Obesity as an Effect Modifier in Sleep-Disordered Breathing and Postcardiac Surgery Atrial Fibrillation

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BACKGROUND: Because the interrelationships of objectively ascertained sleep-disordered breathing (SDB), postcardiac surgery atrial fibrillation (PCSAF), and obesity remain unclear, we aimed to further investigate the interrelationships in a clinic-based cohort.

METHODS: Patients with polysomnography and cardiac surgery (coronary artery bypass surgery and/or valvular surgery) within 3 years, from January 2009 to January 2014, were identified, excluding those with preexisting atrial fibrillation. Logistic models were used to determine the association of SDB (apnea hypopnea index [AHI] per 5-unit increase) and secondary predictors (central sleep apnea [CSA] [central apnea index ≥ 5] and oxygen desaturation index [ODI]) with PCSAF. Models were adjusted for age, sex, race, BMI, and hypertension. Statistical interaction and stratification by median BMI was performed. ORs and 95% CIs are presented.

RESULTS: There were 190 patients who comprised the analytic sample (mean age, 60.6 ± 11.4 years; 36.1% women; 80% white; BMI, 33.3 ± 7.5 kg/m²; 93.2% had an AHI ≥ 5 ; 30% had PCSAF). Unlike unadjusted analyses (OR, 1.06; 95% CI, 1.01-1.1), in the adjusted model, increasing AHI was not significantly associated with increased odds of PCSAF (OR, 1.04; 95% CI, 0.98-1.1). Neither CSA nor ODI was associated with PCSAF. A significant interaction with median BMI was noted ($P = .015$). Effect modification by median BMI was observed; those with a higher BMI > 32 kg/m² had 15% increased odds of PCSAF (OR, 1.15; 95% CI, 1.05-1.26; $P < .003$).

CONCLUSIONS: SDB was significantly associated with PCSAF in unadjusted analyses, but not after taking into account obesity; those with both SDB and obesity may represent a vulnerable subgroup to target to reduce PCSAF and its associated morbidity.

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KEY WORDS: atrial fibrillation; cardiac surgery; obesity; sleep apnea

ABBREVIATIONS: AF = atrial fibrillation; AHI = apnea hypopnea index; CABG = coronary artery bypass graft; CAI = central apnea index; OAH = obstructive apnea hypopnea index; ODI = oxygen desaturation index; PCSAF = postcardiac surgery atrial fibrillation; PSG = polysomnogram; SDB = sleep-disordered breathing

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Sleep-disordered breathing (SDB) is characterized by repetitive upper airway collapse afflicting upward of 17% of the general population. The prevalence of SDB is markedly high in the perioperative cardiac surgery patient setting, with estimates of 50% to 90%.¹ SDB has been recognized as an independent risk factor for major postoperative cardiopulmonary complications in addition to increased consumption of economic resources and increased hospital stay duration.² Because emerging literature has highlighted the strong association of SDB and atrial fibrillation (AF),^{3,4} the influence of SDB on the development of postcardiac surgery atrial fibrillation (PCSAF) has garnered particular interest. PCSAF prevalence ranges from 10% to 65% and holds clinical importance given its association with increased morbidity and mortality.⁵⁻⁷ In fact, a longitudinal investigation of a large cohort demonstrated that new-onset postcoronary artery bypass graft (CABG) surgery AF portends increased mortality in excess of 20%, even after consideration of a broad range of potential confounding factors.⁶

