Perioperative Auto-titrated Continuous Positive Airway Pressure Treatment in Surgical Patients with Obstructive Sleep Apnea

A Randomized Controlled Trial

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ABSTRACT

Background: Obstructive sleep apnea (OSA) may worsen postoperatively. The objective of this randomized open-label trial is to determine whether perioperative auto-titrated continuous positive airway pressure (APAP) treatment decreases postoperative apnea hypopnea index (AHI) and improves oxygenation in patients with moderate and severe OSA.

Methods: The consented patients with AHI of more than 15 events/h on preoperative polysomnography were randomized into the APAP or control group (receiving routine care). The APAP patients received APAP for 2 or 3 preoperative, and 5 postoperative nights. All patients were monitored with oximetry for 7 to 8 nights (N) and underwent polysomnography on postoperative N3. The primary outcome was AHI on the postoperative N3.

Results: One hundred seventy-seven OSA patients undergoing orthopedic and other surgeries were enrolled (APAP: 87 and control: 90). There was no difference between the two groups in baseline data. One hundred six patients (APAP: 40 and control: 66) did polysomnography on postoperative N3, and 100 patients (APAP: 39 and control: 61) completed the study. The compliance rate of APAP was 45%. The APAP usage was 2.4–4.6 h/night. In the APAP group, AHI decreased from preoperative baseline: 30.1 (22.1, 42.5) events/h (median [25th, 75th percentile]) to 3.0 (1.0, 12.5) events/h on postoperative N3 ($P < 0.001$), whereas, in the control group, AHI increased from 30.4 (23.2, 41.9) events/h to 31.9 (13.5, 50.2) events/h, $P = 0.302$. No significant change occurred in the central apnea index.

Conclusions: The trial showed the feasibility of perioperative APAP for OSA patients. Perioperative APAP treatment significantly reduced postoperative AHI and improved oxygen saturation in the patients with moderate and severe OSA.

What We Already Know about This Topic

- Continuous positive airway pressure automatically adjusted by continuous analyses of flow profiles is an effective treatment for obstructive sleep apnea, but its effectiveness and acceptance in perioperative period are unknown

What This Article Tells Us That Is New

- In this randomized open-label clinical trial enrolling 177 patients with obstructive sleep apnea, auto-titrated continuous positive airway pressure successfully reduced the apnea hypopnea index, whereas, it remained abnormally high without the treatment
- Despite the effectiveness, only 26–48% of the patients used the continuous positive airway pressure for more than 4 h per night during the perioperative nights

OBSTRUCTIVE sleep apnea (OSA) is a common comorbidity in surgical patients.[1,2] Some surgical patients with OSA may not have been diagnosed or treated before their surgery.[3] OSA may have serious implications for anesthetic management, with an increased incidence of perioperative adverse events.[4–7]

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Continuous positive airway pressure (CPAP) is the mainstay treatment for the patients with moderate and severe OSA. Utilization of CPAP in the nonsurgical OSA patients significantly decreases the frequency of apnea and hypopnea. It also reduces the number of arousals, increases oxygen saturation,[8] reverses the increased incidence of hypertension in OSA patients,[9] and improves daytime sleepiness[10] and the quality of life.[11]

Postoperative CPAP treatment had been shown to decrease the incidence of postoperative complications in non-OSA patients undergoing abdominal surgeries.[12,13] To date, there has been no published literature to test the feasibility and effectiveness of perioperative CPAP utilization in the surgical patients with OSA, to prevent postoperative worsening of sleep apnea and perioperative adverse events.

Auto-titrated CPAP (APAP) is a special type of CPAP. On the basis of breath-by-breath measurement of flow, APAP adjusts the delivered pressure over the course of the night to the minimal pressure necessary to maintain an unobstructed airway. Starting treatment with APAP can be as effective as CPAP treatment with polysomnography titration.[14–16] The advantages of APAP include that treatment can be initiated without in-laboratory CPAP titration and the pressure applied can respond to the changes in airway resistance. These features can be very helpful for the surgical patients with suspected OSA because the time interval between the preoperative visit and the scheduled surgery is usually short. It may be difficult to assess a patient suspected of OSA and initiate CPAP treatment without delaying the scheduled surgery. Also, a pressure setting established by in-laboratory polysomnography on an outpatient setting may not be equally effective in the perioperative environment, with possible fluid shift, sedation due to narcotics and changes of body positions.

The objective of this trial is to determine if perioperative APAP treatment decreases postoperative apnea hypopnea index (AHI) and improves oxygenation in the surgical patients with moderate and severe OSA. Our hypothesis is that utilization of the perioperative APAP is an effective pathway to prevent the postoperative exacerbation of AHI and oxygen desaturation in the surgical patients with moderate and severe OSA.

Materials and Methods

Study Design

This is a prospective randomized controlled trial, which has been registered at "http://clinicaltrials.gov" (NCT01249924). Perioperative administration of APAP (S8 Auto Set II; ResMed Corp., San Diego, CA) at night is the trial intervention. The primary outcome was the AHI detected by polysomnography on the postoperative night 3 (N3). The AHI was defined as the number of apneas and hypopneas per hour of sleep. The secondary outcomes were the oxygen desaturation index and the cumulative time percentage with SpO_2 less than 90% (CT90) measured from nocturnal oximetry on 3 preoperative, and 5 postoperative nights. Oxygen desaturation index was defined as the average hourly number of desaturation episodes with at least 4% desaturation and lasting at least 10 s.

