Preoperative STOP-BANG Scores and Postoperative Delirium and Coma in Thoracic Surgery Patients

Running Head: STOP-BANG Scores and delirium and coma

Sophia Wang*, MD[1,2]; Ninotchka Liban Sigua*, MD[3,] Shalini Manchanda[3], MD; Steve Gradney, MD[3] Sikandar H. Khan, DO[3], Anthony Perkins, MS[4,5], Kenneth Kesler MD[6], Babar Khan, MD, MS[2,3,7]

*Drs Wang and Sigua contributed equally to this work.

[1]Department of Psychiatry, Indiana University School of Medicine, IU Health Neuroscience Center, 355 W. 16th Street, Suite 4800, GH, Room 4250, Indianapolis, IN. 46202-7176
[2]Sandra Eskenazi Center for Brain Care Innovation, Eskenazi Hospital, Indianapolis, IN
[3]Division of Pulmonary, Critical Care, Sleep and Occupational Medicine, Department of Internal Medicine, Indiana University School of Medicine, Indianapolis, IN
[4]Center of Health Innovation and Implementation Science, Center for Translational Science and Innovation, Indianapolis, IN
[5]Indiana Clinical and Translational Research Institute, Indiana University School of Medicine, Indianapolis, IN
[6] Department of Cardiothoracic Surgery, Indiana University School of Medicine, Indianapolis, IN
[7]IU Center of Aging Research, Regenstrief Institute, Indianapolis, IN

Classifications: thoracic surgery, STOP-BANG, obstructive sleep apnea, delirium, postoperative complications

Word count: 4912

Corresponding author
Sophia Wang, MD
355 W 16th Street, Suite 4800 GH, Room 4250, Indianapolis, IN 46202
Email: sophwang@iupui.edu

This is the author's manuscript of the article published in final edited form as:Wang, S., Sigua, N. L., Manchanda, S., Gradney, S., Khan, S. H., Perkins, A., … Khan, B. (2018). Preoperative STOP-BANG Scores and Postoperative Delirium and Coma in Thoracic Surgery Patients. The Annals of Thoracic Surgery. https://doi.org/10.1016/j.athoracsur.2018.05.089

ABSTRACT

Background: Obstructive sleep apnea (OSA) is associated with higher rates of postoperative delirium. The relationship between preoperative OSA risk and postoperative delirium and coma in thoracic surgery patients hospitalized in the intensive care unit (ICU) is not well understood. This study tests the hypothesis that thoracic surgery patients hospitalized in ICU with a higher preoperative risk for OSA are more likely to develop postoperative delirium and coma, resulting in longer hospital stays.

Methods: Preoperative OSA risk was measured using the STOP-BANG questionnaire. STOP-BANG scores of ≥ 3 were defined as intermediate-high risk for OSA. 128 patients who underwent major thoracic surgery completed the STOP-BANG questionnaire preoperatively. The Richmond Agitation and Sedation Scale was used to assess level of consciousness. The Confusion Assessment Method for the ICU was used to assess for delirium. Linear regression was used to assess the relationship between risk of OSA and outcome measures. Results were adjusted for age, gender, body mass index, Charlson Comorbidity Index, instrumental activities of daily living, and surgery type.

Results: 96 out of 128 patients (76%) were in the intermediate-high risk OSA group. Adjusted analyses showed that the intermediate-high risk OSA group had a longer duration of postoperative ICU delirium and coma compared to the low risk OSA group (1.4 days ± 1.3 vs 0.9 days ± 1.4; $P = 0.04$). Total number of hospital days was not significantly different.

Conclusions: Higher preoperative risk for OSA in thoracic surgery patients was associated with a longer duration of postoperative delirium and coma.

Postoperative delirium is defined as an acute change in mental status after a surgical procedure, and is characterized by new onset disturbances in attention and awareness. It is associated with longer hospital stays, increased risk of institutionalization, and higher mortality rates.[1] The prevalence of postoperative delirium ranges from 5.3-42% in thoracic surgery patients,[2-8] to 16-92% in post-surgical ICU patients.[9,10] Despite growing recognition of the need to prevent postoperative delirium,[1] strategies which target potentially modifiable risk factors in the preoperative setting are limited.