The pathophysiology of PCSAF encompasses multifactorial etiologic bases, including a vulnerable physiologic substrate characterized by preexisting cardiac pathology, progressive cardiac remodeling, and

chronic systemic inflammation.⁸ Obesity serves as risk for SDB and also has been described as a risk in the development of PCSAF. Most studies conducted thus far examining the relationship of SDB and PCSAF have several limitations, including involvement of smaller sample sizes,^{9,10} proneness to misclassification because of a lack of objective sleep monitoring data to ascertain SDB indices,^{9,11-14} involvement of primarily post-CABG surgery ascertainment without consideration of valvular surgery,⁹⁻¹³ and did not carefully take into consideration the potential confounding influences of obesity.^{9,11} We therefore attempted to address some of these existing knowledge gaps by conducting an examination of SDB and PCSAF using a clinic-based cohort involving systematic, prospective collection of perioperative data. We hypothesize that increasing severity of SDB as defined by the apnea hypopnea index (AHI) is associated with increased PCSAF, even after taking into consideration confounders including obesity, and postulate that this relationship will be modified by obesity such that those who are more obese will show a stronger magnitude of association of SDB and PCSAF. We also postulate that the frequency of oxygen desaturations as ascertained by the oxygen desaturation index (ODI) will be associated with increased PCSAF.

Methods

Study Population and Study Design

The Cleveland Clinic Sleep Disorders Center's polysomnogram (PSG) database was queried to identify adult patients (> 18 years of age) who underwent in-laboratory full night or a split-night (only data from the diagnostic portion of the study considered for analyses) PSG between January 2009 and January 2014. These records were cross-referenced with The Cleveland Clinic Cardiovascular Information Registry, which contains prospectively collected clinical and laboratory data. Patients who underwent CABG surgery, valvular heart surgery, or a combination of both, at Cleveland Clinic Main Campus, within 3 years of the PSG, were identified. There were 285 patients initially identified. Those who had a current history of AF were excluded ($n = 70$). Postoperative AF was defined based on the Society of Thoracic Surgeons' practice guidelines¹⁵ as new-onset AF or flutter requiring treatment in the postoperative period and not present at the time of surgery (ie, patient entered the operating room in normal sinus rhythm). Patients with inconclusive sleep study data were excluded ($n = 25$) (these included titration studies incorrectly labeled as diagnostic PSG and studies with an absent final report), resulting in a final analytic sample of 190 patients (Fig 1). Among patients who underwent multiple PSGs, the study with the closest approximation to the date of surgery was used in analyses. For patients who had multiple cardiac surgeries, data collected from the first surgery were considered. The study was approved by the Cleveland Clinic institutional review board (No. 14-115) with an informed consent waiver.

Figure 1 – Study population. PSG = polysomnogram.

Data Collection

Polysomnography: Attended overnight sleep studies were conducted using the Nihon Kohden platform. Standard sleep parameters were monitored, including encephalography (F3-M2, C3-M2, O1-M2, F4-M1, C4-M1, and O2-M1), bilateral electrooculography, submental and bilateral anterior tibial electromyography, body position, ECG, thoracic and abdominal respiratory inductance plethysmography, capnography, and finger pulse oximetry.

Respiratory events were scored in accordance with “The AASM Manual for the Scoring of Sleep and Associated Events.”¹⁶ Hypopnea was defined as a 30% reduction in nasal pressure signal excursions from baseline lasting for ≥ 10 s, associated with a $\geq 3\%$ oxygen desaturation and/or arousal. An apnea was defined as a 90% reduction in nasal airflow for ≥ 10 s. The event was categorized as obstructive if effort persisted on thoracoabdominal inductance channels vs central if there was no effort detected. Indices per hour of sleep were calculated and included the AHI (number of obstructive and central apneas and hypopneas), obstructive apnea hypopnea index (OAHI) (number of obstructive apneas and hypopneas), and central apnea index (CAI) (number of central apneas). Furthermore, the ODI was scored considering an oxygen desaturation of $\geq 3\%$, and alternatively as $\geq 4\%$.

Predictors and Outcomes: The primary predictor was the AHI considered as a continuous measure and alternatively considered using a standard moderate to severe cutoff of > 15 . Because there are prospective data which implicate central sleep apnea and incident development of AF,¹⁷ we chose to examine alternative SDB predictors, including the CAI and also the OAHI, to observe for any differential associations of central vs obstructive apnea with PCSAF. Given the putative role of hypoxia in the development of atrial arrhythmia,¹⁸ we also examined the ODI as a measure of intermittent reductions in oxygen saturation. Consistent with the Society of Thoracic Surgeons’ definition,¹⁵ PCSAF was defined as new onset of AF/atrial flutter requiring treatment occurring after the surgical procedure and before hospital discharge.

