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# Postoperative Complications in Patients with Obstructive Sleep Apnea.

**Abstract: 235 words**

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## Postoperative complications in patients with Obstructive Sleep Apnea.

Roop Kaw, Vinay Pasupuleti, Esteban Walker, Anuradha Ramaswamy, Nancy Foldvary-Schaefer.

### Abstract

**Background.** Unrecognized obstructive sleep apnea (OSA) is associated with unfavorable perioperative outcomes among patients undergoing non-cardiac surgery (NCS).

**Methods.** Our study population was chosen from 39,771 patients who underwent internal medicine preoperative assessment between January 2002 and December 2006. Patients undergoing NCS within 3 years of polysomnography (PSG) were considered for the study, whileas those < 18 years of age; with history of upper airway surgery and minor surgery under local or regional anesthesia were excluded. Patients with an apnea-hypopnea index (AHI)  $\geq 5$  were defined as OSA and those with AHI < 5 as controls. For adjusting baseline differences in age, sex, race, BMI, type of anesthesia, American Society of Anesthesiology class and medical co-morbidities, the patients were classified into five quintiles according to a propensity score.

**Results.** Out of a total of 1759 patients who underwent both Polysomnography and NCS, 471 met the study criteria. Of these 282 patients had OSA and the remaining 189 served as controls. Presence of OSA was associated with higher incidence of postoperative hypoxemia (OR= 7.9; p=0.009), overall complications (OR= 6.9; p=0.003); ICU transfer (OR 4.43; p=0.069) and higher length of hospital stay, (OR= 1.65; p=0.049). Neither AHI, nor use of home CPAP before surgery was associated with postoperative complications (p=0.3; 0.75 respectively) or length of stay (p = 0.97; 0.21 respectively).

**Conclusions.** Patients with OSA are at higher risk for postoperative hypoxemia, ICU transfers and longer hospital stay.

## **Abbreviation list:**

OSA: Obstructive Sleep Apnea

PSG: Polysomnography

NCS: Non-cardiac Surgery

BMI: Body-mass index

AHI: Apnea-Hypopnea index

CPAP: Continuous positive airway pressure

PAP: Positive airway pressure

IMPACT: Internal Medicine Preoperative Assessment, Consultation & Treatment

RF: Respiratory failure

MI: Myocardial infarction

CHF: Congestive heart failure

DM: Diabetes Mellitus

COPD: Chronic obstructive pulmonary disease

CAD: Coronary artery disease

REM: Rapid eye movement

ODI: oxygen desaturation index

RDI: respiratory distress index

ASA: American Society of Anesthesiology

LOS: Length of Stay

## Introduction

Obstructive Sleep Apnea (OSA) has been known to be associated with heterogeneous manifestations of cardiovascular disease<sup>1</sup> and is now known to be an independent risk factor for increased mortality.<sup>2</sup> Recent studies have also reported OSA to be a risk factor for increased postoperative morbidity and mortality.<sup>3-8</sup> In 1993, approximately 4% of men and 2% of women in the age group of 30-60 years were estimated to have OSA syndrome.<sup>9</sup> No epidemiologic studies have been conducted to determine the prevalence of OSA in the general surgical population. The problem is further hindered by the difficulty in diagnosing OSA, as patients with OSA may present for surgery without a prior diagnosis. Depending upon the reported series the prevalence in patients presenting for surgery has been estimated to be 1 to 9%<sup>10</sup> and 24% when Berlin questionnaire was used for preoperative screening.<sup>11</sup> It was notable that OSA has not been diagnosed in the majority of the preoperative population.

It is estimated that between 1990 and 1998, there was a 12 fold increase in the diagnosis of OSA in surgical outpatients.<sup>12</sup> In a more recent series of 433 patients undergoing general surgery, 18 of 41 patients suspected to have sleep apnea agreed to undergo polysomnography (PSG) and the majority (78%) were found to have OSA as defined by Apnea Hypopnea Index (AHI)  $\geq 5$ .<sup>13</sup> As such, a significant number of patients with sleep apnea may present for surgery without receiving a prior diagnosis. Although published guidelines exist, OSA is often neither suspected preoperatively nor considered clinically relevant enough to warrant preoperative screening or intervention.<sup>6</sup> Additionally the existing guidelines lack scientific evidence and for the most part are based on expert consensus.