One such potentially modifiable risk factor may be preoperative obstructive sleep apnea (OSA). OSA is a sleep disorder caused by repetitive upper airway obstruction resulting in intermittent hypoxia and sleep fragmentation. It is associated with a higher risk of postoperative delirium.[11-14] The prevalence of OSA is 9-24% in the general population,[15,16] but is significantly higher in surgical populations (33-70%).[13,17] In fact, preoperative rates of undiagnosed OSA may be as high as 80%.[18] It is not known whether OSA is associated with postoperative coma, a common phenomenon in ICU patients. Taken together, these findings suggest a need to better understand the relationship between preoperative OSA risk and acute changes in cognitive functioning (namely delirium and coma) in post-surgical patients who are hospitalized in the ICU. This study tests the hypothesis that thoracic surgery patients hospitalized in ICU who have a higher preoperative risk for OSA are more likely to develop postoperative delirium and coma, resulting in longer hospital stays.

PATIENTS AND METHODS

Data Source

The data in this study were collected as part of the PEPOD (PrEventing Postoperative Delirium) trial (Clinical Trial Registration Number NCT02213900). The PEPOD trial was a randomized, double blind, placebo-controlled single center clinical trial whose primary aim examined the

effects of low-dose haloperidol on postoperative delirium in patients undergoing major thoracic surgery. The STOP BANG study was a planned a priori exploratory subanalysis nested in the original trial of the PEPOD study. The Institutional Review Board of Indiana University Purdue University Indianapolis approved the study. Patients provided the informed consent prior to enrollment.

Study Population

The trial was conducted at Indiana University Hospital, a 257-bed tertiary hospital that serves the population of Indianapolis, Indiana, from October 2013-June 2015. Patients were eligible to be enrolled in the study if they were English speaking, older than or equal to 18 years of age, and undergoing major thoracic surgery. Patients were excluded if they had a history of schizophrenia, Parkinson's disease, severe dementia, alcohol abuse, neuroleptic malignant syndrome, haloperidol allergy, pregnant or nursing, on cholinesterase inhibitors or levodopa, or a corrected QT (QTc) interval > 500 milliseconds. Study personnel identified eligible patients who fulfilled the inclusion and exclusion criteria and were undergoing pre-operative evaluation at the outpatient surgery center prior to their surgery. Eligible patients were then approached for informed consent.

Pre-operative risk assessment and chart documentation of OSA

Consented patients completed the STOP-BANG questionnaire during their pre-operative evaluation. Briefly, the STOP-BANG is an 8 item validated questionnaire to screen for OSA.[19,20] The acronym STOP-BANG is based on the first letter of each of the screening questions: Snoring, Tired, Observed (to stop breathing), Pressure (high blood pressure), Body Mass Index more than 35 kg/m^2, Age (older than 50), Neck size ≥ 40 centimeters, Gender (male). The risk for OSA is categorized with STOP-BANG scores 0-2 is considered to be low risk; 3-4 to be intermediate risk for OSA, and 5-8 to be high risk for OSA. Based on validation studies of the

STOP-BANG questionnaire and clinical trials utilizing STOP-BANG to identify patients who may benefit from OSA treatment, a score of STOP-BANG ≥3 was used to demarcate patients with OSA, *i.e.* the intermediate and high risk groups were combined to create the intermediate-high risk group for OSA.[21,22]

Charts were also reviewed for diagnosis and treatment of pre-operative OSA. Eighteen patients had a chart diagnosis of preoperative OSA that was confirmed with a sleep study. Three of them had a resolution of OSA with weight loss or surgery; 5 were using the CPAP at home; 2 were using bilevel positive airway pressure (bilevel PAP) at home; 3 used a CPAP or bilevel PAP in the hospital; and 8 were not compliant or not using CPAP or bilevel PAP at home.

