

SCIENTIFIC INVESTIGATIONS

Obstructive Sleep Apnea Increases the Perioperative Risk of Cardiac Valve Replacement Surgery: A Prospective Single-Center Study

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Study Objectives: Sleep apnea is common in patients referred for cardiac valve replacement (CVR). We aimed to determine the association of obstructive sleep apnea (OSA) and central sleep apnea (CSA) with perioperative events in CVR surgery in patients with rheumatic valvular heart disease (RVHD).

Methods: Between April 2010 and April 2014, 290 patients with RVHD undergoing CVR were screened for sleep apnea 1 to 7 days before CVR. Baseline medications, cardiac function, sleep parameters, perioperative events, and related risk factors were evaluated.

Results: OSA patients had longer duration of intensive care unit (ICU) stay and mechanical ventilation compared with no sleep-disordered breathing and CSA patients. Patients with CSA had a higher rate of pacemaker use and higher first dose of dobutamine in ICU. NYHA Class and the presence of OSA were independently associated with overall worsening of postoperative recovery (ICU stay ≥ 25 h). Age, NYHA class, and the presence of OSA were independently associated with postoperative respiratory insufficiency (mechanical ventilation ≥ 20 h). Preoperative atrial fibrillation, pulmonary hypertension, and OSA were independently associated with postoperative pacemaker use.

Conclusions: RVHD patients with OSA have an increased incidence of perioperative adverse events. OSA was independently associated with overall postoperative recovery, respiratory insufficiency, and higher rate of postoperative pacemaker use, while CSA was not associated with postoperative events.

Keywords: cardiac valve replacement, central sleep apnea, obstructive sleep apnea, perioperative risk, rheumatic valvular heart disease

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INTRODUCTION

Sleep-disordered breathing (SDB) is evident in approximately 10% of adults; in patients with heart failure, its prevalence can exceed 50%.¹ Previous studies suggest that SDB is also common among candidates for heart surgery.²⁻⁶

SDB may affect postoperative outcomes. Several studies report that SDB increases risk in ambulatory surgery, coronary artery bypass surgery, vascular surgery, and general surgery.^{2,4,6-11} The American Society of Anesthesiologists recently issued practice guidelines for the perioperative management of obstructive sleep apnea (OSA),¹² in order to reduce the risk of adverse outcomes in patients with OSA and to improve perioperative care.

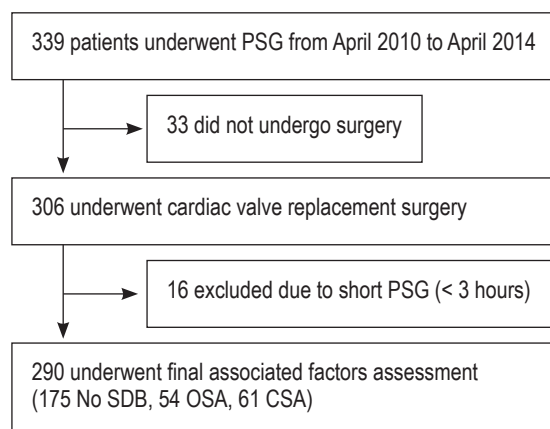
OSA has been found to be highly prevalent in patients undergoing cardiovascular surgery.² However, in this particular study population, OSA was not found to be associated with adverse postoperative outcomes due to the relatively small sample size (107 patients).² Another study was performed to observe the association of OSA on cardiovascular death, myocardial infarction, stroke, and unplanned revascularization in patients treated with percutaneous coronary intervention from eight centers in five countries; the results of this investigation are expected to be presented in 2016.¹⁰

BRIEF SUMMARY

Current Knowledge/Study Rationale: We have previously reported a high prevalence of sleep apnea (SA) among rheumatic valvular heart disease (RVHD) patients undergoing cardiac valve replacement (CVR) surgery; however, whether the presence of SA increases the perioperative risk of CVR is not well established. We explored the potential association of obstructive SA (OSA) and central SA (CSA) with perioperative events of CVR surgery in RVHD patients.

