Original Article

Prevalence of Obstructive Sleep Apnea in Thai Patients with Severe Symptomatic Aortic Stenosis

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Background: Obstructive sleep apnea (OSA) is prevalent in patients with severe aortic stenosis (AS). The present study evaluated the prevalence of OSA and factors associated with OSA risk in Thai patients with severe symptomatic AS.

Materials and Methods: Patients with severe symptomatic AS were screened for OSA using the STOP-Bang questionnaire prior to transcatheter aortic valve replacement. Patients were classified into low, intermediate, and high risk groups in accordance with the STOP-Bang score. Baseline characteristics, comorbidities, and echocardiographic parameters were recorded.

Results: Of 24 patients (median age: 79 years; 54.2% male) included in the present study, 22 (91.7%, 95% confidence interval (CI) 74.2% to 97.7%) had an intermediate-to-high risk of moderate-to-severe OSA. Male gender (odds ratio (OR) 22.5, 95% CI 2.1 to 240.5; p=0.005), current or former smokers (OR 8.6, 95% CI 1.3 to 55.0, p=0.035), and hypertension (OR 21.0, 95% CI 1.0 to 427.0, p=0.019) were significantly associated with a high risk of moderate-to-severe OSA.

Conclusion: The prevalence of OSA is high among Thai patients with severe symptomatic AS. Major factors associated with the risk of OSA include male gender, current or former smokers, and a history of hypertension.

Keywords: Severe symptomatic aortic stenosis, Obstructive sleep apnea, STOP-Bang questionnaire

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Patients with obstructive sleep apnea (OSA) experience snoring, abnormal daytime sleepiness, fatigue, and impaired memory, which results from oxygen deprivation during sleep. OSA is present when a patient has an apnea-hypopnea index (AHI) of ≥5 per hour during a polysomnographic study. However, polysomnography is not widely available because it is costly and usually has a long waiting list. Currently, the STOP-Bang questionnaire is widely used as a screening tool for OSA. The questionnaire consists of eight categories: the STOP components include loud snoring, daytime sleepiness, observed sleep apnea, and high blood pressure, and the Bang components include a body mass index (BMI) of >35 kg/m^2, >50 years of age, neck circumference of >40 cm, and male gender. Each category has one mark. Validation studies indicate high sensitivity (≥90%) and moderate specificity (approximately 40%) in predicting moderate-to-severe OSA (AHI >15) at a cut-off score of ≥3[1,2]. Modification of the scoring system by considering a score of ≥2 from the STOP components together with either one of BMI, neck circumference, or male gender from the Bang components has considerably improved the specificity to 75% to 85%[2].

OSA is associated with various conditions including hypertension, cardiovascular disease, insulin resistance, and type 2 diabetes mellitus[3], certain malignancies[4,5], and all-cause mortality[6,7]. OSA may coexist with severe aortic stenosis (AS) and aggravate its symptoms[8]. Treatment of OSA alleviates the severity of cardiac symptoms and improves quality of life[9-11].

The prevalence of OSA is around 11% in the general Thai population[12] and about 6% among pregnant Thai women[13]. The prevalence of OSA among severe symptomatic AS patients in various countries could be as high as 70% to 77%[8,14]. The authors studied the prevalence of OSA and factors associated with OSA identified by the STOP-Bang questionnaire in Thai patients with severe

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symptomatic AS.

Materials and Methods

Study design

This was a cross-sectional study of patients with severe symptomatic AS, who were admitted for transcatheter aortic valve replacement (TAVR) at the Cardiology Center, Chulabhorn Chalermprakiet Medical Center, Chulabhorn Hospital, during August 2019 to July 2020. The protocol of this study was approved by the Ethics Committee of Chulabhorn Research Institute (No. 069/2562).

Patients

Patients with severe symptomatic AS in accordance with clinical and echocardiographic parameters (aortic valve area of ≤1.0 cm^2, peak velocity across aortic valve of ≥4 m/s, or mean pressure gradient across aortic valve of ≥40 mmHg), who were admitted for TAVR were included in the study. Patients who could not complete the STOP-Bang questionnaire were excluded.

Patient evaluation

Each patient was assessed by a cardiologist. Basic information was recorded and data collection included age, gender, body weight, height, BMI, smoking status, hypertension, diabetes mellitus, hypercholesterolemia, history of coronary heart disease, history of previous myocardial infarction, history of heart failure, atrial fibrillation, previous cardiovascular or thoracic surgical interventions, Society of Thoracic Surgeons (STS) score, chronic kidney disease, current alcohol consumption, blood pressure, and heart rate.

Aortic valve pathology, hemodynamics, and cardiac functions were evaluated using an echocardiographic system. The left ventricular ejection fraction, valvular pathology, aortic valve area, aortic mean pressure gradient, aortic peak pressure gradient, and aortic peak velocity were recorded.