Delirium assessment and management

Postoperative patients were screened for coma and delirium twice a day using the Richmond Agitation Sedation Scale (RASS)[23,24] and the Confusion Assessment Method for the ICU (CAM-ICU) respectively, throughout their entire hospital stay.[25,26] RASS was first administered to all patients to determine the level of consciousness. Coma was defined as a RASS score of -4 or -5. Research assistants then administered the CAM-ICU in patients who had a RASS score ≥ -3. Patients were considered delirious if they had a positive CAM-ICU result, achieved by showing signs of acute change in mental status or fluctuating course, displaying features of inattention, and either disorganized thinking or altered level of consciousness. If the subject screened positive for delirium with the CAM-ICU on either assessment during that day, they were considered to be delirious for that day. Duration of postoperative delirium and coma was defined as the total number of days a patient was either comatose or CAM-ICU+ during their entire hospital stay.[27-30] Delirium severity was measured using the Delirium Rating Scale-Revised-98 (DRS-R-98).[31] Trained and blinded research assistants collected all data points.[26]

A delirium rescue protocol was implemented to manage symptoms in both the control and treatment arms who developed delirium while enrolled in the study. The protocol focused on pain control through use of fentanyl, morphine, or hydromorphone, and management of agitation/sedation through use of propofol in mechanically ventilated patients and dexmedetomidine in non-mechanically ventilated patients. Open label antipsychotics were discouraged during the intervention phase, but the primary services were not otherwise restricted in their prescribing of haloperidol or other anti-psychotics.

Statistical Analysis

Patients in both the placebo (n = 67) and treatment (n = 68) arms were included in the final analyses. Treatment assignment was included in the final analyses. Given the few patients with known OSA which required treatment (*n* = 15) and who were treated with CPAP and biPAP while in the hospital (*n* = 3), treatment of OSA with CPAP and bilevel biPAP was not included in the model as a covariate.

Fisher's Exact Test was used to test for differences in categorical variables between the intermediate-high risk and low risk groups. Due to the skewed distribution of the continuous variables, the Wilcoxon Rank Sum test was used to test for differences for continuous variables between the risk groups. Models were adjusted for covariates ($P \leqslant 0.10$), including age, gender, body mass index (BMI), Charlson Comorbidity Index (CCI), instrumental activities of daily living (IADLs), surgery type, and treatment assignment. Logistic regression was used to determine the association of OSA risk with the incidence of delirium and postoperative complications (arrhythmia, QT prolongation, deep venous thrombosis, physical restraints, re-intubation). Generalized linear models was used to determine the association of OSA risk with all continuous outcomes. The dependent variables for these models was transformed using the transformation log(days+1) to account for the skewedness of the outcome measures.

To ensure logistic regression results were not affected by surgery type, a propensity score analysis was also performed. The predicted probability of esophagectomy was estimated using the following variables: age, surgery duration, previous chemotherapy, estimated blood loss, and benzodiazepine dose during surgery. These probabilities were grouped into quintiles, and we then performed a stratified logistic reqression of OSA risk with coma/delirium incidence. Results were similar to the logistic regression (OR 3.3 (1.3-8.4); p=0.013). Hence logistic regression results were included in the manuscript. All data analyses were conducted using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

128 patients who underwent major thoracic surgery completed the STOP-BANG questionnaire. Thirty-one patients were considered to be at low risk for OSA. Sixty patients were intermediate risk (STOP-BANG scores 3-4), and thirty-seven were high risk (STOP scores 5-8). There were no differences between the intermediate and high risk groups in the prevalence rates of delirium (26.7% vs 27.0%) and of coma and delirium (78.3% vs 83.8%). Therefore, the intermediate and high risk groups were combined into the intermediate-high risk group for the rest of the analyses. Table 1 compares the baseline and clinical characteristics for low risk versus intermediate-high risk for OSA. Patients in the intermediate-high risk group were more likely to be older, male, have a higher BMI, have a lower number of independent IADLs, and higher number of comorbidities compared to the low-risk group (all $P < 0.05$). There were no differences in ethnicity, education level, procedure type, or intraoperative characteristics.

