Postoperative Changes in Sleep-disordered Breathing and Sleep Architecture in Patients with Obstructive Sleep Apnea

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ABSTRACT

Background: Anesthetics, analgesics, and surgery may profoundly affect sleep architecture and aggravate sleep-related breathing disturbances. The authors hypothesized that patients with preoperative polysomnographic evidence of obstructive sleep apnea (OSA) would experience greater changes in these parameters than patients without OSA.

Methods: After obtaining approvals from the Institutional Review Boards, consented patients underwent portable polysomnography preoperatively and on postoperative nights (N) 1, 3, 5, and 7 at home or in hospital. The primary and secondary outcome measurements were polysomnographic parameters of sleep-disordered breathing and sleep architecture.

Results: Of the 58 patients completed the study, 38 patients had OSA (apnea hypopnea index [AHI] >5) with median preoperative AHI of 18 events per hour and 20 non-OSA patients had median preoperative AHI of 2. AHI was increased after surgery in both OSA and non-OSA patients ($P < 0.05$), with peak increase on postoperative N3 (OSA *vs.* non-OSA, 29 [14, 57] *vs.* 8 [2, 18], median [25th, 75th percentile], $P < 0.05$). Hypopnea index accounted for 72% of the postoperative increase in AHI. The central apnea index was low (median = 0) but was significantly increased on postoperative N1 in only non-OSA patients. Sleep efficiency, rapid eye movement sleep, and slow-wave sleep were decreased on N1 in both groups, with gradual recovery.

Conclusions: Postoperatively, sleep architecture was disturbed and AHI was increased in both OSA and non-OSA patients. Although the disturbances in sleep architecture were greatest on postoperative N1, breathing disturbances during sleep were greatest on postoperative N3. **(ANESTHESIOLOGY 2014; 120:287-98)**

OBSTRUCTIVE sleep apnea (OSA) is a common disease. In the general population, OSA, defined by an apnea hypopnea index (AHI) of 5 or greater, affects 22% of men and 9% of women. Moderate to severe OSA (AHI ≥15) affects 7–14% of men and 2–7% of women.[1] The prevalence of OSA in surgical patients may vary with the different surgical populations. Recent studies show that documented OSA was found in 5.5% of orthopedic patients, 2.7% of the general surgical patients,[2] and 7.2% in patients undergoing a variety of surgeries.[3] Because a large proportion of OSA patients remain clinically undiagnosed,[4] the point estimates from these studies may be an underestimation. However, 7 of 10 patients undergoing bariatric surgery were found to have OSA.[5]

Obstructive sleep apnea is associated with an increased morbidity and mortality. It is a significant predictor of coronary heart disease in men younger than 70 yr of age.[6] It is also associated with atrial fibrillation,[7] ischemic stroke,[8] and an increased risk of cardiovascular mortality in patients with coronary artery disease.[9] The all-cause mortality increased with the severity of sleep-disordered breathing.[10]

With regard to the anesthetic implications, children with OSA are highly sensitive to general anesthetics and narcotics.[11–13] OSA patients have an increase in upper airway collapsibility[14–16]

What We Already Know about This Topic

- Previous small sample studies suggest that anesthesia and surgical interventions may change sleep architecture and sleep-disordered breathing in patients with obstructive sleep apnea

What This Article Tells Us That Is New

- In this prospective cohort study, both nonobstructive sleep apnea (n = 20) and obstructive sleep apnea (n = 38) patients suffered sleep disturbance particularly on postoperative night 1 and significantly increased frequencies of sleep-disordered breathing particularly on postoperative night 3

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and are particularly vulnerable to airway obstruction during the postoperative period. Accumulating evidence support that the OSA patients could have an increased incidence of perioperative adverse events with case reports of death.[2,17–22]

Understanding the extent and timing of postoperative changes in sleep-disordered breathing and sleep architecture is necessary for developing evidence-based perioperative care protocols. However, little information is available on this important issue. Sleep architecture was studied in 10 healthy patients undergoing cholecystectomy without postoperative opioid[23] and 12 young patients undergoing abdominal surgery.[24] Postoperatively, rapid eye movement (REM) sleep was found to be immediately suppressed followed by rebound over 1 week.[24,25] Slow-wave sleep was significantly depressed first 2 nights after surgery.[25] The sleep disturbance seems related to the magnitude of surgical procedure. Compared with laparotomy, laparoscopic cholecystectomy caused less pronounced sleep alterations.[23,26]

To date, there is little literature on the perioperative change in sleep-disordered breathing and sleep architecture in OSA patients. The objective of the study was to address the paucity in information regarding perioperative influences on sleep by determining the changes in sleep architecture and breathing disturbances during sleep in the week after surgery relative to preoperative values. We hypothesized that patients with OSA would experience greater changes in these parameters than those without OSA.

Materials and Methods

Study Design

This is a prospective observational study. There was no intervention. The primary outcomes were polysomnography parameters measuring the sleep-disordered breathing. The secondary outcomes were polysomnography parameters measuring the sleep architecture.

Study Subjects

Approvals from the Institutional Review Boards were obtained from Toronto Western Hospital and Mount Sinai Hospital at Toronto, Ontario, Canada. All patients of 18 yr or older, who were American Society of Anesthesiologists physical status I–IV and scheduled for elective surgical procedures, were approached by the study coordinators for written informed consent. Patients who were unwilling or unable to give informed consent or patients who were expected to have abnormal electroencephalographic findings (*e.g.*, brain tumor, epilepsy surgery, patients with deep brain stimulator) were excluded. If a patient used continuous positive airway pressure (CPAP) therapy on any perioperative night, the patient was excluded from the final analysis. The patients were recruited between November 2007 and December 2009. The quality of the portable polysomnography recordings of 41 patients was reported in a previous method article.[27]

Sleep Studies and Follow-up

The recruited patients underwent sleep studies with a 10-channel portable polysomnography device (Embletta X100; Embla, Broomfield, CO) preoperatively (preop) at home and on postoperative (postop) nights (N) 1, 3, 5, and 7 in hospitals or at home. Embletta X100 is a level-2 diagnostic tool for OSA[28] and has been validated against laboratory polysomnography.[27] The polysomnographic recording montage consisted of two electroencephalographic channels (C3 and C4), left or right electroculogram, chin muscle electromyograms, nasal cannula (pressure), thoracic and abdominal respiratory effort bands, body-position sensor, and pulse oximetry.

