Title: Postoperative Respiratory Complications in Patients at Risk for Obstructive Sleep Apnea: A Single Institution Cohort Study

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Abstract

Background: Obstructive sleep apnea (OSA) is a prevalent condition that is associated with early postoperative respiratory complications (PRC). As the majority of patients with OSA are undiagnosed, preoperative screening remains the most efficient method to identify suspected OSA.

Methods: This retrospective study was performed on patients undergoing anesthesia in a single academic medical center. We assigned OSA risk class retrospectively to all patients in the study by using the Perioperative Sleep Apnea Prediction Score (PSAP). The interaction between suspected OSA and surgical risk was assessed to determine need for stratified analyses. We evaluated the relationship between PSAP categories and early postoperative invasive airway placement after adjusting for several preoperative and intraoperative factors previously associated with PRC occurrence across high and low risk surgical procedures.

Results: Interaction between PSAP risk categories and surgical risk was observed, with significant increase in estimates across surgical risk strata. With high risk surgery, moderate PSAP score [AOR 1.6; 95% CI 1.2, 2.3; p=0.003] and high PSAP score categories [AOR 2.0; 95% CI 1.3, 3.1; p=0.002] were independently associated with early postoperative intubation when compared to low PSAP risk of OSA. High PSAP score was associated with postoperative intubation with low risk surgery [AOR 2.7; 95% CI 1.7, 4.2]. Several risk factors reflecting anesthetic agent, relaxant and opioid administration were also independently associated with early PRC.

Conclusions: In summary, we report that suspected OSA based on the PSAP score is independently associated with increased risk of early PRC with varying effect sizes across surgical risk strata. Specific anesthetic techniques are independently associated with early PRC in the multivariate model, pointing to the potential for examining risk modification through these

exposures in future studies.

Introduction

The early postoperative period, defined as the first 72 hours following surgery has been associated with a heightened risk for respiratory morbidity.[1, 2] Early postoperative respiratory complications (PRC) occur in 0.2-3.8% of cases and are associated with an independent 9-fold increase in mortality.[3]PRCs are associated with a 12-fold increase in patient care costs.[4] The increased risks on the first postoperative day may be related to opioid analgesic and sedative use,[5] whereas postoperative hypoxia and sleep disordered breathing typically peak on the third to fifth postoperative nights.[6, 7]

OSA presents a minimally explored target condition for studying the perioperative modifiability of early PRC.[8] First, OSA is a highly prevalent condition that affects ~ 25% of middle-aged men and ~ 10% of middle-aged women, with significant impact on quality of life, life expectancy, cardiovascular disease, respiratory disease and several other end-organ abnormalities.[9-12] Second, recent evidence points to an independent 3 to 6-fold increase in the rate of early PRC in patients with OSA.[13, 14]We have recently shown that preoperative diagnosis and treatment with positive airway pressure is associated with a significantly lowered risk of postoperative cardiopulmonary complications.[15]However, this risk modification is likely to need significant preoperative lead time for completion of both testing and fitting of PAP device, with unknown minimum duration for effectiveness. It is possible that only a minority of patients with undiagnosed OSA presenting for preoperative clinic evaluation will have sufficient social and surgical flexibility to have effective preoperative positive airway pressure therapy. This imposes a major management gap in the remaining majority of these patients, as they still carry a higher risk of PRC and require alternative methods of risk modification.

We previously developed and validated a prediction tool called the Perioperative Sleep Apnea Prediction (PSAP) score, using characteristics typically collected during pre-anesthesia

assessment of patients.[16] The accuracy of the PSAP tool is similar to STOP-Bang,[17] but more importantly, it has provided us the added advantage of retrospectively assigning OSA risk to all adult patients in our single-center anesthesia information system database. An estimated 50-80% of patients with OSA are undiagnosed, making preoperative screening through clinical tools the only feasible risk stratification method to apply in the preoperative setting.[12, 18]However, there is no evidence that the mere process of preoperative screening of OSA makes a difference to medium-term or long-term outcomes.[19]We hypothesized that increasing PSAP scorecategories during preoperative screening for OSA would be associated withincreased odds of developing PRC.We additionally hypothesized that if a relationship exists between suspected OSA and higher PRC rates, that patient, surgical and anesthesia risk factors will influence this relationship.

Methods:

This retrospective observational study was performed usingthe Anesthesia Information Management System database at the University of Michigan Health System. Perioperative comorbidity, anesthesia and procedural data of all adult patients (18 years and older) that presented for a surgical procedure between Jan 2007 and December 2013 were extracted for the creation of the study database. The study was approved by the Institutional Review Board (IRB# HUM00085276), with waiver of need for patient consent, since all data were observational in nature. This database query was created from two related sources, the Centricity Anesthesia Information Management System (GE Healthcare, Waukesha, USA) and the local multicenter perioperative outcome group data.[20-23]The latter has access to other hospital system databases through the institutional research data warehouse. The categorical data fields of interest are entered using prepopulated pick-lists with option for additional text entry. All data were evaluated for completeness, and text entries were manually coded using a de-identified interface provided by the Multicenter Perioperative Outcomes Group

(MPOG)system.[23]

Patient population

Patients with the following conditions were excluded from the study: an existing airway documented on preoperative evaluation (i.e., have an endotracheal tube or tracheostomy in place), preoperative ventilator dependence, liver transplantation, labor and delivery procedures, cesarean section, patient transferred to ICU without extubation, pediatric age group (age younger than 18 years), pancuronium usage, >4 unit PRBC transfusion intraoperatively and emergent procedures.. Additionally, data fields with suspected documentation errors for key study elements and specific medication administration were converted to missing data. These conditions included body mass index less than 10 or greater than 80 $kg.m^{-2}$, height less than 4 feet or greater than 8 feet, anesthesia duration below 1st centile or above 99th centile within the database, intraoperative morphine dose greater than 50 mg, fentanyl greater than 500 micrograms or hydromorphone greater than 5 mg.

Study exposures

The primary exposure in the study was a patient's risk for obstructive sleep apnea as measured by the PSAP score. The methods for its calculation and its performance characteristics are further described in Ramachandran et al in 2010.[16] PSAP scores between 3 and 9 had between 1.9 to 42.4 times likelihood of having OSA. Patients meeting the inclusion criteria were retrospectively classified into the groups at low, moderate and high risk of OSA using the PSAP score (<3, 3-5 and >5 respectively). The PSAP score variables were pre-defined in the study data fields. Three demographic variables: age >43 years, male gender, and obesity; three history variables: history of snoring, diabetes mellitus Type 2, and hypertension; and three airway measures: thick neck, modified Mallampati class 3 or 4, and reduced thyromental distance make up the PSAP score.

Study Outcomes

The primary health outcome of interest for this study was invasive airway placement within the first three postoperative days. Invasive airway placement was defined as postoperative reintubation or intubation of a previously non-intubated patient after anesthesia end.[3]These conditions were identified through a combined search strategy of multiple possible sources: clinical event documentation using pre-defined pick-lists in the anesthesia information management system, nursing information management system, free text search of the intraoperative and PACU nursing charts for “intubation”, safety event notification specifying emergent intubation, documentation of laryngoscopy in the post-extubation period in the operating room or PACU, and documentation of postoperative intubation using preexisting procedure notes. Safety events are reported using an institutional reporting form that triggers automatic event review by the local unit where the event occurs.