Study Impact: RVHD patients with SA have an increased incidence of perioperative complications. OSA was independently associated with overall worsening of postoperative recovery (longer duration of ICU stay), respiratory insufficiency (longer duration of mechanical ventilation), and higher rate of postoperative pacemaker use; while CSA was not associated with postoperative events.

In our previous study of patients with rheumatic valvular heart disease (RVHD), we demonstrated that 16.2% suffered from predominant OSA and 22.7% had predominant central sleep apnea (CSA).¹³ Despite the high prevalence of sleep apnea (SA) among patients referred for heart surgery, whether the presence of SA increases the perioperative risk of cardiac valve replacement (CVR) surgery is not well established. We hypothesized that SA increases the perioperative risks of CVR. Therein, we explored the potential associations between SA and perioperative events in CVR surgery in RVHD patients.

Figure 1—Flowchart of patient enrollment.

METHODS

Patients

Between April 2010 and April 2014, 339 RVHD patients undergoing CVR were screened for SA by overnight polysomnography (PSG) 1 to 7 (3.7 ± 1.6) days before CVR. Of them, 33 did not undergo cardiac surgery and 16 had an unqualified PSG (PSG time < 3 h). Finally, 290 underwent associated factors assessment (**Figure 1**). Baseline medications, cardiac function, perioperative events, and associated factors were evaluated. All patients were admitted to the cardiothoracic intensive care unit (ICU) for continuing treatment after CVR surgery. All the enrolled patients did not receive any sleep apnea-related treatment during the study.

Details on patient recruitment were previously reported.¹⁴ Patients were excluded if they had a previous diagnosis of SA, history of stroke or clinical signs of peripheral or central nervous system disorders, decompensated heart failure, and CVR combined with other cardiac surgery. At our institution all patients scheduled to undergo elective cardiac valve surgery are required to be admitted to the hospital for full preoperative assessment at least 7 to 14 days before the actual day of surgery.

Sample size calculation: According to the pre-trial results (OR = 3 for the postoperative outcome of postoperative respiratory insufficiency in patients with OSA vs. no OSA), we calculated a sample size of 153. With a presumed 20% exclusion rate due to unwillingness to do PSG or failure to undergo surgery, we planned to observe at least 200 patients. As we enrolled a total of 290 patients, under similar assumptions, there would be 97% power at a 0.05 significance level to detect a change in the OSA groups. This change corresponds to an odds ratio of 2.50.

This study was approved by the Clinical Study Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (#2012-SR-144) and registered in the Chinese Clinic Trial Registry Center (#ChiCTR-OCH-12002757). All the enrolled patients provided written informed consent prior to study participation.

Polysomnography

The sleep study was performed by unattended overnight PSG (Embla S4500 System, USA) as described previously.^{13,14} We

used the 2012 standard of the American Academy of Sleep Medicine (AASM) to score SA types and associated events:¹⁵ obstructive apnea—complete cessation of airflow with continued paradoxical chest and abdominal excursion ≥ 10 s; central apnea—complete cessation of airflow as well as complete cessation of chest and abdominal excursion ≥ 10 s; and hypopnea—reduction of airflow > 50% baseline lasting ≥ 10 s and associated with $\geq 4\%$ desaturation. The apnea-hypopnea index (AHI) was defined as the number of apneic and hypopneic events per hour of sleep. An AHI ≥ 5 events/h was considered diagnostic for sleep apnea. SA in which > 50% of events were central was defined as CSA; if > 50% of events were obstructive, it was defined as OSA. PSG data from April 2010 to 2012 were re-scored based on 2012 AASM criteria.

Cardiac Function Evaluation

New York Heart Association (NYHA) classification was assessed immediately after patients were enrolled. Atrial fibrillation (AF) was detected by 12-lead electrocardiography. Two-dimensional Doppler echocardiography was performed to assess left ventricular ejection fraction (LVEF). Patients were evaluated prospectively for the presence of pulmonary hypertension (PAH) (systolic pulmonary artery pressure ≥ 35 mm Hg) preoperatively by echocardiography.¹⁶

The 6-minute walk test (6MWT) was performed within 3 days after hospital admission, according to the guidelines issued by the American Thoracic Society.¹⁷ For those whose lower limb joints were damaged by rheumatic fever, 6MWT was not conducted.