## **Methods and Materials**

*Specific Aims.* Our study had the following specific aims:

1. To study the frequency and nature of postoperative complications in patients with unrecognized or previously diagnosed OSA undergoing elective non-cardiac surgery.
2. To analyze the impact of severity of OSA as measured by the apnea-hypopnea index on the incidence of postoperative complications.

### *Study Population*

The study population was chosen from 39,771 patients who underwent preoperative physical examination and assessment at the IMPACT (Internal Medicine Preoperative Assessment Consultation and Treatment) center between January 2002 and December 2006. This electronic record was cross-referenced with the sleep laboratory database to identify patients who underwent NCS within 3 years of PSG. We chose an arbitrary cut-off of 3 years given that OSA develops over time and patients tested later may have had OSA at the time of surgery. All patients undergoing NCS procedure within 3 years of the polysomnography procedure were included in the analysis. Patients under the age of 18 years (n= 178); those who underwent upper airway surgery {including tonsillectomy (n=14); tracheostomy and ENT surgery (n=5 each)}; and minor procedures under local or regional anesthesia were excluded (n=184). Additional exclusions included preoperative visits for multiple surgeries involving the same patient and those that did not undergo surgery; (n=675); incomplete PSG data (n= 278) and patients with duplicate patient identification numbers.(n=25). Among patients who underwent

multiple surgeries, the NCS in closest approximation to the date of PSG was chosen for analysis. Demographic, clinical, diagnostic, and postoperative data were collected from outpatient electronic records, inpatient hospital admission records, and surgical procedure dictation records. Patients with OSA were defined as those with an AHI>5. Preoperative morbidity data and postoperative outcomes were collected for the NCS procedure in closest approximation to the date of the overnight polysomnography. Respiratory events were characterized on PSG using nasal pressure transducers, oro-nasal thermal sensors, thoracic/abdominal effort piezo belts and pulse oximetry. Hypopnea was defined as  $\geq$  50% reduction in nasal pressure signal excursions from baseline lasting for  $\geq$ 10 seconds associated with a  $\geq$  3% oxygen desaturation and/or arousal. Major co-morbid conditions were defined according to Hosking et al<sup>14</sup>. We did not have information about perioperative opioid use for pain control. The study protocol was approved by our Institutional Review Board IRB number-09-383 (approved on May 8, 2009). The approval included a waiver of informed consent.

#### *Definitions of Postoperative Morbidity*

The clinical outcome endpoints for this study were significant postoperative complications including: Postoperative hypoxemia, respiratory failure (RF), congestive heart failure (CHF), myocardial infarction (MI), atrial fibrillation, delirium as defined in the medical record, death within 30 days, hospital length of stay. These data were obtained from electronic medical records, operative notes, post-anesthetic care unit records and discharge summary notes. Postoperative hypoxemia was considered present if the patient developed postoperative respiratory failure; oxygen desaturations<90% and

>4% reduction from last recorded value; or if confirmed by arterial blood gas postoperatively. Postoperative RF was defined as need for prolonged mechanical ventilation (>24h), need for endotracheal reintubation, or tracheostomy. Postoperative CHF was defined as new pulmonary edema, elevated JVP>10 mmHg, use of diuretic or afterload/preload reducing agents, or physician documentation of CHF. Postoperative MI was defined as appearance of new Q waves >0.04s wide and 1 mV in depth accompanied by elevated levels of troponin T (0.03ng/ml) and creatine kinase-MB (>100IU/l).

### *Statistical Methods and Analysis*

T tests and Chi-Square tests were used to compare the OSA and non-OSA groups with respect to baseline characteristics. For purposes of analysis, co-morbidities and complications were dichotomized as either present or absent. Due to extreme skewness the length of stay data was dichotomized using the median as > 2 Days and ≤ 2 days. To adjust for baseline differences, a propensity score for each patient was calculated using logistic regression. The propensity score has the advantage of summarizing the information of a large number of covariates into one score. This is particularly important in calculating adjusted effects when outcomes are rare.<sup>15</sup> The propensity score is an estimate of the probability that each patient has OSA given the baseline values of the covariates. The propensity model used the presence of OSA as the response and included age, sex, race, BMI, use of general anesthesia, American Society of Anesthesiology (ASA) class, number of co-morbidities and their interactions as covariates. The c-statistic for the propensity model was 0.83 indicating a strong predictive power. The baseline characteristics are compared between the groups in Table 1. The unadjusted p-

