reported, the RVM RR's were used for analysis. RR rate values were compared the MV measurements and sensitivity and specificity of RR as a predictor of inadequate ventilation (MV < 40% $MV_{BASELINE}$) were calculated.

RESULTS: Initial analysis on all measurements reveals that although MV is a function of RR (MV=TV*RR), there is a weak correlation between an MV measurement and its corresponding RR measurement (r=0.05) If MV is an actual indictor of respiratory performance, using RR as a proxy is inadequate (Fig 1). Simulating a variety of RR alarm conditions (4-8 breaths/min (bpm)) showed that a substantial fraction of low MV measurements remain undetected. With a RR cutoff of 8 bpm, >70% of all MV measurements < 40% $MV_{BASELINE}$ would be missed. Decreasing the RR cutoff to 4 bpm misses nearly 90% of MV measurements <40% $MV_{BASELINE}$ (Fig 2). A patient alarm based on RR alone (6 bpm) would miss > 82% of all instances of low MV (18.2% sensitivity) while < 40% of all RR alarms would coincide with a low MV (39.4% PPV, Fig. 3). This is not uniform across the cohort (Table 1), and in some patients, a low RR coincides with low MV, and in others they occur independently. Example MV and RR plots for two patients are shown in figure 4.

CONCLUSION: Low RR measurements alone do not reflect episodes of low MV and are not sufficient for accurate assessment of respiratory status. The relative size of each breath or the amount of air moving with each breath is equally critical to assure respiratory sufficiency. Capnography readings are not uniformly available during upper endoscopic procedures, but even if they could provide continuous measurement of RR, these may not adequately reflect respiratory status. RVM provides a new way to collect MV measurements which provide more comprehensive data than RR alone. Further work is ongoing to evaluate specific protocols for use of MV data in the endoscopy suite.

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1. ASGE 2011;

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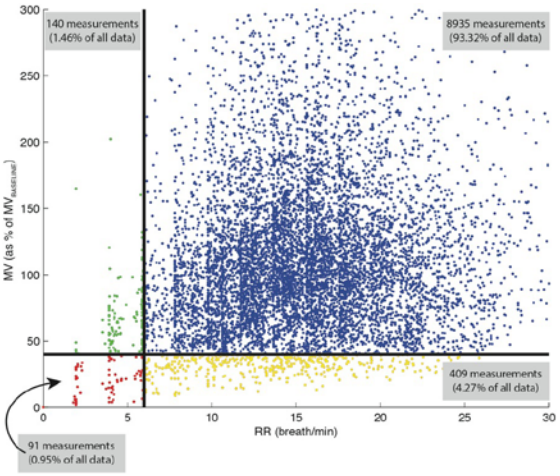

Figure 1: Analysis on all measurements collected (9575) reveals that although minute ventilation (MV) is a function of respiratory rate (RR; MV=TVxRR), there is very weak correlation between any particular MV measurement and its corresponding RR measurement (r=0.05) suggesting that if MV is an indictor of respiratory performance, RR is not a an adequate proxy.

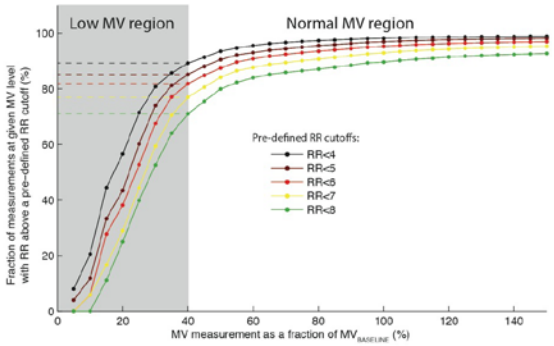

Figure 2: A simulation of a variety of potential RR alarm conditions and the probability they capture a low MV event. Varying RR cutoff from 4 breaths/min (black line) to 8 breaths/min (green line) increases the fraction of low MV events captured by the RR alarm, however, a substantial fraction remains undetected in all conditions. With a RR cutoff of 8 breaths/min (green line), more than 70% of all MV measurements below 40% MVBASELINE level would be missed. Decreasing the RR cutoff to 4 breaths/min misses nearly almost 90% of MV measurements below 40% MVBASELINE (black line). A patient alarm based on RR alone (with a cutoff of 6 b/min) would miss more than 82% of all instances of low MV (red line; 18.2% sensitivity).

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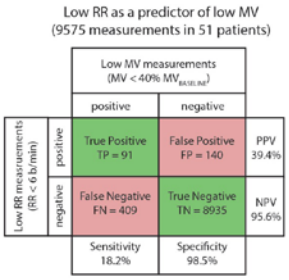

Figure 3: Low RR (RR < 6 b/min) as a predictor of low MV (MV < 40% MVBASELINE). Systematic analysis of 9575 RR measurements from 51 patients showed that RR was a poor predictor MV < 40% of MVBASELINE with a sensitivity of 18.2%, specificity of 98.5%, positive predictive value (PPV) of 39.4% and negative predictive value (NPV) of 95.6%. This demonstrates that RR alone is inadequate for the assessment of respiratory competence.

Table 1: Patient-specific distribution of potential alarm conditions. Theoretical comparison of RR alarms (based on a standard cutoff for low RR alarm of 6 b/min) to MV alarms (based on a cutoff of 40% $MV_{BASELINE}$) within individual patients. In 45% of the population alarms on both MV and RR measurements would have been triggered in unison. In 25% of the population low MV event would have been missed by a low RR alarm and in 35% of the population low RR alarms would have sounded despite MV being in the normal range. In 47% of the studied population, no alarms would have been triggered. Note that the percentages below sum up to more than 100% because a patient could appear in more than one of the first 3 groups (i.e. for a given patient there may be an instance when both low RR and low MV alarms would be triggered in unison (and thus the patient would be counted in the top group) and there may be another instance when a low MV event is missed by a low RR alarm (and the patient would be counted in the second group)

Group n (%)	RR < 6 b/min	MV < 40% $MV_{BASELINE}$	Notes
23 (45%)	YES	YES	In these patients low RR alarms coincide with low MV. **Average of 4.0 alarms per person**
13 (25%)	NO	YES	In these patients low MV events are missed by a RR alarm. **Average of 31.5 missed events per person**
18 (35%)	YES	NO	In these patients RR alarms are triggered w/o a corresponding low MV: **Average of 7.8 potentially false alarms per person**
24 (47%)	NO	NO	In these patients no alarms would be triggered

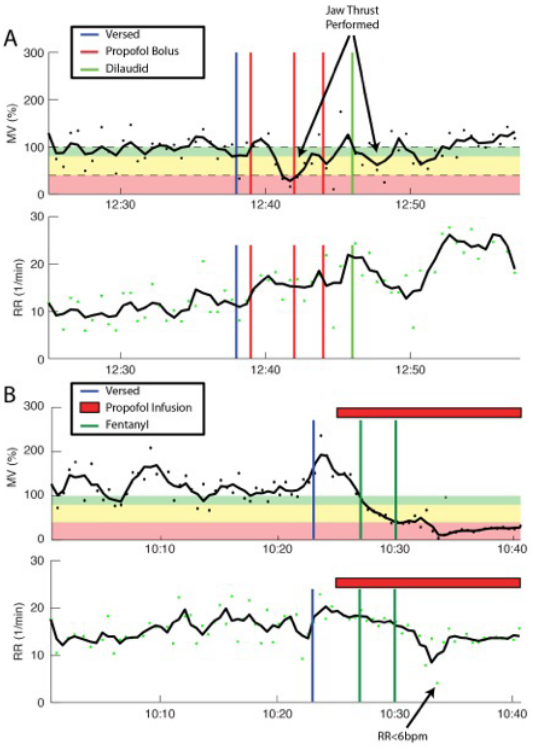

Figure 4: Example plots of individual patient data. Minute ventilation and respiratory rate data recorded with the RVM system during procedural sedation in upper endoscopy. (A) Patient A (Age: 47, BMI: 23) exhibits acute transient hypoventilation in response to sedation. Two jaw lifts were performed by anesthesia staff in response to this hypoventilation. Respiratory rate remained elevated during this period. (B) Patient B (Age: 62, BMI: 30) exhibits respiratory depression in response to sedation. A large decrease in minute ventilation is observed following propofol and opioid administration. Only one respiratory rate measurement was recorded below 6 breaths per minute over this period.

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S-247.

FIRST NATIONAL SURVEY OF PATIENT-CONTROLLED ANALGESIA HOSPITAL PRACTICES: GOOD NEWS AND BAD NEWS FOR PATIENT SAFETY

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OBJECTIVES: Although use of patient-controlled analgesia (PCA) reduces the risk of oversedation, The Joint Commission Sentinel Event Alert on safe use of opioids in hospitals cautions, "While opioid use is generally safe for most patients, opioid analgesics may be associated with adverse effects, the most serious effect being respiratory depression, which is generally preceded by sedation."

Over the six-year period (June 2004 to May 2010), data collected by Pennsylvania Patient Safety Authority revealed approximately 4,500 reports associated with PCA. Moreover, Food and Drug Administration's (FDA) Manufacturer and User Device Experience (MAUDE) database demonstrates PCA-related device events are three times as likely to result in injury or death as reports of device events involving general-purpose infusion pumps.

Our goal was to benchmark the practices hospitals are using to initiate PCA with a patient and to continue to assess that patient's use of PCA.

METHODS: Almost 200 hospitals from 40 states were surveyed on the following five areas: (a) training and the need for training, (b) patient risk factors and information, (c) initiation and continuation of PCA, (d) types of PCA pumps and monitoring used, and (d) alarm fatigue. Survey questions were designed with the help of clinicians and prominent healthcare organizations familiar with PCA.

CONCLUSIONS: The survey revealed inconsistencies between hospital practices and recommendations of key healthcare organizations, such as The Joint Commission, Institute for Safe Medication Practices, and Anesthesia Patient Safety Foundation. Key findings included: (a) patient risk factors are not always checked (for example, low body weight is considered only 62.8% of the time); (b) while pump settings are double checked 98.1% of the time, line attachment is only confirmed 68.1%; (c) continuous electronic monitoring is not routinely performed (only 60.9% monitor all patients with pulse oximetry); and (d) more than one out of every five hospitals are either not using PCA pumps that contain safety software and medication libraries, or using such pumps that are more than 10 years old.

Questions were also asked about alarm fatigue. Alarm fatigue is an issue that about 90% of hospitals are concerned about. The survey shows alarm fatigue is impacting work flow and patient safety. Although hospitals that continuously electronically monitor their patients reported experiencing a reduction in adverse events, costs, and expenditures, hospitals would use more monitoring technology if alarm fatigue was not an issue. Moreover, when asked what tools that would like to have to help manage alarms better, hospitals said that would like better tools and training to tackle this issue - about 70% would like a single indicator that incorporates multiple physiological parameters (like respiratory rate, oxygenation, and end tidal C02) and approximately half would like recommendations to more easily assess patients.

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S-248.

GLUCOCORTICOID PRIMING ENHANCES MACROPHAGE MIGRATION INTO EXPERIMENTAL WOUND TISSUE IN HUMANS

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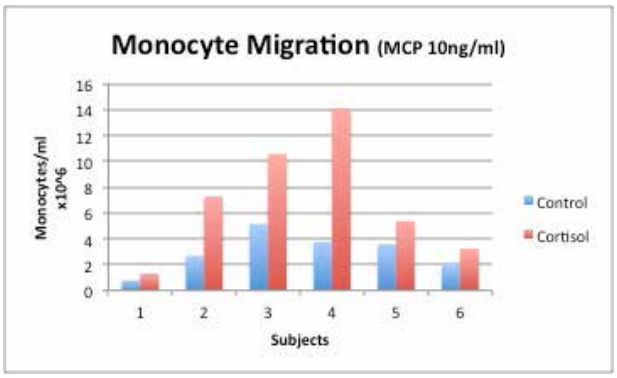
INTRODUCTION: Glucocorticoids (GCs) are well known to suppress inflammation acutely and to suppress immune function (innate and adaptive) chronically when used at pharmacologic concentrations. This potent property of GCs has obscured a previously recognized immune enhancing effect that can be observed after transient exposure to GCs during a period of stress[1]. 'GC priming' of innate immunity has recently re-emerged as a robust intervention to enhance *in vivo* resistance to bacterial challenge in animal studies[2]. Given the continuing clinical problem of Surgical Site Infections (SSIs) in humans following elective surgery, we examined whether GC priming of the innate immune system could be used to enhance leukocyte effector cell (monocyte/macrophages) entry into a sterile experimental wound in humans, thereby potentially reducing the risk for infection.

METHODS: Following IRB approval and written informed consent, healthy human volunteers had 4 blisters induced on the volar aspect of a single forearm using a commercially available negative pressure instrument (Electronic Diversities, Finksburg, MD.). The device induces painless dermo-epidermal separation through the lamina lucida over 90 minutes[3]. Blisters were raised on Day 1 from 0800 to 0930AM after which the blisters were unroofed and each was covered with a sterile 1ml collection chamber containing normal saline with or without 10ng/ml human monocyte chemoattractant protein 1 (MCP-1). Participants were then given a placebo treatment from 1000 to 1600 hours. The following day, the collection chambers were removed and collection chamber fluid was examined for leukocyte transmigration into the sterile saline. A second set of blisters were placed on the opposite forearm from 0800-0930 at an interval of from 3 to 10 days. From 1000 to 1600 hours subjects then received hydrocortisone to raise plasma cortisol concentrations to ~40-50 ug/dl.

RESULTS: MCP-1 significantly increased monocyte infiltration into blister fluid in both placebo and GC treated individuals. Hydrocortisone treatment increased monocyte infiltration into blister chamber fluid without MCP-1 from an average of 1.44 x 106 (+/-0.5 SE) cells/ml with placebo treatment to 2.61 x 10^6 (+/-1.0 SE) cells/ml with GC treatment. GC treatment increased monocyte infiltration into blister chamber fluid with MCP-1 from an average of 2.99 x 10^6 (+/-1.2 SE) cells/ml with placebo treatment to 4.73 x 106 (+/-1.9 SE) cells/ml with GC treatment. Individual results for MCP containing chambers are shown in Figure 1.



CONCLUSIONS: GC priming increases monocyte infiltration into a sterile inflammatory wound in humans. This suggests that GC priming to enhance *in vivo* resistance to bacterial challenge, as has been observed in animals, may also be an effective intervention in humans.

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S-249.

COMPARATIVE CHANGES IN PSYCHOLOGICAL MOOD AND STRESS AFTER DAYTIME PRACTICE IN CERTIFIED ANESTHESIOLOGISTS AND RESIDENTS

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INTRODUCTION: A short form of the Profile of Mood States (POMS) consists of thirty items which load on six different scales: tension-anxiety, depression-dejection, anger-hostility, vigor, fatigue, and confusion, thereby combining to achieve the mood disturbance score (MDS), an aggregate indicator of overall mood. On the other hand, salivary alpha amylase (SAA) levels have been suggested as a potential indirect marker for sympatho-adrenal-medullary activity and a predictor of plasma cathecholamine levels under a variety of stressful conditions. In terms of psychological mood and stress, we examined how daytime anesthetic practice affects certified anesthesiologists and residents, respectively.

METHODS: Fifteen certified anesthesiologists and residents, respectively, at our department were enrolled in this study. They usually took charge of 1 to 3 patients a day in the operating rooms. They received two measurements. One was the the mood meaured by POMS questionaires at 8:00 and 17:00, and the other was the stress assessed by SAA activity at 8:00, 12:00, and 17:00 using COCORO MeterTM (NIPRO Co, Osaka, Japan). Data were analyzed by paired t-test, or one-way analysis of varience, if appropriate. In all tests, a value of $p < 0.05$ was considered statistically different.

RESULTS: Daytime anesthetic practice significantly decreased the scores of tension-anxiety, depression-dejection, anger-hostility, and vigor in certified anesthesiologists, while only increasing the score of fatigue in residents. However, there were no significant differences in the hourly changes in SAA activity in both of the groups.

CONCLUSIONS: Daytime anesthetic practice decreases tension-anxiety, depression-dejection, anger-hostility, and vigor in certified anesthesiologists, while increasing fatigue in residents.

S-250.

PHENOTYPIC VARIATION IN ANESTHESIA WORK AREA S. AUREUS TRANSMISSION

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INTRODUCTION: Health care associated infections (HCAIs) are a leading cause of morbidity in hospitals today. Previous work has demonstrated that bacteria from reservoirs in the anesthesia work area (AWE) explain at least 30% of 30-day postoperative infections. Further, certain phenotypes/ strain characteristics of AWE bacterial isolates lead to increased virulence defined by increased transmissibility, antibiotic resistance, and/or infection development. Our group has recently shown that patients exposed to the hospital ward are more likely than anesthesia provider hands or the anesthesia work area environment to harbor one of these more virulent S. aureus phenotypes. In this study, we sought to identify potential genetic mechanisms explaining this variability. We hypothesize that this information can lead to improved intraoperative infection control.

METHODS: All *S. aureus* isolates obtained from a multicenter study involving three academic medical centers were processed for DNA extraction. These samples included 24 patient, 87 provider hand, and 30 environmentally-derived isolates. Total genomics analysis was conducted on a randomly selected subset of methicillin-resistant and methicillin-sensitive organisms. This led to identification of a novel plasmid containing a qac gene, an upstream enhancer element, and a protein of unknown function. While the qac gene had been previously identified as a genetic region coding for biocide resistance via an efflux mechanism, including chlorhexidine, the combination of the qac gene, enhancer element, and protein was unique. Polymerase chain reaction analysis was utilized to screen for the presence of this plasmid across all *S. aureus* isolates. In addition, patient and provider hand-derived *S. aureus* isolates were subjected to various concentrations of chlorhexidine in order to compare the degree of chlorhexidine resistance. Fisher's exact and Student's T-Test were utilized to compare rates of plasmid positivity and chlorhexidine resistance, respectively.

RESULTS: The plasmid was more likely to be associated with the more virulent patient-derived phenotype than all other phenotypes (RR 9.5, 95% CI 1.67-53.9, p=0.018). The patient-derived phenotype was more resistant to chlorhexidine than the provider-hand derived phenotype with a 2.6 fold increase in colony forming units (CFUs) at a 10-2concentration, $p<0.001$.

CONCLUSIONS: This work partially explains increased *S. aureus* virulence and the biology of S. aureus transmission in the anesthesia work area environment. These results may help to develop novel screening tools for more virulent S. aureus strains and/or to develop new targets for antibiotic and disinfection therapy.

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S-251.

ADD-ONE ASA CLASS: REDEFINING THE ASA CLASSIFICATION SYSTEM TO FORMALLY INCORPORATE FUNCTIONAL DEPENDENCE TO BETTER PREDICT POSTOPERATIVE MORTALITY

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INTRODUCTION: The American Society of Anesthesiologists (ASA) physical status classification remains one of the most significant predictors of preoperative morbidity and mortality, but does not formally incorporate patients' functional capacity - a variable repeatedly identified to be an independent predictor of mortality in subsets of the general population.[1] Our objective was to assess whether patients' functional capacity was an independent predictor of 30-day and long-term mortality in a general population providing evidence to assess weather it should be formally incorporated into the routine ASA classification system.

METHODS: All data were extracted from the Veterans Affair Surgical Quality Improvement program (VASQIP), a perioperative prospectively maintained computerized database. Patients were reclassified into subgroups "A" or "B" in addition to their ASA class, with "A" representing patients who were functionally independent to perform activities of daily living and "B" representing partially or fully dependent patients. In this database, mortality data (primary outcome) was reliably available for all patients up to a 120-month follow-up period.

RESULTS AND MAJOR FINDINGS: 12,345 patients were assessed. Kaplan-Meier and multivariate analyses indicated that both 30-day and long-term mortality were significantly higher for each ASA class' "B" patients compared to their "A" counterparts. Interestingly, odds ratios for mortality were significantly higher for each ASA class' "B" patients when compared to the subsequent higher ASA class' "A" patients, indicating improved survival in the higher class' "A" patients.

CONCLUSION: Functional capacity was a strong independent predictor of 30-day and long-term survival for each ASA class, indicating that it should be incorporated into the routine preoperative evaluation. With an exception of ASA 5 patients, functionally dependent patients' ASA classes should be increased by 1 class-point to better reflect their perioperative risk.

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ASA Class-Subclass Odds Ratios for Mortality			
ASA Class-Subclasses Being Compared	Odds Ratio	95% C.I.	P-value
1/2A	0.18	0.10-0.31	<0.0001
2A/2B	0.14	0.09-0.22	<0.0001
2B/3A	1.92	1.23-2.99	0.004
3A/3B	0.29	0.25-0.33	<0.0001
3B/4A	1.29	1.06-1.57	0.0099
4A/4B	0.5	0.40-0.63	<0.0001
4B/5	2.03	1.06-3.91	0.034

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S-252.

TOO MANY COOKS IN THE KITCHEN? A COHORT STUDY OF ANESTHESIA PROVIDER VOLUME AND RISK OF POSTOPERATIVE COMPLICATIONS

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AFFILIATION: [1]Anesthesiology, Mayo Clinic, Rochester, MN, [2]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA, [3]Endocrinology, Mayo Clinic, Rochester, MN

INTRODUCTION: In an anesthesia care team, a patient undergoing surgery may receive anesthesia care from several providers. The safety of this model, involving multiple transitions of care, has not been evaluated. We tested if the number of anesthesia provideres involved in an operation was associated with the 30-day risk of postoperative complication.

METHODS: A cohort study of surgical patients in an academic tertiary care center with a stable anesthesia care team model participating in the American College of Surgeons - National Surgical Quality Improvement Program (ACS-NSQIP).

RESULTS: We identified 927 patients who underwent elective colectomy with comparable surgical intensity. In all, 71 (7.7%) patient had major nonfatal complications and 7 (0.7%) died. One anesthesiologist provided all care for 530 (57%) patients, two anesthesiologists for 287 (31%) and three or more for 110 (12%). Number of attending anesthesiologists was associated with increased risk of postoperative complication (unadjusted OR=1.52, 95%CI 1.18-1.96; p=0.0013; adjusted OR 1.44, 95%CI 1.09-1.91; p=0.0106). Similarly, associations were found for increasing number of in-room anesthesia residents and nurse anesthetists (adjusted OR=1.39, 95%CI 1.01-1.92; p=0.0446) and for all anesthesia providers (adjusted OR=1.58, 95%CI 1.20-2.08; p=0.0012). Findings were robust across multiple alternative adjustments, exclusions and sensitivity analyses.

CONCLUSION: In our study, care by additional anesthesia providers was independently associated with an increased risk of postoperative complications. These findings challenge the assumption that anesthesia transitions are care-neutral and not contributory to surgical outcomes.

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S-253.

EFFECT OF PREOPERATIVE ORAL HYDRATION AND CARBOHYDRATE LOAD ON GASTRIC VOLUME AND PH IN PATIENTS AWAITING SURGERY

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AFFILIATION: [1]Department of Anesthesiology, PennState Hershey Medical Center, Hershey, PA, [2]Anesthesiology, Penn State Hershey Medical Center, Hershey, PA

INTRODUCTION: Patients were typically fasted for 6 to 8 hours prior to elective surgery in order to reduce the likelihood of pulmonary aspiration of gastric contents during induction of anesthesia. The critical values for volume & pH of the aspirate traditionally have been 25 ml & 2.5 respectively. The practice of preoperative fasting to decrease the risk of aspiration continues today despite literature supporting the benefits of clear liquids. ASA Guidelines recommend an 8-hour fast from fatty foods, & allow clear liquids up to 2 hours before surgery. Our goal was to determine the effect of preoperative ingestion of a specific clear liquid, a nutritional supplement, Nestlé Resource Breeze™, on the gastric volume & pH of patients awaiting elective laparoscopic gynecologic surgery & compare it to those who underwent standard preoperative fasting.

METHODS: In this pilot study, sixty adult patients, who consented to participate were studied in an academic hospital over a 2 month period. It as an open label study & patients were not randomized to either group. While 30 patients (controls) received standard preoperative fasting instructions, fasting from solid food after midnight prior to surgery, 30 study patients were instructed to drink the clear liquid 2 hours before their scheduled time of surgery (usually just before arriving to the hospital). The liquid was Nestlé Resource Breeze (Nestle HealthCare Nutrition, Inc., NJ). One 8 oz. serving (237 ml) contains 9 grams of protein as amino acids (protein source is whey isolate) & 250 Calories (86% carbohydrate, 14% protein, 0% fat). The liquid was being dispensed to patients by their gynecologic surgeon at the time of scheduling surgery, as one element of an IRB approved ERAS pathway. Patients were also instructed to take famotidine prior to their arrival to the hospital. Gastric volume & pH were assessed in both groups. Following induction of anesthesia & tracheal intubation, once a multi-orificed orogastric tube had been inserted, the gastric contents were suctioned into a syringe & its volume was measured using a 70 mL Toomey syringe (Bard Medical Covington, GA). Its pH were estimated with a Gastroccult Test (Beckman Coulter Inc, Brea, CA).

RESULTS: In patients who had ingested Nestle Breeze & received famotidine the mean gastric volume was 12.39 ml (SD 13.42) with a pH of 3.48 (1.62). In contrast, in patients who fasted the mean gastric volume & pH were 23.07 ml (SD 15.34) & 1.71 (1.27) respectively while those who had received oral famotidine in addition had a lower gastric volume of 9.94 ml (12.80) with a higher pH of 4.13 (1.30) .

DISCUSSION: A clear liquid oral nutritional supplement, given 2 hours prior to elective surgery, did not increase gastric volume or decrease pH over the traditional practice of fasting. We propose that it is an efficient way of safely providing nutrients to fasting patients awaiting surgery.

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Table 1: Gastric Volume & pH, Fed vs. Fasting

Parameter	Study patients-given Breeze (n=30)		Control patients-fasting (n=30)	
Time since last meal in hours, mean (SD)	4.19 (1.49)		13.21 (4.67)	
Oral famotidine	with famotidine	without famotidine	with famotidine	without famotidine
Number of patients (famotidine)	28	2	16	14
Time since famotidine in hours, mean (SD)	4.07 (4.68)		5.50 (5.33)	
Number of patients in whom gastric volume was suctioned	23	2	15	14
Gastric volume in ml, mean (SD)	12.39 (13.42)	8 (5.65)	9.94 (12.80)	23.07 (15.34)
Number of patients with gastric volume > 25 ml	5	0	2	8
Gastric pH, mean (SD)	3.48 (1.62)	3 (2.83)	4.13 (1.30)	1.71 (1.27)

Table 2: Oral Famotidine and Trend of Gastric pH

No. of patients in whom gastric aspirate was zero & pH could not be measured	Study patients, Fed5	Control patients, fasting1
Famotidine taken night before surgery	3	4
Famotidine taken morning of surgery	5	5
Famotidine given in the preoperative holding area	20	7
did not receive famotidine	2	14
Gastric pH 6	11	10
Gastric pH 4	3	3
Gastric pH 3	2	2
Gastric pH 2	4	4
Gastric pH 1	5	10

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S-254.

WITHDRAWN.

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Pediatric Anesthesiology

S-255.

USE OF ULTRASOUND FOR PEDIATRIC CAUDAL BLOCKS IN A RESIDENCY TRAINING PROGRAM

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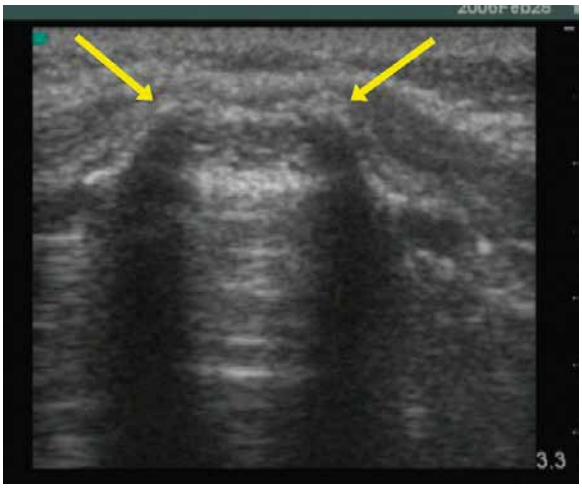
AFFILIATION:[1]Department of Anesthesiology, Baystate Medical Center, Springfield, MA, [2]Division of Nursing, Baystate Medical Center, Springfield, MA

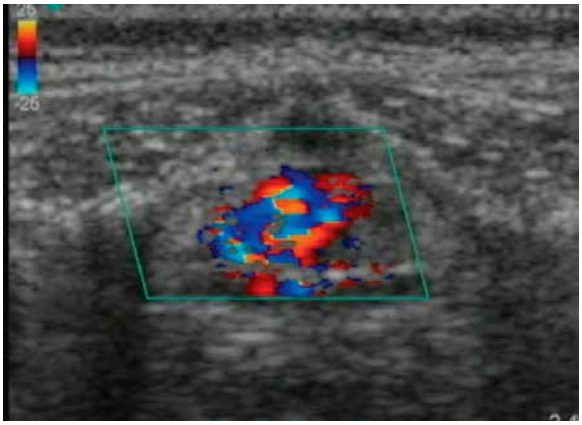
INTRODUCTION: Ultrasound can assist in the placement of caudal blocks[1,2]. Some in our department began using ultrasound as a caudal teaching tool for resident trainees in 2008. Anecdotal feedback indicated that children receiving caudal blocks with ultrasound appeared more comfortable than those without. We conducted a retrospective chart review to see if caudal blocks done by anesthesia residents under ultrasound guidance resulted in improved analgesia, looking at opioid administration as a measure of caudal quality.

METHODS: After IRB approval the medical records of children < 7 years who underwent a circumcision requiring general anesthesia at our hospital between 2008 and 2012 were reviewed. Excluded were combined procedures, penile reconstructions, and cases where the caudal was not performed by a resident. In the ultrasound group, identification of the sacral hiatus and confirmation of sacral canal flow in the transverse plane was carried out (see images). Fentanyl dosing was at the discretion of anesthesia during surgery and PACU nurses postoperatively. Data collected included ultrasound use; bupivacaine dose and volume; caudal clonidine use; intra, post and total narcotic administered. Statistical analysis was accomplished using the unpaired t-test. $P < 0.05$ was considered significant.

RESULTS: A total of 131 charts were reviewed, 70 with ultrasound (+US) and 61 without (-US). Mean age was 45.9 months. Mean bupivacaine dose and volume was 1.7 mg/kg and 0.86 ml/kg for +US and 1.9 mg/kg (p=0.005) and 0.92 ml/kg (p=0.017) for -US. Clonidine (clon) was used in 51 of 70 +US and 19 of 61 -US. Intraoperative, postoperative and total fentanyl doses were 0.12, 0.05 and 0.29 mcgs/kg for +US and 0.36 (p=0.0006), 0.13 (p=0.087) and 0.49 mcg/kg (p=0.25) for -US. When correcting for clonidine use (+US/+clon vs -US/+clon and +US/-clon vs -US/-clon) +US fentanyl dosing remained significantly less.

CONCLUSIONS: Our data suggests that in children getting a caudal block for circumcision by a resident trainee, ultrasound use resulted in lower opioid requirements. The ultrasound group used clonidine more frequently and this may account in part for the difference. However, when correcting for clonidine use, fentanyl administration was still lower when ultrasound was used. We hypothesize that seeing the injectate within the sacral canal with ultrasound correlates with a higher quality caudal block. The retrospective nature of our study cannot control for certain variables such as intra-op opioid administration which may not always be in response to a perceived painful stimulus, but rather reflect individual practice. Liu, et al. described improvements in pediatric caudal blocks when using ultrasound including less puncture attempts and a higher overall success rate[3]. We believe that ultrasound is an invaluable caudal teaching tool for resident trainees in identifying sacral landmarks and confirming correct placement. Our study suggests that caudal quality may improve with ultrasound use.





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S-256.

THE USE OF KETOROLAC FOR POSTOPERATIVE ANALGESIA IN CHILDREN UNDERGOING MYRINGOTOMY AND PLACEMENT OF EQUALIZATION TUBES

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BACKGROUND: Bilateral myringotomy with placement of pressure equalization tubes (BMT) is one of the most common outpatient surgical procedures in children[1]. Despite the brief duration of the procedure, postoperative analgesia is normally required. More than 70% of children undergoing BMT who do not receive preoperative analgesics will require pain medication in the early postoperative period[2]. At our institution, BMT is most often performed without IV cannulation. Therefore, pain relief by an alternate route is needed, which normally occurs by the intranasal (IN) or intramuscular (IM) routes. This retrospective study compares the efficacy of adding IM ketorolac to IN fentanyl in pediatric patients undergoing BMT. Outcomes to be studied include total post-anesthesia care unit (PACU) time, need for additional pain medication, and postoperative nausea and vomiting.

METHODS: A retrospective cohort of pediatric patients who underwent first-time ambulatory BMT at Vanderbilt Children's Hospital from 2008 to 2013 was analyzed. Patients who received only IN fentanyl for postoperative analgesia were propensity matched to patients who received both IN fentanyl and IM ketorolac based on age, weight, gender, and ASA classification. A caliper width of 0.01 was utilized for the matching. Population characteristics and univariate analyses were examined using the Student t-test with or without Welch's correction, Wilcoxon Rank Sum test, or Fisher exact test, as appropriate for the distribution of the data. Analysis of covariance (ANCOVA) was then performed to further analyze predictors of PACU times in this population. Lastly, logistic regression was performed with need for additional analgesia as the response variable and a modified stepwise selection was used to fit the regression models. All statistical analyses were performed using SAS software (version 9.3, SAS Institute, Inc., Cary, NC). $P < 0.05$ was considered statistically significant.