Table 2 compares postoperative ICU delirium, postoperative ICU delirium and coma, and hospital outcomes for high risk versus low risk OSA groups. A logistic regression model was used to examine the incidence of postoperative delirium and incidence of postoperative delirium

and coma while controlling for age, gender, BMI, CCI, IADLs, and surgery type. There was no significant difference in the incidence of postoperative delirium (P = 0.7). The intermediate-high risk group was 3.6 times more likely to have postoperative delirium and coma compared to the low risk group (P = 0.035). Generalized linear models were used to examine the duration of postoperative delirium and coma, duration of delirium, hospital or ICU length of stay, and number of days on mechanical ventilation, while controlling for age, gender, BMI, CCI, IADLs, and surgery type. The intermediate-high risk group had a longer duration of postoperative delirium and coma compared to the low risk group (1.4 days vs 0.9 days; P = 0.04). There were no statistical differences between the high and low risk OSA groups for duration of delirium, hospital or ICU length of stay, and number of days on mechanical ventilation.

Table 3 compares postoperative procedures, clinical outcomes, and complications. There were no significant differences between procedures (transfusion, sedating medications administered), clinical outcomes (postoperative pulse oximetry or hemoglobin) or complications (arrhythmia, QTc prolongation, deep venous thrombosis, restraints, intubation) between the low risk and the intermediate-high risk OSA groups.

COMMENT

Acute changes in the cognitive status of postoperative patients predict poorer clinical outcomes, including higher rates of mortality and morbidity. Our study showed that postoperative delirium affects nearly a quarter of thoracic surgery patients hospitalized in the ICU. We also found that patients with higher preoperative OSA risk were more than three times likely to develop postoperative delirium and coma. However, there was no association between preoperative OSA risk and delirium prevalence, or length of stay in the ICU or hospital. One possible reason we did not detect these expected differences may have been that we used the RASS and CAM-ICU, which are screening tools for delirium. The gold standard for the diagnosis of delirium is a

clinical assessment by delirium experts using the criteria from the *Diagnostic and Statistical Manual of Mental Disorders,* criteria. Another reason is that if a patient had two negative screens on the same day, this counted as a delirium free day. A patient could have had detectable delirium between the times of these evaluations. Therefore, it is possible that we did not detect all cases of delirium.

Our findings about the correlation between OSA and postoperative coma and delirium are significant because previous studies have examined only postoperative delirium as the major outcome. Several landmark studies of ICU delirium have examined coma and delirium as a single clinical outcome, rather than delirium alone, because it may more accurately reflect the acute changes in the cognitive status in this population. Critically ill patients are often comatose due to severity of medical illness, mechanical ventilation, and medications administered for pain and agitation. Patients who are comatose cannot be assessed for delirium. One possible reason that we found a difference for coma and delirium but for not delirium alone could be that this combined outcome may be more sensitive to acute cognitive changes in the ICU. This difference could not be explained by medications administered or perioperative events, and suggests that the higher risk of OSA may predispose towards the development of coma.

Our findings are not consistent with previous literature, which suggests a connection between OSA and postoperative delirium. Flink, *et al.* have shown in a prospective observational study in patients undergoing elective knee arthroplasty that OSA was associated with more than 4-fold increased risk for incident postoperative delirium.[13] In patients undergoing cardiac surgery, increased risk of postoperative delirium was associated with a preoperative Apnea-Hypopnea Index (AHI) of more than 19 events per hour.[12] These inconsistencies may have been due to type of different populations, the use of polysomnography (PSG) to assess OSA, and a lack of power in our study to detect a difference in the rates of delirium.