A full-night sleep study with Embletta X100 was carried out as previously described.[27] At bedtime, the portable polysomnography device was connected to the patients by a polysomnography technician at their home or in hospital. The overnight recording itself was unattended. The patients were taught how to disconnect the device, which was picked up by the same sleep technician the following morning. The patients were asked to keep a sleep diary. The sleep technician picking up the device ensured that the sleep diary was completed.

The recordings from the portable polysomnography device were scored by a certified polysomnographic technologist and reviewed by a sleep physician. Somnologia Studio 5.0 (Embla) was the platform used for scoring polysomnography recordings. The polysomnography recordings were manually scored epoch by epoch by the polysomnography technologist, according to the manual published by American Academy of Sleep Medicine in 2007.[29] Apnea was defined as at least 90% decrease in air flow from baseline, which lasts at least 10 s. Apneic episodes were further classified as obstructive if respiratory effort was present or central if respiratory effort was absent during the event. Mixed apnea is the apnea episodes with characteristics of both obstructive and central apnea. Apnea index is the average number of apnea episodes per hour. Hypopnea was defined as at least 50% reduction in air flow which lasts at least 10 s and is associated with at least 3% decrease in arterial oxyhemoglobin saturation or associated with arousal. Hypopnea index is the average number of hypopnea episodes per hour. AHI is the average number of apnea and hypopnea episodes per hour. REM AHI is AHI during REM sleep, and non-REM AHI is AHI during non-REM sleep. Respiratory arousal index is average hourly sleep arousals due to respiratory events. Oxygen desaturation index is defined as the average number per hour of episodes with 4% or greater desaturation and lasting 10 s or longer.

In this study, all polysomnography recordings were scored after the patients were discharged from the hospitals. The anesthesiologists and the surgeons caring the study patients were blinded to the results of the polysomnography recordings. During the study period, the healthcare team provided routine care to these patients. The decision of oxygen therapy or CPAP therapy for patients was made by the perioperative care team. According to the institution protocol, if

pulse oxygen saturation (Spo_2) on oximeter monitoring is less than 94%, oxygen therapy will be provided. If they suspected a patient who might be suffering from OSA, they could refer the patient for further evaluation and provide the patient with CPAP treatment. The patients with an AHI of greater than five events per hour on the preoperative home polysomnography were defined as OSA patients. Their family physicians were notified after surgery, so that the patients could be referred to sleep physicians for further clinical management. The patients with an AHI of five events per hour or less on the preoperative home polysomnography were defined as non-OSA patients.

Anesthesia and Postoperative Pain Control

A balanced anesthesia technique was used in all patients. In general anesthesia, patients received an induction dose of propofol; a narcotic such as fentanyl, morphine, or hydromorphone; an inhalational agent such as sevoflurane or desflurane; and a muscle relaxant such as rocuronium. The muscle relaxant is usually reversed with neostigmine and glycopyrollate. In spinal anesthesia, patients received local anesthesia, epimorph, and an intraoperative propofol infusion. Both groups received narcotic in the postoperative period.

All patients were reviewed twice daily by the Acute Pain Service team, as per our institutional standard of care. Pain was evaluated by a score of 0–10 with 0 as no pain and 10 as the most excruciating pain. Intravenous morphine through patient-controlled analgesia was initiated when the verbal pain score was 4 or greater. If pain is not controlled by patient-controlled analgesia, the Acute Pain Service team increased the immediate-release oxycodone dose and/or added controlled-release oxycodone to achieve a verbal pain score 4 or less for pain.

Data Analysis and Statistics

Sample Size Estimation. Our primary outcome measurement is the postoperative AHI in OSA or non-OSA patients. Because there is no published study on the postoperative AHI change in OSA or non-OSA patients, we based our sample size estimation on our pilot data of 16 patients who did preoperative and postoperative N1 and 3 polysomnography. The AHI was 22.4 ± 15 events per hour on the preoperative polysomnography and 50.1 ± 38 events per hour on the postoperative N3 polysomnography. If we treat data as paired and power = 0.9, and $\alpha = 0.05$, the estimated sample size would be 21.

Data Analysis. Data were entered into a specifically designed Microsoft Access database and checked for possible errors. SAS 9.2 for Windows (SAS Institute, Cary, NC) was used for data analysis. All the statistical tests were two-tailed test. *P* value of less than 0.05 or adjusted *P* value of less than 0.05 was accepted as statistically significant.

The demographic data and summary of data from polysomnography were presented with descriptive statistics. Categorical data were presented as frequency with percentage, and the statistical significance was checked by chi-square test or Fisher exact test. The mean ± SD was used for continuous data with normal distribution, and the statistical significance was checked with Student independent two-sample *t* test. The median (25th, 75th percentile) was used for continuous data with skewed distribution, and Mann–Whitney U test was used to check the statistical significance for continuous data with skewed distribution.

The evolution of sleep architecture and parameters measuring sleep-disordered breathing in OSA and non-OSA patients were first summarized across the different perioperative nights. The measurements from the different perioperative nights were treated as repeatedly measured data. Mixed models with polysomnography parameters as outcome and preoperative OSA status and the night of polysomnography as predictors were used to analyze the difference between the different perioperative nights in OSA and non-OSA patients. Preoperative OSA status and the night of polysomnography were treated as fixed effect and subject was treated as random effect. The postoperative value of parameters was compared with the preoperative baseline, respectively. The Holm–Bonferroni method was used to adjust *P* value for multiple comparisons.

Results

Patient recruitment and study implementation were shown in flow chart (fig. 1). A total of 4,013 patients were approached and 904 patients (22.5%) gave consent to participate in the study and 243 patients (26.9%) withdrew before performing preoperative polysomnography. Of 661 patients who did preoperative polysomnography, 80 patients were on CPAP therapy on one or more nights while undergoing polysomnography. Fifty-one patients who completed polysomnography recording on 5 nights (preoperative, postoperative N 1, 3, 5, and 7) and seven patients who completed polysomnography recording on 4 nights (preoperative, postoperative N 1, 3, and 5) were included in this report.