Model Covariates

Candidate variables for the adjusted analyses were based on a previously validated model of early postoperative respiratory failure.[3] Patient level variables included smoking, alcohol intake, preoperative benzodiazepine intake, myocardial infarction, chronic obstructive pulmonary disease, liver disease, renal disease, congestive heart failure, neurological conditions, seizures, cancer, preoperative steroid use, preoperative pneumonia, pulmonary hypertension, coma, sepsis, American Society of Anesthesiologists physical status and admission type (outpatient, admission on the day of surgery or inpatient). Preoperative opioid intake was identified if the preoperative admission medication listcontained any of the following: dilaudid, morphine, vicodin, methadone, percocet, hydrocodone, fentanyl, vicoprofen, norco, duragesic, oxycodone, roxicodone, fioricet, percodan, lortab, lorcet, codeine, opium,

hydromorphone, oxycontin, suboxone, endocet, or buprenorphine. Intraoperative anesthesia interventions evaluated were anesthesia type (regional anesthesia, general anesthesia or combined), anesthetic agents used (propofol infusion alone, volatile alone, propofol infusion with volatile), anesthetic exposure (population quartiles of the time duration of estimated minimum alveolar concentration [MAC] above 1.0),[24] number of packed red blood cell units transfused, number of fresh frozen plasma units transfused, intraoperative opioid agents used, number of intraoperative opioids used, dose of intraoperative opioids (population quartiles of intraoperative morphine equivalent dose normalized for ideal body weight and anesthesia time), use of naloxone, and aminoglycoside administration. The surgical complexity score was derived using a previously established technique from the primary CPT code.[25, 26] This approach computes a continuous score using a logistic regression model to predict the study primary outcome. The continuous surgical complexity score was converted to a dichotomous variable as high risk (≥75th centile score) or low risk (<75th centile score), to classify surgical exposure.

We used a composite approach to isolate the NMBA exposures of interest. We first limited the number of NMBAs of interest to three drugs: vecuronium, cistracurium and rocuronium in order to account for the fact that these agents are predominantly used in current state. Next, we normalized the NMBA dose by adjusting for ideal body weight, and anesthesia time. We identified the population distribution of each of these intraoperative NMBA dose per kg per minute and converted them into a binary concepts of high dose (equal to or greater than 75th centile) for each NMBA separately. For this dataset, these were defined as a dose greater than in mg per kg ideal body weight per hour 0.115 mg.kg-IBW^{-1}.hr^{-1} for cisatracurium, 0.069 mg.kg-IBW^{-1}.hr^{-1} of vecuronium and 0.494 mg.kg-IBW^{-1}.hr^{-1} of rocuronium. The relationship between NMBA exposures and outcomes was evaluated by inclusion of these independent categorical variables in the logistic regression models: NMBA used (none, cisatracurium, rocuronium or vecuronium), use of high dose of NMBA, use of neostigmine reversal and use of neuromuscular

monitoring. These variables are fully described in Appendix 1.

Statistical analysis

Descriptive statistics were performed to examine the univariate relationships between the primary study outcome of PRC, namely reintubationwith the exposure variable and the covariates of interest. Differences in distribution were analyzed with the Pearson chi-square test for categorical variables and the t-test for continuous variables. A p value of <0.05 was accepted as significant.

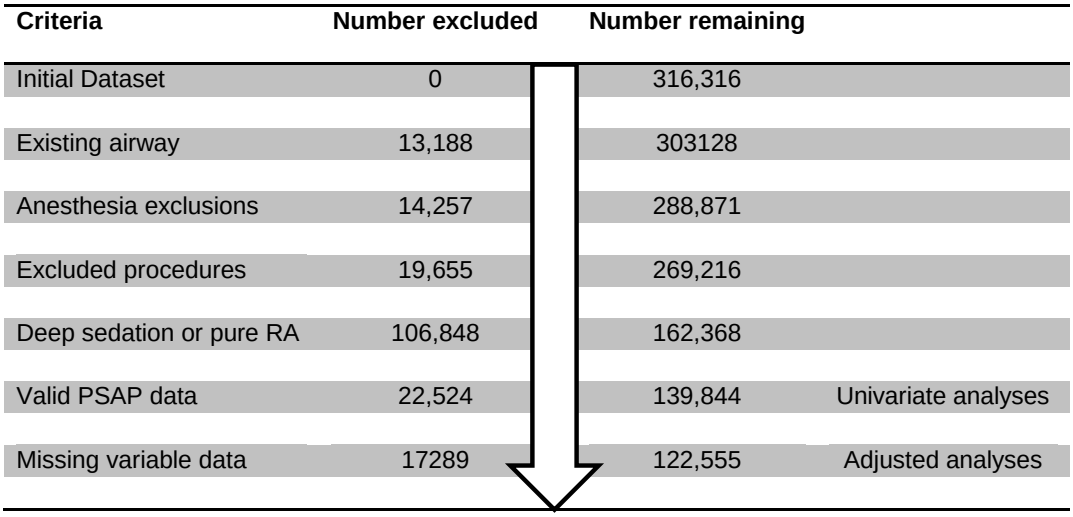
As surgical service was expected to be a strong effect modifier, we first evaluated the presence of significant interaction between OSA risk levels and surgical procedure, by examining the change in estimates across a 2x3 interaction matrix. If there was evidence of significant interaction, subsequent analyses were stratified by high and low surgical risk strata. A logistic regression model was developed using variables described in the univariate analysis section and identified to have univariate associations or determined to be clinically relevant by the investigators. The PSAP risk score was the primary independent variable. A low PSAP score was considered the reference group against which the two higher risk categories of PSAP score were compared. We did not evaluate the influence of individual component variables of the PSAP score in the multivariate model. The dependent variable of the primary model was the occurrence of unplanned early postoperative intubation. Each of the preoperative, and intraoperative characteristics indicated above were evaluated as independent risk factor variables. We evaluated the assumption of linearity of logits for each ordinal or continuous exposure or covariate by plotting the logits and examining the incremental ORs to determine the need for ordinal or indicator variable coding. Variables with a linear relationship with the outcome were used as ordinal categorical variables, whereas variables were coded as indicator variables when the assumption of linearity was not met. Once the form of the variable was

finalized, each variable was initially included in the multivariate model. To determine if a variable should remain in the final multivariate model, we applied a change in estimate criteria. Starting with the fully specified model, the covariate with the largest Wald p-value was removed. When the change in estimate as judged by ln[ORfull/ORfull-1] was >10%, the covariate was retained as a potential risk factor. When the change in estimate was <10%, the covariate was removed from the model. To arrive at a parsimonious set of characteristics in the final multivariate model, the assessment continued until the first variable was reached that produced a change in estimate of >10%. Study estimates were presented as Adjusted Odds Ratios (AOR) and 95% confidence intervals (CI). Missing data frequencies were examined for presence of >5% missingness. In this eventuality, we planned to perform unadjusted 2x2 analyses to compare the PRC rates between patients with missing and complete data. Model discrimination was examined by the c-statistic. Model diagnostics were performed to test model stability and multicollinearity. Variables with variance inflation factors of greater than 10 were considered suspect, and thus evaluated for removal from the model. Additionally, the Hosmer-Lemeshow test and condition indices were evaluated. Acondition index threshold of 30 was imposed, in the eventuality of which we planned Pearson correlation matrices to identify specific pairs of correlated variables. The goodness-of-fit of the models was evaluated using the omnibus tests of model coefficients. If there was poor fit, we planned to perform internal model validation using Somers Dxy optimism estimates on the bootstrapped data.