To obtain a stable clinical status for all patients, optimal drug therapy was used, including digoxin, diuretics, nitrates, angiotensin-converting enzyme inhibitors, and β -blockers.

Cardiac Valve Replacement

CVR was performed in accordance with American College of Cardiology/American Heart Association guidelines, and indications for valve replacement in patients with valvular heart disease.¹⁸ The selection of valve prosthesis type was at the discretion of the operating surgeon. All procedures were performed under cardiopulmonary bypass with mild systemic hypothermia (30°C to 34°C). Myocardial protection was achieved with cold blood cardioplegia.

Perioperative Risk Assessment

Since length of ICU stay reflected overall postoperative condition, a length of ICU stay ≥ 25 h was considered to be an overall worse postoperative recovery. As mechanical ventilation duration stood for postoperative recovery time of respiratory function, postoperative respiratory insufficiency was defined as the need for prolonged mechanical ventilation (mechanical ventilation ≥ 20 h). Pacemaker use was recorded, and indicated whether postoperative cardiac rhythm is stable or not.

The following baseline parameters were selected as probably associated factors for perioperative events: age, NYHA Class, presence of AF, presence of PAH, LVEF, 6MWT distance, presence of OSA, and presence of CSA. Age, NYHA Class, AF, PAH, LVEF, 6MWT distance, OSA, and CSA were used as independent variables to analyze the following 3 perioperative

events one by one respectively: length of ICU stay ≥ 25 h, mechanical ventilation ≥ 20 h, pacemaker use.

Statistical Analysis

Statistical analyses were performed using SPSS statistical software (SPSS Inc., Chicago, IL, USA). Results are expressed as the mean \pm standard deviation, median (interquartile range) or percentage. Differences among the 3 groups (no SDB, CSA, and OSA) were compared using one-way analysis of variance (for normal distribution data) or Kruskal-Wallis H test (for non-normal distribution data). The Student-Newman-Keuls method was used for post hoc multiple comparisons. Comparisons between non-postoperative respiratory insufficiency and respiratory insufficiency, non-postoperative arrhythmia and arrhythmia were performed by t-tests. The χ^2 or Fisher exact univariate tests were used to analyze differences in proportions for the categorical data.

Binary logistic regression (forward stepwise regression) was used to model the association between various baseline predictor factors and perioperative events. Before logistic regression analysis, 2 dependent variables (length of ICU stay, mechanical ventilation) were split into 2 groups by the integers nearest to the mean. The following 3 perioperative events were dependent variables introduced in the binary logistic regression models one by one respectively: length of ICU stay ≥ 25 h, mechanical ventilation ≥ 20 h, and pacemaker use. The candidate independent variables were age, NYHA Class, AF, PAH, LVEF, 6MWT distance, OSA, and CSA. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for each of the significant risk factors. All values of $p < 0.05$ were considered to be statistically significant. Goodness of fit tests and cross-validation for detecting and preventing over-fitting were made for 3 dependent variables (length of ICU stay ≥ 25 h, mechanical ventilation ≥ 20 h and pacemaker use). The sensitivity/specificity and probability cutoffs were approximately 0.7, which proved that the models were reliable.

RESULTS

Baseline Characteristics

Of the 290 patients, 126 (43.4%) were males and 164 (56.6%) were females. The average age was 51.4 ± 10.4 years. Based on NYHA classification, 15.9, 64.8, and 19.3% of the patients were in NYHA classes II, III, and IV, respectively. Digoxin, diuretics, nitrates, angiotensin converting enzyme inhibitors, and β -blockers were used by 83.1, 90.7, 26.9, 48.6, and 47.9% of the patients, respectively.