Measurement of the neck circumference was carried out with patients standing upright, gazing directly forward and without neck flexion or extension. A flexible measuring tape was used to measure the neck circumference at the level of the thyroid prominence around the neck in a perpendicular plane to the neck axis.

Each patient completed the STOP-Bang questionnaire regarding snoring habits, daytime sleepiness, observed sleep apnea, high blood pressure, BMI, age, neck circumference, and gender. A cardiologist explained the questionnaire to a patient who could not read. The risk of moderate-to-severe OSA (AHI >15) was determined by the STOP-Bang score. Patients with STOP-Bang scores of 0 to 2 were classified as the low risk group. Patients with STOP-Bang scores of 5 to 8 were classified as the high risk group. Patients with STOP-Bang scores of 3 to 4 were designated the high risk group if they had either STOP ≥2 and male gender, STOP ≥2 and BMI >35 kg/m^2, or STOP ≥2 and neck circumference >40 cm. The remaining patients (STOP-Bang scores of 3 to 4 and not fulfilling the high risk criteria) were categorized as the intermediate risk group[15].

Statistical analysis

Categorical variables are presented as the frequency and percentage. Continuous variables are summarized as the median and interquartile range. Fisher's exact test was applied to compare categorical variables and the Mann-Whitney U-test was employed to compare continuous variables. Associations between various factors and the risk of moderate-to-severe OSA (low-to-moderate risk group vs. high risk group in accordance with the STOP-Bang score) are represented by the odds ratio (OR) and their 95% confidence interval (CI) calculated using univariate logistic regression models. If at least one cell in a 2×2 contingency table contained a value of 0, a value of 0.5 was added to all cells in that table to estimate the OR. Data were analyzed using STATA 12.1 statistical software.

Results

Twenty-four patients who were admitted for TAVR participated in the study. Baseline characteristics of all participants are presented in the first column of Table 1. All subjects were elderly with a median age of 79 years. Almost half of the subjects were female. One-third of the subjects (8/24) were obese in accordance with the Thai standard (BMI ≥25 kg/m^2). Prevalent comorbidities included hypertension, heart failure, hypercholesterolemia, coronary artery disease, diabetes mellitus, and chronic kidney disease. All patients had severe aortic stenosis (median aortic valve area of 0.50 cm^2, and mean and peak pressure gradients across the aortic valve of 58.3, and 94.2 mmHg respectively). Most patients had a normal left ventricular systolic function.

Prevalence of moderate-to-severe obstructive sleep apnea

At a cut-off STOP-Bang score of 3 or greater, which defined intermediate and high risk groups, the prevalence of moderate-to-severe OSA was 91.7% (95% confidence interval (CI) 74.2% to 97.7%) (Table 2). At a more stringent cut-off score of 5 or greater, which denoted a high risk of moderate-to-severe OSA, the prevalence was 41.7% (95% CI 24.5% to 61.2%). By including subjects with STOP-Bang scores of 3 to 4 with at least one high risk feature as the high risk group, the prevalence was still 41.7% because no subjects with STOP-Bang scores of 3 to 4 met the high risk criteria.

Association between various factors and the risk of moderate-to-severe OSA in accordance with the STOP-Bang score

Comparisons between STOP-Bang low-to-intermediate and high risk groups regarding various factors are presented in columns 2 to 4 of Table 1. Males were much more likely than females to have a high risk of moderate-to-severe OSA (OR 22.5, 95% CI of OR 2.1 to 240.5; p=0.005). Smoking status was significantly associated with the risk of moderate-to-severe OSA with a higher likelihood for current

Table 1. Characteristics of study participants and comparisons between STOP-Bang risk groups