There is a high rate of undiagnosed OSA in patients undergoing elective surgery as these patients frequently do not undergo routine PSG, the gold standard to diagnose OSA. To address the concern about undiagnosed OSA, we administered the STOP-BANG questionnaire, a rapid screening tool that categorizes patients into different OSA risk categories. The STOP-BANG was initially validated in the surgical population, and its use has been extended to include preoperative and primary care clinics.[13,31] The sensitivity for a STOP-BANG score of 3 or more to predict any severity OSA, moderate to severe OSA, and severe OSA is at 83.9%, 92.9% and 100%, respectively.[21] Nevertheless, the STOP-BANG has its limitations. One clinical trial found that the STOP-BANG was a poor predictor of OSA severity as measured by residual Apnea–Hypopnea Index (AHI),[33] and it is noted that residual AHI strongly correlated to delirium in both non-ICU and ICU patients.[12,33] This possible limitation of the STOP-BANG may also explain why we only saw a difference for delirium and coma outcome but not for delirium alone.

Although studies have shown that postoperative delirium is associated with longer hospital and ICU stays, we found that there were no association between preoperative OSA risk and length of ICU and hospital stays. Possible reasons for inconsistent results include the differences in the setting and type of surgeries. Earlier studies were completed in the general hospital setting and patients mostly underwent non-cardiothoracic surgeries. Since the patients in our study were placed in the ICU immediately after their surgery, they were monitored more closely, which in turn may have minimized adverse outcomes that would prolong the hospital and ICU length of stay, and mechanical ventilation days. Second, a systematic review showed that there was no differences in ICU or hospital stays between patients who had OSA compared to those without OSA.[11] These findings and our results suggest that OSA alone does not affect length of stay.

The exact mechanism connecting OSA and postoperative ICU delirium is still not well understood. The correlation between residual AHI and postoperative delirium suggest that intermittent hypoxia and/or sleep fragmentation are two potential etiologies. Intermittent hypoxia that occurs in OSA results in a chronic oxidative state, which may lead to cholinergic neuronal injury, and eventually increase vulnerability to delirium. Sleep fragmentation from OSA results in cognitive impairment, which may then lead to the development of delirium.[11,13] Postoperative oxygenation and hemoglobin levels were not significantly different between the low and intermediate-high risk groups, which argues against hypoxia being an explanation for the difference in the delirium and coma. However, continuous oxygen monitoring measurements and data about supplemental oxygen use were not available, so this interpretation needs to be confirmed. Sleep fragmentation was not assessed, and therefore, its contribution to the differences in delirium and coma cannot be determined in our study.

In summary, this study supports a connection between OSA and postoperative delirium and coma in thoracic surgery patients who have been hospitalized in the ICU. Future studies will be needed to validate these findings in a larger population and will need to use more sensitive, objective measures of hypoxia and sleep fragmentation (e.g. residual AHI, continuous monitoring of postoperative oxygen levels) in order to better understand the mechanisms of how preoperative OSA may lead to the development of postoperative delirium and coma in ICU patients.

REFERENCES

1. American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. J Am Coll Surg. 2015 Feb;220(2):136-48.e1.

2. Yonekura H, Hirate H, Sobue K. Incidence, Risk Factors, and Effects on Outcome of Postoperative Delirium in Patients Undergoing Esophagectomy. *Masui*. 2015;64:597-602.

3. Jeong DM, Kim JA, Ahn HJ, et al. Decreased Incidence of Postoperative Delirium in Robot-assisted Thoracoscopic Esophagectomy Compared With Open Transthoracic Esophagectomy. *Surg Laparosc Endosc Percutan Tech*. 2016;26:516-522.

4. Shiono S, Abiko M, Sato T. Postoperative complications in elderly patients after lung cancer surgery. *Interact Cardiovasc Thorac Surg*. 2013;16:819-823.

5. Yildizeli B, Ozyurtkan MO, Batirel HF, et al. Factors associated with postoperative delirium after thoracic surgery. *Ann Thorac Surg.* 2005;79:1004-1009.

6. Markar SR, Smith IA, Karthikesalingam A, Low DE. The clinical and economic costs of delirium after surgical resection for esophageal malignancy. *Ann Surg.* 2013;258:77-81.

7. Booka E, Tsubosa Y, Matsumoto T, et al. Postoperative delirium after pharyngolaryngectomy with esophagectomy: a role for ramelteon and suvorexant. *Esophagus*. 2017;14:229-234.