Study Population

The study was carried out at the Anesthesia Departments of Toronto Western Hospital of University Health Network, and Mount Sinai Hospital in Toronto, from December 2009 to November 2011. Approvals from the Institutional Review Board of both hospitals were obtained. The approval numbers are 09-0093-B for University Health Network and 09-0037-E for Mount Sinai Hospital. The inclusion criteria of patients approached for consent in the preoperative clinics were: (1) a minimum of 3 nights of hospital stay; (2) age: more than 18 and less than 80 yr old; (3) identified as high risk of OSA or a history of OSA without CPAP treatment. The exclusion criteria of patients were: (1) unwilling or unable to give informed consent; (2) undergoing nasal, eye, head/neck surgery, intracranial, or cardiac/thoracic surgery; (3) currently undergoing treatment for sleep apnea including CPAP; (4) requiring prolonged postoperative ventilation; (5) New York Heart Association functional class III and IV; (6) valvular heart disease, dilated cardiomyopathy, implanted cardiac pacemaker, or unstable angina; (7) myocardial infarction or cardiac surgery within 3 months; (8) chronic obstructive pulmonary disease, or asthma; (9) presence of tracheostomy, facial, neck, or chest wall abnormalities; (10) abdominal aortic aneurysm surgery, chemotherapy, or immunosuppressive therapy within 3 months; (11) visiting preoperative clinic less than 3 days before surgery; and (12) requiring postoperative nasogastric tube.

Patient Recruitment, Intervention, and Follow-up

As shown in the flow chart (fig. 1), the patients visiting preoperative clinics for their scheduled surgery were approached by research coordinators. The eligible patients were invited to answer the STOP-Bang questionnaire.[17] Informed consent were obtained from the patients identified as high risk of OSA by the STOP-Bang questionnaire (score ≥3) or a history of OSA without CPAP treatment. They were scheduled for a home polysomnography with a portable device (Embletta X100; Embla, Broomfield, CO), as previously described.[18]

The patients with AHI more than 15 events/h were randomized into two groups: control or APAP group by blocks of 20 generated with SAS 9.2 (SAS Institute Inc., Cary, NC). The allocation of patients was made by a research analyst not involved in patient enrollment or follow-up. The control group was managed by the anesthesiologists and surgeons as per routine practice, including CPAP treatment, if necessary. For the APAP group, the patients were treated for 2 to 3 preoperative nights (N1–3) at home, and 5 postoperative nights (postoperative N1–5) in the hospital or at home, in addition

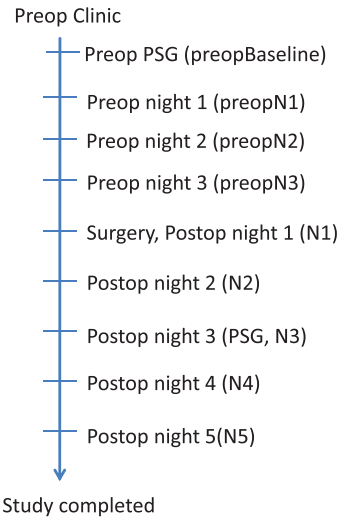

Fig. 1. Study flow chart. Patients were treated with auto-titrated continuous positive airway pressure + routine care or routine care only, for 3 preoperative and 5 postoperative nights. Patients were monitored with oximetry on all nights. Polysomnography (PSG) was done at home preoperatively as baseline and on the postoperative night 3. N = night; Postop = postoperative; Preop = preoperative.

to the routine management by the anesthesiologists and surgeons (fig. 1). The use of APAP for preoperative N1–3 was to familiarize patients with the devices. Supplemental oxygen, if needed, was administered through a "Y" shape connector between the mask and the APAP device, at the discretion of the physician in charge. A research coordinator instructed and assisted patients with APAP at home and in hospital.

Because several studies showed that S8 Auto Set II (ResMed Corp.) has an equivalent effect to the traditional fixed pressure CPAP,[14,15,19,20] it was chosen as the intervention device for the study. S8 Auto Set II has an operating pressure range of 4–20 cm H_2O with expiratory pressure relief. The device also tracks the usage, leak, respiratory events, and pressure.

All study patients were asked to undergo polysomnography with Embletta X100 on postoperative N3 in hospital, as previously described,[18] except that the nasal flow was measured *via* a nasal prong in the control group, and *via* a tubing connected with the oxygen therapy orifice on the CPAP mask in the APAP group. They were also monitored for oxygen saturation with nocturnal oximetry PULSOX-300i (Konica Minolta Sensing, Inc., Osaka, Japan) for preoperative N1–N3, and postoperative N1–N5. Oximeter data were processed as previously reported.[21] The study coordinator visited patients daily to assist them with the devices, collect data, and document adverse events during the hospital stay, or called patients daily when at home.

Data Analysis and Statistics

Sample Size Estimation. Because there has been no published literature on APAP in the surgical patients with OSA, we based our estimation of the sample size on the changes in AHI after CPAP treatment in the OSA patients. According to the Lee study,[22] after 3 weeks of CPAP treatment, the mean change in AHI was −30.7 events/h (SD 23.1) in the CPAP group and −5.8 events/h (SD 18.3) in the placebo group.[22] If we assume that AHI change was similar in the APAP and the control group, two-tailed *t* test with α error = 0.025 and power = 0.9 was used, and the estimated sample size was 20 for each group. The withdrawal rate was expected to be high and estimated as 50%. The number of patients randomized into each group is estimated to be 20 × 2 = 40 with the total sample size of 80.

Data Analysis

Data were entered into a specifically designed Microsoft (Redmond, WA) Access database and checked for possible errors. SAS 9.2 for Windows (SAS Institute Inc.) was used for data analysis. A descriptive statistics was done on the demographic characteristics and the parameters measuring sleep breathing disorders on the preoperative baseline polysomnography. The usage of APAP was analyzed based on intention-to-treat analysis by imputing missing data with zero. Polysomnography data on postoperative N 3 were first analyzed based on intention-to-treat by imputing missing data with preoperative value (last observation carried forward). Supplementary analyses were carried out according to the dropout and the compliance, when necessary. The statistical tests were two-tailed tests, and a *P* value less than 0.05 was accepted as statistically significant. The continuous data with normal distribution were presented as mean ± SD, and the comparison between two groups was checked by independent two-sample *t* test. The data with skewed distribution were presented as median (25th, 75th percentile) and the comparison between two groups was checked with nonparametric test—Mann–Whitney U test. The *P* values for comparisons of oxygen desaturation index and cumulative time percentage with pulse oxygen saturation less than 90% between two groups at each perioperative night were adjusted with the Holm–Bonferroni method. The categorical data were presented as frequency and percentage, and chi-square test was used for statistical significance check. To adjust for the effect of APAP treatment on AHI in the context of confounding factors, analysis with generalized linear model was carried out.