Results

Overall, the cohort was middle-aged, obese, and consisted of predominantly white men with a high burden of cardiovascular risk factors, including hypertension, diabetes mellitus, and heart failure. Of the patients, 177 (93.2%) had an AHI ≥ 5 . PCSAF occurred in 57 patients (30%). As anticipated, those with moderate to severe SDB were older, more likely to be men, and were more likely to undergo CABG surgery than those with lesser SDB or those without SDB (Table 1). In univariate analyses, consistent with existing literature describing standard risk factors for PCSAF,⁷ age was a significant predictor of PCSAF (per unit increase; OR, 1.04; 95% CI, 1.01-1.07), as was white race (OR, 2.7; 95% CI, 1.06-6.9), BMI (per unit increase; OR, 1.05; 95% CI, 1.01-1.10), and hypertension (OR, 4.8; 95% CI, 1.4-16.5). There was an overall moderate degree of SDB in the sample with a median AHI of 25.1 (25th-75th percentile, 10.3- 50). The Hosmer-Lemeshow test indicated no evidence of poor model fit ($P = .19$).

Covariate Data: The PCSAF data and covariate data were systematically collected from multiple electronic data sources prospectively. Additional available data extracted from electronic medical records included subject characteristics, such as age, sex, race, and BMI, and comorbid factors, such as hypertension, diabetes mellitus, heart failure, COPD, creatinine, pre- and postoperative cardiac medications (antihypertensives, antiarrhythmics, lipid-lowering medications, and anticoagulants), intraoperative data, and postoperative complications (eg, use of an intra-aortic balloon pump).

Statistical Analyses

Data are presented as mean $\pm$ SD or median (25th-75th percentiles) for continuous variables and number of participants (%) for categorical variables. Comparisons by univariate analysis were performed between patients with an AHI < 15 and AHI ≥ 15 . A Student t test or Wilcoxon rank-sum test was used to compare continuous variables, χ^2 test or Fisher exact test was used in comparisons of categorical factors, and a Cochran-Armitage trend test was performed in ordinal factors to test whether there was a trend of having a high AHI in the ordinal levels. Logistic regression was used to assess the odds of PCSAF considering SDB measures as predictors in different models. The primary predictor was considered the AHI as a continuous variable (per 5-unit increase), and alternatively as an AHI ≥ 15 , given literature that has referenced this level of apnea exposure as increasing cardiovascular risk and mortality.^{19,20} ORs and 95% CIs were calculated from unadjusted and adjusted logistic models. Covariates included in the multivariable logistic models were age, sex, race, and then BMI and hypertension. Sensitivity analyses were performed excluding those who reported history of positive airway pressure use for sleep apnea. Because there are reported synergies of SDB and obesity in relation to AF,²¹ we examined tests of the statistical interaction of AHI groups and median BMI (binary variable BMI < 32 vs ≥ 32 kg/m²), and stratification analyses by median BMI were performed. All analyses were performed based on an overall significance level of 0.05, using SAS software (version 9.3; SAS Institute).

In unadjusted analyses, when considering the AHI as a continuous measure, the AHI per 5-unit increase was associated with a 6% increase in the odds of PCSAF (OR, 1.06; 95% CI, 1.01-1.12; $P = .026$). In the model adjusted for age, sex, race, BMI, and hypertension, the relationship of SDB defined by the AHI per 5-unit increase and PCSAF was attenuated and no longer statistically significant (OR, 1.04; 95% CI, 0.98-1.1). However, moderate to severe SDB defined as an AHI ≥ 15 was not significantly associated with PCSAF (OR, 1.7; 95% CI, 0.85-3.5) (Table 2). The CAI and OAHI were not significantly associated with PCSAF. Furthermore, although of borderline significance, the ODI (associated with $\geq 3\%$ oxygen desaturation) was not significantly associated with PCSAF (OR, 1.01; 95% CI, 0.98-1.04) in adjusted analyses (Table 2). In sensitivity analyses, restricting to those without report of history of sleep apnea on positive airway pressure therapy (resulting in a total number of participants of 145), there was no statistically significant association of SDB and PCSAF. Sensitivity analyses including only