Results

After study exclusions, a study cohort of139,844 patients wasincluded for descriptive analyses (Fig 1). Based on the PSAP score, 67,284(48%) were screened to be at low risk,61,372(44%) at moderate risk and 11,188(8%) at high risk of having OSA. Of the cohort, 51,137(37%) did not receive NMBA, cisatracurium was administered in 8,630(6%), rocuronium in 5933 (4%) and vecuronium in 74144 (53%). Additionally, 21995 (16%) received a high dose of NMBA.427 patients developed early PRC requiring unplanned tracheal intubation.

Fig 1: Study flow



PSAP perioperative sleep apnea prediction score

Univariateanalysis

Unadjusted analysis revealed significant differences in the distribution of study variables across the outcome and control groups (Table 1). The following conditions were more frequent among patients who developed PRC: higher PSAP score categories, history of smoking, myocardial infarction, chronic obstructive pulmonary disease, liver disease, renal disease, congestive heart failure, neurological conditions, seizures, cancer, steroid use, pneumonia, pulmonary hypertension, sepsis and higher ASA physical status. There were significant differences in most

of the intraoperative anesthesia interventions, with the exception of high dose NMBA, number of packed red blood cell units and hydromorphone usage.Among patients who developed early PRC, there was a significantly higher frequency of NMBA administration, NMBA administration with reversal agent and use of TOF monitoring. Similarly, patients with early PRC had significantly higher frequency of regional anesthesia usage.

Table 1: Frequency distribution of study variables across outcome groups

Variable	**No Early Postoperative Intubation N=139,417**	**Early Postoperative Intubation N= 427**	**p-value**	**Odds Ratio (95% Confidence Interval**
Risk for OSA (PSAP categories)				
Low Risk	67,146 (48)	138 (32)	<0.001	N/A
Moderate Risk	61,163 (44)	209 (49)		
High Risk	11,108 (8)	80 (19)		
PSAP variables				
Age ≥ 43 years	97, 983 (70)	344 (81)	<0.001	1.8 (1.4 – 2.2)
Male	64,030 (46)	244 (57)	<0.001	1.6 (1.3 – 1.9)
BMI ≥ 30 kg/m^2	51,533 (37)	177 (42)	0.056	1.2 (1.0 – 1.5)
History of Snoring	47,950 (34)	172 (40)	0.012	1.3 (1.1 – 1.6)
History of hypertension	55,066 (40)	236 (55)	<0.001	1.9 (1.6 – 2.3)
History of diabetes mellitus	18,244 (13)	101 (24)	<0.001	2.1 (1.6 – 2.6)
Mallampati 3 or 4	25,774 (19)	121 (28)	<0.001	1.7 (1.4 – 2.2)
Thick Neck	20,096 (14)	89 (21)	<0.001	1.6 (1.2 – 2.0)
Short thyromental distance	6,169 (4)	26 (6)	0.093	1.4 (0.9 – 2.1)
Preoperative conditions				
Smoking	18,180 (13)	70 (16)	0.041	1.3 (1.0 – 1.7)
Alcohol intake	9,849 (7)	33 (8)	0.578	1.1 (0.8 – 1.6)
Myocardial infarction	81 (0)	2 (1)	0.027	8.1 (2.0 – 33.0)
COPD	7,659 (6)	68 (16)	<0.001	3.3 (2.5 – 4.2)
Liver disease	8,124 (6)	39 (9)	0.005	1.6 (1.2 – 2.3)
Renal disease	11,802 (9)	80 (19)	<0.001	2.5 (2.0 – 3.2)
Congestive heart failure	4,015 (3)	32 (8)	<0.001	2.7 (1.9 – 3.9)
Neurological disease	17,664 (13)	81 (19)	<0.001	1.6 (1.3 – 2.1)
Seizures	3,576 (3)	17 (4)	0.088	1.6 (1.0 – 2.6)
Cancer	39,102 (28)	147 (34)	0.004	1.3 (1.1 – 1.6)
Steroid treatment	5,555 (4)	38 (9)	<0.001	2.4 (1.7 – 3.3)
Pneumonia	4,201 (3)	34 (8)	<0.001	2.8 (2.0 – 4.0)
Pulmonary hypertension	1,786 (1)	16 (4)	<0.001	3.0 (1.8 – 5.0)
Coma	748 (1)	4 (1)	0.299	1.8 (0.7 – 4.7)
Sepsis	967 (1)	8 (2)	0.011	2.7 (1.4 – 5.5)
ASA physical status				

Class 1, 2 or 3	134,542 (97)	371 (89)	<0.001	4.3 (3.2 – 5.8)
Class 4 or 5	3,964 (3)	47 (11)		
Pre-operative Opioid	34,664 (25)	127 (30)	0.020	1.3 (1.0 – 1.6)
Pre-operative Benzodiazepine	15,121 (11)	66 (16)	0.003	1.5 (1.2 – 2.0)
Admission Status				
Outpatient	66,601 (48)	90 (21)	<0.001	N/A
Admit on day of surgery	56,408 (41)	222 (52)		
Preoperative admission	16,408 (12)	115 (27)		
Anesthesia duration quartiles				
<25th centile	10,347 (7)	2 (1)	<0.001	N/A
25 - 49th centile	34,501 (25)	25 (6)		
50 - 74th centile	47,764 (34)	136 (32)		
≥ 75th centile	46,805 (34)	264 (62)		
Intraoperative aminoglycoside	14,717 (11)	58 (14)	0.045	1.3 (1.0 – 1.8)
Anesthesia technique				
General Anesthesia	125,496 (90)	365 (85)	0.001	1.6 (1.2 – 2.0)
General + Regional Anesthesia	13,921 (10)	63 (15)		
Primary general anesthetic technique				
Propofol infusion	16,445 (12)	24 (6)	<0.001	N/A
Volatile anesthetic	109,809 (79)	254 (60)		
Combined propofol infusion and volatile	13,163 (9)	149 (35)		
Quartile of duration of MAC above 1				
<25th centile	5,774 (4)	30 (7)		
25 - 49th centile	12,992 (9)	69 (16)	<0.001	N/A
50 - 74th centile	56,226 (40)	211 (49)		
≥ 75th centile	64,425 (46)	117 (27)		
NMBA administered				
~~No NMBA used~~	~~51,065 (37)~~	~~72 (17)~~	<0.001	N/A
Cisatracurium	8,599 (6)	31 (7)		
Rocuronium	5,893 (4)	40 (9)		
Vecuronium	73,860 (53)	284 (67)		
NMBA dose ≥75th centile	21,941 (16)	54 (13)	0.086	0.8 (0.6 – 1.0)
No NMBA administered	51,065 (37)	72 (17)	<0.001	N/A
NMB with reversal agent administration	87,303 (17)	350 (82)		
NMB without reversal agent administration	1,049 (1)	5 (1)		
Any TOF use	52,741 (38)	190 (45)	0.005	1.3 (1.1 – 1.6)
Opioid analgesic use	34,664 (25)	127 (30)	0.020	1.3 (1.0 – 1.6)
Reversal use	82,823 (59)	325 (76)	<0.001	2.2 (1.7 – 2.7)
PRBC administration	2,959 (2)	25 (6)	<0.001	2.9 (1.9 – 4.3)
FFP administration	583 (0)	4 (1)	0.107	2.3 (0.8 – 6.0)
Intraoperative opioid				
Fentanyl	130,879 (94)	381 (89)	<0.001	0.5 (0.4 – 0.7)