RESULTS: 136 patients were included in each group in this analysis. Population characteristics were similar in both groups (Table 1). Average total PACU time was 39.6 min in the fentanyl/ketorolac group and 40.7 min in the fentanyl group (P value = 0.628). Using ANCOVA, the only variables that significantly affected PACU time were nausea and intraoperative time. Nine patients (6.6%) in the fentanyl group received additional analgesics compared to two patients (1.4%) in the fentanyl/ketorolac group (P value = 0.061). There was no difference in nausea between the two groups (five patients in each group).

Table 1 - Demographics

Characteristic	Fentanyl + Ketorolac (N = 136)	Only Fentanyl (N = 136)	P value
Age (years)	2.43 ± 2.1	2.28 ± 2.1	0.54
Weight (kg)	13.9 ± 6.7	13.5 ± 6.7	0.64
Male/Female	75/62 (55.1%)	82/54 (60.3%)	0.46
ASA class (2/1)	91/45 (66.9%)	104/32 (76.5%)	0.11

CONCLUSIONS: This analysis shows that there may be no additional benefit of adding IM ketorolac to IN fentanyl for first-time BMTs in terms of PACU time, need for additional analgesics, and postoperative nausea. Ultimately, a larger sample size is needed to provide more power to our analysis.

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ULTRASOUND-GUIDED THORACIC PARAVERTEBRAL BLOCK CATHETER EXPERIENCE IN TWO NEONATES

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INTRODUCTION: Use of thoracic paravertebral block (TPVB) as single injection, or landmark based catheter placement in pediatric patients has literature support, including a recent report of 60 infants aged 1-24 months randomized to thoracic epidural or landmark based TPVB catheter placement showing equivalent analgesia and reduced side effects.[1] Since its description in 2009, ultrasound-guided TPVB catheter placement reports in adults have proliferated. Reports of ultrasound-guided TPVB in pediatric patients are sparse.[2] No report exists of an ultrasound guided TPVB catheter being placed in the neonatal period, although extrapleural placement under direct visualization was described.[3]

METHODS: Retrospective chart review of a series of two neonates undergoing tracheoesophageal fistula (TEF) repair whose pain was managed with ultrasound-guided TPVB catheters for 4-5 days. Block catheters were placed after skin closure while still in thoracotomy position. A SonoSite S Series™ machine and 13-6MHz 6 cm linear probe were used in an oblique intercostal viewing pattern with lateral to medial in-plane needle path similar to the initial description by Renes.[4] Catheters were secured with 2-octyl cyanoacrylate (Dermabond®), Mastisol® (Ferndale IP Inc.) and Tegaderm™ (3M, St Paul, MN, USA). Catheters were bolused with 2 ml 2% 2-Chlorprocaine in the operating room. Ropivacaine was diluted to 0.08% and infusion dose was calculated at 0.2 mg/kg/hr[5] which yielded an infusion rate of ~0.25 ml/kg/hr. Infusions ran for 4-5 days.

RESULTS AND MAJOR FINDINGS: Ultrasound-guided TPVB catheters were successfully placed in both neonates. Local anesthetic infusions were able to provide sufficient analgesia to avoid constant infusions of narcotics or sedatives. Morphine equivalent usage on postoperative day #1 was 0.6-1.1 mg/kg-[1], and 0.48-0.6 mg/kg-[1] on the second postoperative day. Prolonged wean from PRN narcotic and benzodiazepine dosing was not required in either neonate.

CONCLUSIONS: Ultrasound-guided TPVB catheter placement in neonates may offer significant advantages over fentanyl and benzodiazepine continuous infusions. Dilute concentrations are required to infuse adequate volume to maintain a successful block. The rapid plasma esterase metabolism of 2-chloroprocaine may be considered for an alternative infusion to allow a higher volume of infusion.[6] Absence of methadone wean or benzodiazepine taper may be a useful outcome measure for effectiveness of analgesic interventions in neonates.

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	Neonate #1	Neonate #2
Age at TEF repair	DOL 2	DOL 2
Weight	2.3 kg	2.7 kg
Associated anomalies	VACTERL with thoracic vertebral anomalies, VSD, ASD, anal malposition	Pierre Robin Sequence, VSD, Esophageal atresia, Aspiration pneumonia/sepsis
Duration of infusion	5 days	4 days
Extubation	POD #7	POD #4
Chest tube removal	POD #5	POD #10
24hr narcotic use	6 x 0.1 mg/kg morphine 0.6 mg/kg/day ME*	6 x 2 µg/kg fentanyl 1.1 mg/kg/day ME
48hr narcotic use	6 x 0.1 mg/kg morphine 0.6 mg/kg/day ME	3 x 2 µg/kg fentanyl 0.48 mg/kg/day ME
72hr narcotic use	1 x 0.1 mg/kg morphine 0.1 mg/kg/day ME	3 x 1 µg/kg fentanyl 0.33 mg/kg/day ME
Methadone wean required?	No	No
Benzodiazepine days?	2	10
Benzodiazepine wean required?	No	No
Notes	Second chest tube placed POD#1 for unresolved pneumothorax	Chest tube drainage x 10 days requiring q 4-6 hr PRN sedation with fentanyl/versed until removal

*ME=Morphine equivalents

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WITHDRAWN.

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S-259.

DOES DEXMEDETOMIDINE CAUSE LESS AIRWAY COLLAPSE THAN PROPOFOL WHEN USED FOR DEEP SEDATION

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INTRODUCTION: Dexmedetomidine (DEX) is a new sedation agent that has the advantage of causing less respiratory depression than most of the other sedatives. In a small non randomized, retrospective review of MRI images from patients who underwent MRI scan using either propofol or dexmedetomidine sedation, there appeared to be a trend towards less airway collapse in the dexmedetomidine group.

There has also been an increased interest in using DEX for deep sedation in those patients with obstructive sleep apnea. Some results from MRI imaging suggest that there may be a benefit of DEX in this group of patients.

The aim of this study was to compare airway patency between Propofol (PROP) and DEX from images obtained from the MRI using previously described methods of assessing the airway

METHODS: After IRB approval and FDA IND (#111330) with informed consent, we plan to enroll 40 children, ages three to seven into our study that meet the inclusion criteria (ASA 1 or 2, elective MRI of head under anesthesia, no allergy to study medications, do not require intubation, no cardiac history not on treatment for ADHD)

After routine monitors are applied an inhalational induction using 8% sevoflurane in 33% oxygen with nitrous oxide will be performed. Once consciousness is lost, intravenous access will be established. Then supplemental oxygen will be delivered at 2 l/m through one side of the baffled nasal prongs with sidestream capnography.

Patients will then receive either (as per randomization) DEX in a 1 mcg/kg bolus followed by a 1 mcg/kg/hr infusion with a bolus of 0.1 mg/kg midazolam at after load completed or a load of 300 mcg/kg/min of PROP over ten minutes followed by a 250 mcg/kg/min infusion.

The baseline MRI images are obtained (prior to patient receiving the study drug infusions). A sagital scout film, an axial SPGR and 2 CINE sequences (figure 1). These images are then repeated 20 minutes later during the study drug infusion for comparison.

Our study will calculate the airway patency using a volume model calculated from the SPGR image and an assessment of airway collapse from the CINE images.

After the conclusion of the MRI scans patients will then be immediately tested by a blinded observer to determine what their level of sedation is as determined by the Ramsey sedation score, The RS will also be assessed on entry into the PACU.

RESULTS: We have recruited 30 patients so far (overall demographics - Table 1). The mean age was 4.9 years. Most of the scans were for MRI of the brain. All of the patients so far were males. Patient 4 data will not be analyzed as before the study drug was started the child required intubation, due to excessive head movement. The randomization code has not been accessed yet and image analysis has yet to be completed.

CONCLUSION:

Both sedation methods were effective, except for movement issues in case 4, no side effects were noted. Image analysis is pending.

S-260.

MALADAPTIVE BEHAVIOR CHANGES IN PRE-SCHOOL AGE CHILDREN AFTER AMBULATORY SURGERY

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INTRODUCTION: Postoperative maladaptive behavioral changes (PMBC) after anesthesia and surgery are common in children, and may be related to young age, preoperative anxiety, child temperament, ethnicity and postoperative pain[1,2]. In our study, we determined the incidence of PMBC in pre-school age children, assessed the role of age, gender, surgery type and medication compliance. We also examined if the type of insurance, as a surrogate indicator of socioeconomic status (SES), affected PMBC, since SES is known to affect neurodevelopment in children[3].

METHODS: This study was approved by the Institutional Review Board, and informed consent was obtained. Male and female ASA PS 1 and 2 patients pre-school age children (1-6 years old) with English-speaking parents, scheduled for ambulatory surgery (Amb Surg) in GU, general surgical, orthopedic, plastic, and ENT procedures were recruited. Parental interviews were conducted at 48 hours and two weeks postoperatively using the Post-Hospital Behavior Questionnaire (PHBQ). Parents assigned a score of 1-5 to each item and PMBC was defined as one or more scores ≥ 3 on PHBQ. Pain was assessed using Faces Pain Scale (FPS) and Parents Postoperative Pain Measure (PPPM). A score >0 in either FPS and/or PPPM was considered to be reporting pain (PainReport) and ≥ 4 was clinically significant pain (c/o pain). Insurance type was divided into: (1) Medicaid or uninsured, and (2) insurance of any kind. Medication compliance was defined as patients who followed the discharge instructions for use of any pain medication. Poisson regression analysis of pain scores and PMBC was performed and $P<0.05$ was deemed significant.

RESULTS: 146 patients, 53 females and 93 males, were included in the study ages 49± 19.7 months (means ±SD). At 48 hours, 73% had PainReport and 55 % had PMBC. At two weeks, 20% had PainReport but only 8% c/o pain , and 16% continued to have PMBC. There was no correlation between PMBC with age or insurance status. Compared to ENT surgery, orthopedic surgery was more associated with PMBC both at 48 hours and at two weeks. Female gender was associated with an increased occurrence of PMBC at 48 hours, but not at two weeks. Medication compliance was correlated with PMBC only at two weeks and not at 48 hours ($p<0.05$). Insurance type was not a significant factor in PMBC at either 48 hours or two weeks.

CONCLUSION: Our study showed that two weeks following Amb Surg, PMBC is more common than clinically significant pain. Incidence of PMBC of pre-school age Amb Surg patients in our study was similar as reported in children over a wider age range[4], but we did not find young age to be a significant factor in PMBC. Insurance type also had no effect. Medication compliance correlated with PMBC, but not pain, at two weeks. We plan to perform further analysis to determine the relationship between PMBC and pain experience in Amb Surg pre-school age children, and identify common risk factors to both.

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S-261.

ISOFLURANE EXPOSURE IN NEONATAL RAT PUPS IS NOT ASSOCIATED WITH DECREASED VENTRAL HIPPOCAMPAL SIZE

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INTRODUCTION: In animals, anesthetic exposure during critical periods of neurodevelopment is associated with neuroapoptosis and cognitive impairment. Rodent studies of anesthesia associated neurotoxicity have shown impaired performance in the Morris Water Maze (MWM), suggesting that early anesthetic exposure is associated with later deficits in spatial learning and navigation. However, our group has been unable to demonstrate consistent impairment of MWM performance in rats following post-natal day 7 (P7) exposure to 4 h of 1 MAC isoflurane. Spatial learning and navigation are dependent upon ventral hippocampal function. To address the discrepancy between our MWM findings and those of other investigators, we determined whether P7 isoflurane exposure in rats is associated with altered hippocampal morphology.

METHODS: After IACUC approval, rat pups were randomized on P7 to undergo either isoflurane (n = 14) or control (n = 10) exposure. Isoflurane was administered in 50% O_2 in a warmed humidified chamber with a servo-controlled heating pad to maintain normothermia. Inspired isoflurane was titrated to maintain a 50% response to tail clamping every 15 min during the 4h exposure. Control pups received 50% O2 for 4h. After exposure, the pups were reunited with their dams and littermates. At P68, rats were anesthetized and underwent transcardial perfusion with saline and 4% paraformaldehyde. Brains were extracted, weighed, and fixed in 4% paraformaldehyde for ≥ 48 hours and frozen. Tilted Coronal sections (50µm) perpendicular to the long axis of the hippocampus were obtained. Alternate slices were mounted and stained with 0.1% thionin. Measurements of dorsal and ventral hippocampal area were made using ImageJ software.

RESULTS: There was no significant difference in ventral hippocampal area between controls (10.8 ± 2.72 mm2) and isoflurane exposed (11.50 ± 2.53mm2) rats (P = 0.69 unpaired t-test). Similarly, there was no difference in dorsal hippocampal area between controls (3.78 ± 0.62 mm2) and isoflurane exposed (3.54 ± 0.80mm2) rats (P = 0.22).

CONCLUSIONS: It is well known that changes in hippocampal volume can be measured in response to stimuli as diverse as spatial navigation training[1], exercise[2], and seasonal navigation[3]. Although it is reassuring that no change in hippocampal size was measurable after exposure to isoflurane in our small sample, we have yet to determine why we were unable to demonstrate the impairment of MWM spatial navigation seen by other investigators - despite equivalent anesthetic exposure during early development.

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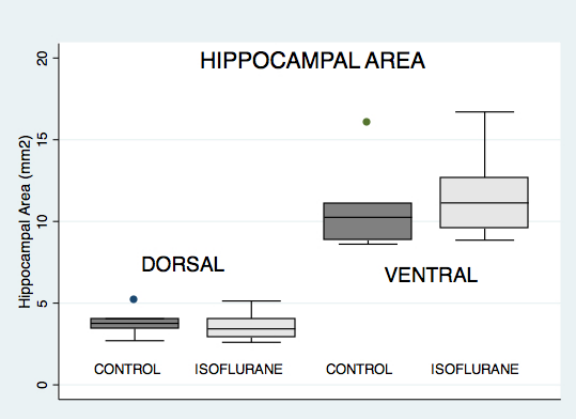

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S-262.

MULTIVARIATE PREDICTORS OF CARDIO-RESPIRATORY AND HEMATOLOGICAL EVENTS FOLLOWING OPEN CRANIOSYNOSTOSIS SURGERY

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BACKGROUND: Infants undergoing craniosynostosis surgery are at risk for significant postoperative complications. We conducted an extensive retrospective chart review to investigate patient variables that might increase or decrease the risk for cardiorespiratory and hematological events and thereby determine the need for ICU admission postoperatively.

METHODS: With IRB approval, the records of infants undergoing open craniosynostosis repair from 2002 to 2012 at Boston Children's Hospital were reviewed.

RESULTS: 225 successive patient charts were analyzed. Table 1 details the patient characteristics of the study cohort.

Univariate analysis identified six variables that were associated with major cardiorespiratory postoperative events (33/225=14.7%); body weight <10kg, ASA level 3 or 4, PRBC transfusion ≥ 60 mL/kg, hemostatic agent transfusion (fresh frozen plasma, platelets, and/or cryoprecipitate), intraoperative complication and intraoperative tranexamic acid (TXA) administration.

These variables were tested using multivariable logistic regression analysis to determine independent risk factors. Four significant independent predictors of a cardiorespiratory event were identified: weight (P<0.001), ASA level 3 or 4 (P=0.003), PRBC transfusion>60 ml/kg (P<0.001), occurrence of an intraoperative complication (p=0.029).

Univariate analysis identified 4 variables that were associated with a major hematological postoperative event (67/225=29.8%); weight <10kg, PRBC transfusion ≥ 60 mL/kg, intraoperative hemostatic blood product transfusion and intraoperative TXA administration. All 4 variables when tested using multivariable logistic regression analysis where determined to be independent predictors of postoperative hematological events: weight (P<0.001), PRBC >60 ml/kg (P<0.001), hemostatic agent transfusion (P<0.001) and TXA administration as a protective factor (P<0.001).

Furthermore, algorithms were developed as a practical clinical tool to predict the probability of a postoperative event (Tables 2 and 3).

Figure 1 shows the odds ratio for multivariate predictors of a significant postoperative event requiring ICU admission.

Figure 2 shows the percentage of postoperative events for the multivariate risk factors identified.

CONCLUSION: Certain craniosynostosis surgery patients are at increased risk for postoperative complications and may benefit from ICU monitoring. Risk factors include body weight <10kg, ASA 3 or 4, transfusion of more than 60 mL/kg PRBC, intraoperative complication, administration of FFP, platelets, or cryoprecipitate. TXA administration was associated less major postoperative hematological events & may reduce the requirement for ICU admission [1-3].

CLINICAL RELEVANCE: A predictive clinical algorithm was developed for pediatric patients having major craniofacial surgery to identify high-risk patients who may require ICU stay. This algorithm can be used to help risk stratify these patients postoperatively.

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Table 1: Characteristics of Study Cohort Undergoing Craniosynostosis Surgery (N = 225)

Variable	Value or Number of Patients	Percentage
Age at procedure, months, median (IQR)	13 (9 - 34)	
Weight, kg, median (IQR)	10 (8.6 - 12.7)	
< 10 kg	112	50%
Gender	119	53%
Male	106	47%
Female		
ASA Class	173	77%
1 or 2	52	23%
3 or 4		
Procedure	158	70%
FOA	67	30%
TCR		
Number of sutures	170	76%
1	37	16%
2	16	7%
3	2	2%
4		
Craniofacial Syndrome*	39	17%
Intraop. PRBC, mL/kg, mean ± SD	32.5 ± 22.8	
Intraop. albumin, mL/kg, mean ± SD	23.2 ± 22.1	
Intraop. hemostatic agents†	19	8.40%
Surgical duration, hrs, mean ± SD (range)	5.4 ± 1.4 (2.2 - 10.6)	
Intraop. TXA Administration	143	64%
Intraoperative Blood transfusion	204	91%

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S-262 • continued

Table 2: Probability Algorithm of Major Postoperative Respiratory or Cardiac Event* Significant Multivariate Clinical Predictor					
Body Weight < 10 kg	**ASA 3 or 4**	**Intraoperative PRBC > 60 mL/kg**	**Intraoperative Complication**	**Probability (%)**	**95% CI**
Yes	Yes	Yes	Yes	89	70 - 96
Yes	Yes	Yes	No	68	46 - 85
Yes	No	Yes	Yes	60	35 - 80
Yes	Yes	No	Yes	55	31 - 77
Yes	No	Yes	No	30	16 - 50
Yes	Yes	No	No	25	14 - 43
Yes	No	No	Yes	20	Oct-35
Yes	No	No	No	7	12-Mar
No	Yes	Yes	Yes	74	45 - 91
No	Yes	Yes	No	45	20 - 72
No	No	Yes	Yes	36	15 - 67
No	Yes	No	Yes	31	15 - 54
No	No	Yes	No	14	5 – 35
No	Yes	No	No	12	5 – 25
No	No	No	Yes	8	3 – 20
No	No	No	No	3	7-Jan

Table 3: Probability Algorithm of Major Postoperative Hematological Event* Significant Multivariate Clinical Predictor					
Body Weight < 10 kg	**Intraoperative PRBC > 60 mL/kg**	**Intraoperative Hemostatic Agents Given**	**TXA Given**	**Probability (%)**	**95% CI**
Yes	Yes	Yes	No	97	85 - 99
Yes	Yes	Yes	Yes	93	68 - 98
Yes	Yes	No	No	86	66 - 95
Yes	No	Yes	No	78	45 - 93
Yes	Yes	No	Yes	70	42 - 88
Yes	No	Yes	Yes	58	26 - 84
Yes	No	No	No	40	25 - 56
Yes	No	No	Yes	20	13 - 31
No	Yes	Yes	No	94	68 - 99
No	Yes	Yes	Yes	85	45 - 98
No	Yes	No	No	74	42 - 92
No	No	Yes	No	62	26 - 88
No	Yes	No	Yes	53	21 - 82
No	No	Yes	Yes	39	13 - 73
No	No	No	No	24	Dec-37
No	No	No	Yes	10	18-Jun

Figure 1: Odds Ratios for Multivariate Predictors of Postoperative Events

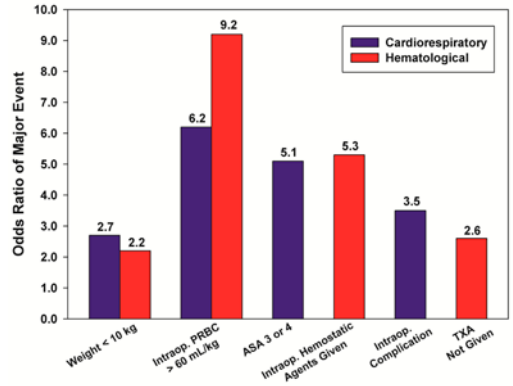
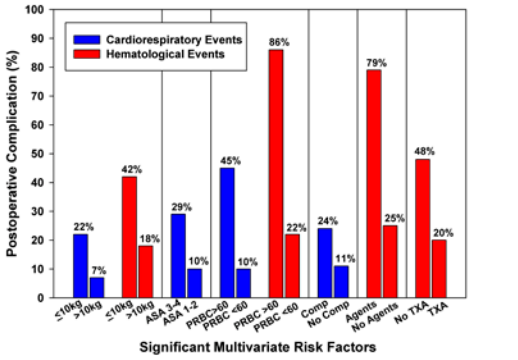


Figure 2: Percentage of Postoperative Events For The Multivariate Risk Factors Identified



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S-263.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) AS A MONITOR OF INTRAOPERATIVE VENTRICULAR VOLUME, FUNCTION AND IV FLUID MANAGEMENT: IMPACT ON INTRA AND POSTOPERATIVE FLUID MANAGEMENT IN THE PARTIAL SEPARATION OF CONJOINED TWINS

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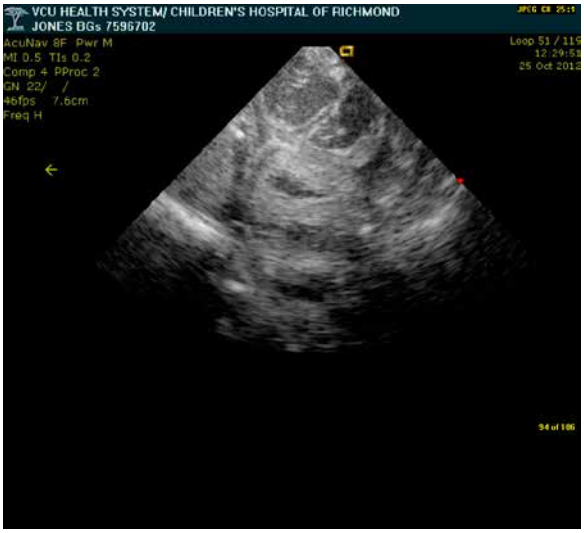
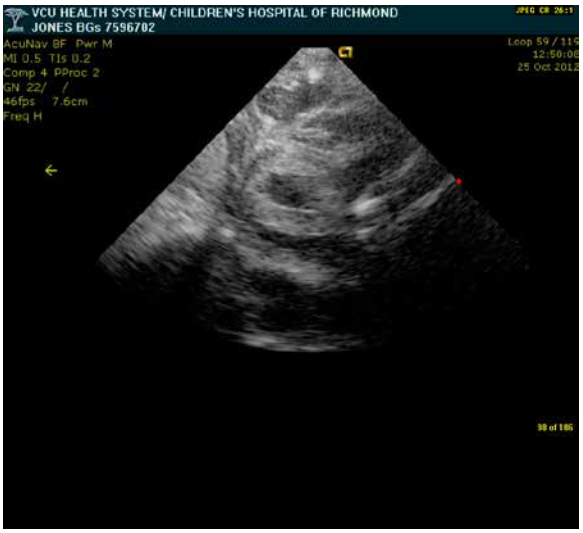
INTRODUCTION: Conjoined thoraco-omphalopagus twins with shared liver parenchyma came to our attention for separation. Delivered at 36 weeks gestation by CS, with the combined birth weight was 4570 grams, infants demonstrated separate brains, lungs, kidneys, bladders, and extremities, hearts with shared pericardium, presence of ASD, and common liver, with hepatic cross circulation through a shared portal vein and separate hepatic arteries and a large truncus venosus shunt connecting. Baby Girl 2 became polyuric and hypertensive with Baby Girl 1 developing oliguria by the 2nd day of life.

METHOD: The infants underwent general anesthesia on dol 7 for surgical liver separation. Medication was injected based on their total weight. Intraoperative TEE was performed by pediatric cardiology via a 6F intravascular echo probe in the esophagus of BG1. The hearts of both babies were able to be visualized simultaneously via this approach. After hepatic division, we noted an immediate increase in the caliber of the IVC and hepatic veins of BG1 and a simultaneous increase in ventricular volume in BG1. Conversely, BG2's left ventricle appeared grossly under filled. This was coincident with a drop in blood pressure and oxygen saturation. BG2 received 15 ml/Kg intravascular fluid bolus with notable improvement in LV filling, systemic blood pressure and oxygen saturation without any observed change in cardiac filling volume in BG1.

CONCLUSION: The utilization of a TEE probe was a helpful addition in the cardiovascular management of these conjoined thoraco-omphalopagus twins allowing us to witness and react to the physiological cardiac responses in real time, and facilited decisions in the amount of IV fluid administration.





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S-264.

NEONATAL MICE RECIEVING SEVOFLURANE DO NOT SHOW AUTISTIC BEHAVIOR

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INTRODUCTION: Numerous animal studies have shown early exposure to general anesthesia causes neurodegeneration and long lasting behavioral deficits, such as impaired learning and deficits in sociability. Early childhood anesthesia has also been implied to increase the risk of developmental behavior disorders and cause long-term language differences in humans.

Autism is a neurodevelopmental disorder which is characterized by impaired sociability and communication and restricted, repetitive behaviors. Due to fact that neonatal anesthesia induces social deficits in mice and increases the risk of developmental behavior disorders in humans, we studied whether neonatal anesthesia could induce autistic behavior in mice.

METHODS: C57BL/6 mice were exposed to sevoflurane at P6-7 for 6 hrs. In order to maintain a relatively constant MAC of 0.6-0.8, sevoflurane was reduced twice during the anesthesia (3% sevoflurane for 90 min, 2.5% for 90 min and 2% for 180 min).

All behavioral studies were performed with age matched male mice (2-4 months). Well described behavioral studies related with autistic behavior were used: 3 chamber assay (sociability) and ultrasonic vocalization (USV, social communication) .

RESULTS: When compared with control mice who received only fresh gas (control group), mice which received sevoflurane (anesthesia group) did not show any difference in all tests:

Anesthesia group showed similar preference to the chamber containing a novel mouse when compared with the control group (see figure).

The total number of calls and latency to first call was also similar between groups in the USV test (see figure)

CONCLUSIONS: Neonatal anesthesia using sevoflurane did not cause autistic behavior in mice. Further studies are needed to explain discrepancy between studies.

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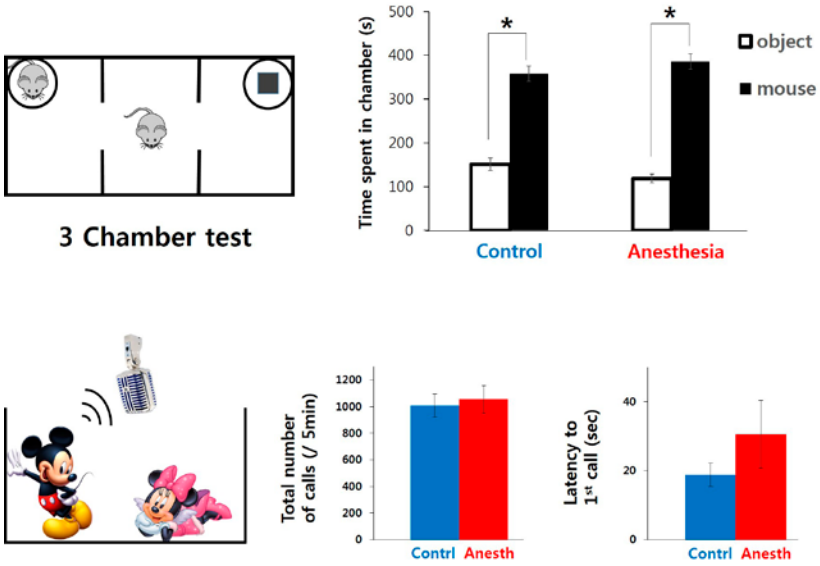

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S-265.

FACTORS INFLUENCING POSTOPERATIVE PAIN EXPERIENCES FOLLOWING DISCHARGE IN PEDIATRIC AMBULATORY SURGERY PATIENTS

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INTRODUCTION: The control of postoperative (postop) pain after hospital discharge in pediatric ambulatory surgical (Amb Surg) patients contributes to the overall postop experience and parent satisfaction[1]. Since a significant portion of the recovery occurs at home, identifying factors important in the postop pain experience during recovery from Amb Surg is needed to improve the quality of pediatric Amb Surg care[2]. We hypothesized that factors contributing to the postop pain experience in Amb Surg pediatric patients include surgery type, insurance status, and pain medication compliance.

METHODS: This study was approved by the Institutional Review Board, and informed written consent was obtained from parents of all participants. Patients undergoing Amb Surg in urological, general surgical, orthopedic, plastic, and otolaryngologic (ENT) procedures were recruited for the study. Inclusion criteria included age of 1-6 years, English-speaking parents, and American Society of Anesthesiologists (ASA) physical status I or II. Data on patients' postop pain experience was collected through patient charts and phone surveys at 48 hours and two weeks after discharge. Parents were asked to rate their child's postoperative pain on the Faces Pain Scale (FPS) and Parents Postoperative Pain Measure (PPPM). Scores ≥4 signified moderate or severe pain on FPS. Insurance status was (1) insured or (2) Medicaid/uninsured. Pain medication compliance was defined as adherence to discharge instructions regarding use of pain medications at home. Poisson regression analysis was performed and statistical significance was defined as $P<0.05$.

RESULTS: 146 children completed the study (age = 49±19.7 months, mean±SD; 64% males). 49% of patients experienced moderate or severe pain in the post-anesthesia care unit (PACU), but only 8% of patients had moderate or severe pain at two-week follow-up. The number of children experiencing no pain increased at each sequential follow-up after surgery (Table 1). 56% of patients were discharged with pain medication prescriptions, and 66% of these patients received prescription pain medications at home.

At 48-hour follow-up, medication compliance, type of surgery, and insurance status affected postop pain experiences. Lower pain ratings negatively correlated with medication compliance ($P<0.05$). Orthopedic procedures ($P<0.001$), and urologic procedures ($P<0.05$) had higher pain ratings than ENT procedures. Pain ratings for insured patients were significantly lower than for Medicaid or uninsured patients ($P<0.001$).

Table 1. Percentage of patients with no postoperative pain on FPS, PPPM, or FPS and PPPM in the PACU

	# of 0-point ratings on FPS	# of 0-point ratings on PPPM	# of 0-point ratings on FPS and PPPM
PACU	25.30%	6.80%	6.10%
48 hours post discharge	44.50%	32.90%	26.70%
2 weeks post discharge	86.30%	80.80%	80.10%

CONCLUSIONS: In the majority of pediatric Amb Surg patients, postop pain resolved within 2 weeks of discharge. Type of surgical procedure and insurance status are correlated with postop pain ratings. The negative correlation between medication compliance and pain scores indicate that discharge instructions may be an area for improvement in the postop pain experience of pediatric Amb Surg patients.

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S-266.

THE INFLUENCE OF INTRAOPERATIVE HYPOTHERMIA ON ADVERSE SURGICAL OUTCOMES IN CHILDREN UNDERGOING SPINE SURGERY

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INTRODUCTION: Hypothermia (core body temperature < 36°C) during surgery has been associated with surgical site infection[1,2]. The infection rate for pediatric scoliosis surgery is approximately 2.6%[3]. A recent retrospective audit[4], of temperature data in children who underwent spine surgeries found that preoperative warming reduced the percentage of the case spent hypothermic by a median of 22% (36% vs. 13%; $p < 0.001$, 95% CI 15-27%). The purpose of this study is to evaluate the effects of intraoperative hypothermia on 30-day surgical site infection rates, length of hospitalization, and bleeding in children undergoing spine surgery.

METHODS: Temperature data from children who underwent spine surgeries between November 1, 2009 and December 31, 2012 was obtained [4]. MATLAB (The Mathworks Inc., Natick, MA, USA) was used to plot temperature trends, and identify episodes of hypothermia and their level of severity. The percentage of a case spent hypothermic is calculated as the summed durations of all hypothermia episodes divided by the duration of temperature monitoring. Surgical outcomes were obtained by retrospective chart review of all cases for which intraoperative temperature data were available. Data were analyzed using R (R Foundation for Statistical Computing, Vienna, Austria) to obtain summary statistics, and receiver operating characteristics curves for outcome variables.