TABLE 1] Patient Characteristics by Sleep-Disordered Breathing Category

Factor	Overall (N = 190)		AHI < 15 (n = 58)		AHI ≥ 15 (n = 132)		P Value
	No.	Value	No.	Value	No.	Value	
Demographics							
Age	190	60.6 ± 11.4	58	58.0 ± 12.4	132	61.7 ± 10.8	.043 ^a
Sex, female	190	60 (31.6)	58	34 (58.6)	132	26 (19.7)	<.001 ^b
Race, white	190	152 (80.0)	58	47 (81.0)	132	105 (79.5)	.81 ^b
BMI, kg/m ²	189	33.3 ± 7.5	58	33.5 ± 8.9	131	33.2 ± 6.9	.79 ^a
Comorbid factors							
History of hypertension	190	159 (83.7)	58	45 (77.6)	132	114 (86.4)	.13 ^b
History of diabetes	190	66 (34.7)	58	19 (32.8)	132	47 (35.6)	.70 ^b
History of stroke	190	22 (11.6)	58	6 (10.3)	132	16 (12.1)	.72 ^b
Previous myocardial infarction	190	51 (26.8)	58	14 (24.1)	132	37 (28.0)	.58 ^b
History of heart failure	190	46 (24.2)	58	14 (24.1)	132	32 (24.2)	.99 ^b
Previous CABG	190	9 (4.7)	58	4 (6.9)	132	5 (3.8)	.35 ^b
Previous percutaneous coronary intervention	190	36 (18.9)	58	9 (15.5)	132	27 (20.5)	.42 ^b
Most recent ejection fraction prior to surgery	154	57.0 (50.0-61.0)	48	56.5 (53.0-61.5)	106	57.0 (50.0-61.0)	.98 ^c
History of sleep apnea and positive airway pressure therapy	190	45 (23.7)	58	10 (17.2)	132	35 (26.5)	.17 ^b
History of smoking	190	27 (14.2)	58	7 (12.1)	132	20 (15.2)	.58 ^b
Intraoperative variables							
Surgery type	190		58		132		.018 ^b
CABG only		59 (31.1)		11 (19.0)		48 (36.4)	...
CABG plus valvular		29 (15.3)		6 (10.3)		23 (17.4)	...
Valvular only		82 (43.2)		32 (55.2)		50 (37.9)	...
Other		20 (10.5)		9 (15.5)		11 (8.3)	...
Perfusion time	190	87.0 (60.0-112.0)	58	88.0 (52.0-109.0)	132	86.5 (61.0-112.5)	.59 ^c
Tube time	189	11.2 (8.4-18.7)	58	11.0 (7.9-18.8)	131	11.5 (9.0-18.7)	.29 ^c
OR time	190	5.8 (5.0-7.2)	58	5.6 (4.8-7.1)	132	5.9 (5.0-7.2)	.34 ^c
Intra-aortic balloon pump	190	4 (2.1)	58	0 (0.0)	132	4 (3.0)	.32 ^d
Permanent stroke (> 72 h) postoperative	190	1 (0.53)	58	0 (0.0)	132	1 (0.76)	.99 ^d
Reintubated	190	6 (3.2)	58	3 (5.2)	132	3 (2.3)	.37 ^d

Values are presented as mean ± SD, median (25th-75th percentile), or No. of participants (%). CABG = coronary artery bypass graft.

^aStudent *t* test.

^bPearson χ^2 test.

^cWilcoxon rank-sum test.

^dFisher exact test.