Hydromorphone	6,430 (5)	22 (5)	0.573	1.1 (0.7 – 1.7)
Morphine	40,081 (29)	123 (29)	0.999	1.0 (0.8 – 1.2)
Number of intravenous opioids				
0	4,949 (4)	24 (6)	0.003	N/A
1	84,169 (60)	231 (54)		
2	48,232 (35)	159 (37)		
3	2,050 (2)	13 (3)		
4	17 (0)	0 (0)		
Quartiles of intraoperative morphine equivalents				
<25th centile	65,549 (47)	302 (71)	<0.001	N/A
25 - 49th centile	38,521 (28)	70 (16)		
50 - 74th centile	20,350 (15)	38 (9)		
≥ 75th centile	14,997 (11)	17 (4)		
Naloxone	906 (1)	22 (5)	<0.001	8.3 (5.4 – 12.8)
PCA orders	195 (0)	7 (2)	<0.001	11.9 (5.6 – 25.4)

Interaction between surgical services and OSA risk

Surgical procedure classified as high risk proceduresbased on the included CPT codes for surgical interventions involving intracranial, intrathoracic, spinal cord, upper abdominal, or lower abdominal body locations, radiological procedures and surgery for burns. Low risk surgery CPT codes involved CPT codes for surgical interventions involving neck, extrathoracic, perineal, pelvic, upper leg or knee, popliteal, lower leg, shoulder, upper arm, forearm and other body locations. Suspected OSA interacted significantly with high surgical risk as shown in Table 2.

Table 2: Interaction between PSAP score and surgical risk

PSAP risk	Low risk surgery		High risk surgery	
	AOR	p-value	AOR	p-value
Low	0.4 [0.3, 0.6]	<0.0001	0.7 [0.5, 1.1]	0.10
Moderate	0.6 [0.4, 0.8]	0.004	1.5 [1.1, 2.0]	0.12
High	1.7 [1.1, 2.6]	0.015	2.2 [1.5, 3.4]	<0.0001

High surgical riskmodel

Higher PSAP score categories: moderate PSAP score [AOR 1.6; 95% CI 1.2, 2.2; p=0.004] and high PSAP score [AOR 2.0; 95% CI 1.3,3.1; p=0.002] were independently

associated with early postoperative intubationwhen compared to low PSAP risk of OSA (Table 3). Other factors independently associated with the outcome include smoking history, COPD, pneumonia, inpatient status, duration of anesthesia, anesthesia type, duration of anesthetic exposure of greater than 1 MAC, morphine use, high dose vecuronium (protective), , patient controlled analgesia,naloxone administration, and NMBA administration with reversal.

Table 3: Independent predictors of early postoperative tracheal intubation, high surgical risk stratum

	AOR	95% C.I.		p-value
		Lower	Upper	
PSAP Score (OSA risk)				
Low risk (PSAP 1-3)	Baseline			
Moderate risk (PSAP 4-5)	1.6	1.2	2.2	0.004
High risk (PSAP >5)	2.0	1.3	3.1	0.002
Preoperative conditions				
Smoking	1.5	1.0	2.1	0.037
COPD	2.4	1.7	3.4	<0.001
Cancer	1.3	1.0	1.7	0.073
Steroid treatment	1.5	1.0	2.4	0.063
Pneumonia	2.2	1.4	3.4	<0.001
Procedural conditions				
Admission status				
Outpatient	Baseline			
Admit on day of surgery	1.0	0.6	1.6	0.962
Preoperative admission	2.0	1.2	3.1	0.004
Anesthesia duration ≥ 75th centile	1.6	1.1	2.2	0.008
Primary general anesthetic technique				
Propofol infusion	Baseline			
Volatile anesthetic	0.3	0.2	0.6	<0.001
Combined propofol infusion and volatile	1.5	0.8	2.8	0.229
≥ 75th centile of duration of MAC above 1	0.4	0.3	0.6	<0.001
Morphine	0.7	0.5	0.9	0.009
High dose Vecuronium	0.5	0.3	0.8	0.005
Patient controlled analgesia	4.2	1.5	11.7	0.007
Naloxone administration	7.9	4.7	13.4	<0.001
No NMB administration	Baseline			
NMB with reversal agent administration	4.2	2.3	7.5	<0.001

NMB without reversal agent administration	0.0	0.0	0.0	0.995

Low surgical risk model

Among patients undergoing low risk surgery, high PSAP score category was independently associated with early PRC (Table 4). Other factors associated with early PRC with low risk surgery include cancer, admission status, anesthesia duration, duration of anesthetic exposure to MAC above 1, high dose rocuronium, patient controlled analgesia, number of intraoperative opioids, morphine, fentanyl, and hydromorphone usage.

Table 4: Independent predictors of early postoperative tracheal intubation, Low surgical risk

	AOR	95% C.I.		p-value
		Lower	Upper	
PSAP Score (OSA risk)				
Low risk (PSAP 1-3)	Baseline			
Moderate risk (PSAP 4-5)	1.1	0.8	1.7	0.507
High risk (PSAP >5)	2.7	1.7	4.2	<0.001
Preoperative conditions				
Renal Failure	1.6	1.0	2.5	0.060
Cancer	1.5	1.1	2.1	0.016
Procedural conditions				
Admission status				
Outpatient	Baseline			
Admit on day of surgery	2.2	1.4	3.5	0.001
Preoperative admission	3.8	2.3	6.3	<0.001
Anesthesia duration ≥ 75th centile	2.6	1.8	3.9	<0.001
Primary general anesthetic technique				
Propofol infusion	Baseline			
Volatile anesthetic	1.2	0.6	2.4	0.638
Combined propofol infusion and volatile	4.6	2.2	9.9	<0.001
≥ 75th centile of duration of MAC above 1	0.6	0.4	0.8	0.001
High dose Rocuronium	4.6	1.8	11.6	0.001
Patient controlled analgesia	6.4	1.5	27.6	0.013
Number of intraoperative opioids	2.1	1.4	3.2	<0.001
Morphine	0.3	0.2	0.6	<0.001
Fentanyl	0.2	0.1	0.4	<0.001
Hydromorphone	0.3	0.1	0.8	0.019

Model diagnostics

The c-statistic (± standard error) of the primary logistic regression model was 0.81±0.020. The variance inflation factors were below 10 and condition indices of test variables were all below 30. The omnibus test of model coefficients revealed a chi-square of 236.830 for the low surgical risk model and 370.731 for the high surgical risk model with 19 degrees of freedom $p < 0.001$.