Demographic Data and Baseline Information

The demographic data and baseline information of the 58 patients were summarized in table 1. There were 38 OSA patients with median AHI of 18 events per hour and 20 non-OSA patients with median AHI of 2 events per hour. The average age of patients was 57 yr with a higher percentage of women. The main type of surgery was orthopedic (59%) and the main type of anesthesia was spinal/regional (59%; table 2). There was no significant difference in sex, age, neck circumference, type of surgery, and type of anesthesia between the OSA and non-OSA patients. The OSA patients did have a significantly higher body mass index. They also had a higher rate of hypertension, 65.8 *versus* 10%; $P < 0.001$. Although the opioid requirement was higher in non-OSA patients than that in OSA patients at first 24 h, second 24 h, third 24 h, and first 72 h, the difference was not significant ($P > 0.05$; table 1).

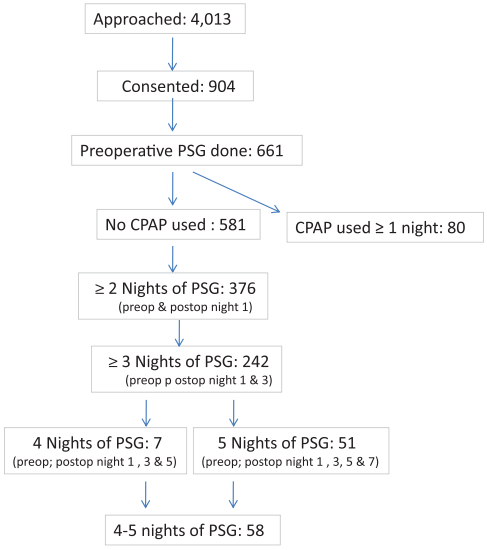

Fig. 1. Patient recruitment and follow-up flow chart. CPAP = continuous positive airway pressure; PSG = polysomnography.

Postoperative Changes in Sleep-breathing Disorder

The parameters measuring sleep-breathing disorders for OSA and non-OSA patients were summarized in table 3, and the major parameters were shown in figure 2, A–D. Compared with the preoperative baseline, the increase in AHI was statistically significant on postoperative N3 in OSA patients and on postoperative N1 and N3 in non-OSA patients. On all observed nights except postoperative N1, AHI was significantly higher in OSA patients than that in non-OSA patients (fig. 2A). Median AHI increased from preoperative baseline 18 (10, 33) (median [25th, 75th percentile]) to 29 (14, 57) events per hour on postoperative N3 for OSA patients (adjusted $P < 0.001$), whereas median AHI increased from 2 (1, 4) to 8 (2, 18) events per hour for non-OSA patients (adjusted $P = 0.007$). AHI remained increased on postoperative N5 and did not completely return to the preoperative level by postoperative N7. A large variation in AHI was observed among the individual patients (fig. 2A).

AHI during non-REM sleep followed a similar change as AHI. AHI during REM sleep (REM AHI) followed a different pattern (table 3). For OSA patients, REM AHI significantly decreased by 91.2% on postoperative N1 *versus* preoperative baseline (3 *vs.* 34 events per hour; adjusted $P < 0.001$) and did not statistically increase on postoperative N3, (45 *vs.* 34 events per hour; adjusted $P = 0.197$). For non-OSA patients, REM AHI changed from five events per hour to one event per hour on postoperative N1 without statistical significance (adjusted $P = 0.654$). But it significantly increased from five events per hour preoperative baseline to 15 events per hour on postoperative N3 (adjusted $P = 0.032$).

Table 1. Demographic Data

	All	OSA	Non-OSA	*P* Value*
n	58	38	20	
Sex, F/M, n (%)†	37 (64%)/2,136%)	24/14	13/7	1.000
Age, yr‡	57 ± 11	58 ± 11	53 ± 12	0.127
Body mass index, kg/m^2‡	30 ± 6	32 ± 6	26 ± 4	<0.001
Neck circumference, cm‡	38 ± 5	39 ± 4	37 ± 4	0.375
Preoperative AHI, events per hour§	10 (4, 24)	18 (10, 33)	2 (1, 4)	<0.001
Opioid requirement in first 24 h (mg)§	30 (9, 38)	29 (6, 35)	34 (23, 50)	0.093
Opioid requirement in second 24 h (mg)§	17 (0, 33)	15 (0, 30)	38 (20, 45)	0.396
Opioid requirement in third 24 h (mg)§	15 (0, 25)	10 (0, 23)	17 (8, 30)	0.222
Opioid requirement in first 72 h (mg)§	63 (16, 91)	60 (11, 82.6)	89 (24, 114)	0.086
American Society of Anesthesiologists physical status, n (%)†				
I	2 (3.5)	1 (2.6)	1 (0.5)	0.058
II	32 (55.2)	17 (44.7)	15 (75.0)	
III	23 (39.7)	19 (50.0)	4 (20.0)	
IV	1 (1.7)	1 (2.6)	0	
Comorbidities, n (%)†				
Hypertension	27 (46.6)	25 (65.8)	2 (10)	<0.001
Diabetes	10 (17.2)	8 (21.1)	2 (10)	0.468
GERD	14 (24.1)	12 (31.6)	2 (10.0)	0.106
Smoker	8 (13.8)	5 (13.2)	3 (15.0)	1.000
Asthma	8 (13.8)	4 (5.3)	4 (20.0)	0.540
COPD	2 (3.5)	2 (5.3)	0	0.540
CAD	4 (6.9)	4 (10.5)	0	0.288
Stroke	3 (3.2)	2 (5.3)	1 (5.0)	1.000
Hypothyroidism	4 (6.9)	2 (5.3)	2 (10.0)	0.602

* *P* value for OSA *vs.* non-OSA. † Data presented as frequency (%). ‡ Data presented as mean ± SD. § Data presented as median (25th, 75th percentile).
AHI = apnea hypopnea index; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; GERD = gastroesophageal reflux disease; non-OSA = patients without obstructive sleep apnea; OSA = patients with obstructive sleep apnea.

Table 2. Type of Surgery and Anesthesia

	All	OSA	Non-OSA	*P* Value
n	58	38	20	
Type of surgery, n (%)				0.174
Orthopedic	34 (59)	24 (63.2)	10 (50)	
Spine	7 (12)	4 (10.5)	3 (15)	
Gynecology	5 (9)	5 (13.2)	1 (5)	
General	4 (7)	1 (2.6)	3 (15)	
Urology	4 (7)	2 (5.3)	1 (5)	
Otolaryngology	2 (3.5)	0 (0)	2 (10)	
Ophthalmology	2 (3.5)	2 (5.3)	0 (0)	
Type of anesthesia, n (%)				0.116
General	24 (41)	12 (31.6)	12 (60)	
Spinal	19 (33)	14 (36.8)	5 (25)	
Regional	15 (26)	12 (31.6)	3 (15)	

Data presented as n (%).