	Total n=24	Low-to-intermediate risk group n=14	High risk group n=10	p-value[a]
Age (years), median (IQR)	79 (75 to 84)	79 (76 to 83)	80 (75 to 88)	0.841
Male gender, n (%)	13 (54.2)	4 (28.6)	9 (90.0)	0.005
Body mass index (kg/m^2), median (IQR)	22.7 (19.6 to 25.4)	23.0 (19.6 to 25.9)	22.7 (19.2 to 24.8)	0.752
Smoking status, n (%)				0.035
Non-smoker	14 (58.3)	11 (78.6)	3 (30.0)	
Current or former smoker	10 (41.7)	3 (21.4)	7 (70.0)	
Hypertension, n (%)	17 (70.8)	7 (50.0)	10 (100.0)	0.019
Diabetes mellitus, n (%)	7 (29.2)	2 (14.3)	5 (50.0)	0.085
Hypercholesterolemia, n (%)	14 (58.3)	6 (42.9)	8 (80.0)	0.104
Coronary heart disease, n (%)	11 (45.8)	5 (35.7)	6 (60.0)	0.408
Previous MI, n (%)	7 (29.2)	3 (21.4)	4 (40.0)	0.393
History of heart failure, n (%)	15 (62.5)	8 (57.1)	7 (70.0)	0.678
Atrial fibrillation, n (%)	4 (16.7)	2 (14.3)	2 (20.0)	1.000
Previous cardiovascular or thoracic surgical interventions, n (%)	2 (8.3)	0 (0.0)	2 (20.0)	0.163
STS score, median (IQR)	3.8 (3.2 to 6.1)	3.8 (3.2 to 6.5)	3.9 (2.9 to 6.4)	0.709
STS score ≥4, n (%)	11 (45.8)	6 (42.9)	5 (50.0)	1.000
Chronic kidney disease, n (%)	8 (33.3)	4 (28.6)	4 (40.0)	0.673
Current alcohol consumption, n (%)	2 (8.3)	1 (7.1)	1 (10.0)	1.000
SBP (mmHg), median (IQR)	131.5 (113.0 to 140.0)	131.5 (111.5 to 141.0)	131.0 (111.8 to 139.5)	0.841
DBP (mmHg), median (IQR)	67.0 (56.2 to 83.8)	73.0 (57.5 to 89.3)	57.0 (54.0 to 73.3)	0.192
HR (beats/min), median (IQR)	68 (62 to 76)	66 (62 to 88)	69 (62 to 76)	0.931
LVEF (%), median (IQR)	64.5 (49.0 to 70.8)	66.0 (56.8 to 70.5)	59.5 (43.5 to 71.5)	0.472
AVA (cm^2), median (IQR)	0.50 (0.40 to 0.62)	0.55 (0.38 to 0.60)	0.50 (0.40 to 0.83)	0.508
AV mean pressure gradient (mmHg), median (IQR)	58.3 (48.9 to 76.6)	57.1 (46.8 to 84.8)	58.4 (47.6 to 65.6)	0.752
AV peak pressure gradient (mmHg), median (IQR)	94.2 (76.8 to 120.9)	96.8 (75.3 to 126.8)	94.2 (80.9 to 107.1)	0.709

[a] Comparison between the STOP-Bang low-to-intermediate risk group and high risk group

AV = Aortic valve; AVA = Aortic valve area; DBP = diastolic blood pressure; HR = heart rate; IQR = interquartile range; LVEF = left ventricular ejection fraction; MI = myocardial infarction; SBP = systolic blood pressure; STS = Society of Thoracic surgery

Table 2. Prevalence of each OSA risk category in accordance with the STOP-Bang score among Thai patients with severe symptomatic aortic stenosis admitted for TAVR (n=24)

Category	n	Prevalence (95% CI)
High risk group	10	41.7% (24.5% to 61.2%)
STOP-Bang score 5 to 8	10	41.7% (24.5% to 61.2%)
STOP Bang score 3 to 4 with a high risk feature[a]	0	0.0%
Intermediate risk group (STOP-Bang score 3 to 4 without high risk feature)	12	50.0% (31.4% to 68.6%)
Low risk group (STOP-Bang score 0 to 2)	2	8.3% (2.3% to 25.8%)

[a] Subjects with STOP-Bang score of 3 to 4 were categorized as high risk if they met either one of the following criteria: STOP score ≥2 + male, STOP score ≥2 + BMI >35 kg/m^2, or STOP score ≥2 + neck circumference >40 cm

or former smokers than non-smokers (OR 8.6, 95% CI of OR 1.3 to 55.0; p=0.035). The risk of moderate-to-severe OSA was higher for hypertensive subjects than normotensive subjects (OR 21.0, 95% CI of OR 1.0 to 427.0; p=0.019). BMI, other comorbidities, the STS score, and echocardiographic parameters were not significantly associated with the risk of moderate-to-severe OSA.

Discussion

The authors assessed the prevalence of OSA among patients with severe symptomatic AS admitted for TAVR. We found a very high prevalence of an intermediate-to-high risk of moderate-to-severe OSA in accordance with the STOP-Bang score among such patients (overall 91.7% with 50% having an intermediate risk and 41.7% with a high risk). We found that gender, smoking status, and hypertension were significantly associated with the risk of OSA.

Our results are consistent with a German study that found a prevalence of sleep-related breathing disorder (SRBD; defined as AHI ≥5/hour) of 77% among severe symptomatic AS patients who underwent TAVR[8]. Another German study also reported a prevalence of sleep apnea (AHI ≥5/hour) of 71% among patients with severe AS[16]. Additionally, many other studies have found significant prevalence of OSA among severe symptomatic AS patients. Thus, screening for OSA in these patients should be considered.