In our study population, 54 patients (18.6%) had predominant OSA and 61 patients (21.0%) had predominant CSA. We compared clinical parameters among no SDB, OSA, and CSA patients (**Table 1**). CSA patients had a significantly higher prevalence of AF and PAH compared with OSA patient and no SDB patients. Compared with patients without SDB or with OSA only, patients with CSA had a remarkably lower LVEF and shorter 6MWT distance. With regards to perioperative events, OSA patients had longer duration of ICU stays and

longer duration of mechanical ventilation compared with CSA patients and no SDB patients. Patients with CSA had a high rate of pacemaker use and a higher first dose of dobutamine. PGS parameters among OSA, CSA and no SDB patients were compared and are shown in **Table 2**. As compared with no SDB patients, patients with OSA and CSA had a short total sleep time, lower sleep efficiency, higher AHI, lower mean, and minimal SpO_2 .

Characteristics between patients with and without postoperative respiratory insufficiency, as well as patients with and without postoperative arrhythmia were compared (**Table 3**). Patients with postoperative respiratory insufficiency were older, with a longer duration of hospital stay and higher prevalence of OSA. Patients with postoperative arrhythmia had a longer duration of hospital stay, a higher incidence of AF and PAH, compared to patients without postoperative arrhythmia.

Predictors of Perioperative Risks

Associated factors of perioperative events were analyzed (**Table 4**). NYHA class and the presence of OSA were independently associated with overall worsening of postoperative recovery (ICU stay ≥ 25 h). Age, NYHA class and the presence of OSA were independently associated with respiratory insufficiency (mechanical ventilation ≥ 20 h). Preoperative AF, PAH, and OSA were independently associated with postoperative pacemaker use.

DISCUSSION

In the present study, we confirmed our previous findings that SDB is common in patients undergoing CVR, and that patients with OSA or CSA had worsened heart function.¹³ Worse heart function may increase postoperative complications; however, whether OSA or CSA leads to adverse postoperative outcomes is not well established. In our study, we found that OSA was independently associated with overall worse postoperative recovery (ICU stays ≥ 25 h), respiratory insufficiency (mechanical ventilation ≥ 20 h) and higher rate of postoperative pacemaker use; while CSA was not significantly associated with postoperative events. We concluded that OSA is one of the major factors associated with perioperative outcomes in CVR surgery.

Previous studies have indicated that OSA is associated with postoperative complications after general and cardiac surgery.^{7,8,19–21} One study evaluated the risk of OSA in patients undergoing ambulatory surgery, and suggested that undiagnosed OSA is associated with increased perioperative events.⁴ OSA also increases the risk of acute kidney injury⁸ and readmission⁷ after coronary artery bypass grafting. In another study, Drager et al. found OSA to be independently associated with a higher rate of long-term cardiovascular events after coronary artery bypass grafting.²²

A recent study found that OSA is highly prevalent in patients undergoing cardiovascular surgery. However, in this population, the authors did not find an association between OSA and adverse postoperative outcomes due to a relatively small sample size (107 patients).² Another study was performed to

Table 1—Comparisons of clinical parameters among No SDB, OSA, and CSA patients.

	No SDB (n = 175)	OSA (n = 54)	CSA (n = 61)	p value
Age (y)	49.13 ± 10.51	54.43 ± 9.49*	55.20 ± 9.05*	< 0.001
BMI (kg/m ²)	22.85 ± 3.22	23.85 ± 3.70	23.32 ± 3.04	0.127
Serum albumin (g/L)	38.23 ± 5.54	37.00 ± 5.91	36.85 ± 6.54	0.175
Sex				0.023
Male, n	65	27	34	
Female, n	110	27	27	
NYHA class				< 0.001
II, n	37	9	0	
III, n	109	39	40	
IV, n	29	6	21	
Symptomatic heart failure				0.598
< 5 y, n	98	31	30	
≥ 5 y, n	77	23	31	
AF, n (%)	86 (49.1)	19 (35.2)*	45 (73.8)*#	< 0.001
PAH, n (%)	45 (25.7)	9 (16.7)*	25 (41.0)*#	0.011
LVEF (%)	62.38 ± 6.39	63.04 ± 5.52	58.97 ± 8.27*#	0.001
6MWT distance (m)	352.77 ± 60.59	316.09 ± 65.19*	274.12 ± 72.55*#	< 0.001
Duration of surgery (min)	250.97 ± 65.67	264.87 ± 69.77	267.87 ± 60.16	0.140
Duration of CBP (min)	114.95 ± 44.00	122.35 ± 46.23	120.79 ± 33.76	0.465
Length of ICU stay (h)	21.5 (19, 32)	27 (21, 63)*	23 (20, 44)	0.003
Duration of mechanical ventilation (h)	16 (11, 19)	17 (14, 24)*	17 (13, 21)	0.006
Pacemaker use, n (%)	45 (25.7)	9 (16.7)*	25 (41.0)*#	0.002
First dose of dopamine in ICU (μg/kg·min)	3.17 ± 2.25	3.53 ± 2.09	3.17 ± 1.80	0.532
First dose of dobutamine in ICU (μg/kg·min)	3.17 ± 1.68	2.64 ± 1.91	3.62 ± 1.59#	0.011
Length of hospital stay (day)	26.82 ± 8.46	26.94 ± 7.74	30.75 ± 9.23*#	0.007
Length before surgery (day)	12.72 ± 6.30	12.39 ± 5.59	14.54 ± 6.88	0.111
Length after surgery (day)	14.08 ± 4.79	14.56 ± 5.39	16.21 ± 7.22*	0.034