RESULTS: All results are reported as median (interquartile range). Temperature and surgical outcome data for 350 patients (248 females) with age 15.4 (13.3-17.2) years weighing 49.5 (38-59.7) kg were available. The skin-to-skin time was 374 (274.5-463.8) min, during which 12 (9-13) levels were instrumented. The percentage time spent hypothermic was 19 (0-35) %. A surgical site infection was detected within 30 days of the procedure in 21 patients; allogenic blood with volume 446.0 (298.5-710.2) ml was transfused to 72 patients, while blood from the cellsaver with volume of 200 (133-180) ml was transfused in 135 patients; length of hospitalization was 6 (5-9) days. Table 1 summarizes the area under the receiver operating characteristics curve results for percent case spent hypothermic. Approximately 242 patients were prewarmed. Prewarming was found to be negatively associated with a length of hospitalization > 6 days (OR 0.50 [95%CI 0.31-0.79]), blood loss exceeding 625 ml (OR 0.53 [95%CI 0.32-0.86]), and use of allogenic blood (OR 0.29 [95%CI 0.17-0.49]), but not for use of cellsaver blood (OR 0.65 [95%CI 0.41-1.04]), nor surgical site infection rates (OR 0.47 [95%CI 0.19-1.13]).

CONCLUSION: Prewarming was found to be an effective strategy in reducing intraoperative hypothermia and was associated with some beneficial postoperative outcomes. However, in this study intraoperative hypothermia was not found to be predictive of surgical site infection rates, nor intraoperative blood product administration.

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Receiver operating characteristics curve results for Percent Case Spent Hypothermic						
Factor	Controls	Cases	AUC [95% CI]	Percent case hypothermic cutoff	Specificity	Sensitivity
Surgical site infection	329	21	0.52 [0.4-0.64]	18.5	0.49	0.57
Transfusion of cellsaver blood	214	135	0.55 [0.49-0.61]	9.5	0.67	0.43
Transfusion of allogenic blood	275	72	0.55 [0.47-0.63]	17.5	0.55	0.56
Length of hospitalization exceeding 6 days	191	159	0.58 [0.52-0.64]	19.5	0.56	0.6
Blood loss exceeding 625mL	244	98	0.58 [0.51-0.65]	17.5	0.57	0.57

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S-267.

ADAPTATION OF THE SOCIETY OF PEDIATRIC ANESTHESIA CRITICAL EVENT CHECKLISTS FOR USE AT A CHILDREN'S HOSPITAL IN A DEVELOPING COUNTRY

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INTRODUCTION: In a simulated setting, the use of critical event checklists has been associated with a marked improvement in surgical team management of common surgical crises such as air embolism, cardiac arrest, and anaphylaxis.[1] The goal of this study was to determine whether the Society for Pediatric Anesthesia (SPA) pediatric-specific critical event checklists could be adapted for use at a children's hospital in a developing country.[2]

METHODS: Following a presentation to anesthesia providers at our study hospital outlining each of the SPA critical event checklists, surveys were distributed to anesthesia providers. Each respondent was asked to select the checklists that would be most valuable in the perioperative setting. Based upon the most frequently selected checklists, we collaborated with local experts to adapt each checklist based on the availability of resources such as diagnostic tests, medications, and treatments at the KBTH. Following completion of the adapted checklists, we re-canvassed the anesthesiologists to assure that the checklists would be useful during the management of the respective critical event scenarios.

RESULTS: Following presentation of the SPA critical event checklists (see figure 1), forty surveys were distributed and completed by anesthesia faculty members, residents, medical students, and nurse anesthetists. Only surveys completed by faculty and residents [N=19] were used to establish the perceived importance of each checklist (see figure 2) as well as which checklists they would most like to have available in the operating room. The four most frequently requested checklists included: cardiac arrest, anaphylaxis, hypoxia, and difficult airway. Collaborating with local residents and faculty members, we adapted the critical care event checklists to specifically match the medications and resources available to anesthesia practitioners at our partner hospital (see figure 3).

CONCLUSION: In collaboration with our international colleagues at a teaching Hospital in a developing country, we were able to successfully adapt the SPA critical care event checklists to their local practice and available resources. We have described the novel adaptation of the SPA critical event checklists as a collaborative quality improvement initiative which may be modeled by others for future international outreach efforts.

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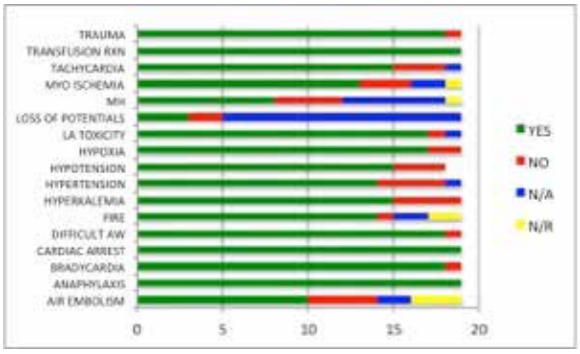

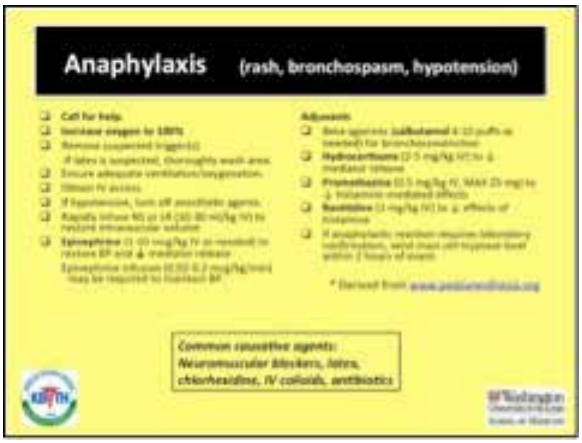

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S-268.

TRANSFUSION ALGORITHMS DECREASE BLOOD TRANSFUSION IN CHILDREN UNDERGOING CRANIOFACIAL RECONSTRUCTION

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BACKGROUND: Craniofacial reconstruction surgery is often associated with large blood loss, coagulopathy, and perioperative blood transfusion.[1-5] Allogeneic blood transfusion is associated with numerous risks and different approaches have been utilized to decrease transfusion during the perioperative period.[6-10] During transfusion surveillance at our institution, we noticed that blood products were being administered without abnormal laboratory values. The purpose of this study was to determine if these guidelines decreased the transfusion of blood products perioperatively.

METHODS: After IRB approval, a chart review was performed on children that underwent craniofacial reconstruction during the period of January 1, 2010 through August 1, 2013. The intraoperative transfusion algorithm was instituted on January 1, 2013

RESULTS: After protocol implementation, the proportion of patients transfused PRBCs intraoperatively decreased by 13.6% while FFP transfusion decreased by 86.4% This corresponded to a decrease in total product use from 0.42 units/kg to 0.13 units/kg per patient. Blood utilization in the postoperative period also decreased when compared to the period before implementation. After guideline initiation, patients transfused PRBCs and FFP postoperatively decreased by 33.4% and 63.5%, respectively. Length of stay in the ICU was not statistically different but total hospital stay was decreased by 1.08 days (P value = 0.02) in the postguideline cohort. There was no significant difference in morbidity and mortality between the two groups.

CONCLUSIONS: These results suggest that using transfusion guided protocols during the perioperative period in major craniofacial reconstruction surgery significantly reduces blood product administration without changes in patient outcome. Total hospital stay was also significantly decreased in this cohort. Further study is warranted to analyze the potential cost savings due to the implementation of this protocol.

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Table 1. Demographics*

	Preguidelines (N = 95)	Postguidelines (N = 22)	*P*-value
Age (years)	0.73 ± 0.49	0.64 ± 0.41	0.426
Weight (kg)	8.42 ± 2.20	8.16 ± 1.89	0.610
Male/Female	53/42 (55.8%)	18/4 (81.8%)	0.091
Proportion			
ASA status %	30.5/69.5/6.3	13.6/84.2/14.3	0.120
(3/2/1)			
Synostosis			0.972
Metopic	41 (44.1%)	10 (45.5%)	
Coronal	10 (10.8%)	3 (13.6%)	
Saggital	29 (31.2%)	6 (27.3%)	
Lambdoidal	1 (1.0%)	0 (0%)	
Multiple	12 (12.9%)	3 (13.6%)	

* These characteristics were examined using the Student *t*-test, Wilcoxon Rank Sum test, Pearson's Chi-square, 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.

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Table 2. Intraoperative Transfusion*

	Preguidelines (N = 95)	Postguidelines (N = 22)	*P*-value
PRBCs	95 (100%)	19 (86.4%)	0.006
FFP	95 (100%)	3 (13.6%)	<0.0001
Platelets	10 (10.5%)	0 (0%)	0.205
Units of product/kg	0.42 ± 0.20	0.13 ± 0.08	<0.0001

* These characteristics were examined using the Student *t*-test, 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 3. Postoperative Transfusion and Length of Stay*

	Preguidelines (N = 95)	Postguidelines (N = 22)	*P*-value
PRBCs	75 (78.9%)	10 (45.5%)	0.003
FFP	69 (72.6%)	2 (9.1%)	0.0001
Platelets	12 (12%)	0 (0%)	0.119
ICU stay (days)	3.98 ± 1.20	4.18 ± 1.18	0.481
Total hospital Stay (days)	7.36 ± 2.10	6.27 ± 0.98	0.020

* These characteristics were examined using the Student *t*-test, 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.

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S-269.

INCIDENCE AND DURATION OF INTRAOPERATIVE HYPOTENSION IN NEONATES AND INFANTS

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INTRODUCTION: There are many factors that may make infants more susceptible to brain injury during anesthesia including prior insults such as birth trauma, prematurity and sepsis. General anesthetics have been shown to be neurotoxic in the laboratory[1], and there is suggestion that in infants, certain anesthetics increase cerebral metabolic demands and lead to a pathologic mismatch of oxygen delivery and consumption[4].

Intraoperative perturbations in vital signs such as hypotension, hypocapnia and hyperthermia can lead to an unfavorable balance of cerebral perfusion. This resulting injury can be exacerbated by hyperoxia[1]. The intraoperative incidence and extent of these potentially morbid physiologic changes have not been well described. The objective of this study is to determine the incidence, duration, and magnitude of intraoperative hypotension.

METHODS: This is an IRB approved, retrospective review of all Anesthesia Information Management System (AIMS) intraoperative records for all patients of American Society of Anesthesia (ASA) class 1 and 2 and less than 12 months of age at our institution.

Hypotension is defined as mean arterial pressure (MAP) <40 mm Hg. Duration of hypotension is defined as the time interval where at least 3 successive blood pressure measurements meet criteria for hypotension. Duration is stratified into 15-25 minutes and >25 minutes. T-tests are used to compare means across groups using Stata (StataCorp LP; College Station, Texas)

RESULTS: 2,688 patients were identified from the AIMs database with a mean age of 4.98 months. 494 patients (18.4%) had periods of hypotension. There were 704 hypotensive intervals amongst these patients with 322 (45.7%) intervals lasting longer than 25 minutes. The mean number of hypotensive episodes per patient was 1.42. The average duration of hypotension was 32.7 minutes. The mean MAP during each hypotensive interval was 35.67 mm Hg. The mean lowest MAP during each hypotensive interval was 32.75 mm Hg.

CONCLUSION: In ASA I and II neonates and infants, there is a 18.4% incidence of hypotension, which is often not simply an isolated occurrence. This is notable given that MAP below 38 and 42 mm Hg in infants is associated with physiologic evidence of decreased cerebral perfusion[2,3]. A current limitation of our study is that patients <40 weeks postmenstrual age are not identified and therefore screened using an age adjusted definition of hypotension. Future studies should include alternate definitions of hypotension (i.e. % change from baseline and systolic blood pressure thresholds) as well as evaluate additional intraoperative variables that influence cerebral perfusion and ultimately examine their association with neurodevelopmental outcomes.

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Study Outcomes			
	Mean	95% CI	p-value
Interval Time (minutes)	32.7	30.92-34.47	
MAP (mm Hg)	35.67	35.58-35.76	
Lowest MAP (mm Hg)	32.75	32.44-33.06	
MAP (mm Hg) by length of interval			
15 - 25min	36.39	36.26-36.53	
>25min	35.29	35.18-35.39	*<0.0001
Lowest MAP (mm Hg) by length of interval			
15 - 25min	33.9	33.53-34.28	
>25min	31.39	30.91-31.86	*<0.0001

Patient Characteristics	
Mean age (months)	4.98
ASA I (% patients)	29.4
ASA II (% patients)	70.6
Mean # hypotensive episodes per patient	1.42
>25 minute intervals (% patients)	45.7

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S-270.

ANESTHESIA-INDUCED NEUROTOXICITY IN THE DEVELOPING MURINE RETINA

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BACKGROUND: Anesthetic agents cause widespread apoptosis in the developing brain. Vulnerability coincides with the peak in synaptogenesis and anesthesia-induced neurodegeneration has been shown to result in loss of neurons, cognitive impairment, and behavioral abnormalities in a variety of newborn animal models. However, it is unknown if anesthesia-induced neurotoxicity occurs in humans because there is currently no modality to assess for neuronal apoptosis *in vivo*. The retina is unique in that it is the only portion of the central nervous system that can be directly visualized by non-invasive means. As in the brain, programmed cell death occurs naturally in the developing retina and is critical for synaptogenesis and elimination of aberrant connections. Thus, we hypothesized that anesthetics can cause neurotoxicity in the developing retina. We aimed to demonstrate that isoflurane induces apoptosis in the retina following exposure. Because high resolution non-invasive methods have been developed to image single cell apoptosis within the retina *in vivo*, we also tested the hypothesis that a systemically injected fluorescent probe could cross the blood-retinal barrier and bind to cells undergoing programmed cell death.

METHODS: The care of the animals in this study was in accordance with NIH and Institutional Animal Care and Use Committee guidelines. 7 day old CD-1 male mouse pups underwent 1 hour exposure to isoflurane (2%) or air. Following exposure, retina was harvested and immunohistochemistry for activated caspase-3, -9, and -8 was performed. Cytochrome c release from retinal mitochondria was assessed and steady-state levels of pro- and anti-apoptotic mediators were determined with immunoblot analysis. Significance was assessed with ANOVA and post hoc Tukey's test and significance set at $P<.05$. The types of cells undergoing apoptosis were identified with double labeling immunofluorescence. Retinal uptake and the ability of fluorescent-labeled annexin V to bind to cells undergoing natural cell death and anesthesia-induced apoptosis in the retina were determined following intraperitoneal injection.

RESULTS: Isoflurane activated the intrinsic apoptosis pathway in the inner nuclear layer (INL) and activated both the intrinsic and extrinsic pathways in the ganglion cell layer of the retina. Immunofluorescence demonstrated that bipolar and amacrine neurons within the INL underwent physiologic cell death in air-exposed controls and were the likely targets of isoflurane-induced neurotoxicity. Following injection, fluorescent-labeled annexin V was readily detected in the INL of both air- and isoflurane-exposed mice and co-localized with activated caspase-3 positive cells.

CONCLUSIONS: These findings indicate that isoflurane-induced neurotoxicity occurs in the developing retina and lays the groundwork for development of a non-invasive imaging technique to detect anesthesia-induced neuronal apoptosis in infants and children. Thus, in future work, it may be possible to exploit neurodegeneration in the human retina as a surrogate for anesthesia-induced brain neurotoxicity.

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S-271.

GENETIC VARIANTS OF BLOOD BRAIN TRANSPORTER, ABCB1 ARE ASSOCIATED WITH OPIOID RELATED RESPIRATORY DEPRESSION IN CHILDREN

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INTRODUCTION: Tonsillectomy is one of the most common and significantly painful surgical procedures children undergo. Opioid-induced respiratory depression is a serious perioperative problem. Use of opioids accounted for many post-tonsillectomy deaths and anoxic brain injuries. In February 2013, the FDA warned against the use of codeine (morphine pro-drug) in children undergoing tonsillectomy based on multiple reports of deaths and serious adverse effects irrespective of the *CYP2D6* genotype and sleep apnea status. Opioids often worsen oxygen desaturations after tonsillectomy in children. Thus, adequate and safe postoperative pain management is essential. Morphine is subject to efflux transport via P-glycoprotein transporter encoded by *ABCB1* gene. *ABCB1* polymorphisms (Figure 1a) may affect blood brain barrier transport of morphine and, therefore, individual response to its central analgesic and adverse effects. This study aims to determine specific associations between common ABCB1 genetic variants and analgesic efficacy and clinically important adverse outcomes associated with intravenous morphine in American children undergoing tonsillectomy.

METHODS: A homogeneous group of 263 children undergoing tonsillectomy who received intravenous morphine as part of standard perioperative care were genotyped for ABCB1. The association between 5 single-nucleotide polymorphisms (SNPs) of *ABCB1* (**Figure 1a**) and the primary safety endpoints, respiratory depression, and respiratory depression resulting in prolonged stay in Post Anesthesia Recovery Room (PACU) were evaluated. The secondary outcome was postoperative morphine requirement.

RESULTS: *ABCB1* polymorphism, *rs9282564*, was significantly associated with increased risk of morphine related respiratory depression in PACU in both 219 white and 44 black children (Table 1). Specifically, in a combined race analysis compared to children with GA genotype, children with GG genotype of *rs9282564* had 4.7 fold increase in the odds of respiratory depression resulting in prolonged stay in PACU (95% CI: 2·-10·8, p=0·0002) (Figure 1b); increased postoperative morphine requirement was associated with CC genotype of the *ABCB1* polymorphism, rs2229109 (p=0·02).

CONCLUSIONS: *ABCB1 rs9282564* polymorphism is associated with increased risk of morphine related respiratory depression resulting in prolonged stays in PACU, and *ABCB1* polymorphism, *rs2229109* is associated with variations in postoperative morphine requirement in children undergoing tonsillectomy. Awareness of genetic variations of drug responsiveness can lead to tailored drug selection on the basis of a patient's genetic makeup and dose adjustment, which are likely to prevent adverse drug reactions.

Table 1. Respiratory depression (RD) and prolonged PACU stay due to RD by genotypes

		White Children					Black Children				
ABCB1 SNP		N	Respiratory Depression %	p	Prolonged PACU due to RD%	p	N	Respiratory Depression %	p	Prolonged PACU due to RD%	p
rs9282564	GG	2	100	**0.04**	100	**<0.01**	0	-	0.20	-	**0.04**
	GA	46	17		20		3	67		67	
	AA	171	16		8		41	27		10	

Figure 1. ABCB1 Transporter Variant is associated with Respiratory Depression in White and Black Children

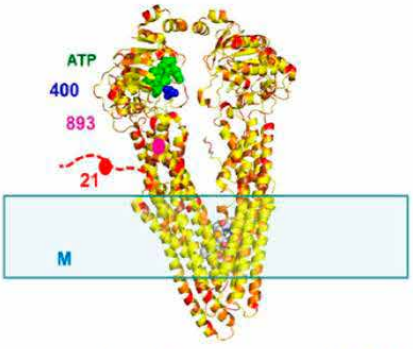

Figure 1a. 3D structure of ABCB1 with Polymorphisms

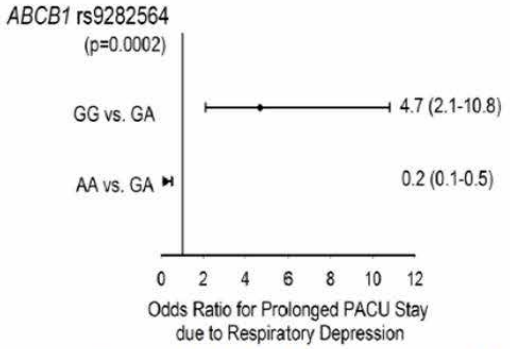

Figure 1b. ABCB1 genotype and risk of Respiratory Depression

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S-272.

WHAT DO CHILDREN REMEMBER ABOUT THE DAY OF SURGERY AND HOW ACCURATE ARE THESE MEMORIES

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INTRODUCTION: Children's declarative memories (i.e., the ability to recall information, sensations, and emotions) are important in medical contexts because the way in which children remember painful and anxiety provoking medical events has been found to be influence their responses to subsequent events[1,2]. Although there has been some previous research on the impact of sedative premedication on implicit and explicit memory formation in the preoperative period, there has been no study that has aimed to examine the accuracy of children's declarative memories for the day of surgery.

METHODS: With IRB approval and parent authorization/child assent, we conducted a prospective cohort study of 34, anesthesia naive 5 to 9 year old children (56% female) who underwent ambulatory ear, nose and throat or dental surgery. Children completed the Children's Fear Scale and Faces Pain Scale-Revised preoperatively and postoperatively. Children did not receive sedative premedication. The preoperative period was structured with standardized cues provided to ensure children attended to contextual details. The anesthetic was also standardized. Recall of contextual details and fear and pain ratings were queried 2 weeks postoperatively via a telephone interview.

RESULTS AND MAJOR FINDINGS: On average, children remembered 66% of the contextual details that they were cued to, with children remembering the fewest details at the time of separation from their parents. 61% of children remembered a standardized prompt provided after one minute of administration nitrous oxide. Thematic analysis indicated that 40% of children remembered negative events or emotions such as needles, their IV, crying, being in pain and feeling scared or nervous. Overall, children's memories of their pain and fear did not significantly differ from their reported pain and fear on the day of surgery, but 17% of children exaggerated their memory of fear and 36% of children exaggerated their memory of pain. Conversely, 21% recalled less fear and 32% recalled less pain than measured.

CONCLUSIONS: Children who receive anesthesia for ambulatory surgery accurately recall two thirds of event that occur on the day of surgery, even late in the induction process. Unpleasant and exaggerated memories are formed in nearly one third of patients, and this may have an impact on children's responses to subsequent medical procedures.

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S-273.

CEREBRAL OXYGEN EXTRACTION MEASURED BY NIRS AND JUGULAR BULB OXYGEN SATURATION DEMONSTRATES THE IMPORTANCE OF HEMOGLOBIN CONCENTRATION IN CONGENITAL HEART DISEASE

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INTRODUCTION: Cerebral O_2 delivery (DO_2) is regulated in part by $CMRO_2$[1]. The increased blood hemoglobin concentration (Hb) that accompanies chronic hypoxemia[2] is believed to be an important compensatory response to support DO_2 in congenital heart disease (CHD) with decreased SaO_2. With respect to cerebral tissue oxygen saturation ($SctO_2$) measured by near-infrared spectroscopy (NIRS), little data exists on the differences between SaO_2 and jugular bulb O_2 saturation ($SjbO_2$) and $SctO_2$ as estimates of cerebral oxygen extraction (CEO_2), particularly in relation to Hb. The aim of this study is to evaluate these differences and to quantify the importance of Hb to DO_2 in CHD.

METHODS: With IRB approval and written informed consent, 65 children (1 month-18 years; 3-50 kg) with CHD undergoing elective cardiac catheterization were enrolled in a validation study of the FORE-SIGHT (CASMED, Branford, CT) NIRS medium sensor (source-detector separation 12 and 40 mm). Validation was performed by comparison of NIRS-measured $SctO_2$ with a reference oxygen saturation (REF CX) calculated by co-oximetry measurement of SaO_2 and $SjbO_2$, whereby REF CX = $0.3SaO_2 + 0.7SjbO_2$[3]. Arterial and jugular samples were drawn twice under the same physiologic conditions: during the baseline hemodynamic and saturation measurements and 5-10 minutes thereafter. Jugular bulb samples were obtained with an end-hole catheter guided under fluoroscopy up the internal jugular vein to the jugular bulb. Extracerebral contamination of $SjbO_2$ was assumed if the difference between the 2 samples was > 10% (absolute) without changes in clinical or blood gas measurements. Data from the 2 time points were averaged for analysis. Pearson correlation and linear regression were used to determine relationships between oxygen saturation parameters and demographic variables. $P < 0.05$ was considered statistically significant.

RESULTS: Acceptable $SjbO_2$ samples were obtained in 57/65 subjects, 58% male and 72% Caucasian. No correlations were found between oxygen saturation variables and age, weight, race or gender. Demographic and saturation data are shown in Table 1, and correlation data in Table 2. The SaO_2 $SjbO_2$ difference (P=.0001) and SaO_2 $SctO_2$ difference (P<.0001) correlated inversely with Hb (Figures 1 and 2).

CONCLUSIONS: Although a weak correlation between $SctO_2$ and Hb has been reported[4], the present study found a stronger relationship between Hb and CEO_2 measured directly (SjbO2) and indirectly ($SctO_2$), thereby providing some clinical validation for NIRS technology. Because of elevated Hb, near 'normal' SctO2 values may be seen with chronically lower SaO_2 in CHD subjects. Conversely, an important clinical implication is that the cyanotic patient who is anemic, particularly in conjunction with decreased cardiac output and/or impaired cerebral autoregulation, may approach $SctO_2$ levels that have been associated with brain injury in laboratory studies[5].

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Table 1.

Variable (N=57)	Median	Minimum	Maximum
Age (y)	3.4	0.2	16
Weight (kg)	13.2	4.6	49.5
Hb (g/dL)	12.1	7.6	17.5
SaO2 (%)	95	70	100
SjbO2 (%)	64	45	99
REF CX (%)	73	55	99
SctO2 (%)	73	56	96
SaO2 - SjbO2 (%)	25	1	46
SaO2 - SctO2 (%)	20	4	35

Table 2.

Pearson Correlation Coefficients (N = 57)
Probability > |r| under H0: Rho=0

	Age (y)	Weight (kg)	Hb (g/dL)	SaO2 (%)
SjbO2	0.208 0.121	0.173 0.197	-0.055 0.683	**0.361** **0.006**
REF CX	0.211 0.115	0.175 0.192	-0.259 0.052	**0.603** **<.0001**
SctO2	0.182 0.175	0.161 0.232	-0.097 0.475	**0.485** **0.0001**
SaO2 - SjbO2	-0.114 0.4	-0.097 0.475	**-0.507** **<.0001**	**0.425** **0.001**
SaO2 - SctO2	-0.061 0.65	-0.063 0.644	**-0.633** **<.0001**	**0.534** **<.0001**
SaO2 - REF CX	-0.114 0.4	-0.097 0.475	**-0.507** **<.0001**	**0.425** **0.001**

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S-273 • continued

Figure 1

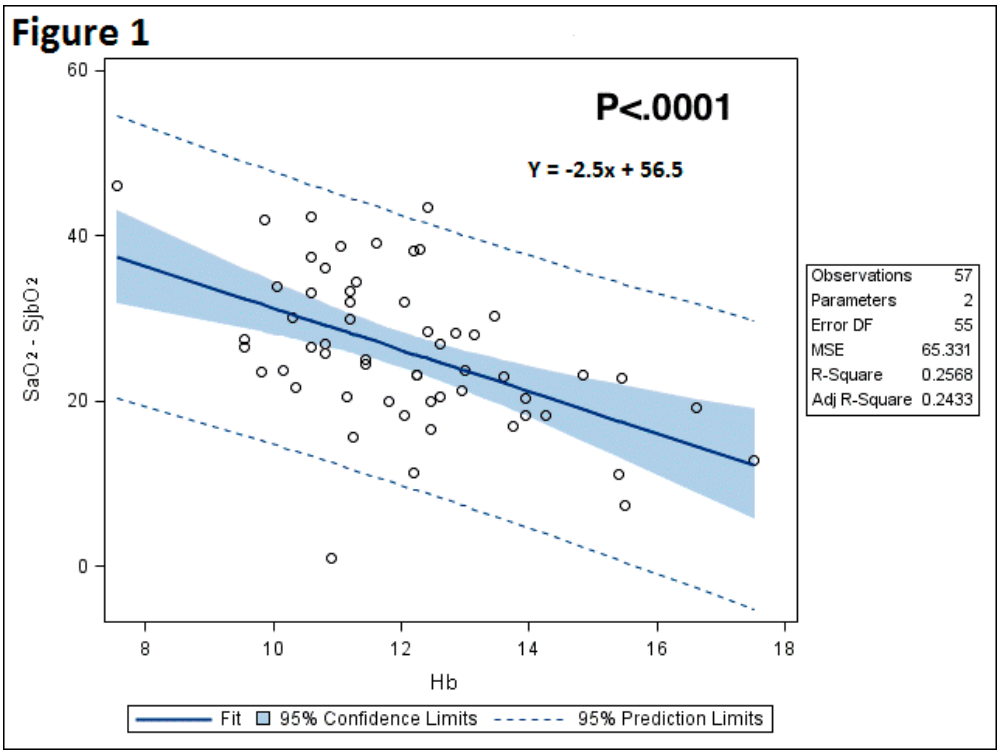
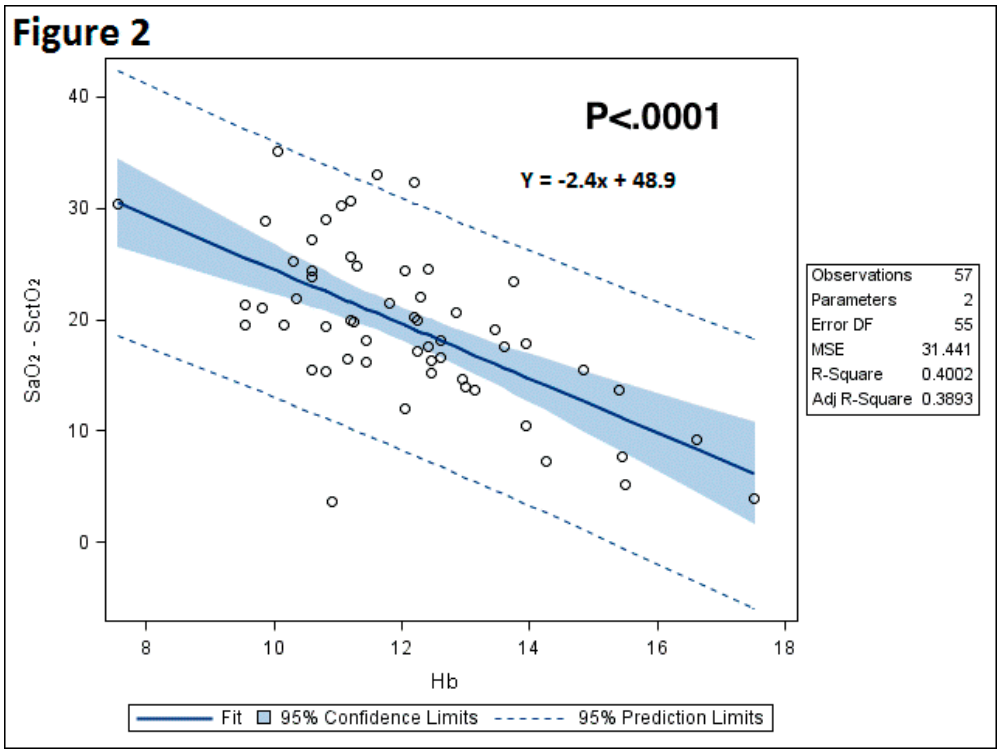


Figure 2



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Regional Anesthesia

S-274.

BRACHIAL PLEXUS NERVE BLOCK IN A PATIENT ON ASPIRIN AND PLAVIX DUE TO RECENT CARDIAC STENT PLACEMENT

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INTRODUCTION: A 52 year old male with a history of HTN, HLD, CAD status post 4 vessel CABG surgery 20 years ago and also recent cardiac stent placement 3 weeks prior to admission, presented to the Emergency Department complaining of chest pain and multiple lacerations from a knife assault. He had a cardiac catheterization shortly after presentation; the patient had two new bare metal stents placed and was continued on aspirin and Plavix. The patient had significant nerve damage to his right hand from the assault and orthopedics recommended that he undergo urgent surgery to preserve motor and sensory function of his hand. Due to the acute stent placement, he had to remain on aspirin and Plavix to prevent stent thrombosis. In addition, the patient was at high risk for general anesthesia due to his recent cardiac history. The decision was made to proceed with surgery using a regional anesthetic technique with sedation.

INTRAOPERATIVE COURSE: The patient was brought to the operating room and standard ASA monitors were placed. A single shot supraclavicular nerve block was performed under ultrasound guidance and a peripheral nerve stimulator. Midazolam 2 mg IV and fentanyl 100 mcg was given for sedation for the block. Upon sonographic visualization of the brachial plexus and functional confirmation with the nerve stimulator, a mixture of 30 cc of 0.5% bupivacaine and 10 cc of 2% lidocaine with epinephrine was injected. During the procedure, the patient was given IV sedation with remifentanil at 0.1 - 0.2 mcg/kg/min and maintained spontaneous ventilation. The surgery lasted approximately 4 1/2 hours and the nerve block provided anesthesia for the entire duration. Postoperatively, the patient recovered function of his operative extremity with no residual motor or sensory deficits following the supraclavicular block. The patient was discharged home the following day.

DISCUSSION: This case presented the anesthesia staff with a difficult clinical scenario. The patient's recent stent placement placed him at high risk for general anesthesia. In addition, the patient was on aspirin and Plavix making him a high risk for complications with a regional block[1,2]. Of particular concern was the risk of hematoma at the site of block placement, which could impinge the arterial circulation and cause ischemia[3]. These concerns were expressed to the surgical team preoperatively; however, the surgeons deemed the procedure to be urgent due to the risk of loss of function in the dominant right hand. The benefits and risks of anesthetic techniques were considered and the decision was made to use regional anesthesia with sedation.

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S-275.

EVALUATION OF THE FEASIBILITY OF DEXAMESTHASONE ADDE TO BUPIVACAINE FOR CONTINUOUS FEMORAL NERVE BLOCK FOR POSTOPERATIVE ANALGESIA AND REHABILITATION AFTER RECONSTRUCTIVE KNEE SURGERY.