Results

Study Population and Baseline Data

The recruitment and follow-up of patients is shown in figure 2. A total of 2,659 patients were screened, with 386 patients giving consent for home polysomnography. One hundred seventy-seven patients with AHI more than 15 events/h were randomized, APAP: 87 and control group: 90. There was no significant difference between the APAP and the control group in terms of the demographic data,

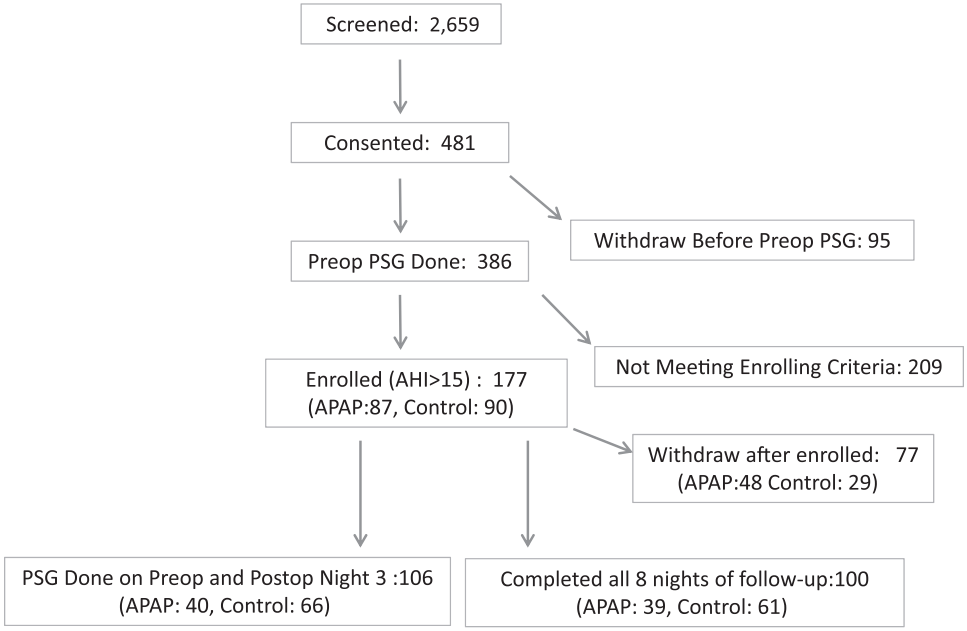

Fig. 2. Patient recruitment and follow-up flow chart. AHI = apnea hypopnea index; APAP = auto-titrated continuous positive airway pressure; Postop = postoperative; Preop = preoperative; PSG = polysomnography.

preoperative AHI, and the type of surgery and anesthesia in all randomized patients or the patients who underwent polysomnography on postoperative N3 (table 1). No difference in sleep architecture was found between the two groups at the baseline (data not shown). The parameters measuring sleep breathing disorder on the preoperative baseline polysomnography was summarized in table 2 and represented in figure 3A. Although a large variation in each measurement

Table 1. Demographic Data

	Randomized Patients			Patients with PSG on N3		
	APAP	Control	*P* Value	APAP	Control	*P* Value
N	87	90		40	66	
Sex, F/M	35/52	36/54	0.862	20/20	28/38	0.448
Age, yr	61 ± 11	63 ± 9	0.271	59 ± 11	53 ± 9	0.095
BMI, kg/m^2	33.5 ± 7	32.9 ± 7	0.589	32.4 ± 6	31.6 ± 6	0.531
Neck circumference, cm	42.8 ± 8	41.1 ± 4	0.112	44.9 ± 13	40.9 ± 3	0.146
AHI, events/h	30.1 (22.1, 42.5)	25.6 (18.8, 39.6)	0.175	30.4 (23.2, 41.9)	29.0 (18.8, 40.8)	0.557
72 h opioid requirement, mg	62 (43, 77)	53 (36, 87)	0.539	63 (53, 85)	57 (34, 93)	0.352
ASA Physical Status						
1	0	1	0.525	0	1	0.367
2	32	39		15	29	
3	53	49		24	35	
4	2	1		1	1	
Type of surgery						
Orthopedic	47 (54)	51 (57)	0.657	20 (50)	40 (60)	0.599
Spine	7 (8)	7 (7)		5 (13)	3 (5)	
Gynecology	3 (4)	4 (5)		2 (5)	4 (6)	
General	20 (23)	20 (23)		10 (25)	13 (20)	
Urology	7 (8)	2 (2)		3 (8)	2 (3)	
Other	3 (4)	6 (6)		0	4 (6)	
Type of anesthesia						
General	54 (62)	49 (54)	0.442	25 (63)	34 (52)	0.377
Spinal/regional	33 (38)	41 (46)		15 (37)	32 (48)	

AHI = apnea hypopnea index; APAP = auto-titrated continuous positive airway pressure; ASA = American Society of Anesthesiologists; BMI = body mass index; F = female; M = male; PSG = polysomnography.

was shown in the box plot (fig. 3A), no significant difference was found between the two groups.

APAP Usage and Compliance

Due to the dropout, 106 patients (APAP: 40 and control: 66) had polysomnography on postoperative N3, and 100 patients (APAP: 39 and control: 61) completed follow-up for postoperative N1–N5. The percentage of patients wearing APAP during all observed nights was 45% (39 of 87). The reasons for noncompliance were listed in table 3. Postoperative generalized discomfort, nausea and vomiting accounted for the majority of withdrawals, 73% in APAP group and 79% in control group.

Because not all patients were ready for APAP on preoperative N1, more patients used CPAP on preoperative N2 (table 4). Subsequently, the number of patients using APAP gradually decreased. By postoperative N5, only 45% (39 of 87) of the randomized patients were compliant with APAP.