Discussion

Suspected OSA as screened by the PSAP score is associated with independent increases in risk of unplanned early postoperative intubation. This outcome relationship in patients with suspected OSA is mediated in part by surgical procedural risk. . This study provides important and novel information on the value of preoperative screening for OSA, as outcome modification may be possible through more judicious use of NMBAs. OSA is a highly prevalent condition that is largely undiagnosed, making preoperative screening relevant to clinicians. Preoperative diagnosis and PAP treatment of patients with OSA is associated with reduced risk of developing postoperative cardiopulmonary complications. The study findings further advance our understanding of the relationship between OSA and surgical risk states.

In this study, we evaluated the interaction between OSA risk and surgical risk in an *a priori* manner. However, other significant conditions and interventions were independently associated with the outcome in the stratified multivariate models. Specific characteristics of NMBA management that influence outcomes have recently been evaluated. Higher doses of NMBA, avoidance of neostigmine, higher doses of neostigmine, and lack of adequate recovery neuromuscular monitoring using train of four have all been implicated in increased risk of developing PRC.[27]In the high risk surgical stratum, use of NMBA with neostigmine reversal was associated with significantly greater odds of early PRC, whereas avoidance of neostigmine was not. This may indicate the usage of neostigmine preferentially in some patients who are demonstrating signs of neuromuscular weakness. It may also reflect inherent limitations in the pharmacodynamics of competitive reversal at the neuromuscular junction, in the setting of residual NMBA effect. Some of this clinical effect may also be attributed to excessive use of neostigmine, as this has been shown to induce muscle weakness. In contrast, avoidance of neostigmine reversal with NMBA was not associated with early PRC. This could be related to the clinical decisions surrounding the timing of tracheal extubation when neostigmine is avoided

in this single institution study. It is possible that some of the patients with clinically detectable residual paralysis were left intubated and transferred to PACU for management of their respiratory care needs. This specific practice pattern would potentially result in the avoidance of reintubation since extubation is then performed in PACU after clinical demonstration of full recovery, without need for reversal. Further, reintubation may not be necessary to manage all patients with residual paralysis. TOF monitoring was also not associated with the study outcome. This may indicate inherent limitations to gross motor responses to qualitative monitoring techniques, in contrast to more objective measures of muscle response such as acceleromyography.[28] Further research is warranted to examine the interactions between OSA risk, specific NMBA agents, and dosing patterns of NMBA with neostigmine with an aim to identify higher risk strategies of NMBA management in patients with suspected OSA.

Study measures of general anesthesia were independently associated with outcome occurrence. The combined use of propofol infusion and volatile anesthesia was associated with early PRC when compared to propofol infusion alone in low surgical risk patients. Longer exposures of MAC >1 seemed protective in bothstratified models, suggesting that clinical behavior may be different in sicker patients at greater risk of PRC, with a tendency to lower levels of anesthesia exposure.[29] Thus, higher MAC exposures in this study may indeed be reflective of the low risk status of the patient in the real-time clinical assessment of the provider. In contrast, longer anesthesia exposures irrespective of MAC level were strongly associated with increased risk. This rather conflicting finding does warrant further investigation to determine if the outcome variance is related to anesthetic depth or anesthetic agent.

We acknowledge the possibility of bias from misclassification of both our primary health outcome and variables of interest. In order to minimize misclassification bias, objective measures were used to define the outcome and covariates whenever possible. By consulting with our programmers, each variable had explicit definitions within defined time-frames and

threshold values where applicable. Retrospective studies may also be prone to selection bias, because the outcome has already occurred and risk factors are known before study inclusion. To avoid selection bias, all inclusion and exclusion criteria were identical across the low, moderate and high PSAP score groups. The same covariates were examined in the entire study population for the primary and sensitivity analyses models. Clinical screening for OSA in itself has significant challenges as we have shown previously.[30] High test heterogeneity and false negative rates are specific concerns. The PSAP score threshold of 3 is associated with a high sensitivity >90%, comparable with the STOP-Bang score. However, the low specificity and positive predictive value, relative to the low outcome prevalence, mean that a significant number of patients screened as having moderate and high risk of OSA will be false positives. The most common consequence of high false positive rates is the risk of potential cost or harm from unnecessary interventions. Prospective studies may be warranted in order to better understand the cost-benefit relationship of wider or stricter use of specific interventions. Unlike previous investigators, we chose a stricter definition of PRC that was not complication-specific. This may have underestimated the number of patients with PRC that required additional respiratory care through application of non-invasive ventilation or extended intensive care unit stay. Despite these limitations and considerations, this study provides novel information about the potential value of preoperative screening for OSA, and identifies suspected OSA patientsas potential targetsfor intraoperative modifiability of early PRC.

In summary, we report that suspected OSA based on the PSAP score is independently associated with increased risk of early PRC requiring invasive airway placement or more intensive respiratory care. Surgical procedural risk modifies early PRC risk by effecting a synergistic interaction with PSAP risk categories. Specific anesthetic techniques were independently associated with early PRC, pointing to the potential for examining effect modification through these exposures in future studies.

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Appendix 1

Patient Characteristics and Risk Factors

DEMOGRAPHICS, ANTHROPOMETRICS, AND COMORBIDITIES VARIABLES

PSAP Score Variables: The following variables are components of the PSAP score.Patients meeting the inclusion criteria will be retrospectively classified into groups at low, moderate and high risk of OSA using PSAP score. The score is calculated as follows:

- Low risk of OSA = <3 variables
- Suspected OSA
    - Moderate risk of OSA = 3-5 variables
    - High risk of OSA = greater than or equal to 6 variables

The variables in PSAP score are: age>43 years, male gender, body mass index >30 kg/m2, history of snoring, history of type 2diabetes mellitus, history of hypertension, documented thick neck (subjective estimation), estimated thyromental distance <6 cm, and modified Mallampati score 3 or 4. These variables are not weighted as per the validation analysis published previously.[19]The presence of moderate or high risk of OSA (PSAP > or =3 variables) will initially be included as an independent variable in the prediction model. Variables will be identified based upon the pre-defined MPOG, AIMS or Centricity data fields.

AGE

-Dataset Location= local UMHS MPOG database
-Variable Name= AIMS_Patient_Age_Years
-Variable Type= Both dichotomous and continuous

Age will be included (either 43 years and over, or under 43 years old) as a dichotomous outcome for the PSAP score. It will be a primary variable used to determine eligibility for the study, and is also one the variables used to determine PSAP score. Thus, age will be evaluated as a risk factor for our primary outcome.

GENDER

-Dataset Location= local UMHS MPOG database
-Variable Name= AIMS_Sex
-Variable Type= Dichotomous

Male gender is one of the factors included in PSAP score, and therefore may be associated with our health outcome of interest. Male gender (yes/no) will be considered a dichotomous outcome for the PSAP score.