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INTRODUCTION: Adequate analgesia after total knee arthroplasty TKA considered to be a challenging; specially in elderly patients; due to the presence of co morbidities[1,2]. Adequate peri-operative analgesia will enhance functional recovery, and reducing postoperative morbidity,and mortality[3].However, the implementation of immediate anticoagulation protocols has raised concerns regarding spinal hematoma with the use of continuous lumbar epidural analgesia[5].femoral nerve block FNB has been found to improve pain control following TKA. Recent trials supported the role of the dexamethasone; that would prolong regional anaesthesia through reducing local anaesthetic absorption,increasing the activity of inhibitory potassium channels on nociceptive C-fibers thus decreasing their activity[14,15].We hypothesed that; adding dexamesathone to bupivacaine for continuous femoral nerve block provides better peri-operative analgesia than standard CFNB.

METHODS: 150 patients scheduled for primary unilateral TKA were enrolled in the study. Patients were allocated to one of three groups. The femoral nerve block with dexamesthasone added to bupivacaine for femoral nerve block FNBD, the standard femoral nerve block FNB, and the control group. All patients enrolled in the study receive general anesthesia; that was implemented after the block in group A,and B patients. As regard group A, and B the block was performed in the block room before pushing to the operating room. Premedication was done using 1 mg dormicum + 50 µg fentanyl.The block needle was attached to a nerve stimulator. The first target point was direct visualization of the needle tip maintained with ultrasound while inserting the needle. The second target used was an ipsilateral quadriceps contraction.On attaining this endpoint and following negative aspiration 25 mL of 0.5% bupivacaine +8 mg dexamesathone were injected slowly in group A patients, and 25 mL of 0.5% bupivacaine was injected slowely in group B patients,a catheter placed 3 - 4. A continuous infusion of 0.25% bupivacaine was started at a rate of 4 ml per hour, after the end of the operation, infusion starting time that was correlated with first time patient reported pain after the end of the procedure was documented, and infusion was continued for 72 h. In case of intra-operative increase in hemodynamic parameters IV remifentanil infusion were started at 0.1 mcg/kg/min. The following parameters were measured; total amount of morphin consumed, NRS, at rest and during movement, satisfaction scores for patient, sergeant, and anesthesia resedant. The primary endpoints of the study were the amount of morphine required in the first 24 hours and comparing the total amount of morphine used in the three studied groups.

RESULTS: Patients in FNBD Group reported lower pain scores on passive movement compared to FNB Group. Cumulative morphine consumption was lower in FNBD Group after recruitment. Conclusion Dexamethasone added to bupivacain prolonged analgesia fromFNB. Further studies will be necessary to demonstrate its safety for perineural use.

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S-276.

COMPARATIVE STUDY BETWEEN CONTINUOUS EPIDURAL ANESTHESIA AND CONTINUOUS WILEYTM SPINAL ANESTHESIA IN GERIATRIC PATIENTS UNDERGOING TURP

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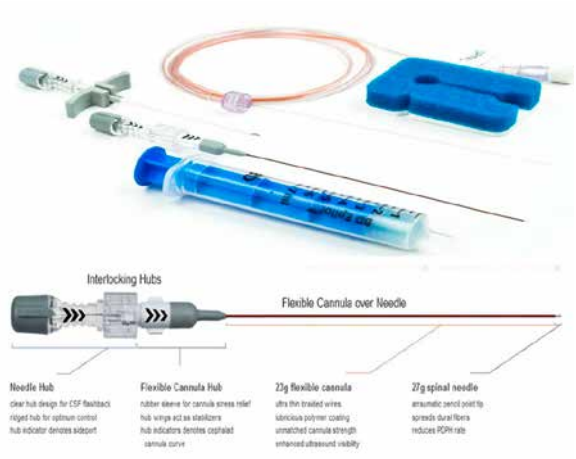
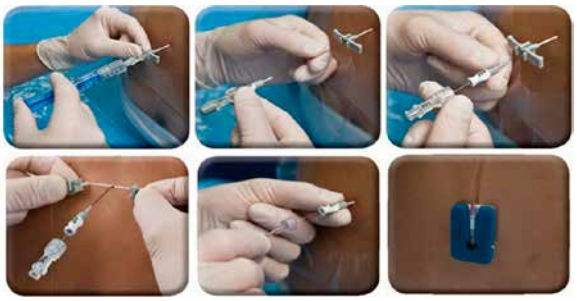
INTRODUCTION: Geriatric patients undergoing transurethral resection of prostate (TURP) have high morbidity rate which is difficult to be detected under general anesthesia[1]. Subarachnoid single dose injection has unpredictable duration and hemodynamic response. Continuous epidural anesthesia extends and intensifies the block providing postoperative analgesia[2]. Continuous spinal anesthesia provides the same advantage with rapid onset, good blockade quality, and low systemic toxicity yet the incidence of post dural puncture headache (PDPH) is unacceptable[3,4]. The Wiley Spinal™ catheter is (Fig-1) an innovative flexible cannula over needle designed for convenient intrathecal access that reduces PDPH[5].





METHODS: After ethical committee approval, 30 geriatric male patients ASA II or III scheduled for elective TURP were allocated into two equal groups: Epidural anesthesia Group (Group EA) who received fentanyl 50 µg and plain bupivacaine 0.5% in 5ml increments and Wiley Spinal anesthesia Group (Group WSA) (Fig-2) who received fentanyl 5µg and plain bupivacaine 0.5% in 0.5ml increments to reach T10 sensory level. The onset time, times to maximum sensory and motor block levels, time to two-segment regression of sensory block, total intraoperative bupivacaine dose, time to full recovery of sensory and motor block, hemodynamic values, and postoperative analgesia as well as adverse effects were recorded.

RESULTS: On comparing WSA group with EA group, the onset time of sensory block to T10 [2 (1-8) vs. 5 (3-20) min], time to reach maximum sensory block [5 (1-20) vs. 7 (3-25) min] and motor block [9 (2-25) vs. 12 (5-40) min], time to two-segment regression [40 (16-75) vs. 80 (30-90) min], time to full recovery of sensory [161.67 ± 28.33 vs. 253.33 ± 52.74 min] and motor block [100.0 ± 27.39 vs. 130.67 ± 19.45 min] respectively being significantly ($P < 0.05$) shorter in WSA group than EA group. Total intraoperative bupivacaine dose was significantly lower in WSA group than EA group ($P < 0.05$). Hemodynamic data showed significant decrease of mean arterial pressure at 3 and 5 min after local anesthetic injected and heart rate at 15 min in Group WSA compared with Group EA ($P < 0.05$); otherwise they were comparable intraoperatively. Number of patients required postoperative analgesia and the incidence of adverse events were comparable.

DISCUSSION: This study revealed that Wiley Spinal anesthesia has more rapid onset and recovery of sensory and motor block with less local anesthetic requirements compared with epidural anesthesia. Both techniques provided almost the same hemodynamic profile. These results go in accordance with Reisli et al[6] but they used prilocaine as local anesthetic. However, Sutter et al[7] showed that continuous spinal anesthesia provided better cardiovascular stability than continuous epidural anesthesia in lower limb surgery.

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S-277.

CLONIDINE AS A LOCAL ANESTHETIC ADJUNCT FOR BRACHIAL PLEXUS BLOCKADE: META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION: Clonidine has been investigated as an adjuvant to local anesthetics (LA) with the goal of improving surgical anesthesia and prolonging postoperative analgesia in regional neural blockade. Whether due to the conflicting results of small-scale randomized controlled trials, or concerns regarding its side effect profile, the use of clonidine in brachial plexus blockade has declined in many institutions over time. Therefore, the goal of this study was to review the available literature and use meta-analysis to quantitatively assess the utility of clonidine as an adjunct in brachial plexus neural blockade.

MATERIALS AND METHODS: A literature search was conducted on the use of clonidine in brachial plexus blockade for upper extremity surgery using PubMed, Ovid and Cochrane databases, including the reference sections of relevant articles. Inclusion criteria stipulated that only prospective/randomized trials of adult patients undergoing brachial plexus blockade be included, that studies directly compare the use of LA to LA plus clonidine (LA+C), and that outcome data be presented in a format suitable for comparative analysis. The primary outcome of interest was duration of analgesia. Other outcomes of interest included rates of block failure, onset and duration of surgical anesthesia and motor blockade and adverse event rates. Random-effects meta-analysis was used to compute effect sizes. Results were considered statistically significant if P<0.05. Analysis of publication bias was completed for all study outcomes.

RESULTS: Fifteen studies (835 patients) met criteria for inclusion. A statistically significant prolongation of the duration of analgesia was found for LA+C (difference in means 117.27min, 95%CI 82.11 to 152.42, P100mcg (diff.means 99.46min, P<0.001) over doses <100mcg (diff.means 138.28min, P<0.001). Duration of surgical anesthesia and motor blockade were similarly prolonged with LA+C. Times to onset of anesthesia (diff.means -1.9min, P=0.130) and motor blockade (diff.means -1.79min, P=0.624) were not significantly different between LA and LA+C. The relative risk of hypotension with LA+C (risk ratio 2.49, 95%CI 1.28-4.86, P=0.008) was found to be non-significant for doses of clonidine 100mcg (RR 4.92, P=0.004). Risks of block failure, bradycardia and desaturation were not significantly different between groups.

DISCUSSION: Previous randomized controlled trials assessing the use of clonidine in brachial plexus blockade have reached disparate conclusions. Random effects meta-analysis of available data from these trials reveals that a statistically and clinically significant prolongation of postoperative analgesia, surgical anesthesia and motor blockade may be achieved with the use of relatively low doses of clonidine. In addition, the use of lower doses appears to mitigate the relative risk of bradycardia.

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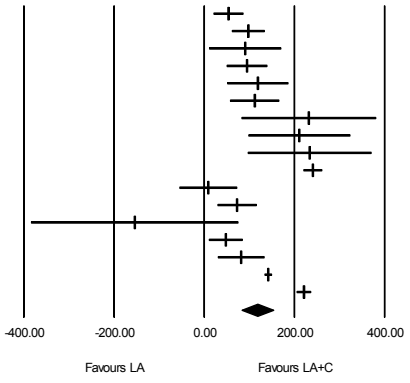
Study name	Subgroup within study	Outcome	Statistics for each study						
			Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Buttner 1992	120mcg vs Mep	Duration analgesia	54.000	17.325	300.173	20.043	87.957	3.117	0.002
Buttner 1992	240mcg vs Mep	Duration analgesia	98.000	18.933	358.442	60.893	135.107	5.176	0.000
Singelyn 1996	0.1mcg/kg vs Mep+Epi	Duration analgesia	91.000	41.202	1697.600	10.246	171.754	2.209	0.027
Singelyn 1996	0.2mcg/kg vs Mep+Epi	Duration analgesia	95.000	23.332	544.400	49.269	140.731	4.072	0.000
Singelyn 1996	0.3mcg/kg vs Mep+Epi	Duration analgesia	119.000	34.941	1220.900	50.516	187.484	3.406	0.001
Singelyn 1996	0.4mcg/kg vs Mep+Epi	Duration analgesia	112.000	28.284	800.000	56.564	167.436	3.960	0.000
Singelyn 1996	0.5mcg/kg vs Mep+Epi	Duration analgesia	232.000	76.630	5872.100	81.809	382.191	3.028	0.002
Singelyn 1996	1.0mcg/kg vs Mep+Epi	Duration analgesia	211.000	58.001	3364.100	97.320	324.680	3.638	0.000
Singelyn 1996	1.5mcg/kg vs Mep+Epi	Duration analgesia	234.000	70.400	4956.100	96.019	371.981	3.324	0.001
El Saied 2000	150mcg vs Rop	Duration analgesia	241.000	11.083	122.826	219.278	262.722	21.746	0.000
Erlacher 2000	150mcg vs Rop	Duration analgesia	9.000	33.007	1089.450	-55.692	73.692	0.273	0.785
Antonucci 2001	1.5mcg/kg vs Rop	Duration analgesia	73.000	22.700	515.300	28.508	117.492	3.216	0.001
Culebras 2001	150mcg vs Bup+Epi	Duration analgesia	-154.000	117.748	13864.575	-384.782	76.782	-1.308	0.191
Broch 2005	1.5mcg/kg vs Prilo	Duration analgesia	48.000	19.612	384.650	9.560	86.440	2.447	0.014
Iohom 2005	100mcg vs Mep	Duration analgesia	82.000	26.730	714.481	29.611	134.389	3.068	0.002
Contreras-D 2006	150mcg vs Mep+Epi	Duration analgesia	142.000	4.655	21.667	132.877	151.123	30.506	0.000
Chakraborty 2010	30mcg vs Bup	Duration analgesia	221.200	8.535	72.846	204.472	237.928	25.917	0.000
			117.267	17.936	321.710	82.112	152.421	6.538	0.000



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S-280.

IMPACT OF REGIONAL ANESTHESIA ON CIRCULATING TUMOR CELLS, CELL-MEDIATED IMMUNITY AND INFLAMMATORY RESPONSE IN PATIENTS WITH NONMETASTATIC BREAST CANCER

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INTRODUCTION: Recent anesthesia research raises an important question: Can the anesthetic technique used during surgical removal of a malignant tumor affect the incidence of cancer recurrence or metastasis? [1,2] One hypothesis is that blockade of pain signals originating from the periphery will result in diminished intraoperative activation of neuroendocrine responses and decreased need of anesthesia and opioids in the perioperative period. As these elements are known immunosuppressants, minimizing them will result in immunocompetence of the host and this may translate to an enhanced ability of the immune system to remove residual tumor cells after the primary tumor is excised.[3,4] The goal of this pilot study was to evaluate the immune system during the perioperative period of women randomized to receive regional anesthesia (RA) or general anesthesia (GA) for surgical excision of primary nonmetastatic breast cancer. In addition we examined peripheral blood for the clearance of circulating tumor cells (CTC) before and after surgery.

METHODS: Eleven women scheduled to undergo unilateral mastectomy or lumpectomy with axillary dissection or sentinel lymph node biopsy were randomized to receive GA or RA [with paravertebral nerve block (PVB)]. GA was achieved with a propofol infusion and intraoperative fentanyl or dilaudid. RA was achieved with T1-T6 PVB, propofol infusion and fentanyl. All postoperative therapies were the same. Blood was sampled within one week of surgery, the morning of surgery, the morning after surgery and within one week after surgery. CTC were enumerated via two enrichment methods (ApoStream and CellSearch), cell populations were analyzed via FACS, cell cytotoxicity was evaluated by granzyme secretion (ELISPOT) and cytokines were evaluated via Luminex.

RESULTS: Five patients had GA and six patients had RA with PVB. Patients randomized to the RA group appeared to have a stronger immune response as analyzed by granzyme secretion as compared to the GA group. When presurgical values of granzyme activation were compared to the morning after surgery values, there was increased granzyme secretion in the RA group and decreased granzyme secretion in the GA group. (Fig. 1) Four out of six patients (67%) in the RA group had no CTCs detected by either enrichment method at the time of the postoperative visit as compared to one out of five patients (20%) in the GA group. (Fig. 2)

CONCLUSIONS: Results demonstrate a trend towards enhanced immunity in the RA group and this trend is accompanied by greater CTC clearance within this group. Long-term benefits resulting from RA may be explained by enhancements within the immune system, something not experienced by patients receiving GA. Regional anesthesia promotes immunocompetence by blunting neuroendocrine responses and reducing amounts of anesthesia and opioids required during the perioperative period, all of which are immunosuppressive. By offsetting these immunosuppressive events, RA may enhance the host's ability to clear residual tumor cells remaining in circulation after removal of the primary tumor and this may ultimately translate to a decrease in future recurrence.

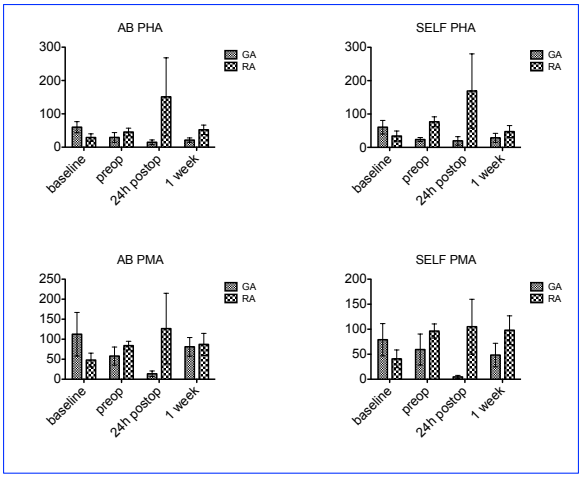

Fig. 1: Anesthesia modulates PBMC granzyme secretion. PBMC were used to determine number of cells capable of secreting granzyme B in response to overnight stimulation with PHA or PMA in culture medium with autologous serum (SELF) or Human AB serum (AB) (ELISPOT assay). Cells from patients randomized to RA (n=6) had a stronger immune response at 24 hours post surgery, compared to patients randomized to GA (n=5).

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S-281.

MOTOR SPARING KNEE BLOCK FOR ANALGESIA FOLLOWING KNEE ARTHROPLASTY: DESCRIPTION OF A NEW APPROACH

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AFFILIATION: Department of anesthesia and perioperative medicine, Western University, London, ON, Canada

INTRODUCTION: Fast track arthroplasty regimens require preservation of motor power to perform early rehabilitation and ensure early discharge [1]. Commonly performed nerve blocks like femoral and Sciatic nerve blocks results in motor weakness thereby not only interfering in early rehabilitation and physiotherapy but may also predispose to patient falls[2,3]. Hence, targeting the terminal branches of the femoral and sciatic nerves around the knee joint under ultrasound is an attractive strategy. The nerves of interest for knee analgesia are the terminal branches of the femoral nerve, the genicular branches of the lateral cutaneous nerve of thigh, obturator and sciatic nerves[4].

METHODS: We modified the technique of adductor canal block performance and combined it with US guided posterior pericapsular injection and lateral femoral cutaneous nerve block to provide analgesia around the knee joint. Femoral artery is traced under the sartorius muscle till the origin of superior geniculate artery. The intermediate cutaneous nerve of thigh travels as a dual nerve between the Sartorius and rectus femoris above the fascia lata which is blocked by 5 ml of 0.5% ropivacaine (LA). The needle is then redirected to enter the fascia of Sartorius to deliver an additional 5ml of LA to cover the medial retinacular branches. The needle is then advanced till the needle tip is seen to lie adjacent to the femoral artery under the Sartorius to perform the adductor canal block with an additional 15-20 ml of LA to cover nerve to vastus medialis, infrapatellar branch of saphenous nerve and the articular branch of the obturator nerve. The lateral cutaneous nerve of thigh is blocked with 10 ml of LA near the anterior superior iliac spine between the origin of Sartorius and tensor fascia lata. The terminal branches of sciatic nerve to the knee joint is blocked by depositing 25 ml of local anesthetic solution between the popliteal artery and femur bone at the level of femoral epicondyles.

RESULTS: Our initial experience with this block has been promising. We have used this technique in 10 patients undergoing knee arthroplasty with good effect. The median (IQR) block duration was noted to be around 20 (±6.5) hours. The median (IQR) pain scores in the first 24 postoperative hours ranged from 0 (±0.5) to 3 (±2.5) at rest and 1.5 (±3.5) to 5.5 (±1) on movement. All patients were successfully mobilized on the morning of the first postoperative day.

CONCLUSION: Motor sparing from the blocks while providing adequate analgesia can be achieved by selectively targeting the sensory innervation of the knee joint. Future comparative studies are needed to evaluate the performance of this block with other modes of analgesia for knee arthroplasty.

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S-282.

DOCUMENTATION OF RISK DISCLOSURE IN UPPER LIMB BLOCKS

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INTRODUCTION: The Association of Anaesthetists of Great Britain & Ireland (AAGBI) recommends documentation of invasive procedures or ones with significant risks in patient's notes, or a separate anaesthetic consent form1. The Royal College of Anaesthetists (RCOA) also recommends auditing this process of consent and states 100% compliance as target for best practice2. The purpose of this retrospective audit was to assess our departmental compliance with documentation of risk disclosure while performing upper limb nerve blocks.

METHODS: In accordance with local practice for audit projects, after approval by the departmental lead for audit, relevant data were collected from anaesthetic records of 50 patients who received upper limb regional nerve block, with or without other forms of anaesthesia. These records were analysed for the documentation of the designation of doctor consenting the patient, type of nerve block performed, risk of infection, bleeding, nerve damage, incidence of nerve damage, risk of pneumothorax (if performing a supraclavicular block) and local anaesthetic toxicity.

RESULTS: Out of 50 patients, 48 were consented by a consultant while 2 patients were consented by a Non-Consultant grade doctor. A clear documentation of the type of block being performed was found in only 46% of the anaesthetic records. The types of block performed as documented are shown below in Table 1.

Table 1. Type of block as documented

Type of block	Number of patients (%)
Documented	23/50 (46%)
Interscalene	4/50 (8%)
Supraclavicular	7/50 (14%)
Axillary	1/50 (2%)
Suprascapular/Axillary	1/50 (2%)
Brachial plexus block	6/50 (12%)
Peripheral nerve block (PNB)	2/50 (4%)
Nerve block	2/50 (4%)
Not documented	27/50 (54%)

Since we considered the use of descriptive terms like nerve block, peripheral nerve block, and brachial plexus block as inaccurate, only 26% (13 out of 50) of the anaesthetic records had an accurate description of the type of block being performed. Only 54% records had a documentation of risk involved with the proposed procedure. These risks are summarised below in Table 2.

Table 2. Documentation of risk disclosure

Risk disclosure	Number of patients (%)
Infection	10/50 (20%)
Bleeding	8/50 (16%)
Nerve damage	25/50 (50%)
Incidence of nerve damage	11/50 (22%)
Pneumothorax	8/19 (42%)$
Local anaesthetic toxicity	1/50 (2%)
Motor block	10/50 (20%)
Numbness	1/50 (2%)
Bruising	1/50 (2%)
Horner syndrome	1/50 (2%)
Failure of procedure	7/50 (14%)

NOTE: Nineteen patients had a supraclavicular block (documented or not) out of which the risk of pneumothorax was documented in 8 records only.

CONCLUSION: In conclusion, our documentation of risk disclosure was well below the recommended target. Some of the reasons for the observations may include a lack of time, lack of patient information leaflets, and disclosure related apprehensions of patients. It was agreed at the departmental meet to introduce patient information leaflets, improve our documentation, preformed risk disclosure stickers and to revise the current anaesthetic record to allow disclosure of risks as a checklist. It was also felt that other regional blocks such as spinal, epidural and lower limb blocks should also be brought under the purview of such measures. A time frame of 6 months was set to introduce these changes, and a re-audit was after a further 6 months. A draft sticker for consent in regional anaesthesia was introduced recently and is shown in figure 1.

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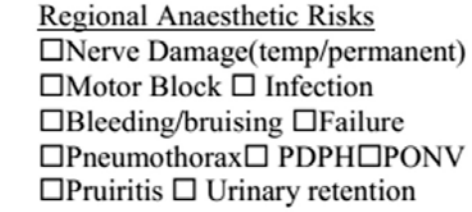
Figure 1. Risk Disclosure Sticker for Regional Anaesthesia procedures



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S-283.

MANAGEMENT OF EPIDURAL BLOOD PATCHING IN PATIENTS WITH LEUKEMIA

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INTRODUCTION: Patients with leukemic diseases get frequent spinal punctures for diagnostic as well as for therapeutic procedures. With the risk of developing post dural puncture headache [PDPH], and the eventual need for epidural blood patch as part of PDPH management, comes the controversy of injecting the patients' own blood to the epidural space. An epidural blood patch (EBP) is the most appropriate treatment of persistent PDPH. However, in these patients, there are no data on the safety of EBP. Instead of autologous blood injection in the epidural space a colloid or saline solution could be an alternative, also insertion of the intrathecal catheter at the time inadvertent dural puncture was also mentioned [1,2].

CASE REPORT: A 43-yr-old, 74-kg patient at a remission of acute lymphocytic leukemia (ALL). Within several hours of his last diagnostic spinal puncture, the patient complained of a severe positional headache. After an initial response to bed rest, oral then IV fluids and ibuprofen, and three 500-mg doses of IV caffeine over 36 h, the patient continued to have a severe positional headache. EBP was recommended to help with the patient's persistent headache [PDPH]. On the grounds that this more invasive treatment could place the patient at increased risk of infectious complications and central nervous system leukemia, consultation with our team of regional anesthesia experts, hematologists, and literature review took place. EBP was considered safe on the basis of normal blood work, and almost seldom chance of central nervous system leukemia. EBP was done under complete sterile conditions. Complete resolution of the headache occurred after a single EBP

CONCLUSIONS: The fluid chosen to be used with epidural patch should be individualized according to the existing medical condition that necessitate the earlier dural puncture. Prospective controlled studies are required to confirm the safety and efficacy of the various methods to treat PDPH.

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S-284.

OPIOID CONSUMPTION IN TOTAL KNEE ARTHROPLASTY PATIENTS: A RETROSPECTIVE COMPARISON OF ADDUCTOR CANAL AND FEMORAL NERVE CONTINUOUS INFUSIONS.

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INTRODUCTION: When compared to femoral nerve blockade (FB), the adductor canal block (ACB) is associated with less motor weakness. Currently, little evidence exists regarding the effect of ACB on opioid consumption when compared to FB. Our purpose in this study was to assess differences in postoperative opioid consumption in total knee arthroplasty patients. Our hypothesis was that when combined with sciatic nerve blockade (SB), ACB does not increase opioid requirements when compared to continuous FB/SB.

METHODS: A total of 96 patient charts were reviewed for this study: 51 patients with continuous FB/SB and 45 with continuous ACB/SB. Patients were matched according to age, height, weight, gender, baseline pain scores, and mean home opioid consumption. The primary outcome of the study was postoperative opioid consumption on postoperative days 0 (POD 0), 1 (POD 1), and 2 (POD 2). Secondary outcomes were postoperative visual analog scale (VAS) scores, use of IV hydromorphone or hydromorphone PCA, incidence of nausea and pruritus, and need for catheter bolus by a physician.

RESULTS: Mean opioid consumption overnight in milligrams of oral morphine equivalent (mean ± CI) from POD 0 to 1 were 38.2mg ± 8.76 in the FB/SB group vs 43.98mg ± 10.02 in the ACB/SB group (p= 0.39). POD 1 mean opioid consumption was 78.06 mg ± 18.08 vs 74.96mg ± 11.19 in the FB/SB and ACB/SB canal groups, respectively (p=0.78). POD 2 mean opioid consumption was 31.88mg ± 6.37 and 28.19mg ± 5.32 in the FB/SB and ACB/SB groups, respectively (p= 0.38). On POD1, median anterior and posterior knee VAS scores at rest, as well as posterior knee VAS scores with knee motion, were equivalent in both the FB/SB and ACB/SB groups (p=0.84 , p=0.22, p=0.21, respectively). Median anterior knee VAS scores with knee motion were higher in the adductor canal group, [1 vs 4 ($p<0.05$)] on POD1, but not statistically different on POD2 either at rest or with motion [1 vs 1 (p=0.67), 3 vs 3 (p=0.96), respectively]. Incidence of nausea, use of intravenous hydromorphone or hydromorphone PCA, as well as need for catheter bolus by a physician on either POD 1 or 2 were not statistically different between the two groups (p=0.77, p=0.62, p=0.37, p=0.74, p=0.13, respectively).

CONCLUSION: In the first two days postoperatively after a total knee arthroplasty, opioid consumption in patients with continuous ACB/SB is not statistically significantly different from patients receiving continuous FB/SB. Continuous adductor canal block seems to provide adequate analgesia when compared to continuous femoral blockade.

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Table 1: Baseline patient characteristics

	FB/SB	ACB/SB	p-value
Age	66.92	64.86	0.32
Height	167.33	167.57	0.91
Weight	90.65	83.29	0.07
% Male gender	33.3	31.1	0.82
% pts on home opioid	21.6	11.1	0.17
Mean home opioid dose	12.8	12	0.85
Baseline pain at rest	1.9	1.2	0.13
Baseline pain with motion	6.5	5.6	0.08

Table 2: Mean opioid consumption in milligrams of oral morphine equivalent, ± confidence interval.

	FB/SB	ACB/SB	p-value
POD 0 to 1	38.2 ± 8.76	43.98 ± 10.02	0.39
POD 1	78.06 ± 18.08	74.96 ± 11.19	0.78
POD 2	31.88 ± 6.37	28.19 ± 5.32	0.38

Table 3: Median postoperative VAS scores with knee at rest

	FB/SB	ACB/SB	p-value
POD 1 , anterior	0	1	0.84
POD 1, posterior	1	0	0.22
POD 2, anterior	1	1	0.67
POD 2, posterior	1	0	0.047

Table 4: Median postoperative VAS scores with knee in motion

	FB/SB	ACB/SB	p-value
POD 1, anterior	1	4	0.02
POD 1, posterior	3	2	0.21
POD 2, anterior	3	3	0.96
POD 2, posterior	4	2	0.002

Table 5: Incidence of secondary outcomes, in percentages

	FB/SB	ACB/SB	p-value
Nausea	29.4	26.7	0.77
Pruritus	7.8	28.9	0.01
Patients requiring IV hydromorphone	62.7	57.8	0.62
Patients requiring hydromorphone PCA	5.88	2.22	0.37
Patients requiring catheter bolus by physician, POD1	15.7	13.3	0.74
Patients requiring catheter bolus by physician, POD2	1.96	8.89	0.13

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S-285.

POST-OPERATIVE PAIN CONTROL WITH TRANSVERSUS ABDOMINIS PLANE BLOCKS WITH LIPOSOMAL BUPIVACAINE VERSUS IV OPIOIDS IN LAPAROSCOPIC COLORECTAL PATIENTS: A RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Transversus abdominis plane (TAP) blocks are gaining popularity as part of a multimodal regimen to decrease post-operative pain and narcotics in abdominal procedures. Studies have shown that TAP blocks with either bupivacaine or ropivacaine decrease post-operative pain and narcotic requirements for the first 24 hours.[1] Liposomal bupivacaine (LB) (Exparel) has been shown to provide pain relief up to 72 hours after infiltration; however, its use in TAP blocks has been minimally reported. [2]

OBJECTIVE: The aim of this study was to evaluate the effect of an ultrasound-guided TAP block with LB on narcotic use in patients undergoing laparoscopic colectomy.

METHODS: In total, 38 patients (median age 60, range 18-82; 22 male, ASA I-III) who underwent a laparoscopic right, left, or total colectomy were retrospectively studied and outcomes were followed for up to 72 hours post injection. The cohort consisted of 19 patients (10/2012 to 7/2013) who received a TAP block and 19 patients (3/2012-9/2012) who did not. Pain intensity was assessed via visual analog scale (VAS) 0-10. Narcotics were delivered via PCA and their use was normalized to micrograms of fentanyl. All charts were analyzed up to 14 days post-discharge for any complications or readmissions for pain.

RESULTS: The two groups had no difference in baseline characteristics. Patients who received a TAP block had decreased total narcotics usage in the first 72 hours post-operatively compared to those who did not (1153 ± 618 mcg vs 1835 ± 1227 mcg, p= 0.04). In the first 24 hours post block and from 24 to 48 hours post-operatively, narcotic usage was less in those who received TAP block compared to those who did not (424 ± 270 mcg vs 633 mcg ± 342, p= 0.04) and (424 ± 295 mcg vs 726 ± 542 mcg, p= 0.04),, respectively. This was also associated with an observed decreased length of stay in those who received a TAP block compared to those who did not (111.4 hours ± 49.4 vs 167.4 hours ± 85.37 p= 0.02). While there was no difference in VAS minimum pain scores between the two groups, there was a decreased VAS maximum pain score on the first 24 hours post block (5.8 ± 2.5 vs 7.8 ± 2.0 p= 0.01) and 48-72 hours post block (3.6 ± 2.2 vs 5.1 ± 2.3 p = 0.049). Three patients in the TAP group had nausea post operatively versus 9 in the control group.

CONCLUSION: In patients undergoing laparoscopic colectomy procedure, performing an ultrasound guided transversus abdominis plane block with lisosomal bupivicaine may decrease narcotics in the first 72 hours post block, decrease overall length of stay, and decrease the maximum VAS pain score compared to those who receive no block.

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S-286.

DEXAMETHASONE AS AN ADJUNCT FOR BRACHIAL PLEXUS BLOCKADE: META-ANALYSIS

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INTRODUCTION: The search for adjuncts in regional anesthesia has lead to the addition of epinephrine, clonidine, tramadol, neostigmine and dexamethasone perineurally. The ideal adjunct prolongs the duration of analgesia, speeds the onset and improves the quality of the blockade. Despite the existence of several randomized controlled trials reporting improved duration of analgesia with dexamethsone. The goal of this study was to review the available literature and use meta-analysis to quantitatively assess the utility of dexamethasone as an adjunct in brachial plexus blockade.

MATERIALS AND METHODS: A literature search was conducted on the use of dexamethasone in brachial plexus anesthesia using PubMed, Ovid and Cochrane databases, including the reference sections of relevant articles. Inclusion criteria stipulated only prospective/randomized trials of adult patients undergoing brachial plexus blockade be included, that studies directly compare the use of local anesthetic (LA) alone to LA plus perineural dexamethasone (LA+D) and that outcome data be presented in a format suitable for comparative analysis. Outcomes of interest included duration of analgesia and onset /duration of sensory and motor blockade. Random-effects meta-analysis was used to compute effect sizes and compare LA/LA+ D groups. Results were considered statistically significant if $P<0.05$. Analysis of publication bias was completed for all study outcomes.