The median usage time of APAP on all observed nights ranged from 0 to 3.8 h/night, mean from 2.4 to 4.6 h/night with 26–48% of patients using 4 h/night or more (table 4). The 95 percentile pressure ranged from 9.0 ± 3 to 10.2 ± 2 cm H_2O. No significant postoperative pressure increase was observed. Although there was a slight increase in median and 95 percentile leakage on postoperative N1–4, the apnea index detected by APAP device did not increase on these nights (table 4).

Parameters Measuring Sleep Breathing Disorders

In the APAP group, AHI decreased significantly from the preoperative baseline: 30.1 (22.1, 42.5) events/h (median [25th, 75th percentile]) to 3.0 (1.0, 12.5) events/h; *P* value was less than 0.001 on postoperative N3, whereas, in the control group, AHI increased from 30.4 (23.2, 41.9) events/h preoperatively to 31.9 (13.5, 50.2) events/h; *P* value was equal to 0.302 on N3 (table 2). To compare the polysomnography parameters of the two groups on N3, data were analyzed based on the intention-to-treat analysis (table 2; "All Patients [Intention to Treat]"), and followed by supplementary analysis based on the available data (fig. 3B and table 2; "Patients with N3 polysomnography"). Both analyses yielded similar results. Compared with the control group, APAP patients had a decreased AHI: 19.8 (3.7, 33.7) events/h (median [25th, 75th percentile]) *versus* 28.6 (17.2, 45.1) events/h, $P = 0.002$ in the control group for intention-to-treat analysis, and 3.0 (1.0, 12.5) *versus* 31.9 (13.5, 50.2) events/h, $P < 0.001$ in the control group for analysis of patients with postoperative N3 polysomnography. The patients treated with APAP also had a significantly lower value in AHI during rapid eye movement sleep and nonrapid eye movement sleep, obstructive apnea index, hypopnea index, respiratory arousal index, oxygen desaturation index, and lowest Spo_2. No statistically significant difference was observed in central apnea index and mixed apnea index.

To further explore the effect of APAP on the perioperative AHI change, individual AHI values from all patients who did polysomnography both preoperatively and on N3 were shown in figure 4A (n: APAP: 40 and control: 66). In general, compared with the preoperative baseline, the AHI decreased significantly on N3 in the APAP group whereas AHI showed a trend of increase in the control group. There was some variability among the APAP patients. Compared with the preoperative baseline, AHI increased in four (10%) patients in the APAP group on N3 *versus* 32 (48.5%) patients in the control group. In patients wearing APAP more than 4 h on N3, the change in AHI was shown in figure 4B (APAP, N = 26 and control, N = 66). In 26 patients with better APAP compliance, three patient experienced AHI increase on N3.

In the control group, no difference in sex, age, body mass index, neck circumference, rapid eye movement sleep percentage, and supine sleep percentage was found between the patients who had postoperative AHI increase and those who did not (data not shown). There was no difference between the two groups in the sleep architecture on postoperative N3 except that the patients in control group had longer stage 1 sleep (table 5).

Oxygen Desaturation Index and Cumulative Time Percentage with Spo_2 Less Than 90% (CT90)

Compared with the control group, oxygen desaturation index in the APAP group was significantly decreased on preoperative N1 and N3 (adjusted $P < 0.05$ for all comparisons; fig. 5A). CT90 in APAP group also was significantly decreased on preoperative N2 and 3 (adjusted $P < 0.05$ for all comparisons; fig. 5B).

Postoperative Oxygen Therapy and APAP Treatment

The percentage of patients on oxygen therapy in the APAP *versus* the control group was 84.5 *versus* 81.7%, respectively, on N1, 54 *versus* 34% ($P = 0.031$), respectively, on N2, and 59 *versus* 33% ($P = 0.008$), respectively, on N3. A multivariate generalized linear model was used to adjust the confounding effect of oxygen therapy on the AHI difference between the APAP and the control group on N3. AHI on postoperative N3 was the response variable. The treatment group, oxygen therapy, preoperative AHI, opioid consumption first 72 h, age, sex, body mass index, the type of anesthesia, and surgery were the independent variables. APAP treatment was found to be the only significant factor for AHI on postoperative N3 polysomnography, with *P* value less than 0.001. The *P* value for all other factors is more than 0.2.

Postoperative Complications and APAP Treatment

As summarized in table 6, no major complications occurred in this study population. No difference in the incidence of postoperative complications was found between the two groups. The most common complication was clinically observed hypoxemia.

Table 2. Polysomnography Data

	Preoperative Baseline		
	All Randomized Patients		
	APAP	Control	*P* Value
N*	87	90	
AHI, events/h†	30.4 (23.2, 41.9)	29.0 (18.8, 40.8)	0.555
REM AHI, events/h†	47.0 (30.2, 57.4)	47.8 (28.0, 55.7)	0.953
NREM AHI, events/h†	25.0 (16.3, 43.4)	22.6 (15.0, 41.8)	0.762
Obstructive apnea index†	9.4 (3.5, 16.2)	7.5 (4.0, 15.6)	0.442
Central apnea index†	0 (0, 1.1)	0 (0, 1.2)	0.956
Mixed apnea index†	0 (0, 0.5)	0 (0, 0.4)	0.853
Hypopnea index†	16.2 (12.0, 22.5)	16.1 (10.6, 23.4)	0.343
Respiratory arousal index†	9.4 (4.3, 14.2)	8.1 (3.8, 13.7)	0.861
Oxygen desaturation index†	25.2 (15.8, 36.1)	20.3 (15.6, 33.4)	0.333
Lowest Spo_2‡	79.2 ± 7.1	79.5 ± 7.1	0.845
CT90†	4.1 (1.0, 13.5)	3.2 (0.7, 9.4)	0.866
Wake Spo_2‡	95.0 ± 1.5	95.1 ± 1.6	0.204

* Data present as "N." † Data present as "median (25th, 75th percentile)." ‡ Data present as "mean ± SD." § $P < 0.05$ *vs.* "preoperative." AHI = apnea hypopnea index; APAP = auto-titrated continuous positive airway pressure; apnea index = average hourly number of apnea episodes; CT90 = cumulative time percentage with Spo_2 <90%; hypopnea index = average hourly number of hypopnea episodes; mixed apnea index = average hourly number of apnea episodes with characteristics of both obstructive or central apnea; NREM AHI = apnea hypopnea index during nonrapid eye movement sleep; obstructive or central apnea index = average hourly number of obstructive or central apnea episodes; REM AHI = apnea hypopnea index during rapid eye movement sleep; respiratory arousal index = average hourly sleep arousals due to respiratory events; wake Spo_2 =average Spo_2 while patient awake during polysomnography.