Data are presented as n (%), mean ± SD or median (Q1, Q3). SDB, sleep-disordered breathing; OSA, obstructive sleep apnea; CSA, central sleep apnea; BMI, body mass index; NYHA, New York Heart Association; AF, atrial fibrillation; PAH, pulmonary hypertension; LVEF, left ventricular ejection fraction; 6MWT, six-minute walk test; CBP, cardiopulmonary bypass; ICU, intensive care unit. *p < 0.05, OSA or CSA vs. no SDB; #p < 0.05, CSA vs. OSA.

investigate the association of OSA with cardiovascular death, myocardial infarction, stroke, and unplanned revascularization in patients treated with percutaneous coronary intervention from eight centers in five countries; these results are anticipated to be presented in the near future.¹⁰

Although several studies have shown that OSA is associated with increased postoperative complications of cardiac surgery,^{20–22} a few reports failed to show a close correlation between OSA and postoperative complications.^{2,9} Therefore, the association between OSA and postoperative complications has not been clearly elucidated until now. In our study, we found OSA was independently associated with a longer ICU length of stay and duration of mechanical ventilation and postoperative pacemaker use. These results may provide some proof to support the correlation between OSA and postoperative complications after CVR. For the first time the current study investigated the difference in effects of OSA and CSA on perioperative risk. There was a significant association between OSA and perioperative events, while CSA displayed no obvious relation to perioperative events. It has been shown that CSA is correlated with poor cardiac function, which may play a more important role in occurrence of postoperative complications than CSA itself.

The mechanisms for OSA to increase perioperative risk were not fully understood. We suspected that apnea causes acute physiological changes, including upper airway muscle dysfunction, vascular endothelial dysfunction, cardiac arrhythmia and alveolar hypoventilation, and other impairments affecting perioperative outcomes.²³ Furthermore, sedatives, narcotics, and anesthetics have been shown to increase pharyngeal collapse, decrease ventilatory response, and impair the arousal response, leading to perioperative and postoperative complications.⁶

In patients undergoing aortic valve replacement for aortic stenosis, PAH increased operative mortality and decreased long-term survival.¹⁶ We found that PAH was associated with high rate of pacemaker use. It is important for surgeons to consider PAH in their preoperative risk assessment of patients undergoing CVR.

Previous studies have suggested that perioperative continuous positive airway pressure (CPAP) use may reduce the risk of postoperative complications.^{21,24} This viewpoint was also supported by the case-control study of Gupta et al., in which patients with known OSA receiving CPAP treatment at home experienced significantly fewer postoperative complications, regardless they used either preoperative or postoperative

Table 2—Comparisons of polysomnography data among No SDB, OSA, and CSA patients.