BODY MASS INDEX

-Dataset Location= local UMHS MPOG database
-Variable Name= AIMS_Body_Mass_Index
-Variable Type= Categorical

To improve clinical usability, body mass index will be classified using the World Health Organization groups: underweight (less than 18.50 kg/m2), normal weight (18.50–24.99 kg/m2), overweight (25.00–29.99 kg/m2), obese class I (30.00–34.99 kg/m2), obese class II (35.00–39.99 kg/m2), and obese class III (>=40.00 kg/m2). Obesity class I and greater will be considered a dichotomous outcome for the PSAP score.

SNORING

-Dataset Location= Centricity
-Variable Name= Pulmonary>Snoring
-Variable Type= Dichotomous

Snoring will be considered a dichotomous (yes/no) outcome for the PSAP score

DIABETES MELLITUS TYPE II

-Dataset Location= Centricity
-Variable Name= Centricity>Endocrine>Diabetes>Type 2
- Variable Type= Dichotomous

Type 2 Diabetes is one of the factors included in PSAP score, and therefore may be associated with our health outcome of interest. It will be considered a dichotomous (yes/no) outcome for the PSAP score

HYPERTENSION

-Dataset Location= local UMHS MPOG database
-Variable Name= 70031 Cardiovascular – Hypertension
-Variable Type= Dichotomous

Patients with a diagnosis of hypertension will be identified as having the condition. It will be considered a dichotomous (yes/no) outcome for the PSAP score. Medications being used to treat existing hypertension will be included in the "home medications" variable.

NECK CIRCUMFERENCE

-Dataset Location= local UMHS MPOG database
-Variable Name= Neck_Anatomy
-Variable Type= Dichotomous

Neck circumference is one of the factors included in PSAP score, and therefore may be associated with our health outcome of interest. Documented estimation of presence of thick neck on anesthesia H&P will be considered a dichotomous (yes/no) outcome for the PSAP score.

MODIFIED MALLAMPATI SCORE

-Dataset Location= local UMHS MPOG database
-Variable Name=
    70001 Airway - Mallampati Score
    70007 Airway - Mallampati_Neutral
-Variable Type= Dichotomous (either 3 or 4, or not 3 or 4)

Mallampati Score is one of the factors included in PSAP score, and therefore may be associated with our health outcome of interest. Mallampati scores 3 and 4 on anesthesia H&P will be considered a dichotomous (yes/no) outcome for the PSAP score.

THYROMENTAL DISTANCE

-Dataset Location= local UMHS MPOG database
-Variable Name= Hyoid_to_Mentum_Subjective
-Variable Type= Dichotomous

Thyromental distance is one of the factors included in PSAP score, and therefore may be associated with our health outcome of interest. Estimated thyromental distance less than 6 cm on preoperative anesthesia H&P will be considered a dichotomous (yes/no) outcome for the PSAP score.

Additional Variables to be Analyzed

IDEAL BODY WEIGHT

- Dataset Location= local UMHS MPOG database
- Variable Name= MPOG_Ideal_Body_Weight
- Variable Type= Continuous

Ideal Body weight will be used to quantify tertile of intraoperative NMB dosage

CURRENT SMOKER

-Dataset Location= local UMHS MPOG database
-Variable Name= 70128 History - Tobacco
-Variable Type= Dichotomous

Smoking will be treated as a dichotomous variable, and evaluated for potential association with respiratory failure postoperatively.

ALCOHOL USE

-Dataset Location= local UMHS MPOG database
-Variable Name= 70126 History - Social History - Alcohol
-Variable Type= Dichotomous

While alcohol use has not been linked explicitly to our health outcome of interest, it is an important patient characteristic that may be a risk factor. Therefore, we are including alcohol use in our analysis as a dichotomous variable; low or no use versus moderate or high use.

DYSPNEA

-Dataset Location= Centricity Cardiovascular>cardiac symptoms>dyspnea at rest OR dyspnea on exertion OR orthopnea OR paroxysmal nocturnal dyspnea
Pulmonary>Symptoms>SOB
-Variable Name= 70040 Cardiac
-Variable Type= Dichotomous

Dyspnea is indicative of respiratory health problems, and may therefore be linked to PRC. Patients with a history of dyspnea will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

PULMONARY HYPERTENSION

-Dataset Location= Centricity>Pulmonary>Other – pulm>pulmonary HTN OR MPOG
-Variable Name= 70036 Cardiovascular - Pulmonary Hypertension
-Variable Type= Dichotomous

Pulmonary hypertension is indicative of respiratory health problems, and may therefore be linked to PRC. Patients with a diagnosis of pulmonary hypertension will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

COPD

-Dataset Location= local UMHS MPOG database
-Variable Name= 70115 Respiratory - COPD General
-Variable Type= Dichotomous

Patients with a diagnosis of COPD will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

PNEUMONIA

-Dataset Location= local UMHS MPOG database
-Variable Name= 70138 Respiratory - Bronchitis / Pneumonia
-Variable Type= Dichotomous

Patients with a diagnosis of pneumonia will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

DIABETES

-Dataset Location= local UMHS MPOG database
-Variable Name= 70046 Endocrine - Diabetes
-Variable Type= Categorical

Patients with a diagnosis of diabetes will be identified as having the condition. The disease will be treated as a categorical variable, with the patient being flagged as either having or not having the condition by type.

LIVER DISEASE

-Dataset Location= local UMHS MPOG database
-Variable Name= 70052 GI - Liver Disease
-Variable Type= Dichotomous

Patients with a diagnosis of liver disease will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

RENAL FAILURE

-Dataset Location= local UMHS MPOG database
-Variable Name= 70060 Renal / Urologic - Renal Failure
-Variable Type= Dichotomous

Patients with a diagnosis of renal failure will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having renal failure.

HISTORY OF CAD

-Dataset Location= local UMHS MPOG database
-Variable Name= 70027 Cardiovascular
-Variable Type= Dichotomous

Patients with a diagnosis of Coronary Artery Disease will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having a history of CAD.

RECENT CAD EVENT

-Dataset Location= Centricity
-Variable Name= Cardiovascular>MI> either “less than 7 days” OR between 7 and 30 days”
-Variable Type= Dichotomous

Recent Myocardial Infarction is a well-known comorbidity affecting negative surgical outcomes.

CONGESTIVE HEART FAILURE

-Dataset Location= local UMHS MPOG database
-Variable Name= 70026 Cardiovascular - Congestive Heart Failure
-Variable Type= Dichotomous

Patients with a diagnosis of Congestive Heart Failure will be identified as having the condition.