8. Takeuchi M, Takeuchi H, Fujisawa D, et al. Incidence and risk factors of postoperative delirium in patients with esophageal cancer. *Ann Surg Oncol.* 2012;19:3963-3970.

9. Abelha FJ, Luís C, Veiga D, et al. Outcome and quality of life in patients with postoperative delirium during an ICU stay following major surgery. *Crit Care*. 2013;17:R257.

10. Theuerkauf, N., Guenther, U., Putensen, C. Postoperative delirium in the PACU and intensive care unit. *Trends Anaesh Crit Care*. 2012;2:148–155.

11. Gaddam S, Gunukula SK, Mador MJ. Post-operative outcomes in adult obstructive sleep apnea patients undergoing non-upper airway surgery: a systematic review and meta-analysis. *Sleep Breath*. 2014 Sep;18(3):615-633.

12. Roggenbach J, Klamann M, von Haken R, et al. Sleep-disordered breathing is a risk factor for delirium after cardiac surgery: a prospective cohort study. *Crit Care* 2014;18:477.

13. Flink BJ, Rivelli SK, Cox EA, et al. Obstructive sleep apnea and incidence of postoperative delirium after elective knee replacement in the nondemented elderly. *Anesthesiology*. 2012; 116: 788–796.

14. Mirrakhimov AE, Brewbaker CL, Krystal AD, Kwatra MM. Obstructive sleep apnea and delirium: exploring possible mechanisms. *Sleep Breath*. 2014;18:19-29.

15. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177:1006–1014.

16. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-1235.

17. Amra B, Niknam N, Sadeghi MM, et al. Obstructive sleep apnea and postoperative complications in patients undergoing coronary artery bypass graft surgery: a need for preventive strategies. *Int J Prev Med*. 2014;5:1446-1451.

18. Wolfe RM, Pomerantz J, Miller DE, et al. Obstructive Sleep Apnea: Preoperative Screening and Postoperative Care. J Am Board. Fam *Med*. 2016;29:263-275.

19. Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A practical approach to to screen for obstructive sleep apnea. *Chest* 2016;149:631-638.

20. Toronto Western Hospital, University Health Network, University of Toronto (2012). Screening - STOPBang.ca. Retrieved from http://www.stopbang.ca/osa/screening.php. Accessed March 11, 2018.

21. Nagappa M, Liao P, Wong J, et al. Validation of the STOP-Bang Questionnaire as a Screening Tool for Obstructive Sleep Apnea among Different Populations: A Systematic Review and Meta-Analysis. *PLoS One*. 2015;10:e0143697.

22. Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. *Chest*. 2016;149:631-638.

23. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med. 2002 Nov 15;166:1338-1344.

24. ICU Delirium and Cognitive Impairment Study Group (2003). Richmond Agitation Sedation Scale (RASS). Retrieved from http://www.icudelirium.org/docs/RASS.pdf. Accessed on March 11, 2018.

25. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-1379.

26. ICU Delirium and Cognitive Impairment Study Group (2003). Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Retrieved from http://www.icudelirium.org/docs/CAM_ICU_training.pdf. Accessed on March 11, 2018

27. Girard TD, Pandharipande PP, Carson SS, et al; MIND Trial Investigators. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. *Crit Care Med* 2010;38:428-437.

28. Page V, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med* 2013;1:515-523.

29. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med* 2014;42:1024-1036.

30. Barnes-Daly MA, Phillips G, Ely EW. Improving Hospital Survival and Reducing Brain Dysfunction at Seven California Community Hospitals: Implementing PAD Guidelines Via the ABCDEF Bundle in 6,064 Patients. *Crit Care Med* 2017;45:171-178.

31. Trzepacz PT, Mittal D, Torres R, et al. Validation of the Delirium Rating Scale-revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci* 2001;13:229-242.