Non-OSA = patients without obstructive sleep apnea; OSA = patients with obstructive sleep apnea.

Among the components of AHI, hypopnea index had a similar perioperative evolutional pattern as AHI and accounted largely for the increase in AHI (fig. 2, A and D). Respiratory arousal index also followed a similar trend (table 3). Although obstructive apnea index was higher in OSA patients, there was no statistically significant postoperative increase in both OSA and non-OSA patients (fig. 2B).

The central apnea index was low in the study population. The central apnea index was only significantly increased in non-OSA patients on N1 *versus* preoperative baseline (2.52 *vs.* 0.02 events per hour; adjusted $P < 0.001$; fig. 2C).

There was a statistically significant correlation between the postoperative opioid requirement and sleep-breathing disorders in the non-OSA patients. The central apnea index and obstructive apnea index on postoperative N1 were correlated with the first 24-h opioid requirement. The Spearman coefficient was 0.654 ($P = 0.003$) for central apnea index and 0.551 ($P = 0.018$) for obstructive apnea index. No significant correlation between the opioid requirement and sleep-breathing disorders was found in OSA patients.

No correlation between opioid requirement in the first postoperative 72 h and preoperative AHI, oxygen desaturation index, cumulative time percentage with Spo_2 less than 90, average Spo_2, and lowest Spo_2 was found.

Postoperative Changes in Oxygen Saturation Level

The change for the parameters measuring oxygen saturation level, including oxygen desaturation index, cumulative time percentage with Spo_2 less than 90%, and lowest Spo_2, followed a different pattern from AHI (table 3). Oxygen desaturation index and lowest Spo_2 improved on postoperative N1, possibly related to a high percentage of patients receiving oxygen therapy on that night.

In OSA patients, oxygen desaturation index was increased on postoperative N3, 5, and 7 *versus* preoperative baseline but decreased on postoperative N1. However, the changes were not statistically significant, the adjusted *P* value was greater than 0.05 for all comparisons (fig. 3A). Cumulative time percentage with Spo_2 less than 90% was significantly increased in OSA patients on postoperative N3 (median 7.2 *vs.* 1.3% preoperative baseline; adjusted $P < 0.001$) and N5 (4.0 *vs.* 1.3%; adjusted $P = 0.031$). In non-OSA patients, a significant increase in cumulative time percentage with Spo_2 less than 90% was observed only on postoperative N3 (median 1.1 *vs.* 0% on preoperative baseline; adjusted $P = 0.018$; fig. 3B).

Postoperative Changes in Sleep Architecture

The data on the sleep architecture from preoperative baseline to postoperative N7 were summarized in table 4, and the changes in the major parameters were shown in figure 4A. Sleep efficiency, REM sleep, and slow-wave sleep were depressed on postoperative N1, then recovered to preoperative level by postoperative N7. Stage 2 sleep was correspondingly increased on postoperative N1.

The sleep efficiency was not statistically different between OSA and non-OSA patients on preoperative baseline (OSA *vs.* non-OSA, 85 *vs.* 89%; adjusted $P = 0.999$). It significantly decreased on postoperative N1 in both OSA and non-OSA patients, with less reduction in OSA patients (OSA *vs.* non-OSA; 71 *vs.* 62%; adjusted $P = 0.083$; fig. 4B).

The postoperative change in REM sleep followed a similar trend as sleep efficiency (table 4). REM sleep dramatically decreased by 18% on postoperative N1 in OSA patients (adjusted $P < 0.001$) and by 20% in non-OSA patients (adjusted $P < 0.001$). Then REM sleep recovered close to the preoperative level by postoperative N7 with a slower recovery in OSA patients (table 4 and fig. 4A).

In OSA patients, the slow-wave sleep was significantly suppressed by 10% on postoperative N1 (adjusted $P = 0.009$). It recovered rapidly close to preoperative baseline