values show that the differences between five of the seven baseline variables were highly significant. However, none of the differences remained significant after adjusting for the propensity score. This means that the propensity score was effective in balancing the differences and allowed a fair comparison between the two groups with respect to outcomes. The effect of OSA on a given outcome was estimated using logistic regression that adjusted by the propensity score and the covariates. Statistical analysis was done using JMP 8.2 software, SAS Institute, North Carolina.

## Results

A total of 1759 patients underwent both PSG and NCS between Feb 2002 and June 2006 at a major tertiary care center. After applying exclusion criteria 471 patients were eligible for the study of which 282 (59.8%) had OSA (AHI>5).(Figure 1). Patients with OSA were older, mean age (55.9 vs 46.3 years), predominantly male (44.7% vs 21.7%), with a higher BMI (38.3 vs 33), higher ASA class and greater medical co-morbidities viz., COPD, HTN, DM, CAD. These differences between the two groups however, were successfully balanced with the propensity score (Table 1). Amongst the surgical procedures the majority (>80%) were intermediate risk, with abdomino-pelvic and orthopedic procedures dominating among both the groups.(Table 2). No differences existed between the types of anesthesia used amongst the two groups of which general anesthesia was more common (>80%). After adjusting for the propensity score, presence of OSA was associated with higher incidence of overall complications (OR = 6.9; p = 0.003); postoperative hypoxemia (OR=7.9; p=0.009),ICU transfer (OR 4.43; p=0.069) & higher length of hospital stay (LOS),(OR=1.65; p=0.049).(Table 3). A total of 131 patients (46%) had severe OSA defined as AHI>30; and 79 (28%) had moderately

severe OSA (AHI 15-30) and the rest were mild OSA cases. Severity of OSA measured by AHI was not associated with postoperative complications ( $p=0.3$ ); ICU transfer ( $p=0.9$ ) or LOS ( $p=0.97$ ). The median LOS in the OSA group was 2 days (IQR:0,4) and 1 day in the control group (IQR: 0,3).

Of the 282 patients with OSA 153 (57%) were recommended some form of positive airway pressure (PAP) treatment after the diagnosis and 106 (70%) were adherent as self reported at their preoperative assessment. Home PAP use prior to NCS was not associated with lower overall postoperative complications ( $p=0.75$ ) or length of stay ( $p=0.21$ ).

## **Discussion**

Although it may be intuitive to suspect that patients with OSA are at higher risk of postoperative complications the literature supporting the claim is conflicting. One of the major limitations in confirming such a claim in case controlled studies has been to have an adequate number of polysomnographically tested controls without OSA ( $AHI<5$ ) at baseline or after treatment with CPAP or surgery. To the best of our knowledge ours is the largest study to date using PSG to define OSA status among surgical patients. All the patients in the control group had an  $AHI<5$  at the time of NCS. A propensity score was used to balance the effect of medical morbidities associated with OSA, including BMI, which may have confounded the perioperative outcomes reported in previous studies. Our study confirms that OSA is independently associated with postoperative hypoxia, higher rate of respiratory failure and ICU transfer, and longer hospital stay after non-cardiac

surgery. Sample size limitations prevented us from studying the possible role of OSA on development of cardiac complications like postoperative arrhythmias especially atrial fibrillation, MI and CHF.