The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

SENSORIUM OR COMA

-Dataset Location= Centricity

-Variable Name= Endo/Neuro/Pain>Neuro sign/Sx>acute altered mental status OR Chronic altered mental status OR Coma OR Delirium Tremens OR Encephalopathy

-Variable Type= Dichotomous

Patients with a diagnosis of coma will be identified as having the condition. Sensorium or coma will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

PRIOR NEUROLOGIC CONDITION

-Dataset Location= local UMHS MPOG database

-Variable Name=

70085 Neuro - Cerebral Aneurysm
70086 Neuro - Cerebrovascular Disease
70087 Neuro - CNS Tumor
70088 Neuro - Cerebrovascular Accident
70089 Neuro - Dementia
70090 Neuro - Other
70091 Neuro - Peripheral Nerve Disease
70093 Neuro - Seizures
70094 Neuro - Symptoms

-Variable Type= Dichotomous/Categorical

Patients with a diagnosis of a preexisting neurologic condition will be identified as having the condition. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having a prior neurologic condition. Conditions listed under “other neurological conditions” include ALS, Alzheimer’s Disease, Cerebral Aneurysm, Cerebral Palsy, Cervical Radiculopathy, CNS tumor, CVA, dementia, developmental delay, Eclampsia, Encephalocele, H/O head trauma, increased ICP, lumbar radiculopathy, mental retardation, migraine headaches, multiple sclerosis, myelomeningocele, neuropathy, Parkinson’s Disease, PNS disorder, Restless Leg Syndrome, Spina Bifida, spinal cord injury, subarachnoid hemorrhage, subdural hemorrhage, Tethered Cord Syndrome, and TIA.

MYASTHENIA GRAVIS

-Dataset Location= local UMHS MPOG database

-Variable Name= Aims_preop, 70090

-Variable Type= Dichotomous

Patients with a diagnosis of Myasthenia Gravis will be identified as having the disease. The disease will be treated as a dichotomous variable, with the patient being flagged as either having or not having cancer.

CANCER

-Dataset Location= local UMHS MPOG database

-Variable Name=

70068 Hematologic - Malignancy
70100 Misc - Malignancy (Solid or Hematologic)
70101 Misc - Solid Organ Malignancy Metastasis

-Variable Type= Dichotomous

Patients with a diagnosis of cancer will be identified as having the disease. The disease will be

treated as a dichotomous variable, with the patient being flagged as either having or not having cancer.

STEROID USE

-Dataset Location= local UMHS MPOG database
-Variable Name= 70076 General - Medications - Chronic Steroid Use
-Variable Type= Dichotomous

Chronic steroid use will be noted from the patients' history and will be treated as a dichotomous variable.

PREOPERATIVE SEPSIS

-Dataset Location= local UMHS MPOG database
-Variable Name= 70039 ID - Sepsis
-Variable Type= Dichotomous

Patients with a diagnosis of sepsis will be identified as having the condition. The condition will be treated as a dichotomous variable, with the patient being flagged as either having or not having the condition.

PRIOR OPERATION WITHIN 30 DAYS

-Dataset Location= Centricity Anesthesia H&P
-Variable Name= Prior Operation
-Variable Type= Dichotomous

This variable will be manually calculated by our programmer. The data query looks at each individual patient identifier and looks for prior completed intraoperative anesthesia record. The variable will be coded in a binary fashion (yes/no). Patients with prior surgery within 30 days are excluded from the analyses.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS (ASA) PHYSICAL STATUS CLASSIFICATION

-Dataset Location= local UMHS MPOG database
-Variable Name= ASA_Class
-Variable Type= Categorical

The ASA status is a mature risk assessment tool with 6 categorical values and has repeatedly been demonstrated to be one of the strongest perioperative risk adjustment variables available.

HOME MEDICATIONS

-Dataset Location= local UMHS MPOG database
-Variable Name= 70077 General-Medications-Current
-Variable Type= Categorical

All home medications are categorized according to the National Library of Medicine RxNorm categorization system, allowing facile retrieval and risk adjustment of underlying patient risk.

PROCEDURAL AND ANESTHETIC RISK FACTORS

SURGICAL COMPLEXITY SCORE: The surgical complexity score was derived using a previously established technique from the primary CPT code.[25, 26] This approach computes a continuous score using a logistic regression model to predict the study primary outcome. Adjusted estimates for each CPT code were then converted to the logarithmic scale and applied to model as an independent variable.

PRIMARY ANESTHESIA CPT CODE (Exclude liver transplant, labor/delivery, caesarian section)

-Dataset Location= local UMHS MPOG database

-Variable Name= Charge_Capture_Primary_Anesthesia_Code

-Variable Type= Categorical

Procedure type will be identified for exclusion purposes. These anesthesia code types are an additional method to ensure the accuracy of data query in completely excluding cases deemed inadmissible for the analysis.

DURATION OF PROCEDURE (ANESTHESIA, IN-ROOM, AND SURGICAL)

-Dataset Location= local UMHS MPOG database

-Variable Name=

Anesthesia_Start_DT
Anesthesia_End_DT
Patient_In_Room_DT
Patient_Out_Of_Room_DT
Procedure_Start_DT
Procedure_End_DT

-Variable Type= Continuous

Duration of the procedure will be recorded as a continuous variable and used for analyses to determine any correlation between length of procedure and postoperative morbidity. We will also use the anesthesia time to determine dose tertiles of NMB use.

AMINOGLYCOSIDE GIVEN

-Dataset Location= local UMHS MPOG database

-Variable Name= Aims_intraopmedications, 10202 (gentamicin), 10203 (gentamicin), 10023 (Amikacin), 10131 (clindamycin), 10313 (neomycin), 10314 (neomycin), 10207 (neomycin)

-Variable Type= Dichotomous

Aminoglycoside administration will be reported as a dichotomous variable: yes/no for use of any of the listed aminoglycosides in the intraoperative medication administration record

USE OF GENERAL ANESTHESIA

-Dataset Location= local UMHS MPOG database/Centricity

-Variable Name= either of the two intubation variables

- Centricity Object_Sys 20442 __ mm __ ET tube taped at __ cm
- MPOG ID 50122 Intubation Endotracheal Tube Size

-Variable Type= Dichotomous

Use of general anesthesia will be identified for inclusion in this study. The variable will be reported as dichotomous: yes/no for use of general anesthesia.

USE OF NEURAXIAL ANESTHESIA

-Dataset Location= local UMHS MPOG database

-Variable Name= 50691 Categorized note - Neuraxial anesthesia

-Variable Type= Dichotomous

Use of neuraxial anesthesia will be reported as a dichotomous variable: yes/no for use of neuraxial anesthesia.

PERIPHERAL NERVE BLOCKADE

-Dataset Location= local UMHS MPOG database

-Variable Name= 50199 Monitoring - Neuromuscular blockade -- peripheral nerve

stimulator placed
-Variable Type= Dichotomous

Use of a peripheral nerve blockade will be reported as a dichotomous variable: yes/no for use of peripheral nerve blockade.

PROPOFOL INFUSION

- Variable(s) Used = (10377, 10378, 10453, 10572, 10577, 10578, 10579, 10597, 10639, 10649
- Dataset Location = local UMHS MPOG database
- Variable Type = dichotomous

Propofol use will be identified. The receipt of propofol will be treated as a dichotomous variable with "No Use of Propofol" serving as the reference group.

USE OF INHALED ANESTHETIC MEDICATION

-Dataset Location= local UMHS MPOG database
-Variable Name= Any of the following >0.5
3260 IsofluraneExp%
3270 SevofluraneExp%
3280 DesfluraneExp%
-Variable Type= Dichotomous

Use of inhaled anesthetic medication will be treated as a dichotomous variable: yes/no if Isoflurane, Sevoflurane, or Desflurane are used in a quantity greater than 0.5. Each inhaled agent will be treated as a distinct dichotomous variable for logistic regression.