Table 3. Parameters Measuring Sleep-breathing Disorders and Oxygen Saturation

Polysomnography Parameters	n	Preoperative Night	Postoperative Night 1	Postoperative Night 3	Postoperative Night 5	Postoperative Night 7
Oxygen therapy, n (%)						
Non-OSA	20	0	11 (55)	0	0	0
OSA	38	0	20 (53)	3 (8)	0	0
AHI, events per hour						
Non-OSA	20	2 (1, 4)	3 (1, 23)*	8 (2, 18)*	3 (1, 22)	4 (1, 9)
OSA	38	18 (10, 33)†	20 (8, 43)	29 (14, 57)*†	22 (10, 38) †	21 (11, 28)†
REM AHI, events per hour						
Non-OSA	20	5 (1, 10)	1 (0, 12)	15 (5, 37)*	8 (1, 14)	9 (1, 24)
OSA	38	34 (23, 55)†	3 (0, 39)*	45 (20, 66)†	37 (15, 58)†	33 (20, 46)†
NREM AHI, events per hour						
Non-OSA	20	1 (0, 2)	3 (1, 21)*	6 (1, 16)*	2 (1, 23)*	2 (0, 7)
OSA	38	12 (4, 31)†	16 (4, 43)*	25 (7, 51)*†	18 (10, 39)*†	20 (6, 27)*†
Obstructive apnea index, events per hour						
Non-OSA	20	0.2 (0, 0.5)	0.3 (0, 3.1)	0.3 (0.1, 1.2)	0.2 (0, 0.7)	0.2 (0, 0.5)
OSA	38	3.7 (1.5, 10.8)	1.8 (0.2, 14.5)	3.3 (0.5, 8.8)	2.7 (0.5, 8.5)	2.3 (0.5, 7.7)
Central apnea index, events per hour						
Non-OSA	20	0 (0, 0) (0.02 ± 0.06)	0 (0, 0.35)* (2.52 ± 5.47)	0 (0, 0.20) (0.61 ± 1.41)	0 (0, 0.1) (0.17 ± 0.39)	0 (0, 0) (0.12 ± 0.43)
OSA	38	0 (0, 0) (0.06 ± 0.18)	0 (0, 0)† 0.07 ± 0.26	0 (0, 0) (0.13 ± 0.44)	0 (0, 0) (0.15 ± 0.72)	0 (0, 0) (0.24 ± 1.12)
Mixed apnea index, events per hour						
Non-OSA	20	0 (0, 0) (0.05 ± 0.12)	0 (0, 0.6) (1.34 ± 4.01)	0 (0, 0.2) (1.85 ± 5.44)	0 (0, 0) (0.85 ± 3.48)	0 (0, 0) (0.23 ± 0.92)
OSA	38	0 (0, 0.3) (0.98 ± 2.88)	0 (0, 0.3) (0.77 ± 2.16)	0 (0, 0.2) (3.39 ± 11.10)	0 (0, 0.1) (3.17 ± 3.48)	0 (0, 0) (3.92 ± 14.77)
Hypopnea index, events per hour						
Non-OSA	20	2 (1, 3)	2 (1, 7)	7 (2, 11)	3 (1, 17)	4 (1, 9)
OSA	38	10 (7, 16)†	13 (3, 24)†	18 (6, 32)*†	15 (8, 26)†	11 (8, 20)†
Respiratory arousal index, events per hour						
Non-OSA	20	2 (1, 3)	2 (1, 13)	5 (1, 13)*	2 (1, 15)	2 (0, 5)
OSA	38	7 (5, 30)†	13 (2, 27)	16 (6, 40)*	15 (5, 28)*	13 (523)†
Oxygen desaturation index, events per hour						
Non-OSA	20	2 (1, 4)	1 (0, 6)	4 (1, 20)	6 (2, 21)	4 (1, 14)
OSA	38	13 (10, 36)†	4 (2, 27)	21 (8, 37)†	22 (11, 34)†	16 (9, 35)†
Time % with Spo_2 <90% (%)						
Non-OSA	17	0 (0, 0.3) (2 ± 5)	0 (0, 0.1) (8 ± 23)	1.1 (0, 30.9)* (17 ± 31)	0 (0, 2.3) (3 ± 6)	0 (0, 1.5) (1 ± 3)
OSA	35	1.3 (0.4, 6.6)† (5 ± 8)	0.6 (0, 10.6) (10 ± 18)	7.2 (1.5, 30.5)* (23 ± 32)	4.0 (1.0, 19.7)*† (15 ± 24)	3.0 (0.4, 11.0)† (8 ± 13)
Lowest Spo_2 (%, mean ± SD)						
Non-OSA	19	90 ± 5	89 ± 8	85 ± 6	88 ± 5	88 ± 5
OSA	37	82 ± 5†	84 ± 10†	78 ± 9*†	78 ± 8*†	81 ± 9†

All data except oxygen therapy and lowest Spo_2 were presented as median (25th, 75th percentile); data also presented as mean ± SD for central apnea index, mixed apnea index, and time percentage with Spo_2 <90%.

* Adjusted $P < 0.05$ for postoperative night 1, 3, 5, and 7 *vs.* preoperative night, respectively. † Adjusted $P < 0.05$ for OSA *vs.* non-OSA on the same night.

Non-OSA = patients without obstructive sleep apnea; NREM AHI = apnea hypopnea index during nonrapid eye movement sleep; OSA = patients with obstructive sleep apnea; REM AHI = apnea hypopnea index during rapid eye movement sleep.

by postoperative N3 and surpassed preoperative value by 4% on postoperative N7. In non-OSA patients, slow-wave sleep followed a similar postoperative change with a faster recovery (fig. 4B).

The opioid requirement in the first postoperative 24 h was negatively associated with REM sleep. The Spearman correlation coefficient (r_s) was −0.458 ($P = 0.004$) in OSA patients and −0.624 ($P = 0.006$) in non-OSA patients.

Postoperative Oxygen Therapy on Sleep-breathing Disorder and Sleep Architecture

On postoperative N1, 20 OSA patients (53%) and 11 non-OSA patients (55%) received oxygen therapy (table 3). Compared with the OSA patients without oxygen therapy, the OSA patients with oxygen therapy had a significantly lower oxygen desaturation index, 0.6 (0.4, 4) events per hour *versus* 16.8 (3.3, 37) events per hour ($P = 0.004$). In non-OSA patients, no difference in oxygen desaturation index