Discussion

To date, our study is the first randomized controlled trial to investigate the effectiveness of perioperative APAP in OSA patients undergoing surgeries. The trial showed the feasibility of the application of perioperative APAP for the surgical patients with untreated OSA. Perioperative APAP treatment effectively decreased AHI and improved postoperative oxygen saturation in the surgical patients with moderate and severe OSA. However, the overall compliance rate of APAP for the surgical patients in the perioperative setting was relatively low at 45%

CPAP is established to be the mainstay treatment for the nonsurgical patients with moderate and severe OSA. Studies

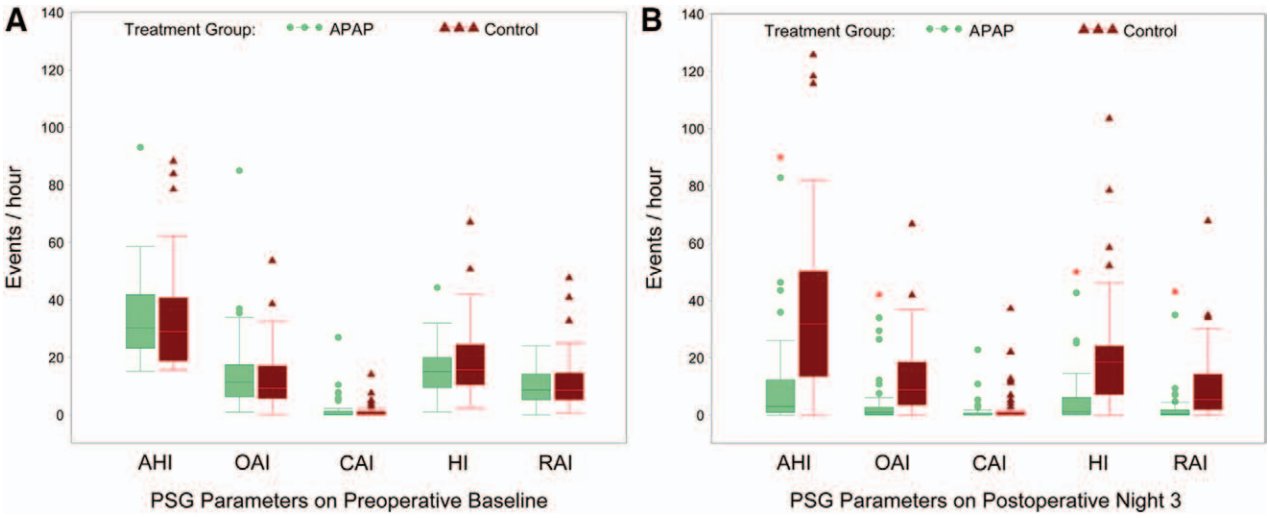

Fig. 3. The polysomnographic parameters measuring sleep breathing disorder on preoperative (*A*) and postoperative night 3 polysomnography (PSG; *B*). The data are presented in box plot. The *box* represents the interquartile range (IQR); the *line* inside the box represents the median; the *upper whiskers* indicate the largest value within 1.5 × IQR from the upper edge of the box; the *lower whiskers* indicate the smallest value within 1.5 × IQR from the lower edge of box; ● and ▲ indicate the outliers beyond 1.5 × IQR. AHI = apnea hypopnea index; APAP = auto-titrated continuous positive airway pressure; CAI = central apnea index; HI = hypopnea index; OAI = obstructive apnea index; RAI = respiratory arousal index. *$P < 0.05$ compared with control group.

Postoperative Night 3					
All Patients (Intention-to-treat)			Patients with N3 Polysomnography		
APAP	Control	*P* Value	APAP	Control	*P* Value
87	90		40	66	
19.8 (3.7, 33.7)§	28.6 (17.2, 45.1)	0.002	3.0 (1.0, 12.5)§	31.9 (13.5, 50.2)	<0.001
29.2 (5.9, 50.8)§	38.3 (20.6, 54.7)	0.030	4.0 (0.9, 8.5)§	40.0 (20.7, 82.0)	<0.001
2.3 (0.7, 11.5)§	29.7 (15.7, 49.6)	<0.001	2.3 (0.7, 11.5)§	30.0 (15.7, 49.6)	<0.001
2.8 (1.0, 10.8)§	7.3 (3.2, 16.3)	0.004	1.0 (0.2, 2.8)§	8.9 (3.5, 18.6)	<0.001
0 (0, 0.8)	0.2 (0, 1.0)	0.320	0 (0, 0.5)	0.2 (0, 0.8)	0.552
0 (0, 0.2)	0 (0, 0.3)	0.756	0 (0, 0)	0 (0, 0.2)	0.088
10.9 (1.3, 19.1)§	17.6 (8.4, 23.9)	<0.001	1.3 (0.3, 6.4)§	18.5 (5.7, 24.2)	<0.001
3.8 (0.4, 10.0)§	5.6 (2.8, 13.1)	0.007	0.4 (0, 1.5)§	5.3 (1.9, 14.3)	<0.001
18.7 (6.5, 33.2)§	26.1 (13.8, 44.7)§	0.010	6.5 (2.1, 23.2)§	28.6 (11.7, 49.0)§	<0.001
80.9 ± 8.2§	77.9 ± 8.7§	0.019	82.5 ± 9.0§	77.1 ± 9.3	0.003
4.2 (0.8, 12.3)	6.9 (1.4, 15.8)§	0.194	3.2 (0.4, 7.8)	7.6 (1.8, 40.5)§	0.087
94.2 ± 2.6§	94.0 ± 2.8§	0.481	93.7 ± 3.5	93.4 ± 3.0	0.677

show that CPAP improves both the subjective and the objective measures of sleepiness,[10,23] the quality of life,[11] the cognitive functions, and psychological well-being in the OSA patients.[24] Long-term follow-up demonstrates that CPAP treatment significantly reduces the incidence of cardiovascular events.[25]