RESULTS: Four studies (246 patients) met criteria for inclusion. A statistically significant difference in favor of LA+D was found for duration of analgesia (difference in means 421.85 min, 95%Cl (270.34-573.46), $P<0.001$). The prolongation of analgesia was found to be significant irrespective of dexamethasone dose (4 vs 8mg) or approach to the brachial plexus blockade (interscalene vs supraclavicular vs axillary). A statistically significant prolongation of the duration of motor blockade was observed for LA+D (difference in means 487.43min, 95%CI 41.94-932.91, $P=0.032$). No significant difference was found in the onset of sensory or motor blockade. Analysis of publication bias for duration of analgesia revealed one “file drawer publication” to the left of the mean, However the addition of imputed data had no effect of the statistical significance of our previous findings.

CONCLUSIONS: Adjuncts have been added to regional blockades with the goal of prolonging duration, improving the quality of the blockade, and speeding the onset. Several studies have assessed the ability of dexamethasone to provide these benefits. Despite a growing volume of retrospective evidence supporting the utility of dexamethasone as an analgesic adjunct, the relatively small scale of various prospective controlled trials demonstrating this effect may be dissuading clinicians from the widespread adoption of dexamethasone for regional anesthesia. Meta-analysis of available data from randomized controlled trials directly comparing the use of local anesthetic alone to local anesthetic plus dexamethasone for regional blockade revealed a significant prolongation in the duration of procedural analgesia.

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S-287.

DIPHENHYDRAMINE BLOCKS RAT SCIATIC NERVE AND EXHIBITS A TOXIC EFFECT ON PC12 CELL

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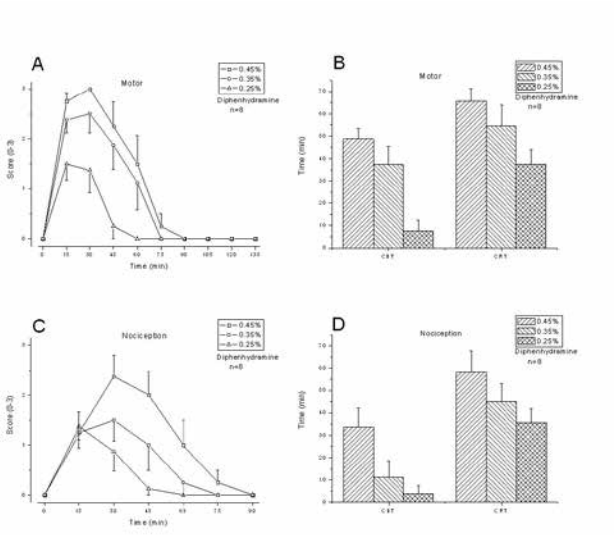
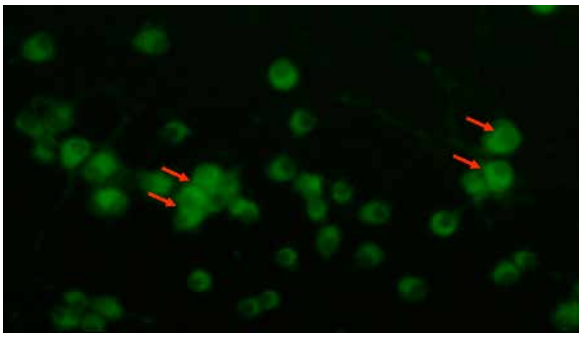
INTRODUCTION: Novel drugs that provide sensory/nociceptive blockade with minimal impairment of motor functions are highly desirable for regional anesthesia. Diphenhydramine is well known working as histamine antagonists by blocking H1 receptor. It also exhibited sodium channel blockade as traditional local anesthetic (e.g. lidocaine and bupivacaine). Because diphenhydramine may be a useful alternative agent and adjuvant of local anesthetics, the authors investigated the local anesthetic properties of diphenhydramine in a rat sciatic nerve block model and the potential toxicity in cultured cells.

METHODS: The study was approved by institutional Animal Care Committee. Anesthetized rats weighing 250-300 grams had their sciatic nerves exposed by lateral incision. Sciatic nerve blockade was achieved with 0.2 ml diphenhydramine at selected concentrations, and the motor and nociceptive blockade was evaluated, respectively (n = 8 per group). The score was graded on a scale of 0 to 3: 0 (baseline or normal), 1 (mildly impaired), 2 (moderately impaired), and 3 (totally impaired). The ED50 was calculated by nonlinear regression analysis with the Hill equation: $E = Emax\ (D/ED_{50})^m / 1 + (D/ED_{50})^m$, where *E* is the measured neurobehavioral score (0, 1, 2, 3); D is dose of drug; *E*max is the full range of response that can be effected by infinite drug dose; ED_{50} is the median effective dose of drug; and *m* is a slope/sigmoidicity parameter. To elucidate the potential toxic effect and confirm dose-dependent toxicity, apoptosis was quantified by flowcytometry based on the staining caspase3,7 as a marker in cultured pheochromocytoma cells (PC12 cells) incubated with diphenhydramine.

RESULTS: The time courses of motor, and nociceptive function of sciatic nerve blockade by selected concentrations of diphenhydramine is shown in figure1. The ED50 of diphenhydramine are 0.24% (95% confidence interval: 0.217 - 0.264) and 0.263% (95% confidence interval: 0.167 - 0.359) in motor function and nociception, respectively. A dose-dependent toxic effect in PC12 cells exposed to diphenhydramine is shown in figure3.

CONCLUSIONS: Diphenhydramine exhibits local anesthetic property in rat sciatic nerve. It may be useful as a local anesthetic and an adjunct to local anesthetics for peripheral nerve blockade. However, with cellular toxicity, it appears to caution for clinical usage because of potential neurotoxicity. Future studies should also include analysis of a safety profile to determine the therapeutic window.





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S-288.

THE USE OF IV PCA WITH OR WITHOUT EPIDURAL ANALGESIA DOES NOT AFFECT RECURRENCE FREE SURVIVAL OR OVERALL SURVIVAL WHEN COMPARED TO EPIDURAL ANALGESIA ALONE AFTER PANCREATIC CANCER SURGERY. A RETROSPECTIVE STUDY.

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INTRODUCTION: Epidural analgesia has well known benefits after pancreatic surgery.[1-2] However, many patients still require intravenous patient controlled analgesia (IV PCA) in addition to epidural analgesia since frequently, epidural infusion rates may be decreased or temporarily held in the first twenty four hours after surgery mainly due to hypotension.[3] Systemic narcotics are not without risks, and can result in not only medical complications, but potentially immunosuppression.[4] The purpose of this study was to compare recurrence free survival (RFS) and overall survival (OS) in patients who received IV PCA with or without concomitant use of epidural analgesia to patients who received epidural analgesia alone.

METHODS: The records of all patients over the age of 18 who had surgery for pancreatic adenocarcinoma at MD Anderson Cancer Center from January 2006 to October 2012 were reviewed. Patients were compared by modality of postoperative pain control. Demographic and clinical data were collected. Variables that were statistically significant on univariate analysis were entered into a multivariate model to assess for effect on RFS and OS.

RESULTS: A total of 425 patients were studied, of which 286 patients received an epidural alone and 139 patients received an IV PCA with or without epidural. The median RFS time for patients receiving an epidural alone (15.41 months; 95% CI: 11.63, 16.56), was no different than patients receiving an IV PCA (14.72 months; 95% CI: 11.56, 18.43), P=0.9538. On multivariate analysis, factors associated with decreased RFS included type of surgery, tumor stage, and diabetes mellitus. (Table 1).

The median OS for patients receiving epidural alone (32.82 months; 95%CI: 29.04, 43.89), was not statistically different than those receiving IV PCA with or without epidural (31.24 months 95%CI: 26.02, 40.14), P=0.7996. On multivariate analysis, factors associated with poorer overall survival included patient age, tumor stage, and estimated blood loss. (Table2).

CONCLUSIONS: The use of IV PCA with or without epidural analgesia did not have a significant effect on RFS or OS in patients undergoing surgery for pancreatic adenocarcinoma when compared to the use of epidural analgesia alone. Unfortunately, we did not have an IV PCA alone group of patients. Robust studies on perioperative factors that may impact RFS and OS after pancreatic cancer surgery are warranted.

We would like to acknowledge the contributions of Jun Yu, Department of Biostatistics, MD Anderson Cancer Center.

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Table 1					
Parameter		**p-value**	**HazardRatio**	**95% CI for HR**	
Postoperative Pain Control	**Epidural alone vs. PCA+/-Epidural**	0.8163	0.969	0.744	1.263
Surgery Type	**Pancreatectomy Total vs. PancreatectomyDistal**	0.0274	0.199	0.047	0.835
Surgery Type	**Pancreaticoduodenectomy vs. PancreatectomyDistal**	0.0154	0.645	0.453	0.920
Surgical Stage	**2 vs. 1**	0.0007	2.649	1.506	4.659
Surgical Stage	**3 vs. 1**	0.0177	2.501	1.172	5.334
Surgical Stage	**4 vs. 1**	0.0373	3.86	1.083	13.757
Log EBL		0.0916	1.18	0.974	1.431
Diabetes mellitus	**Y vs. N**	0.02	1.764	1.094	2.846
pRBC transfused during admission	**Y vs. N**	0.1721	1.21	0.92	1.592
Intraoperative dexamethasone	**Y vs. N**	0.0775	1.281	0.973	1.686

Table 2					
Parameter		**p-value**	**HazardRatio**	**95% CI for Hazard Ratio**	
Age	**<60 vs. > 60**	0.0175	1.021	1.004	1.038
Postoperative Pain Control	**Epidural alone vs. PCA+/-Epidural**	0.7663	0.954	0.702	1.298
Surgical Stage	**2 vs. 1**	0.0009	3.995	1.762	9.061
Surgical Stage	**3 vs. 1**	0.006	4.057	1.494	11.018
Surgical Stage	**4 vs. 1**	0.0017	13.553	2.669	68.821
Log EBL		0.007	1.369	1.09	1.719
pRBC transfused during admission	**Y vs. N**	0.0889	1.347	0.956	1.899

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S-289.

THE EFFICACY OF ULTRASOUND-GUIDED SPERMATIC CORD BLOCK FOR SCROTAL SURGERY

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BACKGROUND: Orchiectomy in treatment of metastatic prostate cancer is often performed in general and neuraxial anesthesia. Most of the patients who undergo orchiectomy are elderly and at high risk for general anesthesia due to worsening physical status associated with cancer progression.Spinal anesthesia is absolutely contraindicated in lumbar metastasis, which often occurred in prostate cancer patients.A blindly performed block may result in a complication(i.e.intravascular injection of local anesthetics, scrotal hematoma, and perforation of the deferent duct).Ultrasound-guided spermatic cord block would reduce complications and risks for general and neuraxial anesthesia and be helpful to postoperative pain management.

METHODS: Fifteen inpatients undergoing orchiectomy were included in this prospective study.All patients received ultrasound-guided spermatic cord block for orchiectomy.The spermatic cord was identified as it emerges from the external inguinal ring and trapped it over or just superior to the pubic tubercle.We tightly held the spermatic cord and lifted it up and applied the ultrasound transducer and discerned the spermatic cord and the deferent duct.A 20 G needle was advanced close to the deferent duct by avoiding vessel perforation,and local anesthetic was infiltrated around the deferent duct under direct visualization.We used a mixture of 5 ml mepivacaine 2% and 5 ml ropivacaine 0.75% for the block and 10 ml lidocaine 1% for the site of the incision because spermatic cord block dose not provide scrotal skin anesthesia.We assessed the pain response immediately after surgery and at 24 and 48 hours after the injection of the local anesthetics,using a numeric rating scale (NRS,0=no pain and 10=unbearable pain). Blocks were considered successful if surgery could be completed without the use of general anesthesia,defined as a propofol requirement of 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ or more,or any use of nitrous oxide or volatile drugs.

RESULTS: No conversion to general anesthesia was needed,although it was necessary to inject another 0 to 13ml lidocaine 1%.Only one patient complained of right side abdominal pain when there was heavy traction on the spermatic cord,but it abated immediately after we injected another 6ml lidocaine 1% into the cord.Fifteen patients did not need any IV pain medication during the 48 hours after the injection.The median NRS score was 0 immediately after surgery,0 at 24 hours after the injection,and 0 at 48 hours after the injection.No complications related to the anesthesia were seen.

CONCLUSION: Good anesthetic management by the ultrasound-guided spermatic cord block was achieved.Our experience suggetsts that ultrasound-guided spermatic cord block is a simple,safe and effective techinique that should become an alternative to general or neuraxial anesthesia in the urological setting and that it would reduce the cost of the operation considerably.

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S-290.

FEASIBILITY AND PERI-OPERATIVE PAIN RELIVING EFFICACY OF ULTRASOUND GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK IN MORBID OBESE PATIENTS UNDERGOING LAPAROSCOPIC BARIATRIC SURGERY.

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INTRODUCTION: The implementation of adequate postoperative analgesia may be beneficial in morbidly obese patients after bariatric surgery due to their higher risk for postoperative pulmonary complication.TAP block is a new regional anesthetic technique,it has been implemented successfully for pain control after laparoscopic surgery in non obese patients.Success with this block is dependent on correct identification of the neuro-fascial plane.The introduction of ultrasound guidance has allowed greater precision of needle placement in the desired tissue plane. This prospective,randomized,double blinded, controlled study was carried out to evaluate the feasibility,and efficacy of ultrasound-guided TAP block in patients with morbid obe¬sity undergoing laparoscopic bariatric surgery. We hypothesed that; USG-TAP block is feasible, and effective in reducing pain scores, and attenuating morphine consumption.

PATIENTS&METHODS: After obtaining approval from Ethics Committee.100 patients underwent laparoscopic sleeve gastrectomy enrolled in the study.Patients with,body mass index > 35 kg/m2, included.patients were allocated by sealed envelops to one of two groups;USG-TAP(50),or to receive standard care regarding regular postoperative analgesia (50), according to the anesthesia department protocol. before extubation;the skin was prepared, the probe was placed on the anterolateral abdominal wall between the iliac crest and the subcostal margin.A 22-gauge needle was inserted medial to the probe by the in-plane technique. When the tip of the needle reached the TAP plane,1 mL of 0.5% bupivacaine were injected into the patients of the TAP block group. after negative aspiration, and the spread of the drugs was confirmed.Then, the remaining 19 mL was injected. these step done bilaterally. The primary endpoints of the study were the amount of morphine required in the first 24 hours.

STATISTICAL ANALYSIS: For sample size calculation, we considered that a clinically important difference in 48 h morphine consumption would be a 25% absolute reduction in the TAP compared with control group.Based on this assumption 35 patients were required for the IV-PCA+TAP block group, and 40 patients were assigned to the IV-PCAgroup. To minimize any effect of data loss, we elected to recruit 50 patients in each group.Comparisons of means were conducted with the Student’s t test for parametric variables and Mann-Whitney for non-parametric ones.

RESULTS: median NRS pain score of (USG-TAP) group was consistently lower at 30 minutes, hourly till 6,6,12, and18 h at rest and on movement,and coughing in the postoperative period. This reduction in NRS showed statistically significant difference in comparison to control group Cumulative morphine consumption was significantly reduced at 24 h,and 48h in patients who received a TAP block.conclusion:ultrasound-guided TAP block is a fea¬sible technique for effective component of multimodal postoperative analgesia in morbidly obese patients undergoing laparoscopic sleeve gastrectomy.

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S-291.

WITHDRAWN.

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S-292.

TRANSVERSUS ABDOMINIS PLANE BLOCK TO AMELIORATE POSTOPERATIVE PAIN OUTCOMES AFTER LAPAROSCOPIC SURGERY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION: Transversus abdominis plane (TAP) block has been used as a component of multimodal strategy to optimize postoperative pain outcomes; However, it remains unclear which type of surgical procedures can benefit from the administration of a TAP block. Several studies have examined the effect of TAP block on postoperative pain outcomes after laparoscopic surgical procedures and generated conflicting results. Our main objective in the current investigation was to evaluate the effect of TAP block on postoperative analgesia outcomes for laparoscopic surgical procedures.

METHODS: A search was performed to identify randomized controlled trials that evaluated the effects of the TAP block compared with an inactive group (placebo or "no treatment") on postoperative pain outcomes in laparoscopic surgical procedures. Primary outcomes included early (0-4 hours) and late (24 hours) postoperative pain at rest and on movement and postoperative opioid consumption (up to 24 hours). Meta-analysis was performed using a random-effects model. Publication bias was evaluated by examining the presence of asymmetric funnel plots using Egger regression test. Meta-regression analysis was performed to establish an association between the local anesthetic dose and the evaluated outcomes.

RESULTS: Ten randomized clinical trials with 633 subjects were included in the analysis. The weighted mean difference (99% confidence interval) of the combined effects favored TAP block over control for pain at rest (≤4 hours, -2.41 [-3.6 to -1.16]) and (at 24 hours, -1.33 [-2.19 to -0.48]) (0-10 numerical scale). Postoperative opioid consumption was decreased in the TAP block group compared with control, weighted mean difference (99% confidence interval) of -5.74 (-8.48 to -2.99) mg morphine IV equivalents. Publication bias was not present in any of the analyses. Preoperative TAP block administration resulted in greater effects on early pain and opioid consumption compared with postoperative administration. Meta-regression analysis revealed an association between local anesthetic dose and the TAP block effect on late pain at rest and postoperative opioid consumption. None of the studies reported symptoms of local anesthetic toxicity.

CONCLUSIONS: TAP block is an effective strategy to improve early and late pain at rest and to reduce opioid consumption after laparoscopic surgical procedures. In contrast, the TAP block was not superior compared with control to reduce early and late pain during movement. Preoperative administration of a TAP block seems to result in greater effects on postoperative pain outcomes. We also detected a local anesthetic dose response on late pain and postoperative opioid consumption.

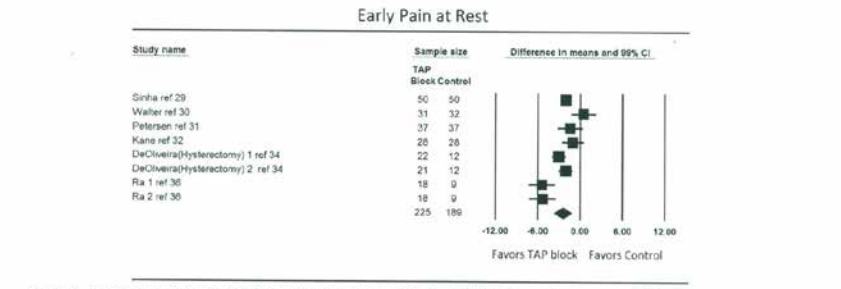

Figure 2. Meta-analysis evaluating the effect of transversus abdominis plane (TAP) block on early pain scores (≤4 hours) at rest compared with control. The overall effect of TAP block versus control was estimated as a random effect. Point estimate (99% confidence interval [CI]) for overall effect was −2.41 (−3.6 to −1.16) (0–10 numerical scale). Weighted mean difference for individual studies represented by square on Forrest plot, with 99% CI of the difference shown as solid line. Larger sized square and thicker 99% CI line denote larger sample size. The diamond represents the pooled estimate and uncertainty for the effects of TAP block compared with control.

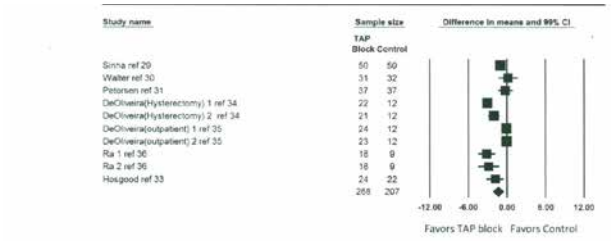

Figure 3. Meta-analysis evaluating the effect of transversus abdominis plane (TAP) block on late pain scores (24 hours) at rest compared with control. The overall effect of TAP block versus control was estimated as a random effect. Point estimate (99% confidence interval [CI]) for overall effect was −1.33 (−2.19 to −0.48) (0–10 numerical scale). Weighted mean difference for individual studies represented by square on Forrest plot, with 99% CI of the difference shown as solid line. Larger sized square and thicker 99% CI line denote larger sample size. The diamond represents the pooled estimate and uncertainty for the effects of TAP block compared with control.

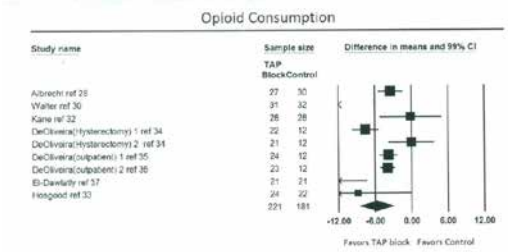

Figure 5. Meta-analysis evaluating the effect of transversus abdominis plane (TAP) block on postoperative opioid consumption compared with control. The overall effect of TAP block versus control was estimated as a random effect. Point estimate (99% confidence interval) for overall effect was −5.74 (−8.48 to −2.99) mg morphine IV equivalents. Weighted mean difference for individual studies represented by square on Forrest plot, with 99% CI of the difference shown as solid line. Larger sized square and thicker 99% CI line denote larger sample size. The diamond represents the pooled estimate and uncertainty for the effects of TAP block compared with control.

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S-293.

RETROSPECTIVE ANALYSIS OF OUTCOMES OF A DEDICATED REGIONAL ANESTHESIA ACUTE PAIN TEAM MODEL

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INTRODUCTION: Regional anesthesia is an excellent modality that provides patients superior pain control[1]. Ubiquitous utilization is often marred by side effect profiles, unfamiliarity with procedures, low surgeon acceptance, high block failure[2]. Resistance seems to stem from lack of uniformity and predictability; impart due to a plethora of providers manning the service. Other anesthesiology driven services have seen improved outcomes from a dedicated team model namely with surgical intensivists, cardiothoracic, transplant[3] and peadatric teams. A regional anesthesia acute pain team would provide standardization through adoption of standard protocols/techniques which would result in improved VAS pain scores, lower incidence of urinary retention, increase in procedural volume, improved surgeon satisfaction and lower block failure rate.

METHODS: After IRB approval a retrospective chart review was conducted for all patients who received a regional anesthetic over a 30 month period, ASA 4 or higher and emergent procedures were excluded. Charts were reviewed from a 15 month time period prior to the implementation of a dedicated team regional acute pain team, and from a 15 month time period after implementation of said team. Data was analyzed for block failure by way of conversion to general anesthesia or a repeat block for inadequate pain control. Additionally, total procedural volume was compared. The average VAS score on all epidurals during this time period over a three day post-operative course was tabulated. Urinary retention based on foley re-insertion during this time period was also tabulated. Continuous variables were compared using ANOVA and two-sided two-sample t-tests. A survey was sent out to the surgeons whom utilize the service assessing satisfaction, desire to refer more patients and impression of an improved pain control experience this was compared using a two sample t-test or Wilcoxon rank-sum tests.

RESULTS: Implementation of a dedicated regional anesthesia acute care team resulted in a 75% increase in procedural volume. Block failure rate was reduced 14%. There was a 42 % reduction in VAS scores, and a 52% reduction in urinary retention for patients whom received an epidural. Of the surgeons who utilized our service 90% observed better pain control, 80% improvement in the service and 75% willingness to refer more patients.

CONCLUSION: A dedicated acute pain regional anesthesia team provides a superior pain control product. We observed improved outcomes, decrease side effects, increase in procedural volume, lower failure rate and improved surgeon satisfaction.

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S-294.

WHICH CONCENTRATION DO YOU CHOOSE 0.2% ROPIVACAINE OR 0.375% ROPIVACAINE? THE COMPARISON OF THE ANALGESIC EFFECT OF THE CONTINUOUS GLUTEAL SCIATIC NERVE BLOCK AFTER RECONSTRUCTIVE SURGERY OF ANKLE AND FOOT.

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INTRODUCTION: Continuous nerve block is commonly performed to provide anesthesia or analgesia for patients undergoing reconstructive surgery of ankle and foot. With fewer side effects compared to other methods, this therapeutic block has been applicable to patients on anticoagulation, patients with transformed back anatomy and hemodynamically unstable patients. We proactively provide these patients with continuous gluteal sciatic nerve block during and after reconstructive surgery of ankle and foot.

METHODS: 42 patients, aged 18-80y with ASA physical status 1 or 2 without asthma, scheduled for reconstructive surgery of ankle and foot were randomly assigned to two groups with continuous sciatic nerve block and general anesthesia. Before inducing general anesthesia, we performed gluteal sciatic nerve block with ultrasound and nerve stimulation guidance. General anesthesia was induced and maintained with propofol, remifentanil (TIVA ; total intravenous anesthesia). From beginning of surgery, patients received 0.2% Ropivacaine: Group A (n=21) or 0.375% Ropivacaine: Group B (n=21) 4ml/h with a possible addition of 3ml every 30 min via a patient-controlled bolus dose at least 24 hour. Postoperative pain score was quantified as the Numeric Rating Score (NRS). Postoperative nausea and vomiting (PONV), numbness and use of analgesics were monitored every 6 hours for 48 hours after surgery.

Our institutional Ethics Committee approved this study and all patients provided written informed consents to participate in all procedures associated to this study.

Data were analyzed by the Mann-Whitney U test and the chi-square test. $P<0.05$ was considered statistical significant.

RESULTS: There was no statistical difference in the incidence of PONV, numbness and the use of analgesics at all periods. Group B's NRS was significantly lower than Group A's at 0h($p=0.030$) and 6h($p=0.047$) after surgery.

CONCLUSION: We obtained high precise analgesia with 0.375% Ropivacaine for continuous gluteal sciatic nerve block after reconstructive surgery of ankle and foot.

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S-295.

ANALGESIA AFTER TOTAL HIP ARTHROPLASTY: PERIARTICULAR INJECTION VERSUS EPIDURAL PCA

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INTRODUCTION AND GENERAL PURPOSE OF THE STUDY: The need for primary total hip arthroplasty (THA) is increasing as the United States population is aging. Unfortunately, the best analgesic regimen to achieve adequate pain control postoperatively is still questionable. This randomized double blind placebo controlled study compares the use of patient controlled epidural analgesia (PCEA) to periarticular injection (PAI). We hypothesized that PAI would lead to earlier readiness for discharge with decreased opioid consumption and lower pain scores.

METHODS: After IRB approval and informed consent, a total of 41 patients received PAI with bupivacaine, morphine, methylprednisolone and cefazolin, while a total of 43 patients had PCEA with bupivacaine 0.06% / hydromorphone (10 μg/ml). In a double blind fashion, patients were randomized to receive either PAI at the end of surgery or PCEA. Preoperatively, both groups received dexamethasone 6 mg PO while the PAI group received a clonidine patch and oxycontin and the PCEA group had a placebo patch and pill. Intraoperatively, all patients received combined spinal/epidural anesthesia. Postoperatively, both groups had an epidural pain pump; the PAI group received normal saline infusion while the PCEA group received a bupivacaine and hydromorphone mixture. Both groups had foley insertion as well.

RESULTS AND MAJOR FINDINGS: Time to readiness for discharge was 2.4 ± 0.7 days vs. 2.3 ± 0.8 days for PAI and PCEA respectively, p=0.86 (Table 1). Mean length of stay was 3.0 ± 0.8 days for PAI vs. 3.1 ± 0.7 days for PCEA, p = 0.46 (Table 1). A significant difference of 0.74 (p=0.01, CI 0.18 - 1.31) for pain scores with ambulation and 0.80 (p=0.03, CI 0.09 - 1.51) with physical therapy was found in favor of the PCEA group (Table 2). Opioid consumption was significantly higher in the PAI group on postoperative day (POD) 0 and POD 0-2, p=0.002 and 0.004 respectively (Table 1). Opioid-Related Symptom Distress Scale (ORSDS) scores were significantly higher in the PCEA group, p<0.05 (Table 1). Quality of recovery scores-40 and patient satisfaction were similar (Table 1).

CONCLUSIONS: PAI did not decrease time to discharge. It was associated with higher pain scores and greater opioid consumption, but less ORSDS scores compared to PCEA. Quality of recovery scores and patient satisfaction were similar. The choice for analgesic regimen may be dependent on threshold for pain and potential side effects. In hospitals in which PCEA is not available or cost prohibitive, PAI is an acceptable alternative for pain relief following THA surgery.

Table 1

	PAI	PCEA	p-value
	Mean ± SD	Mean ± SD	
Discharge (days)			
Readiness	2.4 ± 0.7	2.3 ± 0.8	0.8554*
Actual	3.0 ± 0.8	3.1 ± 0.7	0.4572*
Opioid Intake (oral opioids and PCA)			
POD 0	43.0 ± 20.7	27.6 ± 23.4	0.002
POD 0-2	135.7 ± 59.0	90.0 ± 79.2	0.0037
ORSDS			
Composite Score	0.36 ± 0.35	0.58 ± 0.50	0.0296
QoR-40 Global Score			
POD 1	178.4 ± 10.0	177.1 ± 17.4	0.6749
POD 3	181.9 ± 8.6	179.9 ± 9.2	0.3488
Patient Satisfaction			
POD 1	9.35 ± 0.92	9.32 ± 1.77	0.9163
POD 3	9.39 ± 1.18	8.77 ± 2.00	0.1202

*adjusted for other variables including gender, age, BMI, race and ASA

Abbreviations: ASA = American Society of Anesthesiologists physical status classification, BMI = body mass index, ORSDS = Opioid-Related Symptom Distress Scale, PAI = periarticular injection, PCA = patient controlled analgesia, PCEA = patient controlled epidural analgesia, POD = postoperative day, QoR = Quality of Recovery, SD = standard deviation

Table 2

	Difference Between Groups	p-value
Pain at Rest	0.0441	0.8301
Pain with Ambulation	0.7445	0.0103
Pain during Physical Therapy	0.7995	0.0282

Numeric Rating Scale pain scores were assessed on a 0-10 scale (0 = no pain, 10 = worst pain imaginable)

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S-296.

INCIDENCE OF DEVASTATING COMPLICATIONS OF EPIDURAL ANALGESIA IN THE UNITED STATES, 1998 - 2010: A PERSPECTIVE FROM A MEGA DATA ANALYSIS

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INTRODUCTION: In order to make an informed decision about the use of epidural analgesia (EA), providers and patients need reliable estimates on the risk of devastating complications related to EA. Current evidence is however, controversial[1,2]. The aim of this study was to evaluate the incidence of EA-related complications (EA-RC) in the U.S. using a large national database.

METHODS: The Nationwide Inpatient Sample was analyzed to identify patients receiving EA from 1998 to 2010 in the U.S. EA-RC were identified using appropriate diagnosis and procedure ICD-9 codes. The primary outcome was a composite of any spinal decompression, epidural abscess, spinal ischemia, or spinal MRI occurring during the same admission as the EA. Rigorous criteria were applied to ascertain relationship between EA and outcomes. Outcomes were considered not EA-RC if the principal procedure was a spinal or neurological surgery, the principal diagnosis was a neurological problem, any secondary diagnosis was pathology of the spine or any neurological infection, the outcome occurred before the EA or if the principal procedure was an aortic surgery (for spinal ischemia and MRI). Logistic regression models were conducted to assess patient and hospital characteristics associated with increased odds of EA-RC. Cochrane-Armitage trend tests were used to assess trends on outcomes over time. Results from weighted analyses are presented.

RESULTS: A total of 3,703,755 EA were identified between 1998 and 2010. Most patients (84.0%) were women. Most EA (59.9%) were provided for obstetrical procedures, 12.2% for abdomino-pelvic, 10.8% for orthopedic, 5.2% for cardiothoracic, and 1.2% for miscellaneous surgical procedures. In addition, 10.6% of the EAs were provided for non-surgical analgesia. Adverse outcomes were identified in 957 patients, for an overall complication rate of 25.8 per 100,000 EAs. Trend tests revealed, however, that the incidence of complications did not change over time (P for trend = 0.682). Spinal MRI without further intervention was the most frequent outcome (9.1/100,000) followed by spinal decompression (6.9/100,000), spinal ischemia (5.7/100,000), and spinal abscess (4.9/100,000). Logistic regression models revealed that factors associated with increased odds of EA-RC included higher Charlson Comorbidity scores (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.09-1.18; P < .0001), non-elective surgery (OR, 3.69; 95% CI, 2.56 - 5.32; P < .001), teaching status of hospital (OR, 1.67; 95% CI, 1.12 - 2.50; P = .011), and type of procedure, with higher risk for cardiothoracic procedures, and lower risk for obstetrical procedures (P <0.0001). After adjusting for confounders, patients having an EA-RC were more likely to die during the hospitalization (OR, 3.71; 95% CI, 1.99 - 6.93; P < .001).

CONCLUSIONS: Our analysis of large nationwide inpatient data reveals that the incidence of serious complications is about 26/100,000 EAs. Patients with higher comorbidity scores having non-elective procedures in teaching hospitals are at higher risk for EA-RC.

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S-297.