Gender has long been known to be associated with sleep apnea with males being predominant[17]. In the present study, male patients had about 22 times higher odds of being in the high risk STOP-Bang group than female patients. However, the magnitude of association in the present study may be somewhat overestimated because male gender is a component of the STOP-Bang score, which results in an autocorrelation between gender and the OSA risk. The differences between genders may be attributed to various biological variances such as fat distribution, hormonal balance, and anatomical disparity in tracheobronchial tree and its associated smooth muscle[18].

The authors found that current or former smokers had 8.6 times higher odds of a high risk STOP-Bang score compared with non-smokers. Similarly, a study by Wetter et al yielded an OR of 3 for any SRDB (AHI ≥5/hour) and 4.4 for moderate-to-severe SRDB (AHI ≥15/hour) for current smokers compared with non-smokers[19]. The level of sleep depth and its disturbance are linked to smoking by the blood level of nicotine during sleep and inherent inflammatory state in the tracheobronchial tract. Nicotine in tobacco is believed to stabilize the airway during the day. However, when the blood nicotine level drops at night, the airway reverts to the originally inflamed state, which increases the likelihood of developing OSA.

Our study indicated that high blood pressure was strongly associated with the risk of moderate-to-severe OSA. Although this association may be, to some extent, overestimated in the present study because of the autocorrelation between hypertension and the STOP-Bang score, other studies that have used polysomnography to identify OSA also found a significant association. A study of the general Thai population showed a significant association between hypertension and polysomnography-defined OSA[12]. Similarly, cross-sectional analysis of a large cohort of the US general population found that the OR of hypertension was 2.3 (95% CI 1.8 to 2.9) for participants with high AHI (≥30/hour) compared with those in the lowest AHI category (<1.5/hour) after adjustment for age and demographic characteristics[20]. However, a prospective cohort study in Spain found that the association between OSA and the incidence of hypertension at 7.5 years of follow-up had disappeared after adjustment for confounding factors[21].

Obesity is a significant risk factor for OSA. Changes in body weight were proportionately associated with changes in the respiratory disturbance index (the number of apnea plus hypopnea events with at least a 4% oxyhemoglobin desaturation level divided by the total sleep time)[22]. A study of the general Thai population found a significant association between BMI and the risk of OSA[12]. Nevertheless, we did not find an association between BMI and the risk of OSA in the present study. There are several possible explanations for the lack of such an association in our study. A small sample size may lead to failure to demonstrate an existing association in the statistical analysis (a so-called type 2 error). The present study exclusively enrolled patients with severe AS, which might be different from subjects from the general population in other studies. All our participants were elderly.

A study has revealed that BMI contributes very little to OSA among patients aged 60 years or older[23].

Our study has some major limitations. The sample size was small, which increased the probability of a type 2 error. Additionally, the small sample size contributed to uncertainty in the estimates of the magnitude of the association between factors and the OSA risk as evidenced by the wide confidence intervals of the OR estimates. The small sample size also precluded us from implementing multivariable analyses. The authors enrolled only severe symptomatic patients admitted for TAVR. Therefore, the results may not be generalizable to other patient populations such as AS patients who undergo aortic valve surgery, patients with severe asymptomatic AS, or patients with other valve pathologies.

For practical reasons, the authors did not use polysomnography as the definite diagnostic test to identify subjects with OSA. Alternatively, we used the STOP-Bang questionnaire to identify subjects at risk of moderate-to-severe OSA. The questionnaire was designed to be a screening test for OSA and there certainly are false positive and false negative results. Therefore, the prevalence of OSA in our study should be regarded as an approximation. However, the questionnaire has many advantages over polysomnography. It is readily available, requires less expertise, is much easier to perform, and is much less costly compared with polysomnography. A patient with a certain risk level in accordance with the STOP-Bang score can be considered for further testing by polysomnography. This approach would be more practical and economical than subjecting every patient to polysomnography in a resource-limited country such as Thailand.

Conclusion

The prevalence of OSA in Thai patients with severe symptomatic aortic stenosis who undergo TAVR is high. Major factors associated with the risk of OSA include male gender, current or former smokers, and a history of hypertension.

What is already known on this topic?

The prevalence of OSA among severe symptomatic aortic stenosis patients in various countries could be as high as 70% to 77%. Studies in Thailand indicate that the prevalence of OSA is about 11% among the general population and about 6% among pregnant women.

What this study adds?

The prevalence of an intermediate-to-high risk of moderate-to-severe OSA in accordance with the STOP-Bang score was high (91.7%). Factors significantly associated with a high risk STOP-Bang score include male gender, current or former smokers, and a history of hypertension.

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Potential conflicts of interest

The author declare no conflict of interest.

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