The benefit of perioperative CPAP application in the non-OSA patients may be dependent on the type of surgery. Perioperative CPAP application prevented the occurrence of postoperative pulmonary complications in the non-OSA patients undergoing abdominal surgery,[12,13] but no benefit was found in cardiac surgery.[26]

Data on the perioperative CPAP application in the OSA patients undergoing surgeries are very limited. Reeder *et al.*[27] reported that a patient without diagnosed OSA experienced severe postoperative respiratory obstruction during sleep and was effectively rescued by nasal CPAP. Rennotte *et al.*[28] reported a case series of 16 patients with documented OSA. Two patients without CPAP suffered postoperative complications whereas 14 patients treated with CPAP had uneventful postoperative course. To date, our study is the first randomized controlled trial to investigate the effectiveness of perioperative CPAP in OSA patients undergoing surgeries. Our results show the practical aspect of a perioperative APAP pathway for the surgical patients with untreated OSA. APAP is effective in reducing AHI and improving oxygenation in the surgical patients with moderate and severe OSA. This finding is important to develop an evidence-based perioperative care protocol for the surgical patients with moderate and severe OSA.

Table 3. Reasons for Noncompliance, n (%)

	APAP	Control
Withdraw due to generalized discomfort, nausea or vomiting	35 (72.9)	23 (79.3)
Surgery cancelled	3 (6.3)	2 (6.9)
Withdraw due to changing mind	7 (14.6)	0 (0)
Mouth breather	1 (2.1)	0 (0)
Postoperative gastric tube	1 (2.1)	0 (0)
Severe pain	0 (0)	1 (3.5)
MRSA positive	0 (0)	1 (3.5)
Neurosurgery	1 (2.1)	0 (3.5)
Equipment failure	0 (0)	2 (7)
Total	48	29

APAP = auto-titrated Continuous positive airway pressure; MRSA = methicillin-resistant Staphylococcus aureus.

In the APAP group, a higher percentage of patients received supplementary oxygen therapy on postoperative N2 and 3. The healthcare team might be more likely to prescribe oxygen therapy to the OSA patients wearing APAP. This may interfere with the interpretation of the results. Improvement in oxygen saturation may be due to the oxygen therapy, especially on the first 3 postoperative nights. However, APAP application still played a significant role in improving oxygen saturation in the APAP patients. The reason is that the APAP group had significantly less desaturation on all preoperative nights and postoperative N4 and 5, when no patients were receiving oxygen therapy. The benefit of APAP is evident because obstructive apnea

Table 4. CPAP Usage and Apnea Index Detected by APAP Device (n = 87)

	Time, h*	Time, h‡	N (%)† (≥4 h/Night)	Pressure, cm H_2O‡		Leakage*		Apnea Index*, Events/h
				Median	95% Percentile	Median	95% Percentile	
Preop night1	2.0 (0, 7.0)	4.3 ± 5.3	38 (44)	6.6 ± 2.4	9.2 ± 2.8	0 (0–4.8)	16.8 (9.6, 22.8)	0.7 (0, 3.1)
Preop night2	3.8 (0, 7.1)	4.6 ± 4.6	42 (48)	7.2 ± 2.6	10.2 ± 2.3	1.2 (0–6.0)	16.8 (9.0, 27.6)	1.1 (0.1, 2.8)
Preop night3	2.9 (0, 5.7)	3.6 ± 4.1	37 (43)	6.9 ± 2.1	9.4 ± 2.4	1.2 (0–8.4)	18.6 (9.0, 27.0)	1.1 (0.1, 2.1)
Postop night1	1.8 (0, 7.8)	4.1 ± 5.3	34 (39)	7.0 ± 1.9	9.9 ± 2.3	2.4 (0–10.8)	21.6 (10.8, 30.0)	2.2 (0.7, 5.3)
Postop night2	1.0 (0, 7.0)	4.1 ± 5.9	34 (39)	7.1 ± 2.3	9.5 ± 2.6	2.4 (0–15.6)	21.6 (9.6, 39.6)	0.8 (0.2, 2.9)
Postop night3	1.3 (0, 6.7)	3.6 ± 4.8	30 (35)	6.8 ± 2.0	9.5 ± 2.6	3.6 (0–13.2)	21.6 (12.0, 34.8)	1.6 (0.4, 5.4)
Postop night4	0 (0, 5.2)	2.8 ± 3.9	28 (32)	6.7 ± 2.0	9.1 ± 2.5	0.6 (0–8.4)	21.6 (12.0, 36.0)	0.9 (0, 2.6)
Postop night5	0 (0, 4.6)	2.4 ± 3.6	23 (26)	6.5 ± 1.9	9.0 ± 2.8	0 (0–8.4)	19.2 (8.4, 33.6)	0.6 (0, 4.7)

* Data presented as median (25th, 75th percentile). † Frequency (%). ‡ Data presented as mean ± SD.

APAP = auto-titrated continuous positive airway pressure; CPAP = continuous positive airway pressure; Postop = postoperative; Preop = preoperative.

index, which is not affected by the level of oxygen saturation, was significantly decreased in the APAP group. Due to the small patient number and a low incidence of postoperative complications, a larger sample is needed to test whether APAP treatment could reduce the incidence of postoperative complications.