HEMIDIAPHRAGMATIC PARALYSIS FOLLOWING ULTRASOUND-GUIDED SUPRACLAVICULAR VERSUS INFRACLAVICULAR BRACHIAL PLEXUS BLOCKADE: A RANDOMIZED CLINICAL TRIAL

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AFFILIATION: [1]Department of Anesthesia, St. Paul's Hospital, Vancouver, BC, Canada, [2]Department of Anesthesiology, Pharmacology & Therapeutics, The University of British Columbia, Vancouver, BC, Canada

BACKGROUND: Hemidiaphragmatic paralysis due to inadvertent phrenic nerve blockade is a well-recognized complication of brachial plexus anesthesia whose incidence varies with the anatomical approach. However, the majority of reports on this complication stem from the era before the widespread use of ultrasound and ubiquitous move to ambulatory surgery. While there exists consensus that interscalene blockade carries the highest risk, the incidences associated with contemporary ultrasound-guided supraclavicular versus infraclavicular techniques have not been extensively studied. Hence, the objectives of this study were to define the comparative incidences associated with these two common approaches, and test the hypothesis that ultrasound-guided infraclavicular brachial plexus blockade results in a lower incidence compared to the supraclavicular approach when a standard local anesthetic volume and concentration is used.

METHODS: With institutional human ethics board approval, we enrolled 64 patients undergoing right-sided arm and hand surgery in a randomized, blinded, parallel-group clinical trial. Patients were randomly assigned to receive ultrasound-guided supraclavicular or infraclavicular blockade with 30 mL of 0.5% ropivicaine. We measured diaphragmatic excursion pre-, and at 15 and 30 min post-block with the voluntary sniff (VS) test using M-mode ultrasonography. We assessed sensory brachial plexus blockade by testing for perception of cold and touch in the distributions of the major branch nerves of the brachial plexus. The primary endpoint was the incidence of complete hemidiaphragmatic paralysis at 30 min, defined as a > 75% reduction in diaphragmatic excursion in the VS test; partial paralysis was defined as a reduction between 25% and 75%.

RESULTS: All 64 patients completed the trial (each group, n = 32). Eleven patients (34%) in the supraclavicular group versus one (3%) in the infraclavicular group had complete hemidiaphragmatic paralysis at 30 min (Fisher's exact test, P = 0.001 [one-tailed]; relative risk, 11.00 [95% CI, 1.51–80.32]). The percentages of patients with any (complete or partial) hemidiaphragmatic paralysis were 44% and 13%, respectively (P = 0.006; relative risk, 3.50 [95% CI, 1.29–9.49]). Eight patients (25%) in the supraclavicular group versus 5 in the infraclavicular group reported mild to moderate dyspnea (P = 0.54; range of verbal rating scale [0–10] scores, 1–5). No patients had block failure requiring unscheduled "rescue" conversion to general anesthesia. One patient in the infraclavicular group and none in the supraclavicular group reported residual sensory blockade on postoperative day one.

CONCLUSIONS: Ultrasound-guided supraclavicular brachial plexus blockade with 30 mL of 0.5% ropivacaine produced complete hemidiaphragmatic paralysis in approximately one third of patients. While the infraclavicular approach greatly reduced this risk, it did not completely eliminate it. These data may aid in the selection of the approach to brachial plexus blockade, particularly in ambulatory patients and/or those with respiratory comorbidities.

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Sleep Medicine

S-298.

A META-ANALYSIS OF OVERNIGHT OXIMETRY AS AN INDEPENDENT SCREENING TOOL FOR OBSTRUCTIVE SLEEP APNEA

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INTRODUCTION: Obstructive Sleep Apnea (OSA) is associated with significant comorbidities, early mortality and postoperative morbidity.[1] As overnight polysomnography is time-consuming and expensive, the majority of patients with the condition are undiagnosed, making preoperative screening for OSA an essential step for risk modification. Clinical screening tests have significant prediction heterogeneity and moderate to poor accuracy, with pooled sensitivity of 0.52 and positive predictive value of 0.6 for diagnosis of OSA.[2] The purpose of this study was to perform a systematic review on the accuracy of overnight oximetry as an independent screening tool for OSA.

METHODS: We searched the PubMed database to find clinical studies using various methods of analysis of oximetric data in the diagnosis of OSA. The gold standard comparison in all studies was overnight polysomnography. After a systematic process of study inclusion (Fig 1) and evaluation of quality, we abstracted raw or derived 2x2 data to perform pooled analyses based on each of the four major test types: cumulative time spent under SpO2 90%, oxygen desaturation indices, linear models, and nonlinear models, and generated a Summary Receiver Operating Characteristic (SROC) curve (Fig 2).[3] We then performed DerSimonian-Laird random effects meta-regression to identify variance in prediction accuracy between these methods, after adjusting for available patient demographics and study quality.[3,4] The resulting parameter estimates were back-transformed to relative diagnostic odds ratios (rDOR). Further meta-regression analyses were performed to quantify variance between individual prediction methods.

RESULTS: Thirty-six studies met our inclusion criteria for analysis. Pooled results indicated greater diagnostic accuracy with increasing OSA severity and by test type (rDOR 1.23 95% CI [1.05, 1.44]). The SROC curve presented an AUC=0.90 (SE 0.005). Additional analyses identified increasing accuracy from cumulative time spent under SpO2 90%, oxygen desaturation index, linear models, to nonlinear models. Pooled estimates [95% CI] for nonlinear models for diagnosis of OSA were sensitivity 0.84 [0.83, 0.85], specificity 0.77 [0.76, 0.78] and diagnostic odds ratio 19.28 [16.30, 22.81]. The positive predictive value [SD] was 0.85 ± 0.05. Pooled estimates are presented in Table 1. Of the nonlinear methods, multilayer perceptron networks and logistic regression analysis were associated with highest diagnostic accuracy (Table 2).

CONCLUSIONS: Overnight oximetry is a relatively cheap but highly accurate method of predicting OSA. The vastly superior sensitivity and positive predictive value compared to traditional clinical screening tests makes preoperative overnight oximetry screening relevant for clinical decision making and resource utilization. Diagnostic accuracy is significantly enhanced by using nonlinear modeling of SpO_2 time series data.

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Figure 1: Flowchart of study inclusions

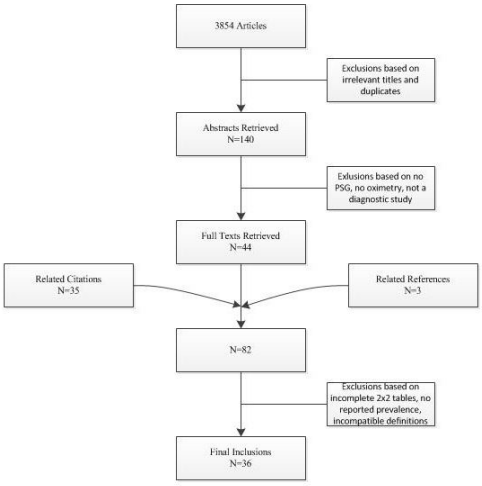

Figure 2: Summary Receiver Operating Characteristic (SROC) curve of all included studies

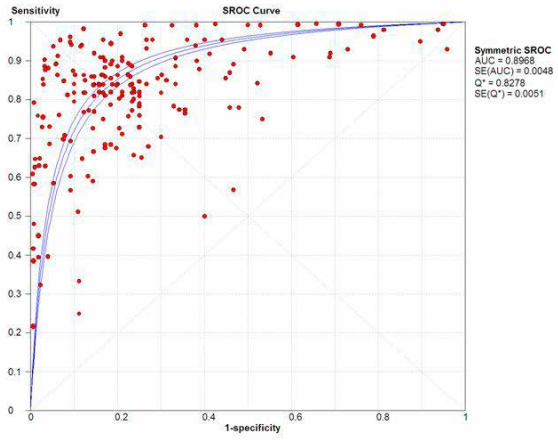

Table 1: Pooled Estimates for Index Tests at Diagnostic Thresholds (AHI[1] 5 or 10)

Method	Sensitivity [95% CI][3]	Specificity [95% CI]	Positive Likelihood Ratio [95% CI]	Negative Likelihood Ratio [95% CI]	Diagnostic Odds Ratio [95% CI]
CT90[2]	0.66 [0.62,0.70]	0.77 [0.73,0.81]	3.00 [2.04,4.42]	0.42 [0.32,0.56]	7.97 [5.85,10.85]
Desaturation Index	0.67 [0.65,0.68]	0.86 [0.84,0.87]	6.18 [3.92,9.75]	0.32 [0.26,0.39]	19.12 [13.51,27.07]
Linear Models	0.84 [0.83,0.85]	0.70 [0.68,0.72]	3.01 [2.30,3.93]	0.24 [0.21,0.28]	13.54 [10.36,17.69]
Nonlinear Models	0.84 [0.83,0.85]	0.77 [0.76,0.78]	3.98 [3.17,5.01]	0.21 [0.19,0.23]	19.28 [16.30,22.81]

Pooled Estimates for Index Tests at Moderate Threshold (AHI 15)

Method	Sensitivity [95% CI]	Specificity [95% CI]	Positive Likelihood Ratio [95% CI]	Negative Likelihood Ratio [95% CI]	Diagnostic Odds Ratio [95% CI]
Desaturation Index	0.78 [0.77,0.80]	0.79 [0.77,0.81]	6.00 [4.21,8.56]	0.23 [0.18,0.30]	44.84 [29.33,68.54]
Linear Models	0.68 [0.66,0.70]	0.77 [0.75,0.79]	7.30 [3.08,17.30]	0.26 [0.17,0.39]	34.11 [22.65,51.37]
Nonlinear Models	0.94 [0.89,0.98]	0.79 [0.71,0.85]	4.1 0 [1.84,9.16]	0.07 [0.04,0.14]	74.70 [29.60,188.52]

Pooled Estimates for Index Tests at Severe Threshold (AHI 30)

Method	Sensitivity [95% CI]	Specificity [95% CI]	Positive Likelihood Ratio [95% CI]	Negative Likelihood Ratio [95% CI]	Diagnostic Odds Ratio [95% CI]
Desaturation Index	0.91 [0.89,0.93]	0.70 [0.68,0.72]	6.20 [3.42,11.23]	0.11 [0.05,0.22]	129.24 [84.12,198.56]
Linear Models	0.85 [0.80,0.88]	0.91 [0.87,0.94]	9.44 [6.70,13.13]	0.17 [0.11,0.25]	62.51 [37.18,105.08]

Legend: [1]Apnea-hypopnea Index, [2]Cumulative time spent under SpO_2 90%, [3]95% Confidence Interval

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Table 2: Meta-regression of Nonlinear Models

Variable	Coefficient	Standard Error	P-Value	RDOR[6]	95% CI[7]
Cte.[1]	22.91	61.23	0.71	----	----
S[2]	-0.34	0.10	0.001	----	----
Prevalence	-7.71	8.59	0.37	0.00	(0.00, >100)
Male	-5.78	21.48	0.79	0.00	(0.00, >100)
Age	-0.17	0.45	0.71	0.84	(0.35, 2.06)
BMI[3]	-0.21	1.94	0.91	0.81	(0.02, 38.87)
QUADAS[4]	0.46	1.09	0.67	1.59	(0.18, 14.11)
AHI[5]	-0.03	0.15	0.86	0.97	(0.72, 1.32)
Poincaré	1.20	5.49	0.83	3.33	(0.00, >100)
Probabilistic Neural Network	3.44	5.68	0.55	31.18	(0.00, >100)
Multilayer Perceptron Network	2.11	0.41	0.00	8.27	(3.68, 18.58)
Logistic Regression	1.99	0.47	0.00	7.30	(2.86, 18.67)
Cross Approximate Entropy	0.71	0.27	0.01	2.04	(1.20, 3.48)
Central Tendency Measure	1.54	0.33	0.00	4.67	(2.41, 9.07)
Data Clustering	1.86	0.55	0.00	6.40	(2.13, 19.20)
Lempel-Ziv Complexity	1.16	0.43	0.01	3.20	(1.34, 7.63)
Approximate Entropy	1.16	0.33	0.00	3.18	(1.64, 6.19)
Generalized Measures	2.75	2.65	0.30	15.63	(0.08, >100)

Legend: [1]Constant Coefficient, [2]S Coefficient, [3]Body Mass Index, [4]Quality Assessment of Diagnostic Accuracy Studies, [5]Apnea-hypopnea Index, [6]Relative Diagnostic Odds Ratio, [7]95% Confidence Interval

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S-299.

FATIGUE FROM SLEEP DEPRIVATION WHILE ON CALL PROMOTES RISKY BEHAVIORS ON THE POST CALL DAY

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INTRODUCTION: A 24 hour call with four hours or less of sleep results in physical and mental dysphoria including nausea, headaches, and cognitive decline.[1] Sleep deprivation of this magnitude is equal to a blood alcohol level of 0.05-0.1%, equivalent to inebriation in most states, and clearly hazardous.[2] While information exists about call shifts and cognition, this study is the first to examine anesthesiologist health on the post call day. We hypothesized that health would be negatively impacted and risky activities would occur on the post call day.

METHODS: With IRB approval, an anonymous survey was distributed to both residents and attending anesthesiologists at the NYSSA-PGA meeting. Items were scored with a 5 point Likert scale, and age and gender were collected as demographic information.

RESULTS: 68 surveys were completed at the PGA meeting for this pilot study. “Post-Call Risky Behaviors” included the use of alcohol, recreational drugs, and sleeping pills, as well as unsafe driving. 58% found it extremely difficult to fall asleep on the post call day (after <4 hours of sleep on call). 18% used at least two 80 proof drinks to aid with sleep after arriving home, a majority of whom were over 40 years of age. 15% of those under 40 years of age used marijuana to fall asleep. The use of sleeping pills was reported in only 2 respondents, much lower than the general population. 50% admitted to driving home after call, but only 18% reported falling asleep one or more times at the wheel. Over 95% agreed that it was unsafe to drive after call. 26% of did not go to sleep post call (after <4 hours of sleep on call) until the evening of the post call day. 38% claimed to overeat on their post call day. Age was not a factor in the latter 6 results.

CONCLUSIONS: Call shifts with <4 hours of sleep were disruptive to a majority of participants, although the use of substances for sleep was much lower. Driving home after call is worth re-evaluating, as falling asleep at the wheel is hazardous to the anesthesiologist as well as to bystanders. Although a full quarter of participants stayed awake during the day after call, the physiologic and mental effects of this loss of sleep, especially as it accumulates over time, is unknown. Alcohol to promote sleep could lead to further behavioral issues and disrupted sleeping patterns. LIttle is known about marijuana as a sleep aid. Overeating on a single day is likely not harmful, but the additive effects with frequent call could lead to weight gain and decreased cardiovascular health. This study was performed as a pilot, and the power for the definitive survey will be increased by distribution at the IARS and ASA meetings. The symptoms of severe fatigue reported here warrant further study of severe sleep deprivation while on call and poor coping behaviors after call. Improving the post call physical and mental health of the anesthesiologist will benefit the profession, our patients, and the public.

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S-300.

NEW PERSPECTIVE IN PROPOFOL AND SLEEP INTERACTION

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INTRODUCTION: It is believed that propofol acts on many brain areas that have been implicated in the initiation and maintenance of natural sleep1. Several studies suggested that it satisfies the need for both rapid eye movement (REM) and slow wave sleep (SWS)[1,2]. Other studies proved that though propofol slow wave activity shares many features with SWS yet they are not identical [3]. Most of those studies were based either on animal models or on induced sleep deprivation with no further clinical extrapolation[1,2,4]. In this study we investigate the relation between natural preoperative sleep (REM and SWS) and propofol induction dose and whether or not this relation has clinical impact.

METHODS: After obtaining ethical committee approval 27 ASA I adult male patients scheduled for elective surgery with age(20-40) years and body mass index (BMI)(25-30) were included in this study. The night just before the operation, patients were subjected to at least 8 hours sleep EEG which was scored for the following: Total Sleep Time (TST), % of Slow Wave Sleep(SWS)and % of Rapid Eye Movement (REM). Propofol induction dose (mg kg-1) achieving Bispectral Index (BIS) value between 40 and 60 was recorded in all patients. Correlation between propofol dose and both SWS % and REM % was done. After that Patients were classified according to sleep EEG into good sleepers (10 patients) and bad sleepers (9 patients), 8 patients had borderline values. Propofol dose in good sleepers and bad sleepers was compared.

RESULTS: There was a positive correlation between propofol induction dose and both SWS (%) (r= 0.583; p= 0.003) and REM (%) (r= 0.550; p= 0.005). The median value of propofol induction dose in good sleepers was 1.70 (1.00-2.00); while in the bad sleepers it was significantly lower 1.10 (0.80-1.70) (p value 0.01).

Conclusion: Propofol dose was strongly correlated with preoperative %REM and %SWS which confirms their common neurophysiological pathways. This correlation has clinical impact shown in the significant decrease in propofol dose noticed in bad sleepers. So we recommend adding preoperative sleep quality to routine history taking.

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S-301.

CHRONIC OPIOID USE AND CENTRAL SLEEP APNEA - A REVIEW OF THE PREVALENCE, RISK FACTORS, MECHANISMS, AND PERIOPERATIVE CONSIDERATIONS

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BACKGROUND: Respiratory depression is a well-recognized adverse effect of opioids. Chronic opioid use is associated with the development of sleep disordered breathing such as central sleep apnea (CSA). A large number of patients on chronic opioids may suffer from unrecognized sleep apnea that contributes to unexplained morbidity and mortality.

Currently information regarding the perioperative management of patients with sleep disordered breathing associated with chronic opioid use is limited in the anesthesiology literature. The objectives of this review are to define the prevalence and risk factors of respiratory disturbances occurring during sleep that are associated with chronic opioid therapy.

METHODS: We searched Medline (1946 - November 2013), Medline in process and other Non-indexed citations, Cochrane database of systematic reviews and Cochrane central Registry of Controlled Trials (2005 - October 2013), Embase (1997 - November 2013), PubMed basic search (1946 - November 2013) and sleep medicine meeting abstracts. All prospective, retrospective studies and case reports were included if 1) CSA was confirmed by polysomnography 2) prevalence, opioid medication and dose, concurrent medications and treatment of patients with CSA were reported. Defining feature of CSA was simultaneous absence of airflow and breathing effort $\geq$ 10 seconds. Central apnea index (CAI) $\geq$ 5 events/hr was considered significant.

RESULTS: The search strategy yielded 7 studies and 4 case reports, including 504 patients. All patients were on chronic opioid medication and had completed polysomnography. Three hundred and seventy-three patients were on chronic opioid medication and were referred to sleep clinics for evaluation of sleep disordered breathing. The remaining 131 patients were on methadone maintenance therapy and polysomnography was performed to explore the possibility of sleep disordered breathing.

The overall prevalence of CSA was (34.3%). A morphine equivalent daily dose higher than 200 mg was strongly associated with the severity of sleep disordered breathing, predominantly central sleep apnea. Concurrent use of benzodiazepines, hypnotics and an inverse relationship of body mass index were also associated with the severity of CSA. There were conflicting results for the best positive airway pressure therapy for opioid-induced CSA. Continuous positive airway pressure (CPAP) may be ineffective in eliminating or may even increase CSA but remains as an initial mode of titration. Some reports state, effective therapy with adaptive servo ventilation or bilevel positive pressure ventilation with back-up rate.

CONCLUSION: The overall prevalence of CSA in patients taking chronic opioids was 34.3%. The most important risk factors were a morphine equivalent daily dose higher than 200mg, concurrent use of sedatives or hypnotics and low BMI. CPAP may be ineffective for treatment of CSA. There are limited data available on the peri-operative management of patients with CSA associated with chronic opioid use. There is a need for further prospective studies on the peri-operative risks and management of these patients.

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S-302.

EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON POSTOPERATIVE ADVERSE EVENTS IN OBSTRUCTIVE SLEEP APNEA PATIENTS UNDERGOING SURGERY. A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Obstructive sleep apnea is a commonly encountered co-morbid condition in patients undergoing surgery and is associated with a higher risk of postoperative adverse events. Treatment by continuous positive airway pressure (CPAP) may decrease the risk of adverse events. The objective of this meta-analysis is to determine the effectiveness of CPAP in reducing the risk of postoperative adverse events in obstructive sleep apnea (OSA) patients undergoing surgery.

METHODS: A search of the literature databases Medline (from 1946 to 2013), Medline in-process and other non-indexed citations, Embase (from 1947 to 2013), Cochrane central register of controlled trials, Cochrane database of systematic reviews and Health technology assessment (4th Quarter 2013) was carried out. The search strategy yielded 1970 citations. Irrelevant papers were excluded by title and abstract review, leaving 101 manuscripts. We reviewed the studies that included: 1) A target population of surgical patients with obstructive sleep apnea; 2) CPAP as a study intervention; 3) Effects of CPAP on postoperative adverse events; 4) OSA surgical patients without CPAP as a comparison group. The postoperative complications were cardiac events or respiratory events or any complication requiring ICU admission. Statistical analysis was carried out using the Review Manager 5.2 software. The pooled risk ratio and the number needed to treat to benefit (NNTB) for postoperative complications were estimated.

RESULTS: The meta-analysis was carried out in 6 studies including a total of 1342 patients (CPAP group n=725 and no-CPAP group n=617). Four trials were observational studies[1-4], while two were randomized control trials[5,6]. Overall CPAP significantly reduced the risk of postoperative complications (risk ratio, 0.73; 95% confidence interval, 0.63-0.85) with a corresponding NNTB of 11 (95% confidence interval, 6.8-19.3). The variation in risk ratio attributable to heterogeneity was negligible (I2=14%) and there was a low risk of bias.

CONCLUSION: This meta-analysis suggests that perioperative CPAP decreases the risk of postoperative adverse events in OSA patients undergoing surgery and supports its clinical use in these patients during perioperative period.

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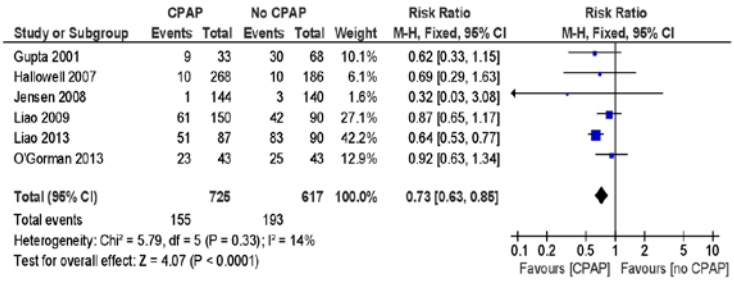

Figure 1: Forrest plot, association of postoperative complications in patients with CPAP vs no-CPAP treatment.

Table 1: Data on postoperative adverse events in surgical OSA patients on CPAP vs no-CPAP group

Authors	Sample size (n)	Intervention	Time delivered		Postoperative adverse events	Groups			
			Preoperative CPAP	Postoperative CPAP		CPAP		no-CPAP	
						Total	Postoperative adverse events (cases)	Total	Postoperative adverse events (cases)
Gupta et al 2001	101	CPAP vs no-CPAP	yes	no	Cardiorespiratory complications ICU admission Length of hospital stay	33	9	68	30
Hallowell et al 2007	454	CPAP vs no CPAP	yes	yes	ICU Admission	268	10	186	10
Jensen et al 2008	284	CPAP vs no CPAP	yes	no	Pneumonia Reintubation Anastomotic leak Death	144	1	140	3
Liao et al 2009	240	CPAP vs no CPAP	yes	yes/no	Respiration complications ICU admissions Additional monitoring Prolonged O2 therapy	150	61	90	42
Liao et al 2013	177	APAP vs no APAP	yes	no	AHI elevation Hypoxemia Bradyearda CNS Complications ICU Admission	87	51	90	83
O'Gorman et al 2013	86	APAP vs no APAP	No	yes	ICU transfer Adjustment of O2 Delirium Atelectasis	43	23	43	25
Total	1342					725	155	617	193

CPAP – Continuous positive airway pressure, APAP – Autotitrating positive airway pressure

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Technology, Computing and Simulation

S-303.

ADHERENCE TO GUIDELINES FOR THE MANAGEMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY IS IMPROVED BY AN ELECTRONIC DECISION SUPPORT TOOL AND DESIGNATED 'READER'

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INTRODUCTION: It has been reported recently that the risk of local anesthetic systemic toxicity (LAST) as a complication of neuraxial or regional anesthesia blocks is rare and may be decreasing in frequency. However, the risk has not been reduced to zero. Thus, when LAST occurs, prompt recognition and treatment must be initiated according to published guidelines in order to ensure the best possible patient outcome.[1] Anesthesiology residents are expected to be able to manage such emergency situations, but prior studies have shown that performance during simulations of perioperative emergencies is often suboptimal when scenarios are managed from memory alone.

In light of this concern, a recent study demonstrated that use of a paper cognitive aid containing the published management algorithm for LAST improved adherence to guidelines.[2] While the results of this study were promising, if the goal is perfect adherence to guidelines in these high-risk iatrogenic perioperative events, the mere presence of a cognitive aid does not ensure a high level of adherence to published guidelines. Addition of a designated 'Reader' of the paper cognitive aid during a study of simulations was found to improve adherence to guidelines.

As such, we conducted a prospective, single-blinded randomized controlled trial using in-situ simulation to test the hypothesis that the addition of a designated 'Reader' with an electronic DST would improve adherence to published guidelines in the management of LAST as compared with management from memory alone.

METHODS: Anesthesiology residents were randomized to Reader+DST (N = 16, rDST) and Control (N = 15, memory alone). The rDST group received the assistance of a dedicated 'Reader' on the response team who was equipped with an electronic DST. The Control group managed the scenarios from memory alone, which is the native behavior for most physicians. The primary outcome measure was adherence to guidelines.

RESULTS: For overall and critical percent correct scores, the rDST group scored higher than Control (99.9% vs. 73.0%, $p < 0.0001$; 99.9% vs. 70.9%, $p < 0.0001$, respectively). In the LAST scenario, 0 of 15 (0%) in the control group performed 100% of critical management steps, while 15 of 16 (93.8%) in the rDST group did so ($p<0.0001$).

CONCLUSIONS: In a prospective, randomized single-blinded study, a designated 'Reader' with an electronic DST improved adherence to guidelines in the management of an in-situ simulation of LAST. Such tools are promising in the future of medicine, but further research is needed to define their proper place in residency training curricula, as this study would suggest that the use of such aids may be of great benefit but training with such tools is not currently a part of most training curricula.

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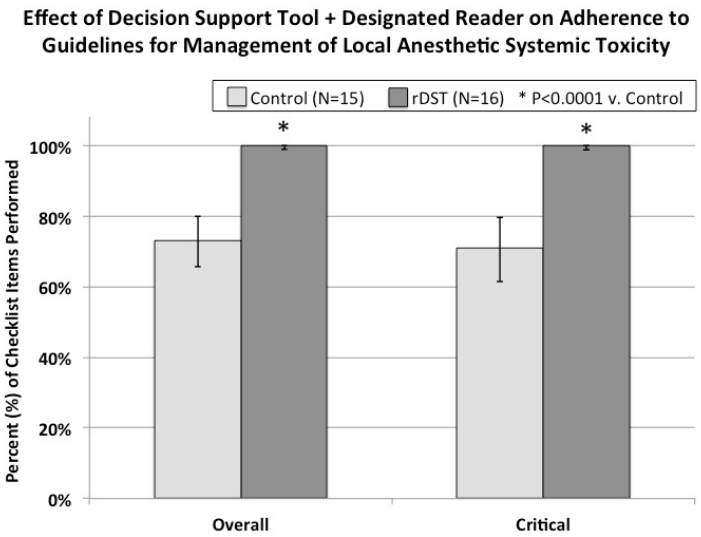

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S-304.

SATISFACTION GUARANTEED? ASSESSING SATISFACTION WITH IPAD APPLICATIONS TO FACILITATE EMERGENCE IN NON-NATIVE ENGLISH SPEAKERS

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INTRODUCTION: According to United States census data, nearly 60 million people speak a language other than English at home. This diversity of language preferences can pose challenges in the perioperative setting where communication barriers between patients and anesthesiologists can compromise both patient safety and comfort. A previous study (Phase 1), which used recorded commands from family members, found a preferential response to a patient's native language upon emergence, even after controlling for differences in responses in the "awake" state. Here we present the results of Phase 2 of the study in which we transitioned to a technological based approach to the challenge of communication with non-English speakers in the perioperative period. In this phase, foreign language commands were generated using commercial translation applications available for the iPad.

METHODS: After obtaining IRB approval, patients whose self assessed language skills were better in a foreign language than in English were enrolled and demographic data were collected. During emergence from general anesthesia, the English and foreign language commands of "open your eyes", "squeeze my fingers", and "wiggle your toes" were played in alternation in each language on an iPad, pausing to allow for a response. The translations were obtained through the iTranslate, Google Translate, and the iHandy Translator apps for the iPad.

RESULTS: 88 patients were enrolled. Compared to Phase 1 of the study, there was not a statistically significant difference in the level of satisfaction of the patients' family members when computerized translations were used instead of recordings of family members (9.93 on a 1-10 ascending scale for Phase 1 versus 9.79 when using translation apps) (table 2). There was a statistically significant decrease in patient satisfaction ($p<0.05$) when using translation apps (mean= 8.7) instead of using recorded commands made by their family members (mean=9.35) (table 1).

DISCUSSION: Our findings demonstrate that both patients and their families have very high levels of satisfaction (8.7 or higher on a 10 point scale) with either technique used to improve the postoperative communication with non-native English speakers. Nevertheless, the statistically significant decrease in satisfaction seen in the patients surveyed when the iPad based system was used suggests that there might be some improvement in patient satisfaction associated with hearing the commands given by the familiar voice of a family member even when patients are in the semi-sedated state associated with emergence from general anesthesia.

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Table 1: Patient Satisfaction

	Phase 1	Phase 2
Mean:	9.35	8.7
Std Dev:	1.268	1.931
Std Err:	0.145	0.294
95% CI:	(9.059, 9.638)	(8.103, 9.292)
N:	76	43
T-Test bw Phases 1 & 2: p=0.0285; p<0.05, significant difference bw phases		

Table 2: Family Satisfaction

	Phase 1	Phase 2
Mean:	9.93	9.79
Std Dev:	0.359	0.38
Std Err:	0.044	0.105
95% CI:	(9.840, 10.013)	(9.563, 10.022)
N:	68	13
T-Test bw Phases 1 & 2: p=0.225; p>0.05, no significant difference bw phases		

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S-305.

MINIMALLY INVASIVE PREDICTION OF $SCVO_2$ IN HIGH-RISK SURGERY: THE INTRODUCTION OF A MODEL INDEX OF OXYGENATION

AUTHORS: H. S. de Grooth, J. Vos, T. Scheeren, P. A. van Beest

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INTRODUCTION: The purpose of this study was to examine the trilateral relationship between cardiac index (CI), tissue oxygen saturation (StO_2) and central venous oxygen saturation ($ScvO_2$) and subsequently develop a model to predict $ScvO_2$ on minimal invasive manner in patients undergoing major elective surgery.

METHODS: The continuous data of thirty-three high-risk non-cardiac surgical patients from a randomized controlled trial (NCT01342900) were analyzed on a between- and within-patient basis using regression on group means, random-effects Generalized Least Squares (GLS) regression. Trend concordance was assessed using a four-quandrant plot. We developed a model Index of Oxygenation (IO) to predict $ScvO_2$ based on CI, StO_2, heart rate (HR), fraction of inspired oxygen (FiO_2) and mean arterial pressure (MAP). The dataset was split by randomizing each patient into an estimation or validation subsample. Randomization was stratified by type of surgery. IO was validated using random-effects GLS regression, a Bland-Altman analysis and four-quadrant concordance.

RESULTS: The patients were monitored for an average duration on 227.5 minutes, giving 7509 observations in total. We could not establish a positive significant association between StO_2 and CI using regression analyses (slope of -1.08 (p=0.15; 95%CI -2.54 to 0.377; within-R2 0.01; figure 1). Trending concordance is non-existent (on a 5-minute basis: 56%) or very weak (on a 60-minute basis: 73%; figure 2). CI was found to be strongly associated with $ScvO_2$ on a within-patient basis, but lacks predictive power in explaining between-patient differences. StO_2, in contrast, was significantly associated with between-patient $ScvO_2$ differences, but does not follow (short term) within-patient $ScvO_2$ variability (figure 3). The mean difference or bias between $ScvO_2$ and IO is 1.07% (95% limits of agreement -14.7% to 16.9%). Concordance for 5-minute and 60-minute trends was 71% and 90%, respectively. The IO model was translated into a linear prediction, which was then scaled back to the mean (78.5) and SD (6.49) of $ScvO_2$ in the estimation sample, according to the following formula (the brackets denote standardized variables):

Figure 4 displays the complete intraoperative $ScvO_2$ data and the IO prediction for two patients in the validation sample.

CONCLUSIONS: StO_2 cannot be considered a flow dependent variable during high-risk surgery. We hypothesize that StO_2 is a gauge of microcirculatory functioning more than a measure of systemic oxygen balance. IO is a better estimator is $ScvO_2$ than either CI or StO_2 alone and could potentially be used for minimally invasive monitoring of systemic oxygenation.

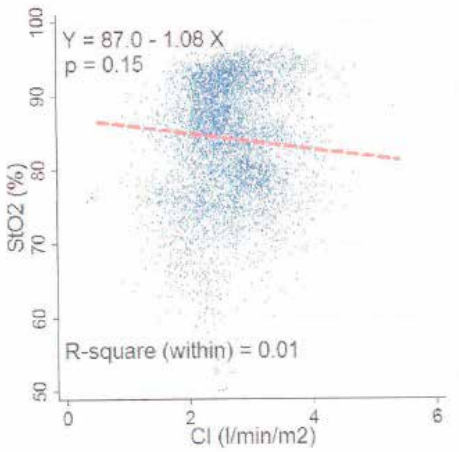

Figure 1. Scatterplot of all CI and StO_2 observations in the dataset. Slope estimate obtained using random-effects GLS regression.