*Characterization of Postoperative Respiratory Complications.*

We report a total of 40(14.2%) complications in 282 patients with OSA undergoing elective NCS compared to a total of 5(2.5%) complications in a propensity matched control group.( $p < 0.0001$ ). As many as 50% (19) of these patients with postoperative complications were transferred to intensive care unit for further management of which only 3 transfers were planned preoperatively. Of all the different postoperative complications, RF accounted for over 35% of the total. While most studies todate have not reported postoperative RF in patients with OSA undergoing NCS, the few studies that did define RF as a postoperative outcome measure<sup>3,5,16</sup> did not find it to be statistically significant. A recent study reporting a large sample of patients from a National inpatient database (NIS) reported 5 fold increase in intubation and mechanical ventilation among OSA patients undergoing NCS, and ARDS was reported as a complication for the first time.<sup>8</sup>

About 10% of patients in the OSA group experienced postoperative hypoxia. This compared to a similar study by Liao et al<sup>16</sup>, which reported 30% of patients having postoperative desaturation although only 2(0.8%) patients developed RF. This may be attributed to a higher rate of ‘planned ICU transfers’ in that study compared to ours. ASA recommends longer (3 hours) postoperative monitoring in OSA patients after ambulatory surgery and 7 hours of monitoring after the last episode of airway obstruction or

hypoxemia while breathing room air in an unstimulated environment prior to discharge from the facility.<sup>6</sup> The guidelines are equivocal about full monitoring in the ICU setting, continuous oximetry by a dedicated observer in the patient's room or low risk patients no longer on continued parenteral narcotics. In a study of patients undergoing predominantly open Roux-en-Y gastric bypass surgery, 1 patient out of 318 among patients undergoing mandatory screening by polysomnography developed respiratory complication requiring ICU stay compared to 11 out of 572 patients who did not get PSG before surgery.<sup>17</sup> A more recent study<sup>18</sup> among patients with OSA undergoing laparoscopic Roux-en-Y gastric bypass; did not show any higher postoperative complication rate among patients with OSA, hence suggesting against routine ICU admission after laparoscopic Roux-en-Y gastric bypass.

In patients with OSA undergoing elective NCS, early postoperative complications may intuitively be attributed to the negative effects of sedative, analgesic, and anesthetic agents, which can worsen OSA by decreasing pharyngeal tone, and the arousal responses to hypoxia, hypercarbia, and obstruction.<sup>19</sup> Later events are, however, more likely to be related to postoperative rapid eye movement (REM) sleep rebound.<sup>20</sup> In a recent study Liao et al reported higher AHI and oxygen desaturation index (ODI) among OSA patients on the third postoperative night compared to the values preoperatively or on the first postoperative night.<sup>21</sup>

#### *Severity of OSA and incidence of postoperative complications*

Our study did not find an association between the severity of OSA as measured by the

AHI and respiratory failure ( $p=0.3$ ); ICU transfer ( $p=0.9$ ) and length of hospital stay ( $p=0.97$ ). Literature is conflicting regarding the severity of OSA and occurrence of postoperative complications. In a study by Gupta et al<sup>3</sup>; severity of OSA as measured by total Respiratory Disturbance Index (RDI) was not associated with postoperative complications however, supine RDI was reported high in most patients. More recent literature supports higher overnight desaturation index (ODI), in patients where polysomnography could not be done, linked with incidence of higher postanesthesia care unit events / postoperative complications.<sup>7,22</sup> Hence, polysomnography may neither be practical nor necessary in the preoperative assessment.

No studies so far have reported any deaths postoperatively directly attributed to OSA. Although respiratory complications dominate, REM rebound has been suggested to contribute to myocardial ischemia and infarction, stroke, mental confusion, and wound breakdown.<sup>23-27</sup> REM sleep rebound and the link to sympathetic tone may be particularly dangerous, leading to myocardial ischemia, infarction, and even unexplained postoperative death. This hypothesis is supported by the finding that majority of unexpected and unexplained postoperative deaths occur at night within 7 days of surgery.<sup>28</sup>

### **Limitations**

Our study is retrospective and used PSG data within 3 years before or after NCS. Getting PSG before NCS in suspected cases is not standard practice and unlike some other disorders symptoms of OSA present and evolve gradually over time. Also we did not have complete information regarding the pre or postoperative use of CPAP or objective PAP adherence data and hence are unable to comment on the impact of perioperative use



of PAP and or possible carry-over effects from use of home CPAP. If resuming PAP after surgery in patient's with known OSA, becomes a clinical standard of care randomized trials addressing the role of PAP in preventing postoperative complications are unlikely to be completed in the future. We did not have pharmacy data to study the impact of pain medications, sedatives and anesthetic agents used on the perioperative outcomes.