APAP has been developed in response to the needs to cope with pressure variation in eliminating the upper airway obstruction in the different sleep stages and positions,[29] and the lengthy waiting period for polysomnography and treatment.[30] APAP has been shown to be as effective as standard CPAP in terms of eliminating respiratory events and improving sleepiness.[31,32]

Patients with undiagnosed and untreated OSA may come for surgery.[3,33,34] Due to edema in the upper airway, possible fluid shift, sedation, and changes of position, the optimal pressure for eliminating sleep breathing disorders may vary after surgery. APAP may be a suitable device to deal with these challenges. Incorporating the screening tools, such as the STOP-Bang questionnaire,[17,35] portable polysomnography,[18] or nocturnal oximetry,[21] it is possible to develop a practical pathway for identifying, diagnosing, and treating the surgical patients with undiagnosed OSA within a limited time frame. In this study, we were able to demonstrate the perioperative feasibility of APAP treatment 3 days before surgery.

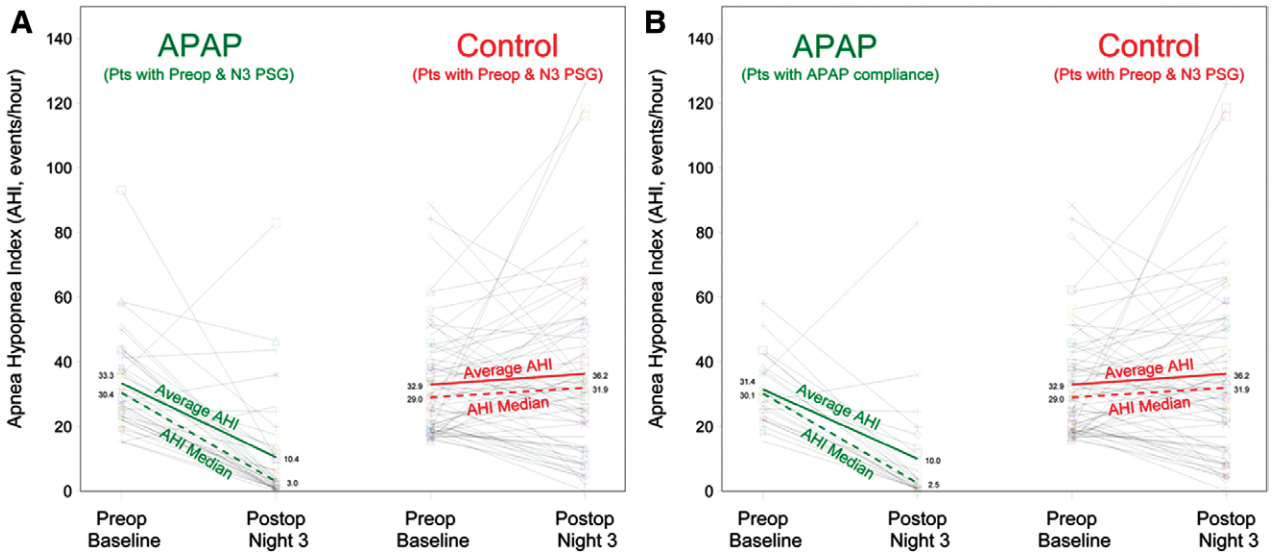

Fig. 4. Apnea hypopnea index (AHI) on preoperative baseline to postoperative night 3 polysomnography (PSG) in the auto-titrated continuous positive airway pressure (APAP) and the control group. (*A*) Represents AHI change in all patients who did both preoperative baseline and postoperative night 3 PSG (APAP, n: 40 and control, n: 66). (*B*) Represents AHI change in the patients with compliance to APAP (using APAP ≥4 h on the first 3 postoperative nights). The control group was same as in *A*: APAP, n: 23 and control, n: 66). The *gray lines* represent individual AHI values for each patient. The *thick solid color line* in each group represents the group average and the *thick broken color line* represents the group median. Essentially, compliance with APAP effectively decreased postoperative AHI. Postop = postoperative; Preop = preoperative.

Table 5. Sleep Architecture

	Preoperative Baseline			Postoperative Night 3		
	APAP	Control	*P* Value	APAP	Control	*P* Value
N*	87	90		40	66	
Total sleep time (min)† preop:preoperative	340 ± 88	338 ± 86	0.890	310 ± 105	304 ± 94‖	0.633
Sleep efficiency, %†	84 ± 12	85 ± 10	0.185	78 ± 16	74 ± 20‖	0.246
REM latency, min‡	91 (69, 130)	92 (62, 131)	0.589	86 (51, 142)	98 (63, 169)	0.572
REM sleep, %†	20.4 ± 6.0	19.3 ± 7.8	0.135	13.1 ± 10.0§	12.4 ± 8.8§	0.727
Stage 1, %†	11.1 ± 8.7	11.1 ± 7.0	0.553	8.5 ± 7.5	12.3 ± 11.4	0.027
Stage 2, %†	58.1 ± 10.1	59.1 ± 11.8	0.526	70.2 ± 14.9§	65.6 ± 20.6	0.383
Slow wave sleep, %†	10.4 ± 7.8	10.3 ± 9.6	0.996	8.3 ± 10.4‖	12.3 ± 11.4	0.510

* Data present as "N." † Data present as "mean ± SD." ‡ Data present as "median (25th, 75th percentile)." § $P < 0.001$ *vs.* "preoperative baseline." ‖$P < 0.01$ *vs.* "preoperative baseline."

APAP = auto-titrated continuous positive airway pressure; REM latency = time from light off to first rapid eye movement sleep; REM sleep = percentage of rapid eye movement sleep in total sleep time; sleep efficiency = percentage of total sleep time in sleep period; sleep stage 1 or 2 = percentage of stage 1 or 2 in total sleep time; slow wave sleep (previous stages 3 and 4) = percentage of slow wave sleep in total sleep time; total sleep time = total time being asleep.