ANESTHETIC EXPOSURE

-Dataset Location= Centricity
-Variable Name=
3260 IsofluraneExp%
3270 SevofluraneExp%
3280Desflurane Exp%
-Variable Type= Continuous

Typically, general anesthesia is maintained by continuous infusion of a modern inhaled anesthesia medication: isoflurane, sevoflurane, or desflurane. Every 60 seconds, the AIMS automatically records the concentration of the medication administered to the patient and expired by the patient. The depth of general anesthesia is calculated using a comparison of expired anesthetic concentration to the ED50 and ED95 for that medication, adjusted for patient age.

The following concepts will be evaluated for inclusion in the model

1. Median calculated depth of anesthesia adjusted for age: MAC (or expired agent) during anesthesia. Each 5 min period has a calculated MAC for the entire case MAC (age adjusted, with Propofol) = Propofol rate (in mcg/kg/min) / 150 + [ExpiredSevoflurane / 1.8 + + [Expired Isoflurane / 1.17 + + [Expired Desflurane / 6.6 + + [Expired Nitrous / 104] x 10 ^ (.00269 x (age of patient – 40)).[24]
2. Highest age-adjusted MAC within 30 min before extubation. This value will be included as an independent continuous variable during sensitivity analyses to evaluate effect on outcome variance.

TOF VALUES AROUND EMERGENCE

-Dataset Location= local UMHS MPOG database
-Variable Name= Aims_intraopphysiologic, 3330
-Variable Type= Continuous

0,1 = deep, moderate (2), mild (3-4) measured within 30 minutes of extubation without subsequent dose NMB. Capture nil value as “no TOF measured.

NMB ADMINISTRATION

-Dataset Location= local UMHS MPOG database

-Variable Name=

cisatracurium MPOG ID 10129
vecuronium MPOG ID 10446
rocuronium MPOG ID 10393
Neostigmine (MPOG ID 10315)
Edrophonium (MPOG ID 10046, 10170)
Physostigmine (MPOG ID 10360)

-Variable Type=dichotomous for use of NMB, categorical for choice of drug

Neuromuscular blocking agents (NMBAs) and agents used for their reversal will be identified. NMBAs include any line item on the day of surgery indicating receipt of:,rocuronium, vecuronium, or cisatracurium. NMBA reversal agents include any line item on the day of surgery indicating receipt of: edrophonium, neostigmine or pyridostigmine.

To evaluate this risk, we will develop an ordinal categorical variable with the reference group being “No NMBA”, group 1 including “Any NMBA use without reversal agent use” and group 2 including “Any NMBA use with reversal agent use”.

NMB AMOUNT

-Dataset Location= local UMHS MPOG database

-Variable Name=

cisatracurium MPOG ID 10129
vecuronium MPOG ID 10446
rocuronium MPOG ID 10393

-Variable Type= continuous for dose, durations

Neuromuscular blocking agents (NMBAs) will be identified. NMBAs include any line item on the day of surgery indicating receipt of: suxamethonium or succinylcholine, rocuronium, vecuronium, atracurium, or cisatracurium. In each patient, we will calculate dose of NMB mg/kg IBW/hour of anesthesia time (continuous) for the relaxant that is used the greatest quantity throughout the procedure. Within each relaxant, the highest quartile of administered NMB/IBW/hr. anesthesia time will be converted to a dichotomous variable of high dose NMB.

OPIOID MEDICATION ADMINISTRATION

- Variable(s) Used = Morphine MPOG ID 10306; Fentanyl MPOG ID 10186; Hydromorphone MPOG ID 10219, Naloxone MPOG ID 10312
- Dataset Location = local UMHS MPOG database
- Variable Type = dichotomous and continuous

Peri-operative (during the procedure and during time in PACU) receipt of opiate pain medications will be identified. The opioids of interest are: Fentanyl, Sufentanil, Alfentanil, Morphine, Hydromophone Oxycodone, Remifentanil. The receipt of an intra- or post - operative opiate use will be treated as a dichotomous variable with “No Use of peri-operative Opiate” serving as the reference group. Additionally, we will explore the use of the opioid antagonist naloxone. The receipt of an intra- or post - operative naloxone use will be treated as a dichotomous variable with “No Use of peri-operative naloxone” serving as the reference group.

OPIOID AMOUNT

- Variable(s) Used = Morphine MPOG ID 10306; Fentanyl MPOG ID 10186; Hydromorphone MPOG ID 10219, Naloxone MPOG ID 10312
- Dataset Location = local UMHS MPOG database
- Variable Type = dichotomous and continuous

Peri-operative (during the procedure and during time in PACU) receipt of opiate pain medications will be identified. The opioids of interest are: Fentanyl, Sufentanil, Alfentanil, Morphine, Hydromophone Oxycodone, Remifentanil. The dose of opioid per mg/kg IBW/hour of anesthesia time (continuous) will be calculated for each patient. When multiple opioids are used total opioid equivalence will be calculated. Within each opioid, the highest quartile of administered opioid/IBW/hr. anesthesia time will be converted to a dichotomous variable of high dose NMB. (**for mg/kg calculations, use both IBW and TBW for sensitivity analyses**)

FLUID BALANCE

-Dataset Location= local UMHS MPOG database

-Variable Name= Fluids in/Fluids out

MPOG_EBL_ml_Actual
MPOG_EBL_ml_CE
MPOG_Urine_ml_Actual
MPOG_PRBC_ml_Actual
MPOG_PRBC_Unit_Actual
MPOG_Salvaged_Blood_ml_Actual
MPOG_Salvaged_Blood_Unit_Actual
MPOG_Salvaged_Blood_ml_Eq
MPOG_Salvaged_Blood_ml_CE
MPOG_FFP_ml_Actual
MPOG_FFP_Unit_Actual
MPOG_FFP_ml_Eq
MPOG_FFP_ml_CE
MPOG_Cryoprecipitate_ml_Actual
MPOG_Cryoprecipitate_Unit_Actual
MPOG_Cryoprecipitate_ml_Eq
MPOG_Cryoprecipitate_ml_CE
MPOG_Platelet_ml_Actual
MPOG_Platelet_Unit_Actual
MPOG_Plat_Bags_Given
MPOG_Platelet_ml_Eq
MPOG_Platelet_ml_CE
MPOG_WBC_ml_Actual
MPOG_WBC_Unit_Actual
MPOG_WBC_ml_Eq
MPOG_WBC_ml_CE
MPOG_Crystalloid_ml_Actual
MPOG_Crystalloid_Unit_Actual
MPOG_Crystalloid_ml_CE
MPOG_Crystalloid_Unit_CE
MPOG_Colloid_ml_Actual
MPOG_Colloid_Unit_Actual

MPOG_Colloid_ml_CE
MPOG_Colloid_Unit_CE

-Variable Type= Categorical and Continuous

All patient fluid input and output, including intravenous fluids, blood products, urine output, estimated blood loss, surgical drains (chest tube, wound drains, gastric tubes, etc.) are recorded in detail. These data will be collected from the local UMHS MPOG dataset.

The following concepts will be included in the model

a. Total fluids given in ml/kg/hour
b. PRBC used – number of packs
c. FFP used – number of packs
d. Platelets used – y/n