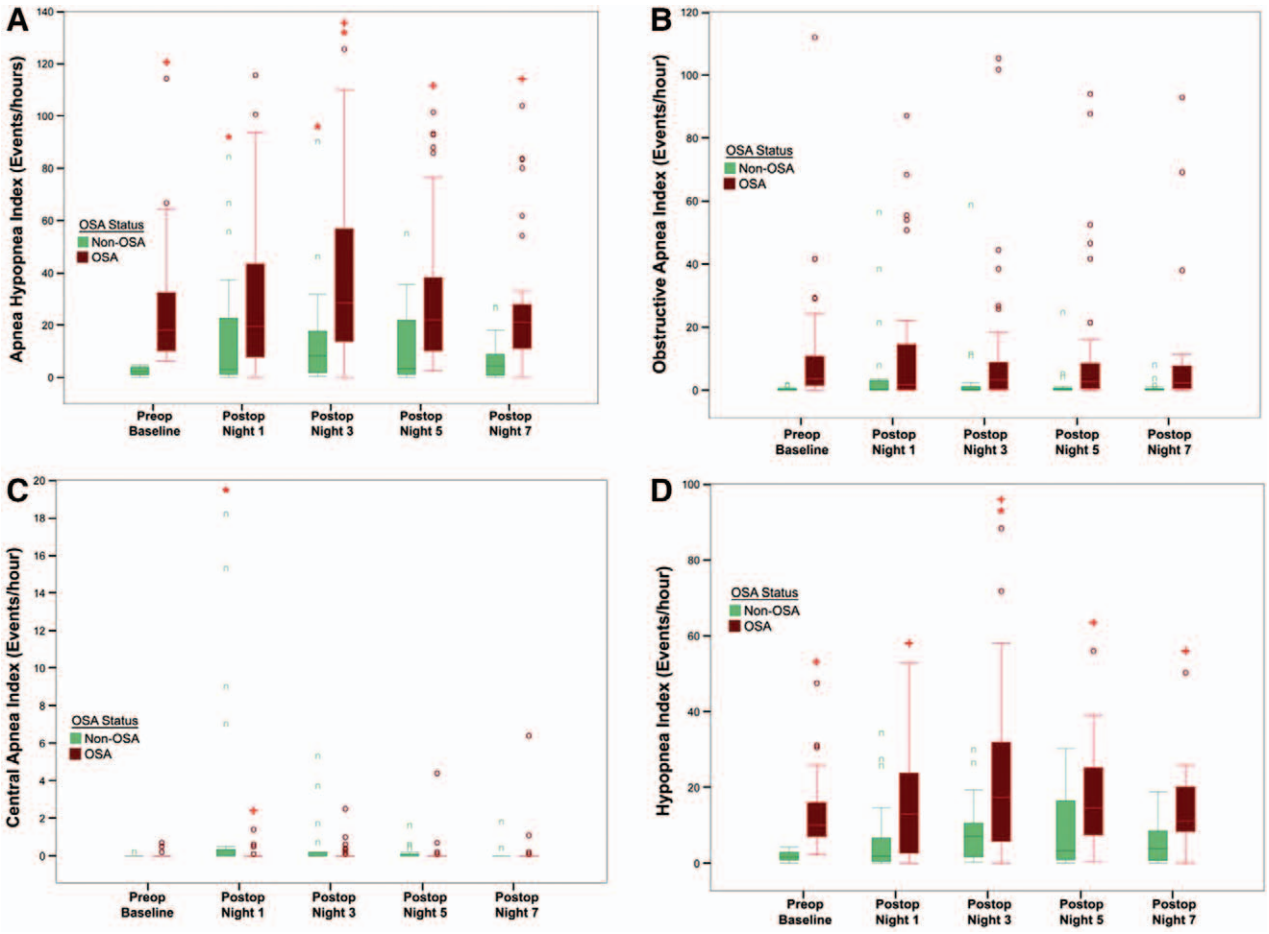

Fig. 2. Box plot for postoperative change in polysomnography parameters measuring sleep-breathing disorders in obstructive sleep apnea (OSA) and non-OSA patients: (*A*) apnea hypopnea index, (*B*) obstructive apnea index, (*C*) central apnea index, and (*D*) hypopnea index. The *box* represents the interquartile range (IQR); the *line* inside the box represents the median; the *upper whisker* is drawn from the upper edge of the box to the largest value within 1.5 × IQR; the *lower whisker* is drawn from the lower edge of box to the smallest value within 1.5 × IQR; *green "n"s* and *brown circles* indicated the values outside 1.5 × IQR. *Adjusted $P < 0.05$ *versus* preoperative measurement; +adjusted $P < 0.05$ *versus* same parameter in non-OSA on the same night.

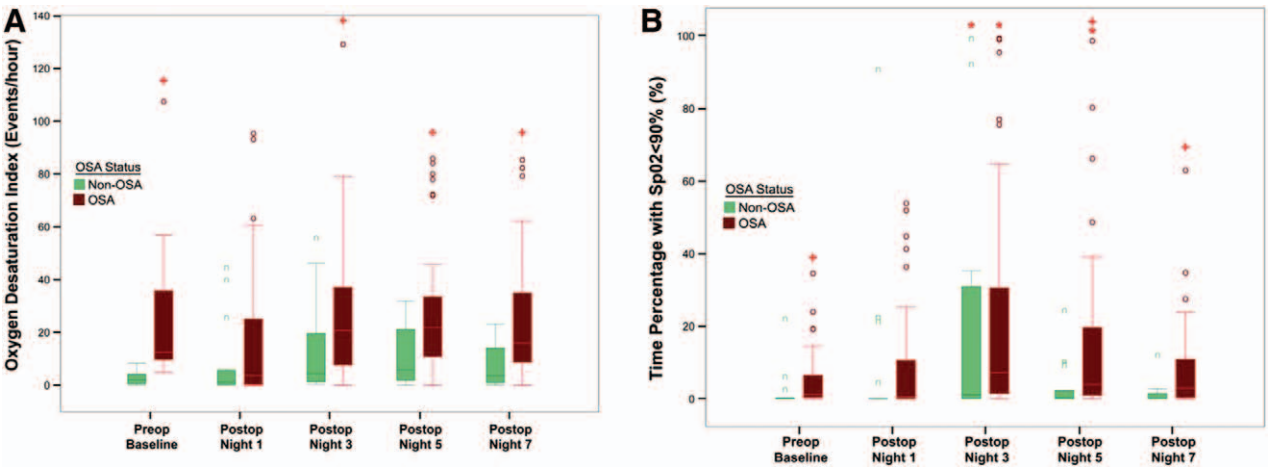

Fig. 3. Box plot for postoperative change in oxygen desaturation index (*A*) and cumulative time percentage with Spo_2 <90% (CT90, *B*). The *box* represents the interquartile range (IQR); the *line inside the box* represents the median; the *upper whisker* is drawn from the upper edge of the box to the largest value within 1.5 × IQR; the *lower whisker* is drawn from the lower edge of box to the smallest value within 1.5 × IQR; *green "n"s* and *brown circles* indicated the values outside 1.5 × IQR. *Adjusted $P < 0.05$ *versus* preoperative measurement; +Adjusted $P < 0.05$ *versus* same parameter in nonobstructive sleep apnea (OSA) OSA on the same night.

Table 4. Sleep Architecture in Patients

	N	Preoperative Night	Postoperative Night 1	Postoperative Night 3	Postoperative Night 5	Postoperative Night 7
Total sleep time (min)*						
Non-OSA	20	354 ± 58	272 ± 117‡	355 ± 60	324 ± 78	342 ± 78
OSA	38	349 ± 68	341 ± 98§	352 ± 73	347 ± 67	356 ± 74
Sleep efficiency (%)*						
Non-OSA	20	89 ± 8	62 ± 23‡	79 ± 10‡	79 ± 11‡	79 ± 15‡
OSA	38	85 ± 14	71 ± 18‡	79 ± 12	82 ± 12	83 ± 10
REM sleep (%)†						
Non-OSA	20	24 (19, 27)	4 (0, 10)‡	15 (11, 22)‡	22 (12, 25)‡	20.6 (16, 24)
OSA	38	21 (17, 27)	3 (0, 12)‡	14 (8, 22)‡	20 (14, 26)	17 (11, 22)‡
Stage 1 (%)†						
Non-OSA	20	3 (2, 4)	7 (4, 11)‡	4 (3, 7)	5 (3, 8)	4 (2, 7)
OSA	38	5 (3, 7)	6 (3, 10)	4 (3, 7)	5 (2, 8)	5 (2, 6)
Stage 2 (%)†						
Non-OSA	20	57 (42, 67)	80 (72, 88)‡	65 (59, 78)‡	60 (50, 70)	53 (49, 59)
OSA	38	60 (51, 70)	77 (69, 91)‡	70 (58, 78)‡	61 (47, 69)	62 (53, 71)
Slow-wave sleep (%)†						
Non-OSA	20	15 (10, 26)	2 (0, 14)‡	10 (2, 18)‡	16 (5, 22)	21 (11, 26)
OSA	38	11 (4, 20)	1 (0, 11)‡	10 (4, 20)	14 (5, 27)	15 (9, 19)

* Data presented as mean ± SD. † Data presented as median (25th, 75th percentile). ‡ Adjusted $P < 0.05$ *vs.* preoperative night. § Adjusted $P < 0.05$ for OSA *vs.* non-OSA on the same night.