TABLE 2] Logistic Regression Analyses of Sleep-Disordered Breathing Indices and Postcardiac Surgery Atrial Fibrillation

Predictors	Unadjusted		Model 1 ^a		Model 2 ^b		Model 3 ^c	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
AHI (per 5-unit increase)	1.06 (1.01-1.12)	.026	1.06 (1.00-1.13)	.048	1.04 (0.98-1.11)	.19	1.04 (0.98-1.11)	.21
CAI (per 5-unit increase)	0.52 (0.19-1.45)	.21	0.37 (0.10-1.31)	.12	0.42 (0.12-1.44)	.17	0.45 (0.14-1.41)	.17
ODI 3% (per 5-unit increase)	1.02 (0.99-1.05)	.13	1.02 (0.99-1.05)	.15	1.01 (0.97-1.04)	.73	1.01 (0.98-1.04)	.58
ODI 4% (per 5-unit increase)	1.02 (0.99-1.05)	.17	1.02 (0.99-1.05)	.18	1.00 (0.97-1.04)	.80	1.01 (0.97-1.05)	.68
AHI ≥ 15 vs < 15	1.73 (0.85-3.54)	.13	1.59 (0.72-3.53)	.25	1.51 (0.65-3.47)	.34	1.47 (0.63-3.39)	.37

AHI = apnea hypopnea index; CAI = central apnea index; ODI = oxygen desaturation index.

^aModel 1 covariates include age, sex, and race.

^bModel 2 covariates include age, sex, race, and BMI.

^cModel 3 covariates include age, sex, race, BMI, and hypertension.

those with a PSG prior to surgery (n = 90) yielded similar findings to the primary analyses (fully adjusted model: OR, 1.05; 95% CI, 0.96-1.2).

Given the observed interrelationships of obesity and AF in clinic-based studies,²¹ we chose to examine the effect of modification of median BMI on the association of change in AHI and PCSAF by examining the statistical interaction and conducting stratified analyses. The statistical interaction of AHI and BMI in relation to PCSAF was statistically significant ($P = .015$) (Fig 2). In logistic models adjusted for age, sex, race, and hypertension, in those with a BMI ≥ 32 kg/m² (median BMI), a 15% increase in PCSAF per 5-unit increase in the AHI was observed. No statistically significant association of AHI and PCSAF was observed in those with a BMI < 32 kg/m². Similar findings were observed with ODI and BMI (OR, 1.15; 95% CI, 1.04-1.28) (Table 3).

Although the overall statistical interaction of AHI and sex relative to PCSAF was not statistically significant ($P = .80$), in stratified analyses, men had a 7% increase in PCSAF (OR, 1.07; 95% CI, 1.00-1.14), a finding not observed in women (OR, 1.04; 95% CI, 0.91-1.18).

Discussion

In this clinic-based sample of patients undergoing CABG and/or valvular surgery, in unadjusted analyses, SDB defined as the AHI considered as a continuous variable was associated with PCSAF, translating to a 6% increased odds of PCSAF per 5-unit increase in the AHI. However, after adjustment for confounders, including age, sex, race, BMI, and hypertension, this relationship was attenuated. We did not identify threshold effects at which moderate to severe levels of SDB conferred an increased odds of PCSAF. The association of intermittent oxygen desaturation frequency at both ≥ 3% and ≥ 4% thresholds of oxygen desaturation did not achieve statistical significance in terms of an association with PCSAF. Finally, we observed effect modification by obesity such that in the more obese group, there was a stronger association of both sleep apnea severity and frequency of oxygen desaturation with PCSAF, an association which was not observed in those with a lesser degree of obesity.