S-305 • CONTINUED ON NEXT PAGE

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S-305 • continued

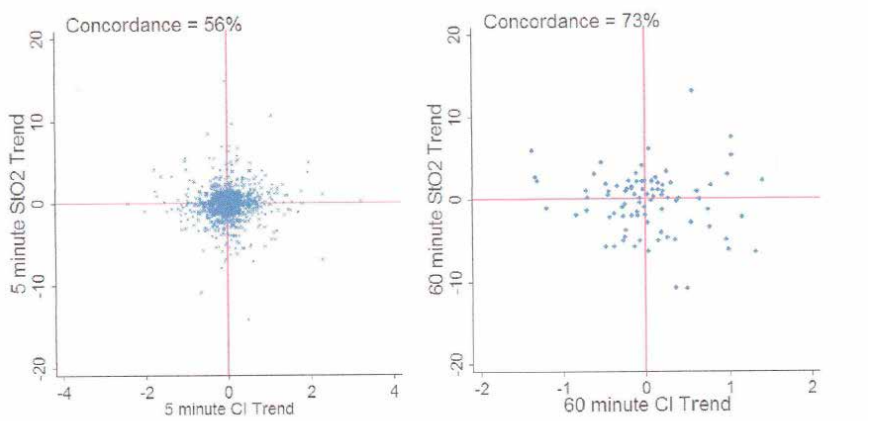

Figure 2. Four-quadrant plots of 5-minute (left) and 60-minute (right) trends in StO_2 and CI. 5-minute trend concordance is 56%, 60 minute trend concordance is 73%.

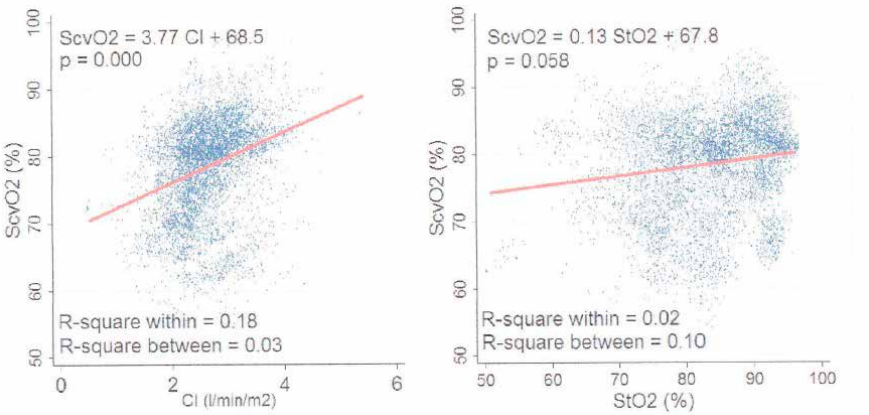

Figure 3. Left: Scatterplot of all (7509) CI and $ScvO_2$ measurements. Right: Scatterplot of all StO_2 and $ScvO_2$ measurements. Slope estimates obtained using random-effects GLS regression.

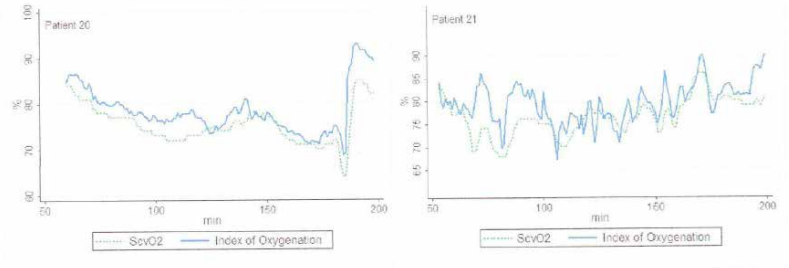

Figure 4. Complete tracing of intraoperative $ScvO_2$ measurements and Index of Oxygenation (IO) $ScvO_2$ prediction based on CI, StO_2, HR, FiO_2 and MAP for two patients in the validation sample.

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S-306.

EVALUATION OF A DECISION SUPPORT SYSTEM TO IMPROVE TIMELY PERIOPERATIVE ANTIBIOTIC REDOSING AND CHARGE CAPTURE OF INVASIVE LINE PLACEMENTS

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AFFILIATION: [1]Anesthesiology, Ochsner Medical Center and Ochsner Clinical School - University of Queensland, New Orleans, LA, [2]Anesthesiology and Pain Medicine, University of Washington, Seattle, WA

INTRODUCTION: Anesthesia Information Management System (AIMS) based decision support modules have been shown to improve quality of care and revenue capture. These modules have been primarily evaluated in institutions where they were originally developed[1]. This study will evaluate the effectiveness of a decision support module, Smart Anesthesia Manager (SAM), at an institution different from where it was originally developed.

METHOD: SAM, originally developed at the University of Washington (UW) (Seattle, WA), was implemented at Ochsner Medical Center (New Orleans, LA) to improve timely redosing of perioperative antibiotics and documentation of invasive lines. SAM would generate real-time "popup" reminders on the AIMS computer screen when the administered antibiotic was due for a redosing based on institutional guidelines. Antibiotic redosing compliance was determined if the antibiotic was given within ±15 minutes of the redosing time interval. Similarly, notifications were also issued when either a valid arterial or central venous blood pressure measurement was detected, but no corresponding documentation for the placement of the invasive line was provided. No reminders were issued for pulmonary artery catheter placement. After Institutional Review Board (IRB) approval, perioperative antibiotic redosing and invasive line documentation compliance data was extracted from the AIMS database before and after instituting SAM reminders.

RESULTS: Baseline compliance for timely antibiotic redosing was 14.2%, which increased to 59.4% after the decision support module, SAM, was initiated ($p<0.001$). [Table 1] Similarly, baseline compliance for completed documentation of arterial and central venous lines increased from 85.7% to 94.4% ($p<0.001$) and from 84.6% to 92.9% ($p<0.001$) respectively. [Table 2] This translated to an additional 39 arterial and 15 central venous lines that were correctly documented per month. This resulted in an increased charge capture of $181,440 per annum. With no reminders for pulmonary artery catheter documentation, compliance for completed documentation remained the same (76.5% baseline, 72.6% intervention, $p=0.23$).

SUMMARY: Both timely antibiotic redosing and invasive line documentation improved with SAM reminders. Improvement in antibiotic redosing at Ochsner (45.2%) was higher than that at UW (21.4%)[2]. However, the improvement in the documentation of arterial (8.7% vs 25.7%) and central venous lines (8.3% vs 9.6%) was lower at Ochsner when compared with UW3. This study shows that an anesthesia clinical decision support module developed at another institution can be effective elsewhere.

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3. Improved billing of invasive line procedures through real-time notification of documentation errors. American Society of Anesthesiologists Annual Meeting, San Diego 2010.

Table 1: Effect of SAM reminders on timely perioperative antibiotic redosing

	Case needing antibiotic redosing	Cases with timely redosing	Compliance
Baseline (12 Months)	2481	352	14.20%
Without SAM reminders			
Intervention (12 Months)	2631	1563	59.40%
With SAM reminders			
p-value (Chi-square test)	<0.001		

Table 2: Effect of SAM reminders on invasive lines documentation

	Baseline (4.5 months) Without SAM reminders			Intervention (4.5 months) With SAM reminders			p-value (Chi-square test)
	Total Lines	Complete Documentation	Compliance	Total Lines	Complete Documentation	Compliance	
Arterial	2102	1802	85.70%	1952	1843	94.40%	<0.001
CVC	878	743	84.60%	784	728	92.90%	<0.001
PAC	438	335	76.50%	372	270	72.60%	0.23

CVC - Central Venous Catheter, PAC - Pulmonary Artery Catheter

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S-307.

RELATIONSHIP OF AWAKE BISPECTRAL INDEX TO POSTOPERATIVE MEMORY FORMATION

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INTRODUCTION: Anesthesia awareness is a rare but significant complication of general anesthesia[1]. As such, "awareness" monitors have been developed to target to the appropriate depth of anesthesia. One such device, the Bispectral Index (BIS) (Covidien) uses an algorithmic analysis of EEG and EMG to generate a score from zero (indicating electrical silence) to 100 (indicating complete wakefulness). Initial studies indicated that BIS improved upon other anesthetic monitoring techniques in preventing awareness[1], but subsequent studies have indicated that BIS is no better[2] or worse[3] than existing protocols. To date, these monitors have not been linked directly to memory formation. This study was designed to characterize whether BIS is correlated with a subject's ability to form memories, a prerequisite for reporting awareness events, by assessing recall of words spoken to the subject during the recovery from general anesthesia.

METHODS: Following IRB approval and informed consent, 167 adult subjects were enrolled in the study. All subjects were undergoing surgical procedures involving administration of general anesthesia. BIS Vista Monitors (Covidien) recorded BIS values as words were spoken to subjects at intervals of 20 minutes following arrival in the post-anesthesia care unit. Each word was repeated six times for a total of six unique words over two hours. If nursing staff anticipated discharge in less than two hours, the intervals between words were decreased to space word delivery evenly throughout the recovery time. Word recall was assessed approximately 24 hours following discharge via in-person interview (for subjects admitted to the hospital) or phone call (for subjects discharged home). A mixed effects logistic regression analysis was performed to determine the relationship between BIS value and word recall.

RESULTS: BIS values for words recalled versus those not recalled were determined to be significantly different as measured by mixed effects logistic regression analysis ($p<0.05$). The odds ratio of recalling a word for each one-point increase in the BIS value was calculated to be 1.06 (95% CI 1.01-1.10) by this model.

CONCLUSIONS: The difference in BIS values for words recalled as compared to words not recalled suggests an association between BIS and memory formation. However, this difference was small, and significant overlap in BIS scores for subjects recalling versus not recalling words precludes the use of BIS as a predictive tool for memory formation in the post-operative setting.

1. Lancet 2004; 363(9423):1757-63
2. NEJM 2008; 358(11):1097-108
3. NEJM 2011; 365(7):591-600

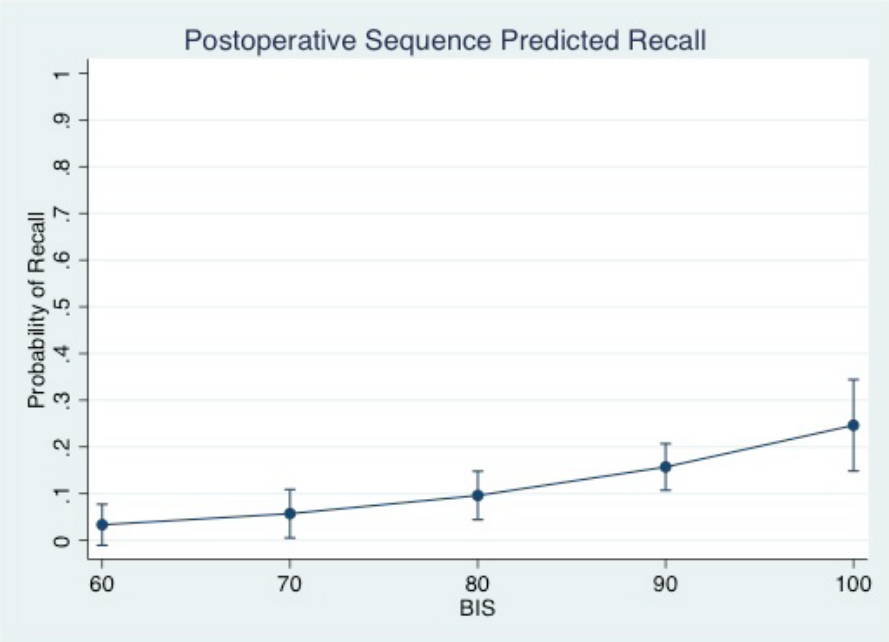

Figure 1: Predicted probability of recall of a word in postoperative sequence for a given BIS value, as modeled by a mixed effects logistic regression. BIS = Bispectral Index.

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S-308.

NONINVASIVE ESTIMATION OF LEFT VENTRICULAR AORTIC COUPLING IN HUMANS

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AFFILIATION: [1]Anesthesiology & Reanimatology, University of Fukui Hospital, Fukui, Japan, [2]Cardiovascular Dynamics, Natl Cerebral and Cardiovascular Ctr, Suita, Japan, [3]Fuclty of Medical Sciences, University of Fukui, Fukui, Japan

INTRODUCTION: Measurement of the left ventricular pressure-volume relationship is invasive; therefore, left ventricular aortic coupling (Ees/Ea) has not been monitored. Without measuring left ventricular pressure and volume, Hayashi et al. developed a framework in animal experiments for noninvasive estimation of Ees/Ea using pre-ejection period (PEP), ejection time (ET), end-systolic arterial pressure (Pes) and diastolic arterial pressure (Pad)[1]. Based on Hayashi's equations, as well as data sets from a study by Senzaki et al.[2], we developed a new equation for humans in clinical settings.

METHODS: We used left ventricular pressure-volume datasets from 48 patients included in the study by Senzaki et al. First, we estimated single-beat elastance using a ventricular time-varying elastance curve represented by two straight lines, one for the isovolumic phase, and the other for the ejection phase. The curve was characterized using the slope ratio, k, of these two lines. The calculated Ees/Ea was expressed as Ees/Ea = Pad/Pes [1+k(ET/PEP)] - 1 (Equation 1). Next, we empirically estimated the relationship between measured k and measured Ees/Ea(Equation 2). We solved these simultaneous equations using Newton's method and compared both the measured and calculated values of Ees/Ea.

RESULTS: The empirical relationship between measured k and measured Ees/Ea in human was described as follows: k = 0.59(Ees/Ea)^0.39 (r = 0.69) (Equation 2). Using Equations 1 and 2, we then calculated Ees/Ea. The correlation coefficient between calculated and measured Ees/Ea was 0.72, the bias was +0.37, and the 95% confidence interval was ±0.64.

CONCLUSIONS: Ees/Ea is able to be estimated noninvasively using two equations in Humans.

REFERENCES:

1. Hayashi et al. Anesthesiology. 2000; 92:1769-76.

2. Senzaki et al. Circulation. 1996; 94:2497-506.

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S-309.

EMPOWERING PATIENTS TO REDUCE IV INFUSION PUMP ALARM INCIDENCE

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AFFILIATION: Anesthesiology, U. of Florida, Gainesville, FL

INTRODUCTION: With more electronic devices in the hospital, the incidence of audible alarms is increasing, promoting alarm fatigue and distressing patients [1,2]. Empowering patients to reverse caution/impending alarm conditions before they develop into audible alarms may reduce alarm incidence and spare the attendant time and effort of clinicians. We applied the concept of active patient participation to intravenous (IV) line occlusions that cause about 40% of IV pump alarms[3].

METHODS: A caution condition (yellow light) triggered by a pressure increase inside the IV tubing is indicative of a potential downstream occlusion in an IV infusion pump (Alaris PC 8015 Series, CareFusion, San Diego, CA). If the caution condition is corrected within 15 seconds, an alarm will not sound. A verbal prompt was retrofitted to the IV pump to instruct patients to "straighten your arm" when a caution condition occurs. After IRB approval, a catheter (supplied with normal saline by the modified pump via an IV infusion set) was taped to the antecubital surface of 11 consenting, supine, blinded lay volunteers. Subjects were instructed to fold the arm with the IV catheter across their chest (creating the occlusion) and to act as if alone in a hospital room and, if needed, to press a provided nurse call button. In the initial control stage, the verbal prompt was disabled. If volunteers did not spontaneously straighten their arm, the occlusion caused a yellow caution light (out of the volunteer's sight) to blink for 15 seconds; the subsequent alarm was allowed to sound for 105 seconds before ending the first stage. In the next, intervention stage, upon detection of a caution condition, a verbal prompt to "straighten your arm" was triggered. If the caution condition was not reversed within 6 seconds, a more assertive prompt "straighten your arm now" was issued; if the caution was not reversed within 15 seconds, the alarm sounded. The subjects' use of the nurse button and the subjective appearance of comfort level were recorded.

RESULTS: With the verbal prompt disabled, no subject prevented the alarm. With the verbal prompt enabled, 10 of 11 subjects corrected the caution within 6 s. One subject required a second verbal prompt. All subjects reversed the occlusion, prevented the alarm and resumed the infusion ($P < 0.001$). Overall, the volunteers reacted positively to a talking pump and its usefulness.

CONCLUSION: An IV pump occlusion from kinked IV tubing may lend itself to being corrected without clinician intervention by empowering patients. With the increasing concern for alarm fatigue and the time and effort spent correcting alarm conditions (that may lead to alarms being disabled) and reducing noise in the hospital, patient-empowering devices may offer a novel opportunity to decrease alarm incidence.

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1) Association for the Advancement of Medical Instrumentation. AAMI Clinical Alarms: 2011 Summit.

2) Medical device alarm safety in hospitals. The Joint Commission: Sentinel Event Alert 8 Apr. 2013: 1-3. Issue 50.

3) Monitoring consciousness via pulse oximeter motion artifact. American Society of Anesthesiologists. 2012 abstract.

Table: Post-Procedural Subject Questionnaire

Questions	Volunteer #1	Volunteer #2	Volunteer #3	Volunteer #4	Volunteer #5	Volunteer #6	Volunteer #7	Volunteer #8	Volunteer #9	Volunteer #10	Volunteer #11
Do you trust software to diagnose alarms?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unsure	Yes	Yes	Yes
Would you follow automated instructions if you were a patient?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Did you feel empowered by this approach?	Yes	No	Yes	No	NA	Yes	Yes	No	Unsure	NA	Yes
How concerned were you (0 no concern-10 panic) when the alarm sounded?	2	1	3	0	3	8	1	1	3	0 (irritated)	5
Did you utilize the nurse call button?	Yes	No	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes
Would you prefer a female (F) or male (M) voice instruction?	M/F	M/F	M/F	M/F	F	M/F	F	M/F	M/F	M/F	M/F

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S-310.

INHALATIONAL INDUCTION FOR DIFFICULT AIRWAY, FACTORS AFFECTING SPONTANEOUS AIRWAY RECOVERY AFTER OBSTRUCTION: A COMPUTATIONAL SIMULATION

AUTHORS: M. Vijjeswarapu[1], A. S. Kuo[2], J. H. Philip[1]

AFFILIATION: [1]Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and Women's Hospital, Boston, MA, [2]Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, MA

INTRODUCTION: The strength of inhalational induction for difficult airway is based on the assumption that if airway patency is lost, drug delivery also ceases and anesthetic depth will spontaneously lighten until airway patency is recovered. [1,2] However, there is no clinical data in the literature to guide management. The event of cannot-ventilate cannot-intubate is rare, potentially catastrophic, and difficult to study. Computer modeling and simulation provide a method for exploring these situations. We used computer simulation to investigate factors affecting time to spontaneous recovery after airway obstruction during inhalation induction.

METHODS: We used GasMan®, a commercially available computer simulation program based on a physiologic multi-compartment model of inhalation anesthetic. [3,4] The circuit was primed with fresh gas flow at 10liters/min and alveolar ventilation was initiated. This was continued until the Vessel Rich Group (VRG) reached the Airway Obstruction Threshold (AOT), measured as a fraction of MAC concentration for the agent. Then alveolar ventilation was stopped and the simulation continued until VRG concentration fell below the AOT. This time was designated the Time to Spontaneous Recovery (TSR) of airway patency. We examined the effect of AOT, induction concentration, cardiac output (CO), functional residual capacity (FRC), volatile anesthetic solubility, and VRG perfusion on TSR.

RESULTS: Overall, lower induction concentration (Fig. 2), higher anesthetic solubility (Fig. 5), and higher AOT (Fig. 1-5) markedly sped spontaneous recovery. The trend of higher VRG perfusion (Fig. 4), lower CO (Fig. 1), and higher FRC (Fig. 3) slowed spontaneous recovery.

CONCLUSION: The results of this study provide guidance in the clinical management of inhalation inductions to speed recovery after airway obstruction. Lower induction concentrations should be used when possible to reduce TSR. Increased anesthetic solubility can also decrease TSR, but clinically sevoflurane is often preferred over the more soluble agents. Higher AOT resulted in decreased TSR, thus drugs that may reduce AOT, such as sedative pre-medications should be avoided. Relatively increased VRG perfusion, as seen in infants, increases TSR. Lower cardiac outputs, such as heart failure or cardiogenic shock, also prolong TSR. Hyperdynamic, high cardiac output states decrease TSR. Decreased FRC reduced TSR, while increased FRC increases TSR. This study demonstrates that computer based simulation offers an approach to scenarios in anesthesia practice that are difficult to study in the field. It also provides a method to enhance the education and experience of both trainees and experienced practitioners.

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3. GasMan-an example of goal oriented computer-assisted teaching which results in learning. J Clin Monit Comput. 1986;3:165-73.
4. User Manual for GasMan® 4.1.5022 http://www.gasmanweb.com/. Downloaded 5/20/2013.

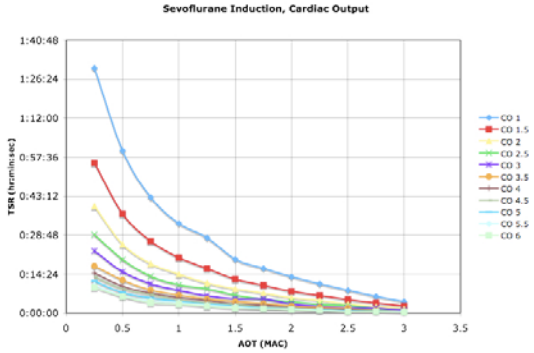

Figure 1: This figure shows the effect of cardiac output (CO) on TSR for a given AOT. AOT is reported as a fraction of MAC for sevoflurane on the x-axis and TSR is on the y-axis.

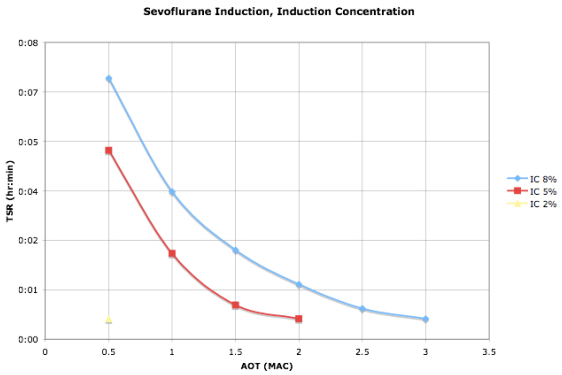

Figure 2: This figure shows the effect of induction concentration (IC) in vapor concentration on TSR for a given AOT. AOT is reported as a fraction of MAC for sevoflurane on the x-axis and TSR is on the y-axis.

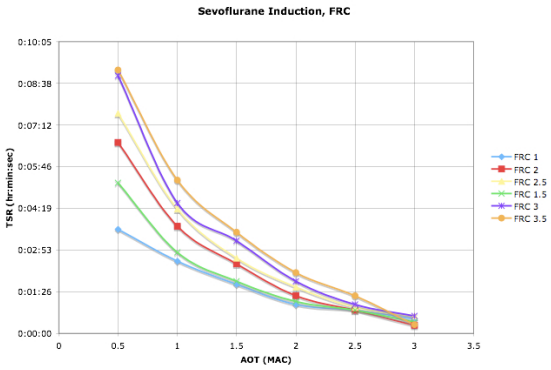

Figure 3: This figure shows the effect of functional residual capacity (FRC) on TSR for a given AOT. AOT is reported as a fraction of MAC for sevoflurane on the x-axis and TSR is on the y-axis.

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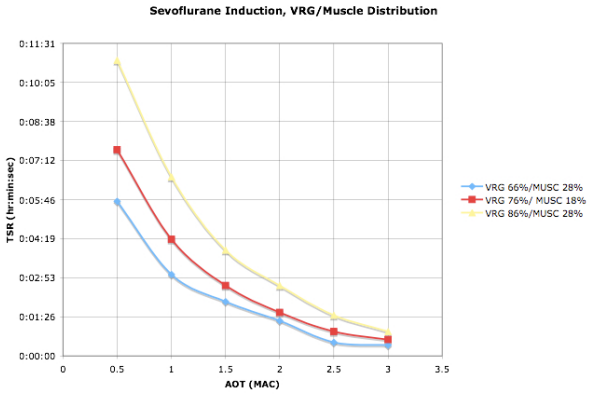

Figure 4: This figure shows the effect of changes in vessel rich group (VRG) perfusion and corresponding changes in muscle group (MUSC) on TSR for a given AOT. AOT is reported as a fraction of MAC for sevoflurane on the x-axis and TSR is on the y-axis.

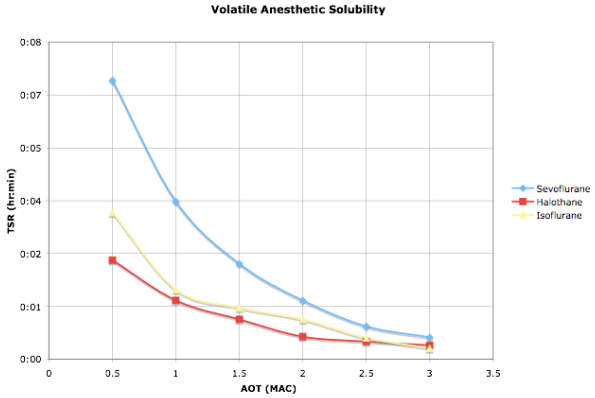

Figure 5: This figure shows the effect of volatile anesthetic solubility on TSR for a given AOT. AOT is reported as a fraction of MAC for each volatile anesthetic on the x-axis and TSR is on the y-axis.
**Solubility of sevoflurane:0.65, Solubility of halothane: 2.4. Solubility of isoflurane: 1.4.*

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S-311.

R ALGORITHM FOR BAYESIAN POWER MODEL OF CONTINUAL REASSESSMENT METHOD TO DETERMINE ED95

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INTRODUCTION: Continual Reassessment Method (CRM) was originally designed for dose-finding phase I cancer drug trials. The primary goal of CRM is to identify maximum tolerated dose of a new drug which is typically defined as the dose with a dose-limiting toxicity probability that is closest to the target toxicity rate. A 'bcrm' package suitable for R is available on Comprehensive R Archive Network (CRAN) http://cran.r-project.org/

However, the package is not readily suitable to determine ED95, as it requires modifications in data entry and data output to yield the required results. This abstract presents a straightforward R algorithm developed for the purpose. An application of the methodology could be to determine MAC-ED95 of inhalational agents since the traditional up-down study design (Dixon method) determines the concentration to produce an effect in half the subjects, not the clinically relevant ED95.

METHODS: R algorithm was developed using the standard formulas for Bayesian one parameter power model of CRM (Figure 1).[1] The ED95 is defined as the 5th percentile of dose-failure relationship which is modelled as $P\alpha$, where α is the parameter of interest which is continually updated based on observed data in each cohort. As negative values are not compatible with the power model, two types of distributions for α are applicable. They are lognormal (mean = 0 and SD = 2) and gamma (shape=1 and scale=1). The algorithm permits the user to choose the type of distribution. Data input requires entry of initial guess of failure probabilities for a dose level and corresponding values related to size of cohort and number of subject exhibiting failure of a defined clinical response. Updated failure probability closest to the 0.05 target yielded by the output of algorithm is chosen as the current ED95 and given to the next cohort. The algorithm was validated with different datasets using bcrm package as standard.

RESULTS: The present algorithm is simple in terms of data entry and interpretation of output. The output of datasets by the present algorithm was comparable with those obtained by the bcrm package.

DISCUSSION: Power model of CRM is a model-based dose finding approach that uses a single unknown parameter to link true probabilities with pre-specified probabilities corresponding to the prior mean probability set. The probabilities are related to 'toxicity' in phase I trials, whereas they are related to 'failure' in trials to determine ED95. Recently, the method was employed to determine ED95 of a standard drug for an established technique.2 While the authors used R software version [2].10#(R CRAN, Vienna, Austria) for analysis, the exact R algorithm was not described. After presentation of this abstract, the algorithm along with detailed documentation for computations will be made available through a web source. This presentation is intended to encourage future researchers, including those novices to the subject, to use the methodology with better understanding of the scheme.

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Figure 1: Formulas used in the algorithm

The dose-failure (probabilities of failure at each dose) model is of the form

$$\pi_j(\alpha) = p_j^{\alpha},$$

Where P_j s are prior guesses of failure at each dose and α is the unkown parameter
We use Bayesian approach and so density of prior distribution is

$$f(\alpha) = \frac{1}{\alpha\sigma\sqrt{2\pi}} e^{-\frac{(\ln(\alpha)-\mu)^2}{2\sigma^2}},$$

μ = 0 and σ = 2, when one uses lognormal distribution

OR

$$f(\alpha = x) = \begin{cases} \exp(-x) & X > 0 \\ 0 & X \leq 0 \end{cases}$$

Shape = 1 and scale = 1, when one uses gamma distribution

Assuming observed data D = $\{(n_j\ y_j),\ j=1,\ldots..j)\}$ and nj patients treated at dose level j, y_j patients experienced failure, the posterior distribution of α is

$$f(\alpha|D) = \frac{f(\alpha)L(\alpha; D)}{\int_0^{\infty} f(\beta)L(\beta; D)d\beta},$$

Where the likelihood is

$$L(\alpha; D) = \prod_{j=1}^{J} \pi_j(\alpha)^{y_j}(1 - \pi_j(\alpha))^{n_j - y_j}.$$

The failure probabilities (plug-in mean) can be estimated by

$$\widehat{\pi}_{j1} = \pi_j \left(\int_0^{\infty} \alpha f(\alpha|D)d\alpha \right)$$

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S-312.

COMPARISON OF TOF-COUNT: TOF WATCH MONITOR VERSUS SUBJECTIVE ASSESSMENT BY ANESTHESIA PROVIDERS

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INTRODUCTION: Qualitative monitoring of neuromuscular blockade, using the train-of-four (TOF) count, is widely used to determine the timing and dose of reversal agents for neuromuscular blockers. Current dosing guidelines for sugammadex are based on studies that determined the TOF-count by a TOF Watch monitor, and not by subjective measurement which is still a common clinical practice. We compared the TOF-count determined by the TOF-Watch SX® acceleromyograph to that estimated by anesthesia providers using their usual clinical practice.

METHODS: In 74 patients recovering from an intubating dose of rocuronium or vecuronium, anesthesia providers performed two subjective assessments (tactilely or visually, per usual routine) of the TOF-count at each level of TOF-count measured by a TOF-Watch SX. The anesthesia provider was blinded to the TOF-Watch display. The researcher watched the TOF-Watch, and as soon as it changed to the next higher TOF-count value, asked the provider to subjectively assess the TOF-count. The researcher then asked the provider to assess the TOF-count again 2-5 minutes later. Thus, ideally 10 data points could be collected for every patient (two provider counts at machine count 0, at machine count 1 etc.)

RESULTS: At the first observation at each TOF count, there was agreement between the TOF-Watch and the subjective assessment by the provider in 226 (66%) out of 345 measurements. The agreement was greatest at the extreme levels of TOF counts, i.e. TOF-count of 0 and 4 (92.8%). Of the 206 measurements at TOF counts of 1, 2, and 3, the agreement was 47% (n=97). In the 109 cases of disagreement at TOF-count 1-3, providers overestimated the TOF-count in 93% of cases. For the second observation at each TOF-Count (n=342), the level of agreement was 46.7%, and for TOF-counts 1-3, it was 23.7% (table 1 and figure 1). In the 155 cases of disagreement at TOF count 1-3, providers overestimated the TOF count in 98 % of cases and 28% of assessments at TOF counts of 1 or 2 were inaccurate by two or more twitches.

CONCLUSION: Anesthesia providers tend to overestimate the TOF count, especially at shallower levels of neuromuscular blockade (TOF-count of 1 to 3), as compared to the TOF-watch. This may have implications in determining the dose of reversal agents, in particular with regard to sugammadex for which dosing guidelines are based on the TOF-count measured by TOF-Watch.

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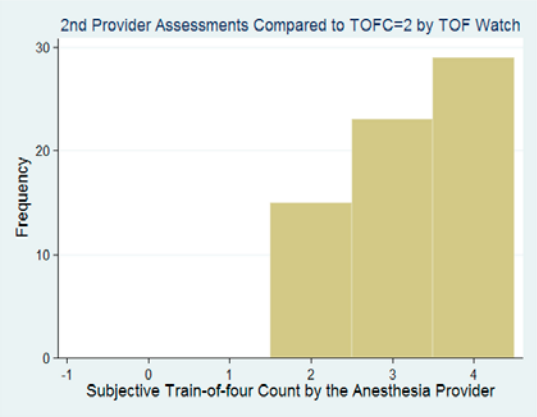

Fig 1. Distribution of anesthesia providers' subjective second assessments of TOF count, at a TOF count of 2 measured by the TOF-Watch.

The table shows the distribution of second anesthesia provider assessments at each level of TOFcount						
n(%)	Provider=0	Provider=1	Provider=2	Provider=3	Provider=4	Total
TOF-Watch=0	47(64)	23(32)	2(3)	0(0)	1(1)	73(100)
TOF-Watch=1	0(0)	29(41)	32(45)	4(6)	6(8)	71(98)
TOF-Watch=2	0(0)	0(0)	15(22)	23(34)	29(43)	67(99)
TOF-Watch=3	0(0)	0(0)	2(3)	4(6)	59(91)	65(100)
TOF-Watch=4	0(0)	0(0)	1(2)	0(0)	65(98)	66(100)

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S-313.