Non-OSA = patients without obstructive sleep apnea; OSA = patients with obstructive sleep apnea; REM = rapid eye movement.

was found between patients with or without oxygen therapy, 0.3 (0, 6.0) events per hour *versus* 1.8 (0, 3.4) events per hour ($P = 0.908$).

Compared with OSA patients without oxygen therapy, OSA patients with oxygen therapy had a lower AHI (13.9 [2.9, 37.9] events per hour *vs.* 29.5 [13.0, 43.4] events per hour) and hypopnea index (11.1 [2.2, 24.4] events per hour *vs.* 19.8 [14.0, 44.5] events per hour) on postoperative N1. However, the difference was not statistically significant ($P = 0.201$ and $P = 0.394$, respectively). In both OSA and non-OSA patients, no statistically significant difference in REM AHI, AHI during non-REM sleep, central apnea index, obstructive apnea index, and hypopnea index was found between patients with and without oxygen therapy.

The patients receiving oxygen therapy had significantly decreased REM sleep in both OSA and non-OSA patients; 0% (0, 8.2) *versus* 10.9% (1.4, 18.3); $P = 0.048$ in OSA patients; and 0% (0, 3.9) *versus* 10.6% (7.0, 18.0); $P = 0.005$ in non-OSA patients.

Discussion

To date, this is the first comprehensive data collection in postoperative change of sleep-breathing disorders and sleep architecture up to postoperative night 7 (N7) in patients with

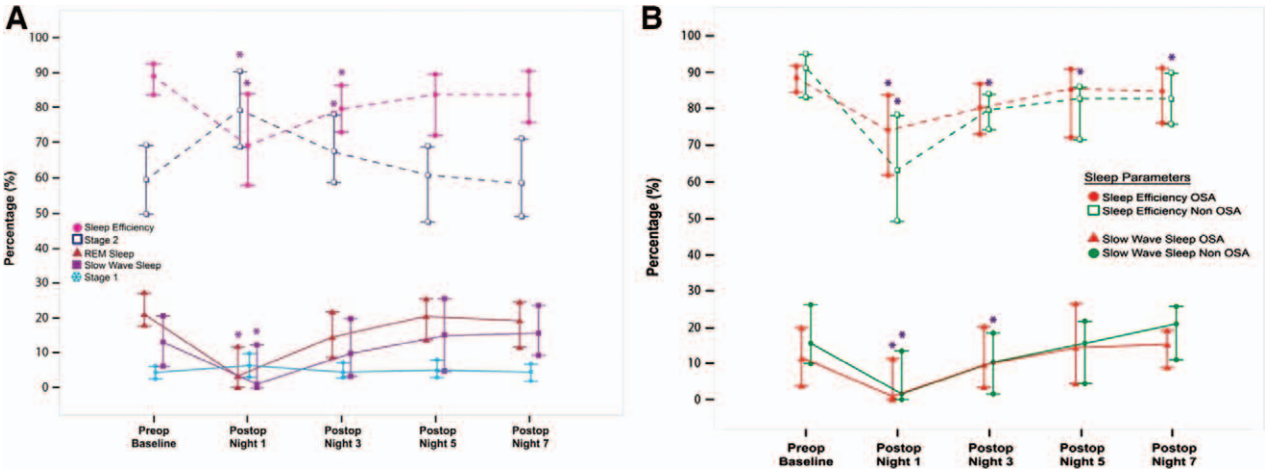

Fig. 4. Perioperative change in sleep architecture in all patients (*A*) and obstructive sleep apnea (OSA) *versus* non-OSA patients (*B*). The *vertical lines* represent the interquartile range and the *points in middle* represent median. *Adjusted $P < 0.05$ *versus* preoperative measurement; + adjusted $P < 0.05$ *versus* same parameter in non-OSA on same night. REM = rapid eye movement.

and without OSA. Overall, AHI and AHI during non-REM sleep were increased after surgery in both OSA and non-OSA patients, with the unexpected greatest increase on N3. AHI was higher in OSA patients with increase in the hypopnea index as the major component. Central apnea index was increased on postoperative N1 in non-OSA patients, which was associated with opioid requirement. A significant decrease in sleep efficiency, REM sleep, and slow-wave sleep occurred in all patients after surgery regardless of OSA status and most considerable on N1. The patients receiving oxygen therapy experienced more substantial depression of REM sleep.

In OSA patients, AHI was increased by 61.1% on N3, accompanied with an increase in oxygen desaturation index by 66% and a fourfold increase in cumulated time percentage with oxygen saturation less than 90%. The lowest oxygen saturation was also present on postoperative N3. The fact that OSA patients suffered from the most severe oxygen desaturation and highest AHI on postoperative N3, instead of postoperative N1, may be related to 53% of patients receiving oxygen therapy on postoperative N1 *versus* 8% on postoperative N3. The oxygen therapy may have attenuated the oxygen desaturation episodes and consequently decrease the number of hypopneic episodes on postoperative N1. Although the decrease in hypopnea index in patients receiving oxygen therapy was not statistically significant in both OSA and non-OSA patients, the difference could become significant in a larger study sample.

The change in the sleep architecture may have also contributed to the finding that the most significant exacerbation of sleep-breathing disorders occurred on postoperative N3. On postoperative N3, REM sleep had greatly recovered from the deep depression on N1 and REM AHI was considerably higher than total AHI. Oxygen desaturation index also followed a similar pattern as REM AHI. This is consistent with the previous observation that postoperative rebound of REM sleep may contribute to the development of sleep-disordered breathing and nocturnal episodic hypoxemia.[25]

In our study patients, hypopnea was the major type of sleep-breathing disorder that was significantly increased after surgery. The depression of respiration and the increased nocturnal episodic hypoxemia may have increased the scoring of hypopnea events. The exact mechanism and the clinical implication of the increased hypopnea events still need to be determined.