32. Finkel KJ, Searleman AC, Tymkew H, et al. Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Med* 2009;10:753-758.

33. Nadler JW, Evans JL, Fang E, et al. A randomised trial of peri-operative positive airway pressure for postoperative delirium in patients at risk for obstructive sleep apnoea after regional anaesthesia with sedation or general anaesthesia for joint arthroplasty. *Anaesthesia* 2017;72:729-736.

Table 1. Preoperative and Intraoperative Clinical Characteristics based on OSA Risk.

Characteristic	Low risk for OSA (N = 31)	Intermediate-High risk for OSA (N = 97)	P-Value
Male, %	51.6 (16)	82.5 (80)	0.001
Age (years)	50.6 (18.0)	62.8 (9.3)	0.001
BMI (kg/m^2)	26.8 (5.6)	30.1 (7.2)	0.019
Caucasian, %	93.6 (29)	97.9 (94)	0.250
Education (years)			
HS Grad or Less	40.0 (N=12)	57.6 (N=53)	0.198
Some College or Less	36.7 (N=11)	28.3 (N=26)	
Bachelor's Degree or More	23.3 (N=7)	14.1 (N=13)	
Preoperative diagnosis of OSA, %	3.2 (N=1)	17.5 (N=17)	0.071
CCI (0-33)	2.3 (2.5)	3.1 (2.2)	0.010
APACHE	16.2 (7.8)	18.3 (7.1)	0.240
ADL	6.0 (0.2)	6.0 (0.2)	1.000
IADL	7.8 (0.5)	7.3 (1.1)	0.002
ASA Class			0.675
I	0.0 (0)	0.0 (0)	
II	3.2 (1)	2.1 (2)	
III	96.8 (30)	96.9 (94)	
IV	0.0 (0)	1.0 (1)	
Surgery type			
Esophagectomy, %	45.2 (14)	67.0 (65)	0.066
Ivor Lewis	11	55	
Other	3	10	
Pneumonectomy	3.2 (1)	3.2 (1)	
Left	1	1	
Thoracotomy, %	51.6 (16)	32.0 (31)	
Lobectomy/bilobectomy with mediastinal dissection, *n*	6	15	
Lobectomy/bilobectomy, *n*	2	4	
Mediastinal dissection, *n*	6	3	
Other, *n*	2	9	
Intra-operative Data			
Duration of Surgery hours	3.9 (1.7) 4.1 (2.3 – 5.0)	3.8 (1.7) 4.0 (2.6-5.1)	0.784
Duration of Anesthesia hours	5.5 (1.7) 5.7 (4 -6.4)	5.4 (1.8) 5.4 (3.8-6.7)	0.740
Estimated Blood Loss ml	212 (172) 125 (100-300)	210 (142) 150 (100-300)	0.757
Amount of Volume Infused Intra-operatively			

Total volume ml	2733 (1535) 2600 (1400-3500)	2478 (1222) 2500 (1500-3100)	0.425
Crystalloid volume ml	2292 (1243) 2100 (1400-3000)	2033 (882) 1905 (1410-2500)	0.330
Colloid volume ml	434 (432) 500 (0-500)	472 (472) 500 (0-750)	0.719
Intra-operative Dose			
Total Opioid Dose	31.1 (12.1) 31.7 (21.7-34.7)	33.5 (14.2) 31.7 (25-38.3)	0.632
Total Fentanyl Dose	255 (117) 250 (150-300)	279 (132) 250 (250-300)	0.368
Total Hydromorphone Dose	0.8 (0.3) 1 (0.5-1.0)	0.8 (0.4) 1 (0.5-1.0)	0.805
Total Benzodiazepine Dose	24.4 (24.1) 12.5 (5-55)	26.0 (23.4) 12.5 (7.5-52.5)	0.556

Continuous variables are expressed as mean (SD). Dichotomous variables are expressed as % (N). Low risk for OSA = STOP-BANG score ≤ 2. Intermediate-high risk for OSA = STOP-BANG score ≥ 3. OSA = obstructive sleep apnea; BMI = body mass index; SD = Standard Deviation; CCI = Charlson Comorbidity Index; APACHE = Acute Physiologic and Chronic Health Evaluation; ASA = American Society of Anesthesiologists; ADL = activities of daily living; IADL = instrumental activities of daily living

Table 2. Delirium and Hospital Outcomes by OSA Risk.