	No SDB (n = 175)	OSA (n = 54)	CSA (n = 61)	p value
Total recording time (h)	462.22 ± 37.36	468.83 ± 46.68	459.36 ± 46.32	0.448
Total sleep time (h)	333.06 ± 41.95	319.70 ± 43.37*	301.80 ± 36.87*#	< 0.001
Sleep efficiency (%)	72.09 ± 7.19	68.37 ± 7.64*	65.84 ± 6.22*#	< 0.001
Arousal index, events/h	3 (2, 5)	13 (8, 24)*	15 (9, 26)*#	< 0.001
Sleep stage				
N1 sleep (%)	15.49 ± 3.03	15.28 ± 3.25	15.84 ± 2.89	0.600
N2 sleep (%)	65.94 ± 3.97	66.96 ± 3.70	67.07 ± 4.46	0.086
N3 sleep (%)	2 (1, 3)	1 (1, 3)	2 (0, 3)	0.567
REM sleep (%)	16.17 ± 3.36	15.67 ± 2.84	14.95 ± 4.02	0.054
SDB severity, n (%)				< 0.001
No SDB	175			
Mild		29	26	
Moderate		18	23	
Severe		7	12	
AHI, events/h	1.59 ± 1.42	16.17 ± 11.50*	21.00 ± 14.34*#	< 0.001
OAH, events/h	1 (0, 2)	10 (5, 18)*	2 (1, 5)#	< 0.001
CAHI, events/h	0 (0, 0)	3 (1, 5)*	14 (7, 23)*#	< 0.001
Mean SpO ₂ (%)	96.45 ± 1.42	95.62 ± 1.55	95.11 ± 2.49*	< 0.001
Minimal SpO ₂ (%)	88.84 ± 6.23	84.11 ± 6.82*	83.31 ± 6.16*	< 0.001
ODI, events/h	1.83 ± 2.11	11.00 ± 9.90*	16.74 ± 13.96*#	< 0.001

Data are presented as n (%), mean ± SD or median (Q1, Q3). AHI, apnea-hypopnea index; OAH, obstructive apnea-hypopnea index; CAHI, central apnea-hypopnea index; SpO₂, pulse oxygen saturation; ODI, oxygen desaturation index. *p < 0.05, OSA or CSA vs. no SDB; #p < 0.05, CSA vs. OSA.

Table 3—Comparison of characteristics between non-respiratory insufficiency and respiratory insufficiency, non-arrhythmia and arrhythmia, postoperatively.

	Postoperative Respiratory Insufficiency			Postoperative Arrhythmia		
	No (n = 221)	Yes (n = 69)	p value	No (n = 192)	Yes (n = 98)	p value
Age (y)	50.05 ± 10.57	55.68 ± 8.52	< 0.001	50.18 ± 11.12	53.76 ± 8.35	0.005
BMI (kg/m ²)	23.28 ± 3.21	22.65 ± 3.54	0.164	23.46 ± 3.18	22.50 ± 3.43	0.020
Serum albumin (g/L)	38.03 ± 5.83	36.70 ± 5.83	0.099	37.71 ± 5.93	37.70 ± 5.72	0.990
Length of hospital stay (day)	26.76 ± 8.11	30.59 ± 9.58	0.001	26.83 ± 8.49	29.33 ± 8.68	0.019
LVEF (%)	61.89 ± 6.77	61.48 ± 7.01	0.667	62.60 ± 5.54	60.21 ± 7.10	0.005
6MWT distance (m)	336.76 ± 67.52	306.70 ± 78.33	0.002	334.33 ± 71.67	320.19 ± 69.90	0.111
NYHA class			< 0.001			< 0.001
II, n	42	4		41	5	
III, n	149	39		124	64	
IV, n	30	26		27	29	
AF, n (%)	109 (49.3)	41 (59.4)	0.143	71 (37.0)	79 (80.6)	< 0.001
PAH, n (%)	54 (24.4)	25 (36.2)	0.055	38 (19.8)	41 (41.8)	< 0.001
OSA, n (%)	36 (16.3)	20 (29.0)	0.020	35 (18.2)	21 (21.4)	0.514
CSA, n (%)	44 (19.9)	17 (24.6)	0.400	36 (18.8)	25 (25.5)	0.182

SDB, sleep-disordered breathing; OSA, obstructive sleep apnea; CSA, central sleep apnea; BMI, body mass index; NYHA, New York Heart Association; AF, atrial fibrillation; PAH, pulmonary hypertension; LVEF, left ventricular ejection fraction; 6MWT, six-minute walk test; CBP, cardiopulmonary bypass; ICU, intensive care unit.