RADIOFREQUENCY BIPOLAR HEMOSTATIC SEALER REDUCES BLOOD LOSS, TRANSFUSION REQUIREMENTS, AND COST FOR PATIENTS UNDERGOING MULTILEVEL SPINAL FUSION SURGERY

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INTRODUCTION: Given the recognized risks and expense of allogeneic blood transfusion in surgical patients, a successful blood management program includes efforts to reduce intraoperative blood loss, as a primary measure of blood conservation. Of the various electrocautery methods that are available, the radiofrequency bipolar hemostatic sealer (RBHS), has been shown in preliminary trials to achieve better hemostasis than traditional cautery used alone. We conducted a retrospective review of blood loss, transfusion requirements and estimated cost savings to assess the benefits of RBHS in patients undergoing multilevel spinal fusion surgery.

METHODS: In a retrospective cohort study, 36 patients undergoing multilevel spinal fusion surgery with the RBHS device (Aquamantys®, Medtronic, Minneapolis, MN), were compared to a historical control group (n=38) matched for important variables related to blood loss. Traditional unipolar cautery and blood salvage were used in both groups. Blood utilization data were extracted from electronic anesthesia records (Metavision®, iMdSoft, Needham, MA) and a blood management intelligence portal, IMPACT Online® (Haemonetics, Braintree, MA). Cost savings were calculated using the acquisition cost as well as the activity-based cost of blood, as described by Shander et al.[1] Data are given as mean ± SEM and $P < 0.05$ defined significance.

RESULTS: The Tables and Figures show the results. Patient characteristics were similar between the two groups, including the number of levels of fusion and preoperative hemoglobin (Hb). Intraoperatively, blood loss was less (by 55%, P=0.002), and the volumes of colloid (by 63%, P=0.04) and returned salvaged blood (by 54%, P=0.003) were less in the RBHS group. Over the entire hospital stay, the average number of units of red cells (by 51%, P=0.01) and plasma (by 56%, P=0.03) were less in the RBHS group. The decrease in Hb was 1.2 g/dL less (P=0.04), and discharge Hb was higher (P=0.01) in the RBHS group. The estimated cost savings per case were substantial by either method of calculation.

CONCLUSION: For patients undergoing multilevel spine fusion surgery, blood loss, transfusion requirements, the decrease in Hb, and costs were substantially less when the RBHS was used to achieve hemostasis. The RBHS method of cautery uses a saline-cooled bipolar delivery of radiofrequency energy, which works by sealing rather than burning tissues. This method has been shown to reduce bleeding and transfusion by more than half in our study, and by similar amounts for total joint replacement surgery.[2,3] In addition to confirming the effectiveness of RBHS in spinal fusion surgery, we have shown a substantial cost savings associated with decreased transfusion. By using this new method of achieving intraoperative hemostasis as part of a comprehensive patient blood management program, the reduced transfusion requirements may result in increased patient safety, improved outcomes, and reduce costs.

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Table 1. Comparison of the Radiofrequency Bipolar Hemostatic Sealer and Control Groups

Variable	RBHS Group (n=36)	Control Group (n=38)	*P* value
Age (yrs)	64 ± 14	59 ± 13	0.17
Sex (male/female)	18/18	23/15	0.33
Body mass (kg)	76.6 ± 18.4	74.1 ± 21.2	0.62
Spinal levels fused [median (IQR)]	4 (3, 9)	4 (2, 7)	0.23
Spinal levels fused (mean±SD)	6.1±4.5	4.9±3.7	0.22
Thoracic or lumbar fusion	22 (61%)	25 (66%)	0.67
Thoraco-lumbar fusion	14 (39%)	14 (34%)	0.67
ASA Class	2.7 ± 0.1	2.5 ± 0.1	0.19
Hemoglobin preoperative (g/dL)	12.5 ± 2.1	12.9 ± 2.1	0.47
Hemoglobin hospital nadir (g/dL)	9.4 ± 1.6	8.5 ± 1.1	0.01
Hemoglobin upon discharge (g/dL)	10.5 ± 1.4	9.7 ± 0.9	0.01
Δ Hemoglobin (admit–discharge) (g/dL)	-2.0 ± 2.2	-3.2 ± 2.1	0.04
Crystalloid (mLs)	6,000 ± 2,000	5,900 ± 2,300	0.88
Colloid volume (mLs)	70 ± 170	190 ± 270	0.04
Cell Salvage (volume returned (mLs)	230 ± 47	500 ± 200	0.003
Estimated blood loss (mLs)	810 ± 530	1,800 ± 1,600	0.002

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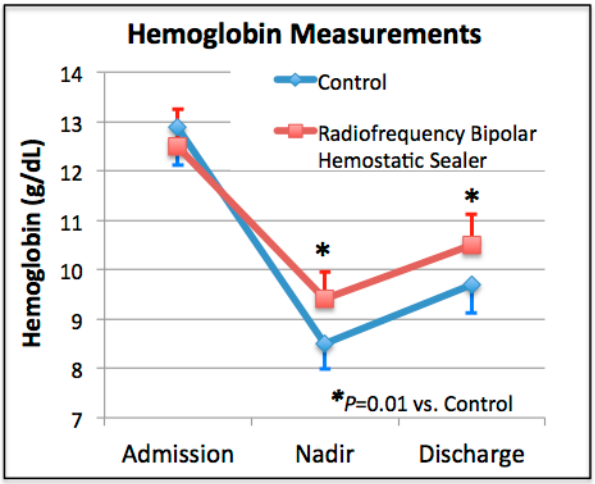
Table 2. Intraoperative and Whole Hospitalization Transfusion Requirements

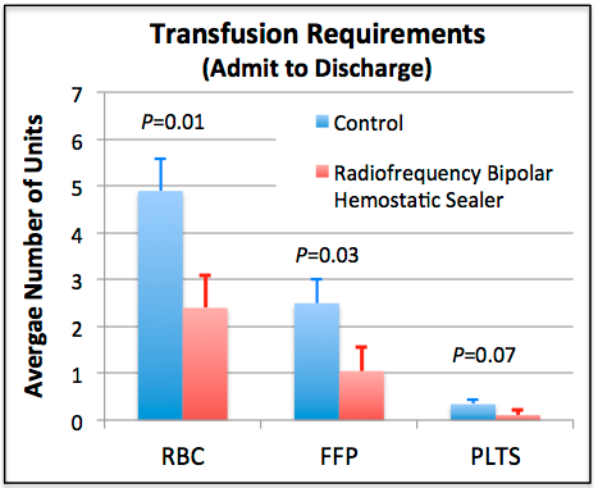
Variable	RBHS Group (n=36)	Control Group (n=38)	*P* value
Transfusion (intraoperative)			
RBC (units/patient)	1.2±1.4	2.8±3.4	0.009
FFP (units/patient)	0.3±0.7	1.8±2.8	0.002
PLTS (units/patient)	0±0	0.1±0.4	0.11
RBCs given	19 (53%)	24 (63%)	0.48
FFP given	7 (19%)	16 (42%)	0.03
PLTS given	0 (0%)	3 (8%)	0.24
Transfusion (whole hospital stay)			
RBC (units/patient)	2.4±3.4	4.9±4.5	0.01
FFP (units/patient)	1.1±2.4	2.5±3.4	0.03
PLTS (units/patient)	0.1±0.5	0.3±0.6	0.07
RBCs given	21 (58%)	30 (79%)	0.05
FFP given	7 (19%)	6 (42%)	0.04
PLTS given	0 (0%)	3 (8%)	0.24

Table 3. Units of Blood Product Saved and Costs Saved per Surgical Case

Blood Component	Units	Acquisition Cost*	ABC (Activity Based Cost)**
Savings in RBCs	2.5	$550	$1,760-2,640
Savings in FFP	1.4	$75	$240-360
Savings in PLTS	0.2	$120	$384-$576
Total Savings		$745	$2,384-$3,576

* - Calculated as $220/RBC unit, $50/FFP unit, and $600/PLTS unit
** - Calculated as 3.2 to 4.8 times acquisition cost (Shander A, *et al*, ***TRANSFUSION*** 2010;50:753-765)[1]





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S-315.

ACCURACY AND CLINICAL RELEVANCE OF NON-INVASIVE RESPIRATORY VOLUME MEASUREMENTS IN OBESE SURGICAL PATIENTS

AUTHORS: R. Schumann[1], C. M. MacNabb[2], Q. Al Hassan[1], I. Bonney[1], A. P. Kwater[3], D. Shoham[3], E. G. Pivalizza[3]

AFFILIATION: [1]Anesthesiology, Tufts Medical Center, Boston, MA, [2]R & D, Respiratory Motion Inc, Waltham, MA, [3]Anesthesiology, University of Texas Medical School, Houston, TX

INTRODUCTION: Obese patients have an increased risk of post-operative respiratory complications. Opioid analgesia, one of the leading causes of post-operative respiratory compromise, is challenging in obese patients because of their variable responses. Enhanced post-operative respiratory monitoring may be beneficial in this population. A novel non-invasive Respiratory Volume Monitor (RVM) has been developed that provides continuous, real-time measurements of minute ventilation (MV), tidal volume (TV) and respiratory rate (RR)[1]. Accuracy of the RVM has been confirmed in non-obese ventilated surgical patients and its clinically relevant accuracy, precision bias and correlation (r=0.97) was demonstrated in non-surgical obese subjects. This study examines the RVM accuracy in the obese surgical population.

METHODS: In a multi-center study, respiratory traces were recorded with an impedance-based RVM system (ExSpiron, Respiratory Motion, Inc. Waltham, MA) from 56 obese patients undergoing elective surgery with general anesthesia. Pre- intra- and PACU data were collected. The MV set for the majority of the surgery was defined as baseline and the RVM was synchronized with the ventilator over a 30 second quiet period (MV_{SYNC}). Two 30 sec RVM segments were selected during quiet periods at the beginning and end of the case to determine accuracy and consistency. RVM measurements in the PACU were compared to preoperative and intraoperative values. MV before and after opioid administration in the PACU was assessed to capture subsequent MV changes. Linear regression and Bland-Altman analyses were used for statistical analysis.

RESULTS: 17 men, 39 women, aged 50 ± 14 years, with a BMI of 44.3 ± 8 were studied with a ventilator time of 153 ± 33 min. Comparison of the RVM and ventilator MV values showed an accuracy of 11%, precision 11% and a 1.5% bias (Example traces Fig. 1, r>0.95). Figures 2 & 3 summarizes the correlation between the RVM and ventilator (r=0.9) and a small measurement error (0.13L/min ± 95%CI [-0.93 to 1.20 L/min]) which remained minimal at the beginning and end of the recording sessions (Fig. 4). The pre-, intra- and postoperative course of MV including during PACU opioid administration is shown in figure 5.

CONCLUSION: The results of this study show a good correlation between the RVM and ventilator volumes with clinically useful accuracy in an obese surgical population, extending prior results from normal weight and obese non-surgical patients. Post-operative opioids caused a substantial but temporary decline in MV, and it is unclear if a dosing change could mitigate such an observation. Continuous RVM measurements providing quantitative respiratory data may be helpful in identifying opioid sensitive obese patients, facilitate post-operative management and improve patient safety.

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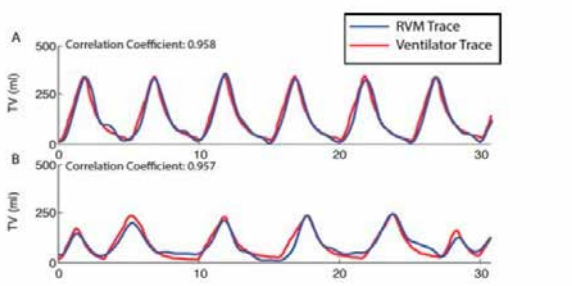

Figure 1: Representative subject traces between the Draeger Apollo[R] ventilator (red) and RVM (blue). Closely correlation at the beginning (A) and end of the case (B, 83 mins later).

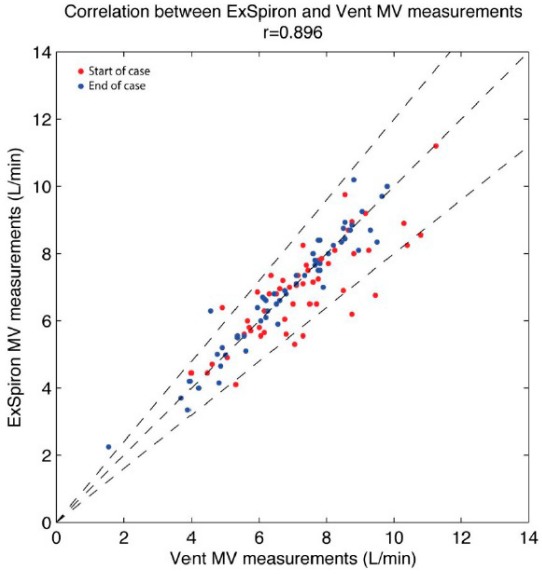

Figure 2: Correlation analysis of MV measurements from RVM and ventilator (n = 56). Each data point is the average of 2 consecutive 30 second MV measurements. Red data points are from the beginning of surgery and blue from the end of surgery.

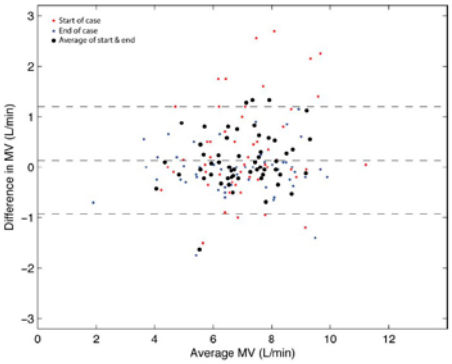

Figure 3: Bland-Altman analysis of MV measurements from the RVM and ventilator. Each data point is the average of 2 consecutive 30 second MV measurements. Red points - beginning of surgery, blue points - end of surgery. The average difference was -0.13 L/min (middle black dashed line) with a 95% prediction interval (± 2SD, -0.93 to 1.20 L/min, upper and lower black dashed lines).

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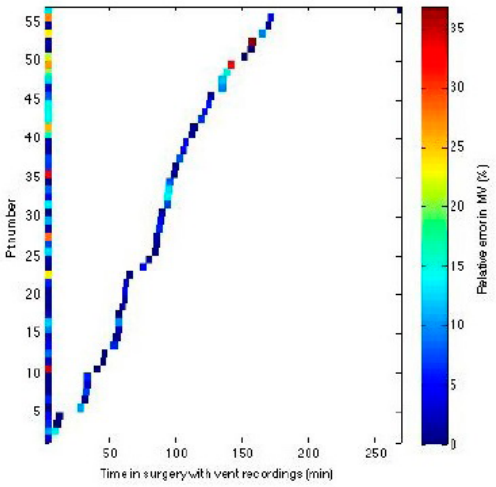

Figure 4: Temporal visualization of the relative measurement error between the RVM and ventilator at the start and end of surgery. The error was computed for each measurement pair according to the Bland-Altman method: 0.5*(RVM-Vent)/(RVM+Vent). Subjects were arranged in order of increasing total recording time and most points were aligned with the time axis (x) indicating beginning of recording. The rightmost points for each subjects are located at the corresponding time from the start of recording when the second set of measurements were taken (e.g. for patient 57 the second point is located at 269 min). The color map corresponds to the relative error with dark blue representing 0% error and dark red representing 37% error.

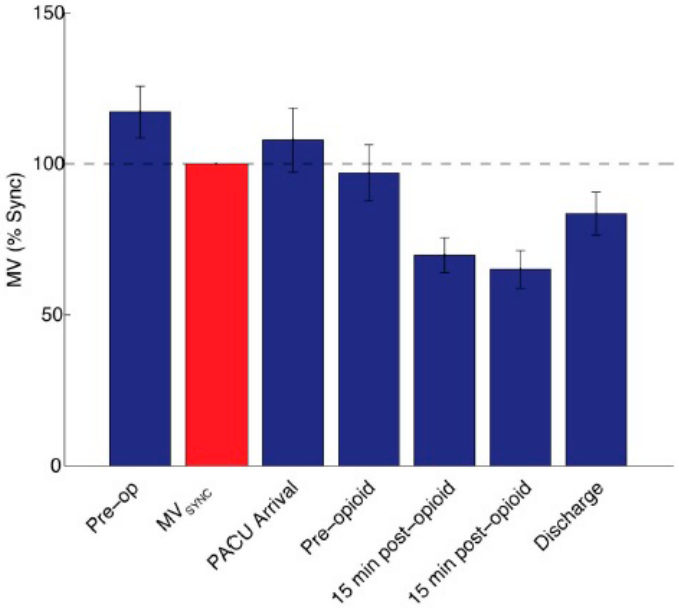

Figure 5: MV during the peri-operative period, calculated as % of intraoperative MV_{SYNC}. MV decreases substantially following first opioid dose (70 ± 6% MV_{SYNC} after 15 min, 65 ± 6% MV_{SYNC} after 30 mins) with partial recovery by PACU discharge (83 ± 7% MV_{SYNC}).

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THE VALIDITY OF BISPECTRAL INDEX VALUES OBTAINED FROM A LATEROFACIAL ELECTRODES

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INTRODUCTION: The bispectral index (BIS) is the most widespread and evaluated parameter to measure the level of consciousness. When it is difficult to attach BIS sensor on the forehead because of the surgical field, the sensor needs to be dislocated. There are a few studies on BIS values obtained from sensors dislocated only for a few centimeters[1] or dislocated to occipital region,[2,3] however credibility is not high. The purpose of this study is to compare the BIS values obtained from a sensor attached on the laterofacial region with the values from a sensor on the forehead.

METHODS: With approval of the IRB, we recruited 21 ASA PS I-II adult patients scheduled for elective abdominal or breast surgeries under general anesthesia (Male/Female; 6/15, age; 33 to 77 years old). Before the induction, 2 BIS electrodes (BIS Quatro sensors connected to BIS-Vista monitors; Covidien, Mansfiled, MA) were placed on the laterofacial region as dislocated and the forehead as standard. The dislocated sensor was mounted as follows: Circle 1 on the outside corner of the right eye, Circle 4 close to earlobe, Circle 2 between Circle 1 and 4, and Circle 3 on the mandible. Anesthesia was induced by propofol, fentanyl and rocuronium, and maintained with sevoflurane. The BIS and Electromyograph (EMG) index values from each sensor were recorded 10 times at the following anesthetic states: awake, loss of response to verbal command, tracheal intubation, 10 minutes after intubation, start of surgery, 10 and 30 minutes after incision, end of surgery, eye opening, and after tracheal extubation. Statistical analyses were assessed by Spearman's rank-correlation coefficient and regression coefficient, and Bland and Altman analysis was also performed.

RESULTS: BIS values of 2 BIS electrode showed strong correlation ($R = 0.878$; $P < 0.01$, $Y = 3.453 + 0.954X$). Bland-Altman analysis of BIS values revealed the mean bias of -0.6 with the 95% limits of agreement at -13.8 to 12.6. While no plot was seen above 2SD, 11 plots were spread below -2SD (indicated in red plots in the figure). Nine measurements among those 11 plots were obtained when EMG from laterofacial region was higher than forehead, hence EMG is suspected to have caused those 9 plots below -2SD. Thus, further studies are necessary to conclude on clinical usefulness and limitations of dislocated BIS sensor.

CONCLUSIONS: BIS values from laterofacial region demonstrated high correlation with standard BIS values. It supports potential clinical usefulness of the dislocated BIS sensor when frontal access is particularly difficult. However, it should be noted that dislocated BIS sensors indicated higher values in some cases with higher EMG values even though BIS sensors placed on the forehead were showing the values between 40-60 which is considered to be the general anesthesia range.

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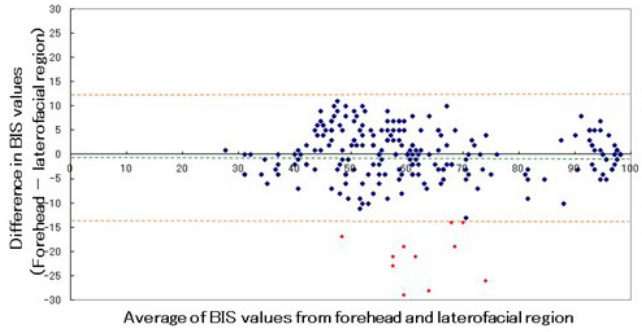
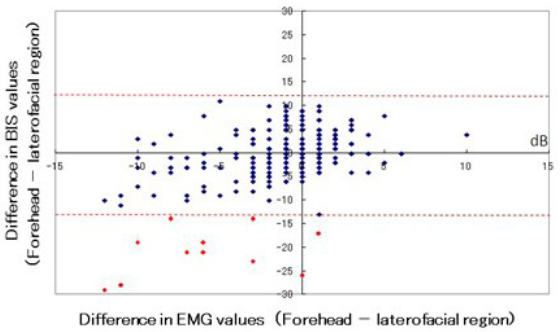


A. Bland and Altman plot of the difference in BIS values between forehead and laterofacial region against the mean of the two measurements.
The dotted green line represents the bias and the red line represents limits of agreement.



B. Difference in BIS values and EMG values between forehead and laterofacial region.
The dotted lines represent the limits of agreement as in **A.**
Red plots are the same measurements as those in **A.**

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S-317.

A THEORETICAL ANALYSIS OF THE EFFECT OF EXTRA-CORPOREAL MEMBRANE OXYGENATION THERAPY ON PULMONARY ARTERIAL PRESSURE: IMPLICATIONS FOR BRIDGE TO LUNG TRANSPLANTATION

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INTRODUCTION: Extracorporeal membrane oxygenation therapy (ECMO) is being used with increasing frequency to offload the right ventricle and reduce pulmonary pressures in patients with pulmonary hypertension awaiting lung transplantation. However, the mechanism by which ECMO reduces mean pulmonary pressure (mPAP) and the relative efficacies of various cannulation strategies on improving perfusion is not known. The purpose of this study was to compare the impact of veno-venous (VV), veno-arterial (VA), hybrid (VAV) and pulmonary arterial to left atrial (PA-LA) ECMO on mPAP and flow.

METHODS: A model of chronic pulmonary hypertension was created (baseline) using time-varying elastances (ventricular contraction) coupled to a series of resistive and compliance elements (the pulmonary and systemic vascular systems). Four different configurations of ECMO (VA, VV, VAV and PALA) were initiated at a flow of 2 liters/minute and hemodynamics recorded. Next, intravascular volume was reduced until total systemic flow returned to the baseline value simulating diuresis.

RESULTS: Initiation of all the cannulation strategies had negligible effects on mPAP except for PALA which reduced mPAP by 13%. Substantial differences in the augmentation of systemic blood flow were observed, with VA and PALA ECMO providing the greatest flow augmentation. The relative reduction in intravascular volume required to return systemic flow back to baseline (Fig 1) was proportional to the augmentation in systemic flow. VA, PALA and VAV ECMO resulted in 43, 36, and 25% reductions in mPAP after diuresis, respectively (Fig. 2).

CONCLUSIONS: Except for the modest reduction seen with PALA cannulation, the initiation of ECMO alone has little direct effect on pulmonary pressures. The benefit of reducing pulmonary pressures is mainly realized through diuresis that is undoubtedly better tolerated with augmented systemic flow. Reductions in pulmonary vascular resistance as a consequence of improved pulmonary oxygen content may also play a role.

Fig. 1

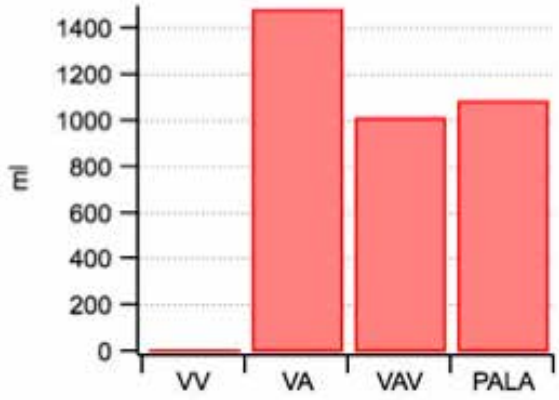
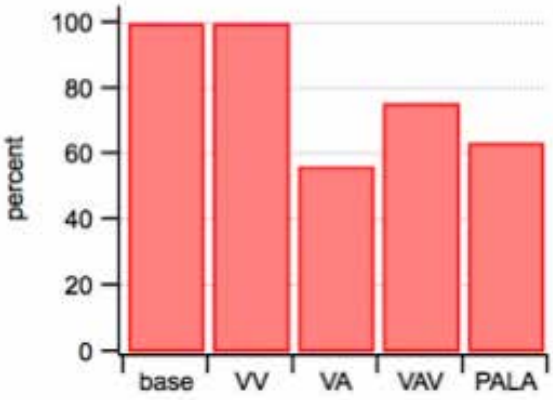


Fig. 2



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S-318.

NOVEL METHOD OF BLOOD VESSEL VISUALIZATION AND CANNULATION USING AUGMENTED REALITY.

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INTRODUCTION: As health care providers we must work with anatomical structures that we simply cannot see. Recently several medical associations and organizations have recommended routine use of ultrasound to better locate central venous structures during central line placement. Augmented Reality is a software process whereby information is blended with a user's view of the real world. This allows a user access to additional data in the context of his or her own environment.

METHODS: Using software developed by our team and a set of video glasses, virtual representations of anatomic structures are presented to the physician user in their *in situ* position. These structures are generated by tracking an ultrasound probe in 3D space and by analysis of the US images. Tracking was accomplished by using a specialized camera to track a card marker which was attached to the ultrasound probe allowing our software to determine this marker's physical position relative to the camera and thus by extension we were able to determine the physical location of the imaged cross-sectional plane of tissue that is projected on the ultrasound machine's screen. Our markers communicate both position, orientation and identification data so that the specific model of ultrasound probe can be determined and each fiduciary marker can be distinguished from other markers designated for tracking needles and other instruments and for maintaining a location lock on the patient. By scanning the ultrasound probe on the patient, a volume of data is generated allowing the reconstruction of 3D virtual representations of anatomic structures. This information remains connected to the patient and the ultrasound probe can be removed. Testing was performed first in clear gelatin phantoms, opaque phantoms and finally in a human test subject (n=3).

RESULTS: The system correctly built virtual representations of structures in both the phantoms and the human subject. We successfully tracked both anatomic structures and a needle below the skin surface. Dye from the phantom vessels and blood from the human subject was successfully aspirated using only the system to guide needle placement.

CONCLUSIONS: Augmented Reality based systems provide a novel method for successful mapping, visualization and cannulation of blood vessels in humans. While our work in its current form is not ready for clinical use due to the size of the system and the time needed for calibration, it does offer exciting possibilities for the future. Further studies are needed to evaluate the use of this technique to target other anatomical structures such as nerves, tumors, etc. Much work and an open field lies before us as we develop the concept of augmented medicine.

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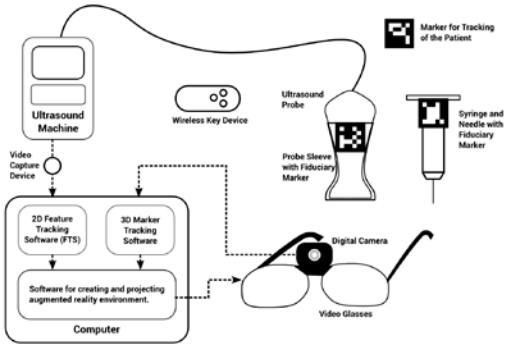

Figure 1: Schematic drawing of the basic set up of the system.

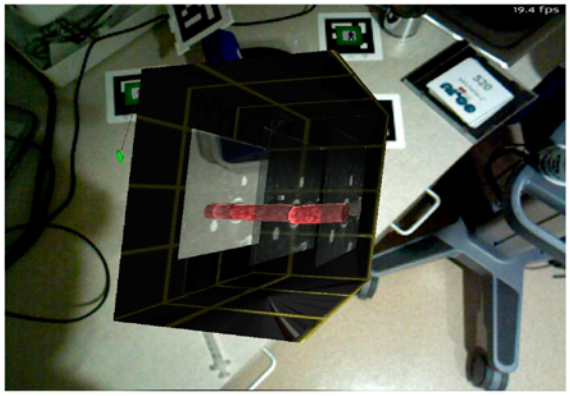

Figure 2: After map generation, the map may be edited to eliminate artifactual structures or to allow the user to identify one anatomic structure among many on which they wish to focus. During editing, the model is presented and slowly rotated directly in front of the user along with ultrasound image slices recorded during the scan. When done the model 'flies' back to its anatomic location within the patient and loses the ultrasound image slices and the grid seen in this image.

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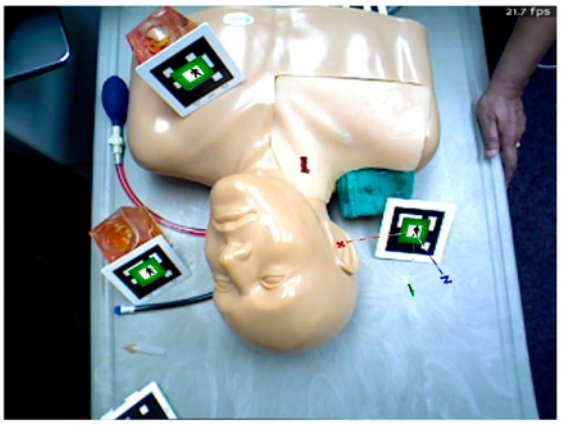

Figure 3- After scanning and map generation with the ultrasound probe. A 2.7 centimeter portion of the phantom's right internal jugular vein is visualized as seen through the head-mounted display. The black-and-white marker cards in the image maintain a positional lock on anatomic structure. The green person glyph over the cards is also an augmentation that simply informs the user that the system has a lock on that marker.

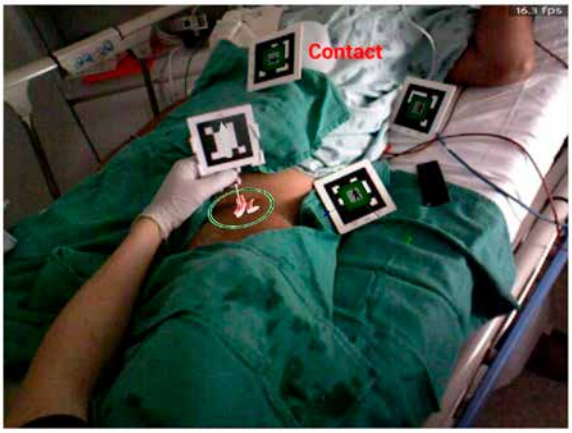

Figure 4- in situ virtual representations of the left femoral vein (left) and left femoral artery (right) as seen through the head-mounted-display. This patient had tortuous vessels but the system was still able to generate accurate representations of the vessels. The needle is overlayed with a virtual representation of the needle (white with aiding green halo) allowing view of the needle below the skin surface.

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CONTROL OF BURST–SUPPRESSION IN A RODENT MODEL OF MEDICAL COMA USING A BRAIN-MACHINE INTERFACE

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INTRODUCTION: Burst suppression is an electroencephalogram (EEG) signature of profound brain inactivation and consists of bursts of electrical activity alternating with periods of electrical suppression. This EEG pattern is targeted in medical coma, a drug-induced brain state used to help recovery after brain injuries and to treat uncontrollable seizures. Medical coma is maintained manually by monitoring the EEG and administering an intravenous infusion of an anesthetic to target a pattern of burst suppression. The coma needs to be maintained for long periods of time, often several hours or days. Hence developing an automated control system could significantly improve the efficiency and accuracy of control. There has been considerable progress in developing these automated systems for control of sedation and general anesthesia in the past 60 years. However, automatic reliable control of medical coma over time-varying target levels or for individual animals has not been demonstrated before.

METHODS: Using a stochastic control framework, we develop a brain-to-pump interface system or brain-machine interface (BMI) for automatic control of medical coma in a rodent model. The BMI works by continuously observing the EEG, estimating the burst suppression level using the EEG, and selecting the real-time propofol infusion rate based on this estimate. To quantify the state of coma, we use the concept of burst suppression probability (BSP) that defines the brain's instantaneous probability of being in the suppressed state. To characterize the effect of propofol on BSP, we use a linear two-dimensional compartment model and fit the parameters of this model in experiments. The BMI consists of two main components: an estimator that computes the BSP from the EEG and a controller that uses this estimate as feedback to adjust the drug infusion rate and achieve a target BSP level. We segment the EEG into a binary time-series by low-pass filtering and thresholding it in small intervals. We derive a two-dimensional state-space algorithm to estimate the BSP in real-time from the segmented EEG. Finally, we design a stochastic controller using both a linear-quadratic-regulator strategy and a model predictive control strategy. We tested the BMI in individual rodents for control of time-varying target BSP levels. Animal studies were approved by the Subcommittee on Research Animal Care, which serves as our Institutional Animal Care and Use Committee.

RESULTS: The BMI enabled prompt transitions between target BSP levels without overshoot or undershoot. The median rise time in the BSP levels was under a minute in individual rodents. The BMI also accurately maintained the BSP at desired target levels in individual rodents in real time. In our experiments the median absolute error and the median bias were both under 5% for each rodent.

CONCLUSIONS: Our results demonstrate the feasibility of automatic control of medical coma in a rodent model using a BMI and suggest that a BMI could be applied in patient care with the potential to enable more accurate and cost-effective control of coma.

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