## Conclusions

Patients with OSA are at higher risk for hypoxia, respiratory failure, unplanned ICU transfers and longer hospital stay. While polysomnography may be neither practical nor necessary in screening patients with suspected OSA about to undertake surgery, future studies need to define the highest risk group among the OSA patients, which may be in particular need of intensive monitoring during and after surgery.

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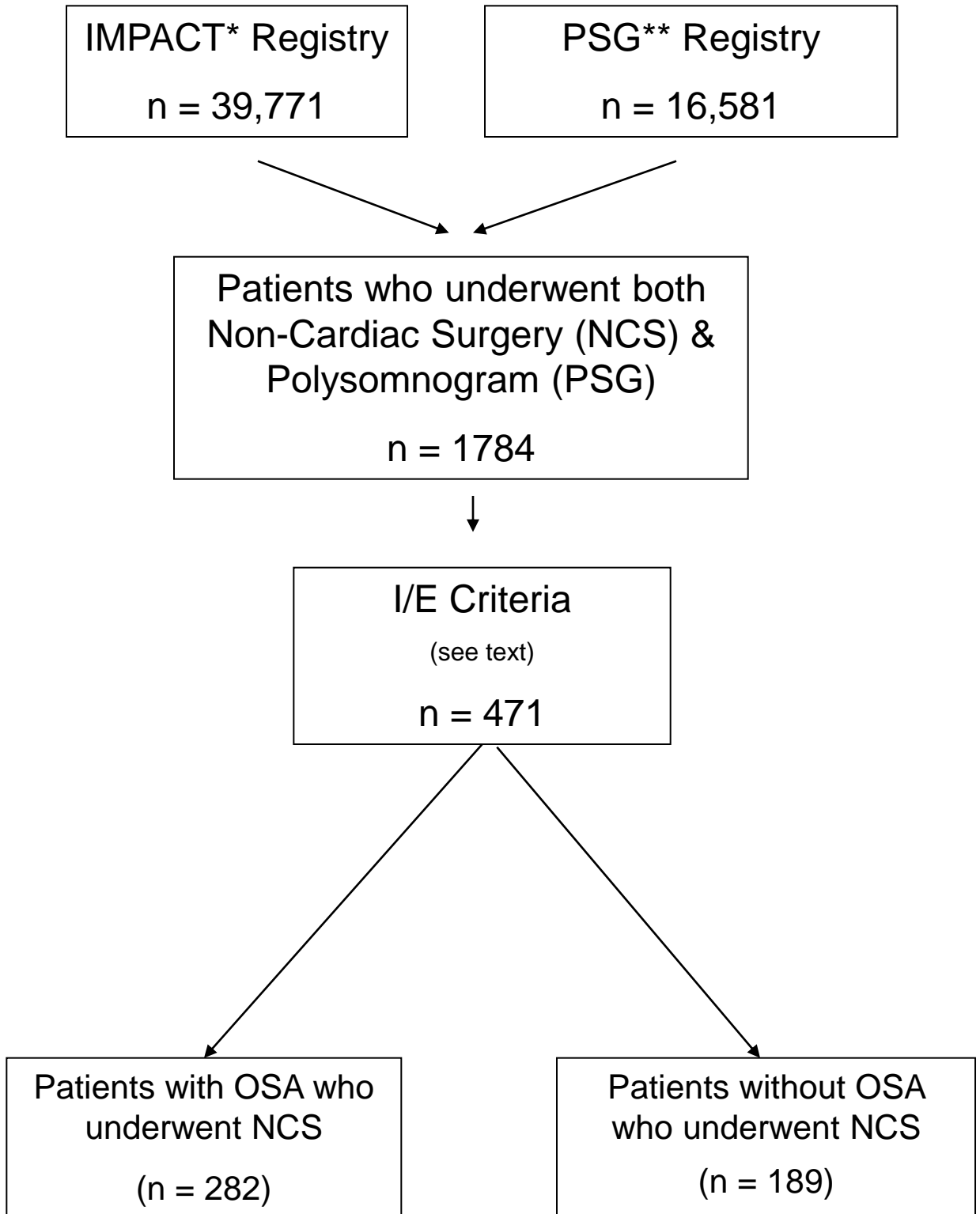
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**Table 1. Baseline Characteristics of Patients with & without Obstructive Sleep Apnea**