CPAP treatment²⁵ A recent systematic review analyzed six studies and found that CPAP treatment can significantly lower postoperative AHI and shorten the length of hospital stay, but did not reduce postoperative adverse events.²⁶ Therefore, the effect of CPAP treatment remains unclear and further research is required with regards to the use of perioperative CPAP in patients with OSA and CSA.

There are several potential limitations with our study. First, this is a single-center study. Although we found OSA was associated with perioperative adverse events in patients undergoing CVR, the similar results may not be translated to the other surgical populations. Second, although catheterization methods are considered the “gold standard” for the diagnosis of PAH, we detected PAH using echocardiography studies;

Table 4—Perioperative risk factors.

	Adjusted OR	p value	95% CI
Length of ICU stay ≥ 25 h			
NYHA Class	3.236	0.008	1.350–7.761
OSA	2.318	0.008	1.241–4.329
Age	1.030	0.028	1.003–1.057
Mechanical Ventilation ≥ 20 h			
NYHA Class	7.560	0.001	2.270–25.178
OSA	2.050	0.041	1.028–4.085
Age	1.056	0.001	1.022–1.092
Pacemaker use			
PAH	2.139	0.017	1.148–3.985
AF	4.051	< 0.001	2.086–7.867
OSA	2.477	0.015	1.196–5.131

Binary logistic regression was used to estimate 95% CI or ORs for dependent variables (perioperative events: Length of ICU stay ≥ 25 h, Mechanical ventilation ≥ 20 h, Pacemaker use). Candidate independent variables were age, NYHA Class, AF, PAH, LVEF, 6MWT distance, OSA and CSA. SDB, sleep-disordered breathing; OSA, obstructive sleep apnea; CSA, central sleep apnea; BMI, body mass index; NYHA, New York Heart Association; AF, atrial fibrillation; PAH, pulmonary hypertension; LVEF, left ventricular ejection fraction; 6MWT, six-minute walk test; CBP, cardiopulmonary bypass; ICU, intensive care unit.

such an estimation method may decrease the overall accuracy of PAH. Third, the long-term effects of SDB on postoperative events were not observed in this study since some recent study revealed the difference between short-term and long-term effects of SDB on postoperative cardiovascular events.²² Thus, long-term follow-up is required to evaluate adverse cardiovascular events in our population.

ABBREVIATIONS

6MWT, 6-minute walk test
 AF, atrial fibrillation
 AHI, apnea-hypopnea index
 CPAP, continuous positive airway pressure
 CSA, central sleep apnea
 CVR, cardiac valve replacement
 ICU, intensive care unit
 LVEF, left ventricular ejection fraction
 NYHA, New York Heart Association
 OSA, obstructive sleep apnea
 PAH, pulmonary hypertension
 PSG, polysomnography
 RVHD, rheumatic valvular heart disease
 SA, sleep apnea
 SDB, sleep-disordered breathing