Epidemiologic data consistently demonstrate support for an association of SDB and AF independent of obesity, cardiovascular risk/disease, and other confounding factors, and experimental data indicate that this likely occurs via a range of pathophysiologic pathways.^{3,4,17} SDB represents a recognized inciting

factor for sympathetic nervous system activation,²² and experimental data support the role of autonomic function in apnea-induced AF,²³ thereby lending support to the biologic plausibility of SDB as a factor increasing PCSAF risk. In addition to autonomic nervous system fluctuations, SDB is also associated with

intermittent hypoxia, hypercapnia, intrathoracic pressure alterations, and upregulation of systemic inflammation and oxidative stress,²⁴ which may either via individual pathways or collectively increase propensity of PCSAF development. In the perioperative setting, superimposed on basal SDB physiology are

TABLE 3] Logistic Regression Analyses of Sleep-Disordered Breathing Indices and Postcardiac Surgery Atrial Fibrillation by Median BMI

Predictors	Unadjusted		Model 1 ^a		Model 2 ^b	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
BMI > 32 kg/m² (n = 95)						
AHI (per 5-unit increase)	1.11 (1.03-1.19)	.004 ^c	1.15 (1.05-1.26)	.003 ^c	1.15 (1.05-1.26)	.003
CAI (per 5-unit increase)	0.53 (0.12-2.25)	.39	0.57 (0.12-2.68)	.48	0.60 (0.15-2.42)	.47
ODI 3% (per 5-unit increase)	1.03 (1.00-1.07)	.076	1.05 (1.00-1.09)	.029 ^c	1.06 (1.01-1.10)	.015
ODI 4% (per 5-unit increase)	1.03 (0.99-1.08)	.089	1.05 (1.00-1.10)	.030 ^c	1.06 (1.01-1.11)	.019
AHI ≥ 15 vs < 15	1.80 (0.63-5.12)	.27	2.00 (0.57-7.04)	.28	1.99 (0.56-7.10)	.29
BMI ≤ 32 kg/m² (n = 94)						
AHI (per 5-unit increase)	0.96 (0.87-1.07)	.48	0.93 (0.83-1.05)	.23	0.93 (0.82-1.05)	.22
CAI (per 5-unit increase)	0.58 (0.15-2.24)	.43	0.32 (0.06-1.68)	.18	0.36 (0.07-1.78)	.21
ODI 3% (per 5-unit increase)	0.98 (0.93-1.04)	.57	0.97 (0.90-1.03)	.31	0.97 (0.90-1.04)	.33
ODI 4% (per 5-unit increase)	0.97 (0.90-1.05)	.45	0.95 (0.87-1.04)	.24	0.95 (0.87-1.04)	.25
AHI ≥ 15 vs < 15	1.49 (0.54-4.08)	.44	1.16 (0.38-3.53)	.80	1.18 (0.37-3.72)	.78

See Table 2 legend for expansion of abbreviations.

^aModel 1 covariates include age, sex, and race.

^bModel 2 covariates include age, sex, race, and hypertension.

acute exposures to provoking triggers such as adrenergic stimulation which may alter atrial refractoriness and promote ectopic activity in addition to volume shifts and electrolyte imbalances.⁸ Preexisting cardiac pathology characterized by the underlying cardiac substrate related to chronic remodeling of the heart, for example because aging, may also enhance postoperative atrial arrhythmic risk, particularly in the presence of SDB.⁸

Several studies have been designed to focus on the investigation of SDB and PCSAF, with inconsistent results characterized by some findings supportive of an association of SDB and PCSAF^{10,12-14} and other studies which did not identify a significant association.^{9,11} In those studies identifying an SDB-PCSAF association, interpretation is somewhat limited given the lack of statistical adjustment for confounders such as obesity,^{12,13} suboptimal assessment of SDB^{9,11-14} (eg, no EEG monitoring, sole use of questionnaire without objective sleep study data collection), and lack of clear exclusion of those patients with baseline AF.¹⁴ Those studies which did not demonstrate a significant SDB-PCSAF association consisted of relatively smaller sample sizes and therefore may have been underpowered to detect an association.^{9,11} Our findings show a significant relationship of SDB and PCSAF in unadjusted analyses which did not persist after adjustment for confounders such as age and obesity. Given the relative stability of the point estimate in the unadjusted and adjusted statistical models (OR reduced from 1.06 to 1.04), it is possible that we did not have sufficient power to effectively capture a statistically significant association. We cannot, however, exclude that a true association of SDB and PCSAF does not exist after taking into consideration confounding factors. There is also the possibility that although SDB does not immediately result in postoperative AF risk, on extended follow-up there is an element of residual increased cardiovascular and arrhythmogenic risk, as has been shown in prior work.¹⁰