That the AHI and oxygen desaturation peaked on postoperative N3 instead of postoperative N1 is surprising and has important clinical implications. According to the American Society of Anesthesiologists guideline, OSA patients are to be in a monitored bed in the postoperative period.[30] It is impractical to monitor OSA patients for a few postoperative nights. Strategies, such as identifying patients with OSA preoperatively, perioperative CPAP, or precautions may mitigate these risks and minimize adverse outcomes in OSA patients.[31]

A large variation in AHI and hypoxemia did exist between the individual patients. In some non-OSA patients, postoperative AHI was increased. The mechanism for this is unknown and needs to be further explored. There are several possible causes. Due to the night-to-night variability in the frequency of sleep apnea and hypopnea,[32,33] and first night effect,[34] some OSA patients might have been missed by a single night of polysomnography. Genetic variations may make some non-OSA patients especially sensitive to opioids.[35–37] The anatomic feature of upper airway may also contribute to the unexpected postoperative AHI increase. The patients with small maxillomandible enclosure are particularly vulnerable to upper airway obstruction.[38,39]

Gislason *et al.*[40] showed that there were increased endogenous opioids in the cerebrospinal fluid of patients with sleep apnea syndrome. As a result, OSA patients had increased sensitivity to opioids. The level of endogenous opioids was decreased 6 months after surgical treatment of the sleep apnea syndrome.[40] The postoperative requirement of opioid was negatively associated with preoperative nadir Spo_2 in children with OSA, which may be due to to an up-regulation of central opioid receptors consequent to recurrent hypoxemia.[41] We did not found a similar association in our patients. Although the opioid requirement in OSA patients was less than that in non-OSA patients, the difference was not statistically significant. We found that in non-OSA patients, the first 24-h opioid requirement was associated with central apnea index and obstructive apnea index on postoperative N1. But a similar association was not found in OSA patients. Opioid can induce central respiratory depression through μ- and κ-opioid receptor.[42] Also, it can inhibit central tonic outflow to the primary upper airway dilator, genioglossus muscle.[42,43] Previous study shows that the perioperative morphine dose was predictive of central apneas for both patients with OSA risk and control patients,[44] which is different from our results in OSA patients. Further research is needed to clarify the relationship between opioids and sleep-disordered breathing in OSA patients.

A significant postoperative decrease in sleep efficiency, percentage of REM sleep, and slow-wave sleep with nadir on N1 has been reported in non-OSA patients.[23–25,45,46] Poor sleep quality characterized with reduced sleep efficiency, slow-wave sleep, and REM sleep was also observed on N1 in pediatric patients undergoing adenotonsillectomy.[47] Sleep efficiency has been shown to decrease as age increase.[48] Two studies have shown that there is a "rebound" in REM sleep and slow-wave sleep on N3.[24,25] In our study, we observed a "rebound" in slow-wave sleep on N3. However, we did not observe that postoperative REM sleep exceeded the preoperative level. On the contrary, the REM sleep did not fully recover to preoperative level by postoperative N7.

The difference may be due to a number of factors. Our preoperative sleep studies were done at home and several days before surgery. The sleep pattern of our patients during

preoperative polysomnography should be very close to their normal sleep pattern. In both the studies by Knill *et al.*[24] and Rosenberg *et al.*,[25] patients had their preoperative polysomnography done in the hospital on the night before surgery. Thus the sleep pattern could be altered by anxiety, change of environment, and also disturbances of sleep by the measurement of vital signs in the hospital. Thus, the amount of preoperative REM sleep in these studies may have represented a suppression of REM sleep.

The difference in the type of surgery, anesthetics and opioid requirement, age, and sex may also contribute to the difference in the results. Both studies by Knill *et al.*[24] and Rosenberg *et al.*[25] were done on younger patients without OSA undergoing abdominal surgery. In our study, we had both OSA and non-OSA patients, 59% patients underwent orthopedic procedures. REM sleep decreases as age increases[49] and laparoscopic cholecystectomy causes less sleep disturbance than open abdominal surgery.[26]

The anesthetics may also contribute to the alterations in sleep architecture. In the previous studies,[24,25] thiopental was used for induction of anesthesia. In our patients, propofol was used to induce anesthesia. Propofol abolished REM sleep[50] and was not associated with REM rebound.[51] Also, the majority of our patients received morphine which might partly account for the REM suppression. Opioids reduce slow-wave sleep and REM sleep through μ-receptor.[52–54]

Our data also show that both OSA and non-OSA patients receiving oxygen therapy had profoundly depressed REM sleep on postoperative N1. It is not clear whether the decrease in REM sleep was directly associated with oxygen therapy or because the patients receiving oxygen therapy had adverse events and required more frequent attention and care from the healthcare team, which might result in more frequent interruption to sleep.

The potential causes for postoperative sleep disturbance include surgical stress response (such as the site and duration of surgery), inflammatory factors (such as pain, opioid requirement), psychological factors, and environmental factors (such as noise, nursing procedures, and light).[55] The increased daytime sleep (including REM sleep) may also decrease nocturnal sleep efficiency, REM sleep, and slow-wave sleep.[46]

There are several limitations of the study. To avoid interference with the perioperative care, we did not control the type of surgery, perioperative medications such as opioids, and oxygen therapy. This may increase the difficulty for data interpretation. Another limitation is that the sleep studies were carried out with a portable level 2 device. Due to the limitation of the portable device, some analyses such as REM density cannot be done.

Also, the sleep monitoring was only done during night time, which might not detect diurnal changes in sleep-wake activity or sleep-disordered breathing. Finally, there may be a selection bias because the patients with OSA-related symptoms were more likely to give consent to the study, the patients wearing CPAP were excluded, and some patients with nausea, vomiting, and severe pain self-withdrew from the study.

In conclusion, this prospective cohort study shows that the OSA patients experienced a significant decrease in sleep efficiency, REM sleep, and slow-wave sleep on postoperative N1 and gradually recovered postoperatively. There was a significant exacerbation in sleep-disordered breathing with the most significant increase in AHI and decrease in oxygen saturation on postoperative N3. The non-OSA patients also followed this pattern of postoperative change in sleep architecture and sleep-disordered breathing to a similar but lesser degree.

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Competing Interests

The authors declare no competing interests.

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