REFERENCES

- Kasai T, Floras JS, Bradley TD. Sleep apnea and cardiovascular disease: a bidirectional relationship. *Circulation* 2012;126:1495–510.
- Foldvary-Schaefer N, Kaw R, Collop N, et al. Prevalence of undetected sleep apnea in patients undergoing cardiovascular surgery and impact on postoperative outcomes. *J Clin Sleep Med* 2015;11:1083–9.
- Mokhlesi B, Hovda MD, Vekhter B, Arora VM, Chung F, Meltzer DO. Sleep-disordered breathing and postoperative outcomes after elective surgery: analysis of the nationwide inpatient sample. *Chest* 2013;144:903–14.
- Stierer TL, Wright C, George A, Thompson RE, Wu CL, Collop N. Risk assessment of obstructive sleep apnea in a population of patients undergoing ambulatory surgery. *J Clin Sleep Med* 2010;6:467–72.
- Danzi-Soares NJ, Genta PR, Nerbass FB, et al. Obstructive sleep apnea is common among patients referred for coronary artery bypass grafting and can be diagnosed by portable monitoring. *Coron Artery Dis* 2012;23:31–8.
- Stierer TL, Collop NA. Perioperative assessment and management for sleep apnea in the ambulatory surgical patient. *Chest* 2015;148:559–65.
- Zhao LP, Kofidis T, Chan SP, et al. Sleep apnoea and unscheduled re-admission in patients undergoing coronary artery bypass surgery. *Atherosclerosis* 2015;242:128–34.
- Kua J, Zhao LP, Kofidis T, et al. Sleep apnoea is a risk factor for acute kidney injury after coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2016;49:1188–94.
- Amra B, Niknam N, Sadeghi MM, Rabbani M, Fietze I, Penzel T. Obstructive sleep apnea and postoperative complications in patients undergoing coronary artery bypass graft surgery: a need for preventive strategies. *Int J Prev Med* 2014;5:1446–61.
- Loo G, Koo CY, Zhang J, et al. Impact of obstructive sleep apnea on cardiovascular outcomes in patients treated with percutaneous coronary intervention: rationale and design of the sleep and stent study. *Clin Cardiol* 2014;37:261–9.
- Fortis S, Colling KP, Statz CL, Glover JJ, Radosevich DM, Beilman GJ. Obstructive sleep apnea: a risk factor for surgical site infection following colectomy. *Surg Infect* 2015;16:611–7.
- Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology* 2014;120:268–86.
- Ding N, Ni BQ, Zhang XL, et al. Prevalence and risk factors of sleep disordered breathing in patients with rheumatic valvular heart disease. *J Clin Sleep Med* 2013;9:781–7.
- Ding N, Ni BQ, Zhang XL, et al. Elimination of central sleep apnea by cardiac valve replacement: a continuous follow-up study in patients with rheumatic valvular heart disease. *Sleep Med* 2014;15:880–6.
- Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2012;8:597–619.
- Melby SJ, Moon MR, Lindman BR, Bailey MS, Hill LL, Damiano RJ Jr. Impact of pulmonary hypertension on outcomes after aortic valve replacement for aortic valve stenosis. *J Thorac Cardiovasc Surg* 2011;141:1424–30.
- ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–7.
- Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation* 2006;114:e84–231.
- de Raaff CA, Bindt DM, de Vries N, van Wagenveld BA. Positional obstructive sleep apnea in bariatric surgery patients: risk factor for postoperative cardiopulmonary complications? *Sleep Breath* 2016;20:113–9.
- Abdelsattar ZM, Hendren S, Wong SL, Campbell DA Jr, Ramachandran SK. The impact of untreated obstructive sleep apnea on cardiopulmonary complications in general and vascular surgery: a cohort study. *Sleep* 2015;38:1205–10.
- Wong JK, Maxwell BG, Kushida CA, et al. Obstructive sleep apnea is an independent predictor of postoperative atrial fibrillation in cardiac surgery. *J Cardiothorac Vasc Anesth* 2015;29:1140–7.

22. Uchoa CH, Danzi-Soares Nde J, Nunes FS, et al. Impact of OSA on cardiovascular events after coronary artery bypass surgery. *Chest* 2015;147:1352–60.
23. Kaw R, Michota F, Jaffer A, Ghamande S, Auckley D, Golish J. Unrecognized sleep apnea in the surgical patient: implications for the perioperative setting. *Chest* 2006;129:198–205.
24. Rennotte MT, Baele P, Aubert G, Rodenstein DO. Nasal continuous positive airway pressure in the perioperative management of patients with obstructive sleep apnea submitted to surgery. *Chest* 1995;107:367–74.
25. Gupta RM, Parvizi J, Hanssen AD, Gay PC. Postoperative complications in patients with obstructive sleep apnea syndrome undergoing hip or knee replacement: a case-control study. *Mayo Clin Proc* 2001;76:897–905.
26. Nagappa M, Mokhlesi B, Wong J, Wong DT, Kaw R, Chung F. The effects of continuous positive airway pressure on postoperative outcomes in obstructive sleep apnea patients undergoing surgery: a systematic review and meta-analysis. *Anesth Analg* 2015;120:1013–23.

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