SDB and PCSAF have several shared risk factors, including age²⁵ and obesity.²⁶ Obesity has been identified as a risk for new-onset AF in epidemiologic data, a relationship that appears to be mediated by left atrial dilatation.²⁷ Other pathways in addition to left atrial dilatation by which obesity may represent an AF risk factor include atrial adaptation, metabolic pathways, paracrine effects, epicardial fat, and adipocytokines.²⁸ Interestingly, individuals who are obese have a 49% increased risk of AF development compared with individuals who are not obese. Furthermore, data demonstrate a two-fold increased risk of AF development

in central SDB, the latter independent of obesity, suggesting an overall relationship of SDB and AF which is independent of obesity.¹⁷ Although data are somewhat inconsistent in terms of the extent that obesity serves as a risk for PCSAF, a systematic review identified obesity as a risk for development of PCSAF, irrespective of the type of cardiac procedure performed, albeit of small magnitude.²⁶ However, many other studies investigating the preoperative predictors of PCSAF did not take into consideration the evaluation of obesity as a potential risk factor. In the current study, in univariate analyses, the BMI is higher in those with PCSAF vs those without (35.5 ± 7.3 vs 32.4 ± 7.5 kg/m², $P = .015$) as was the AHI (23.0 [$9.9, 45.6$] vs 28.0 [$17.0, 73.5$]; $P = .015$). We observed a significant statistical interaction of SDB and obesity in relation to PCSAF such that those with higher levels of obesity (median BMI, > 32 kg/m²) had increased odds of AF (ie, a 10% increased odds per 5-unit increase in the AHI in the adjusted model). These results suggest that individuals who are obese may in fact be most vulnerable to the influences of SDB on PCSAF risk. These findings were also observed with intermittent hypoxia frequency (both $\geq 3\%$ and $\geq 4\%$ oxygen saturation reduction), albeit to a lesser magnitude, suggesting the role of likely both hypoxic and nonhypoxic pathways increasing PCSAF risk in SDB in those who are obese. Although reproducibility of these findings is warranted, the results suggest a risk stratification approach to prioritize identification of SDB in those who are obese to mitigate postcardiac surgery atrial arrhythmogenesis. Although the statistical interaction with sex was not statistically significant, stratified analyses demonstrated potential susceptibility of men to SDB-related PCSAF, a finding not observed in women. These findings require evaluation in future studies to assess for reproducibility.

The strengths of the study include the exclusion of those with baseline AF/atrial flutter, the prospective collection of cardiothoracic data via the Cleveland Clinic Cardiovascular Information Registry, the definition of SDB based on in-laboratory PSG, the consideration of both post-CABG surgery and valvular surgery, the sensitivity analyses excluding those on positive airway pressure, and the consideration of importance of confounding influences of age and obesity among others. Limitations of the work should be recognized. Albeit the high prevalence of SDB observed in our sample is in line with other studies,^{10,29} it is possible that the limited sample of those without SDB or with milder SDB may have limited our ability to detect a significant association of increasing SDB severity and PCSAF. It is

also possible that some patients may have received treatment for SDB prior to surgery which was not self-reported, which would bias findings toward the null hypothesis and would have accounted for the current findings. Other limitations include the lack of analysis of extended follow-up period, limitations of sample size on stratification by surgery type (ie, CABG surgery vs valvular surgery), and limitations of sample size that may have precluded detection of a true association of SDB and PCSAF in adjusted analyses.

Future examination of the impact of SDB treatment on PCSAF in terms of AF burden (ie, duration of time spent in AF), length of stay, and associated morbidity is warranted. Future investigation should also verify our observed enhanced association of SDB and PCSAF in those who are obese because this has implications in risk stratification and targeting those who are obese in terms of more aggressively identifying those with SDB for appropriate treatment and management, with the goal of reducing PCSAF and associated adverse outcomes.

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