Variables	AHI $\geq$ 5 (n=282)	AHI < 5 (n=189)	<i>P</i> value	Propensity Adjusted p value**
Age*	55.9 (12.2)	46.3 (14.3)	<.0001	0.68
Female (%)	156 (55.3)	152 (80.4)	<.0001	0.74
White (%)	198 (70.2)	145 (76.7)	0.12	0.63
BMI*	38.3 (11.1)	33.0 (9.5)	<.0001	0.78
Anesthesia				
General	225 (80.9)	152 (82.6)	0.65	0.35
Others†	53 (19.1)	32 (17.4)		
ASA risk category 1-2 (%)	110 (39.1)	124 (66.0)	<.0001	0.42
Comorbidity $\geq$ 1	230 (81.8)	104 (55.0)	<.0001	0.99
Hypertension	183 (64.9)	63 (33.3)	<.0001	0.36
Diabetes	74 (26.3)	19 (10.0)	<.0001	0.29
Asthma	51 (18.1)	38 (20.1)	0.6	0.24
CAD	43 (15.2)	12 (6.4)	0.003	0.29
COPD	33 (11.7)	7 (3.7)	0.002	0.50
Smoking history‡	85 (30.1)	38 (20.1)	0.02	0.78
Surgical risk category			0.03	0.42
1: High	5 (1.8)	1 (0.5)		
2: Intermediate	250 (88.6)	155 (82.0)		
3: Low	27 (9.6)	33 (17.5)		
AHI**	27 [15, 49]	2.1 [0.8, 3.2]		

\*Values are given as number (%) except for age and BMI expressed as mean (SD). \*\*Propensity model included the first seven baseline characteristics and their interactions.

\*\* Median and IQR

† Spinal anesthesia, local anesthesia, epidural block, and paravertebral block.

‡ Current or previous smoker

ASA = American Society of Anesthesiologists; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease.

**Table 2. Types of Non-Cardiac Surgical Procedures**

Categories	AHI $\geq$ 5	AHI < 5	Total
Abdominopelvic	112 (39.7)	62 (32.8)	174
ENT	4 (1.4)	5 (2.7)	9
Gynecologic	24 (8.5)	29 (15.3)	53
Neurosurgical	10 (3.6)	9 (4.8)	19
Orthopedic	82 (29.1)	45 (23.8)	127
Thoracic	12 (4.3)	16 (8.5)	28
Urologic	18 (6.4)	9 (4.8)	27
Vascular	4 (1.4)	-	4
Other	16 (5.7)	14 (7.4)	30
Total	282	189	471

\*Values are given as number (% of AHI group), unless otherwise indicated.

ENT = ear, nose, and throat.

**Table 3. Postoperative Complications/Outcomes among OSA and non-OSA patients**

Complications	AHI $\geq$ 5 (n=282)	AHI < 5 (n=189)	Propensity Adjusted OR	Propensity Adjusted p value*
Atrial fibrillation	3 (1.1)	0	...	...
Myocardial Infarction	2 (0.7)	0	...	...
Delirium	9 (3.4)	0	...	...
Congestive Heart Failure	3 (1.1)	0	...	...
Postoperative Hypoxemia	35 (12.4)	4(2.1)	7.9	0.009
Respiratory Failure†	14 (4.9)	4 (2.1)	4.3	...
Reintubation†	4 (1.4)	1 (0.5)	9.2	...
ICU transfer	19 (6.7)	3 (1.6)	5.7	0.049
Any Complication	40 (14.2)	5 (2.6)	6.9	0.003
LOS > 2days	135 (48.2)	53 (28.0)	1.65	0.049
Overall LOS	2(0,4)**	1(0,3)	....	.....

( ) indicates%. \*Propensity model included the first seven baseline characteristics and their interactions.

†JMP will not compute a correct *P* Value when numbers in the comparison group are small

\*\* Median and interquartile range

ICU = intensive care unit; LOS = length of stay. OSA= Obstructive Sleep Apnea.

**Postoperative Complications in Patients with Obstructive Sleep Apnea**  
Roop Kaw, Vinay Pasupuleti, Esteban Walker, Anuradha Ramaswamy and Nancy  
Foldvary-Schafer  
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