One major limitation of this study is the high dropout rate and the low rate of compliance in the APAP group. Even with improved CPAP devices, compliance to CPAP is an ongoing challenge to OSA treatment in the general population. In the nonsurgical OSA patients, 5–50% of patients who were recommended CPAP may reject treatment before trying or soon after pressure titration and trial of CPAP.[36] Another 12–25% of patients starting CPAP, abandon it within 3 yr.[36] If adherence is defined as greater than 4 h of nightly use, 46–83% of patients with OSA have been reported to be nonadherent to treatment.[37] Evidence suggests that wearing CPAP for longer than 6 h per night decreases sleepiness, improves daily functioning, and restores memory to normal levels.[37] Recently we have shown that the CPAP compliant patients had a greater reduction in medication for comorbidities than the CPAP noncompliant patients.[38] The severity of OSA and symptoms, the early experience and effective troubleshooting, appropriate and timely education and support, and behavioral and cost factors appear to be the main predictors of uptake and long-term compliance.[36] Standard interventions, including mask optimization, heated humidification, topical nasal therapy, and sleep education followed by a change to flexible bilevel airway pressure, can improve compliance in the previously noncompliant patients.[39] Cognitive behavioral therapy intervention also increases start-up and adherence of CPAP.[40]

There are additional factors, such as preoperative stress, anxiety and postoperative discomfort, adverse events and treatment measures (such as gastric tube), which make the acceptance and adherence to CPAP a greater challenge. In our patients, the percentage of patients wearing APAP on all observed nights was 45%. Approximately 26–48% of all the

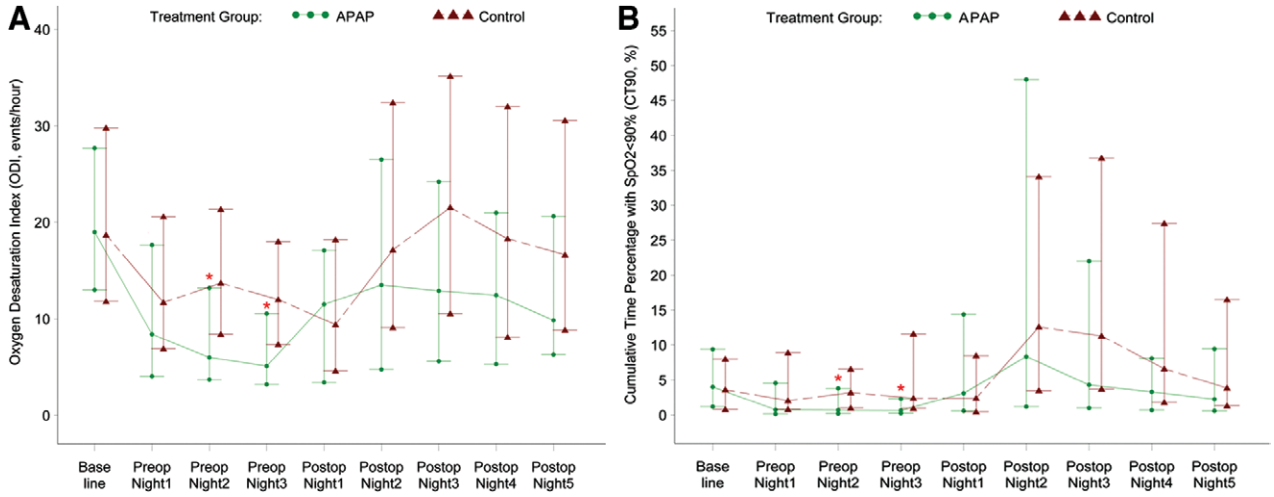

Fig. 5. Perioperative changes of oxygen desaturation index (ODI) (*A*) and cumulative time percentage with SpO_2 less than 90% (CT90) (*B*) from oximeter in the auto-titrated continuous positive airway pressure (APAP) and the control group. Data represented as median (*middle point*) and interquartile range (25th, 75th percentile) *Adjusted $P < 0.05$ compared with control group at the same night. Postop = postoperative; Preop = preoperative.

Table 6. Postoperative Complications

	APAP	Control	*P* Value
N	87	90	
Total postop Cx including hypoxemia	42 (48.3)	43 (48.3)	0.939
Total postop Cx excluding hypoxemia	1 (1.1)	4 (4.5)	0.367
Total cardiac Cx	0	1	
Bradycardia	0	1	
Total respiratory Cx including hypoxemia	42 (48.3)	43 (48.3)	0.939
Total respiratory Cx excluding hypoxemia	0	0	
Hypoxemia (Spo_2 ≤90%)	42 (48.3)	43 (48.3)	0.939
Total neurology complication	0	3 (3.4)	
Confusion	0	2 (2.2)	
Inadequate pain control	0	1 (1.1)	
ICU admission	5 (5.8)	4 (4.5)	
Planned	4	2	
Unplanned	1	2	

Data presented as frequency (percentage). Any patient with one or more events in specific category was counted as one case.
APAP = auto-titrated continuous positive airway pressure; Cx = complication; ICU = intensive care unit; Spo_2 = pulse oxygen saturation.

randomized patients used APAP 4 h/night or more, which is similar to 17–54% in nonsurgical patients.[37] The major reason for nonadherence was postoperative pain or discomfort, nausea and vomiting (73%), followed by changing of mind (15%). If we could better control the postoperative pain or discomfort as well as nausea and vomiting, and provide stronger support and education, compliance to APAP could be improved. To incorporate CPAP into the perioperative care for OSA patents, methods to increase the compliance to CPAP need to be further explored. In this study, patients received arbitrary APAP treatment for three preoperative days before surgery. The optimal timing of the preoperative initiation of CPAP is not known and needs to be further determined.

Another limitation is that the study was not double blinded. Because we want to compare the effect of APAP treatment with routine perioperative care, sham APAP was not used in the control group. This might have introduced bias, which could be responsible for the significantly higher rate of oxygen supplementation in the APAP group on postoperative N2 and 3.

In conclusion, we demonstrate the feasibility of a perioperative APAP program for the surgical patients with moderate to severe OSA. Perioperative APAP treatment decreased postoperative AHI and improved oxygen saturation in the surgical patients with moderate and severe OSA. Perioperative compliance to APAP needs to be improved.

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