Outcome	Low risk for OSA (N = 31)	Intermediate-High risk for OSA (N = 97)	Odds Ratio or Beta (95% CI)	Adjusted P-Value
Delirium and coma, %	45.2 (14)	80.4 (78)	3.6 (1.1 – 11.9)	0.032
Length of Delirium and Coma (days)	0.9 (1.4)	1.4 (1.3)	0.26 (0.01, 0.51)	0.042
Length of delirium and coma in delirious patients	3.0 (2.0)	2.7 (1.6)	0.13 (-0.39, 0.66)	0.603
Delirium, %	19.4 (6)	26.8 (26)	1.3 (0.4, 4.6)	0.679
Length of Delirium (days)	0.2 (0.4)	0.4 (0.8)	0.06 (-0.14, 0.26)	0.522
Duration in delirious patients	1.0 (0.0)	1.5 (0.8)	0.26 (-0.06, 0.58)	0.101
Mean Daily DRS-R-98	0.7 (0.6)	1.5 (1.7)	0.17 (-0.06, 0.41)	0.138
Length of ICU Stay (days)	2.2 (2.5)	2.9 (2.2)	0.16 (-0.13, 0.45)	0.283
Length of Hospital Stay (days)	9.0 (3.8)	10.3 (3.9)	0.06 (-0.07, 0.19)	0.374
Length of Mechanical Ventilation (days)	1.0 (1.9)	1.1 (1.2)	0.19 (-0.04, 0.42)	0.104

Continuous variables are expressed as mean (SD). Dichotomous variables are expressed as % (N). Logistic regression models were used to assess for dichotomous outcomes. Generalized linear models were used to assess for continuous outcomes. All linear regression models were performed on the log transformation. All models were adjusted for age, gender, surgery type, Charlson comorbidity index score, IADL, randomization group, and BMI.
OSA = obstructive sleep apnea; BMI = body mass index; SD = standard deviation; CI = Confidence Interval.

Table 3. Postoperative Outcomes, Procedures, and Complications by on OSA Risk.

Postoperative outcome, procedure, or complication	Low risk for OSA (N = 31)	Intermediate-High risk for OSA (N = 97)	P-Value
Outcome or procedure			
Postoperative transfusion n (%)	6.4 (2)	5.2 (5)	0.676
Initial postoperative pulse oximetry	93.2 (3.3) 94 (91-95)	92.4 (3.1) 93 (91-94)	0.273
Initial postoperative hemoglobin	11.7 (1.8) 11.5 (10.3-12.6)	11.8 (1.5) 11.7 (10.9-12.7)	0.565
Number of days post-operative medications administered			
Opioid	4.0 (2.2) 3 (2-5)	4.8 (3.2) 4 (2-6)	0.310
Benzodiazepines	1 (1.9) 0 (0 -1)	1.2 (2.3) 0 (0-1)	0.968
Antipsychotic	0.1 (0.3) 0 (0-0)	0.5 (1.9) 0 (0-0)	0.660
% Comatose patients who received medication the same day			
Opioid	12.9 (4)	18.6 (18)	0.590
Benzodiazepine	6.4 (2)	6.2 (6)	1.000
Antipsychotic	0.0 (0)	4.1 (4)	0.572
Any opioid, benzo, or antipsychotic	12.9 (4)	20.6 (20)	0.434
Postoperative complications			
Arrhythmia	2 (6.5%)	16 (16.5%)	0.237
QT prolongation	1 (3.2%)	6 (6.2%)	1.000
Deep venous thrombosis	0 (0.0%)	6 (6.2%)	0.335
Physically Restraints	9 (29.0%)	38 (39.2%)	0.393
Re-intubation	3 (9.7%)	5 (5.2%)	0.400

Dichotomous variables are expressed as % (N). Continuous variables are expressed as mean (SD).