

Relationship between Severity and Complexity of Coronary Artery Involvement and Obstructive Sleep Apnea Based on STOP-BANG Questionnaire

Abstract

Background: Obstructive sleep apnea (OSA), which has a known correlation with cardiovascular disease, is a possible risk factor of coronary artery disease (CAD) that is preventable. **Aims:** We sought to put lights on the relationship between OSA based on the STOP-BANG questionnaire (SBQ) and the severity and complexity of coronary artery involvement. **Methods:** This cross-sectional, single-center, retrospective study was conducted among 145 patients who underwent selective coronary angiography (SCA) between October 2018 and March 2019, admitted to the Tehran Heart Center, Tehran, Iran. OSA risk was assessed in patients based on SBQ categories. Also, the severity and complexity of coronary artery involvement calculated according to SYNTAX and Gensini scores. Analysis performed by statistical software SPSS 25. **Results:** Based on SBQ risk assessment categories, 22 (15.2%), 64 (44.1%), and 59 (40.7%) of the patients were low, intermediate, and high-risk for OSA, respectively. By comparing the means of coronary artery involvement, there was no significant difference in SYNTAX score 17.15 ± 13.67 (10.56–23.74) in low, 15.67 ± 9.78 (13.19–18.16) in intermediate, and 16.93 ± 9.21 (14.42–19.45) in high-risk groups; *P* value: 0.754, and Gensini score 66.4 ± 70.75 (35.04–97.77) in low, 66.21 ± 55.05 (52.45–79.96) in intermediate, 74.61 ± 56.33 (59.93–89.3) in high risk groups; *P* value: 0.697 with groups of OSA risks. Also, after adjusting confounding factors, there was still no statistically significant difference in terms of coronary involvement scores. **Conclusions:** There was no statistically significant difference in SYNTAX and Gensini scores of different groups of OSA risk categories based on the SBQ. However, our results can't be extended into the connection between OSA and CAD.

Keywords: Coronary angiography, coronary artery disease, sleep apnea, obstructive

Introduction

Overall, the term “sleep-disordered breathing (SDB)” is used for a group of disorders with difficult breathing in sleep. Obstructive sleep apnea (OSA) is one of these disorders characterized by a repetitive period of upper airway obstruction leading to complete (apnea) or partial (hypopnea) cessation of breath.^[1] According to epidemiologic studies, the prevalence of moderate to severe OSA in 30–70 years adult's population is estimated to be 13% in men and 6% in women, which considerably increases in previous decades.^[2] Although overnight polysomnography (PSG) is a gold standard for diagnosis of OSA,^[3] it's an expensive, time-consuming, and labor-intensive procedure which makes it difficult to use routinely.^[4] Thus, using alternative tools such as questionnaires

and home-based strategies for screening, diagnosis, and management of OSA seems not to be inferior to in-laboratory PSG.^[5]

The importance of OSA is in light of its detrimental complications following it.^[6] OSA as an aggravating factor for cardiovascular disorders including hypertension (HTN), congestive heart failure (CHF), arrhythmias such as atrial fibrillation (AF) and coronary artery disease (CAD) had been well studied.^[7–9] Periods of obstructed breathing result in profound intermittent hypoxia (IH) and hypercapnia which subsequently lead to sympathetic activation (due to reflective response), inflammation, and oxidative stress (due to lack of enough O₂, which itself causes endothelial dysfunction by reactive O₂ species). These mechanisms lead to vasoconstriction and arterial stiffness which finally result in increased blood

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pressure. C-reactive protein (CRP), tissue factor, and heat shock protein-70 (atherosclerosis-associated molecules) upregulated by repetitive hypoxemia in OSA and may be involved in the development of the atherogenic process in OSA.^[10-14]

About CAD as one of the leading causes of mortality and morbidity, primary prevention is preferred to treatment.^[15] A Meaningful relationship between CAD and OSA results in subsequent planning for OSA management in a proper way to prevent its detrimental effects on CAD. Although several studies investigated this relationship, controversial results were achieved.^[16-21] Besides this, there is a lack of enough research which assesses the impact of OSA on microvascular coronary artery involvement. In this study, we sought to investigate the relationship between OSA based on SBQ risk assessment and complexity and severity of CAD characterized by SYNTAX and Gensini scores, to find further preventive strategies for this complication.

Methods

Study design and population

The “relationship between severity and complexity of coronary artery involvement and OSA based on STOP-BANG questionnaire (SBQ) in patients with CAD” study was a cross-sectional, single-center, retrospective study conducted in 2018–2019 in the Tehran Heart Center. The research protocol was approved by the ethics committee of Tehran University of Medical Sciences by ethics code IR.TUMS.MEICINE.REC.1398.302. Three hundred eight consecutive Iranian patients including 85 cases presenting with chronic stable angina and 223 patients with the acute coronary syndrome (79 unstable angina, 98 ST-segment elevations myocardial infarction [STEMI] and 46 non-STEMI [NSTEMI] cases) who underwent selective coronary angiography (SCA) were enrolled between October 2018 and March 2019, Tehran, Iran. Exclusion criteria include patients with no coronary artery involvement in SCA (SYNTAX score = 0 and/or Gensini score = 0), incomplete SBQ due to any reason (ex. misunderstanding information by patients or suspicious answers), patients previously diagnosed as OSA cases, patients with prior history of PCI or CABG.

OSA risk assessment

After SCA, the SBQ completion fulfilled by an interview with the patients on the same day by another expert party who was blinded to the results of the SCA. The interviewer completed the SBQ in collaboration with the patients' partners. SBQ, as a simple and low-cost screening tool, has more than 90% sensitivity and negative predictive value (NPV) for detecting OSA patients, especially in moderate to severe cases.^[22,23] Also, evidence shows the superiority of SBQ in comparison with other OSA screening questionnaires (such as Berlin questionnaire or Epworth sleepiness scales) in terms of predicting the

possibility of the disorder.^[24,25] This questionnaire consists of 8 yes/no questions that originated from STOP-BANG abbreviation.^[22,26] S for snoring: snore, which should be loud enough to be heard through closed doors or mentioned by the partner during sleep. T for tiredness: feeling tired, fatigued, or sleepy during the daytime. O for observed: mentioned stop breathing or choking/gasping during sleep by others. P for pressure: known cases of hypertension. B for body mass index (BMI): BMI more than 35 kg/m². A for Age: age over 50 years old. N for neck size large: greater than 40 cm. G for gender: male gender. Each yes is equaled 1 point. Based on patients' answers, they classified into three groups in terms of risk assessment for OSA:^[22,26]

Low risk: yes to 0–2 questions

Intermediate risk: yes to 3–4 questions

High risk: yes to 5–8 questions

or yes to ≥ 2 of STOP questions + BMI >35 kg/m² and/or male gender

Angiographic study

Two different experienced cardiologists viewed patients' SCA in blindly circumstances and SYNTAX and Gensini scores computed, retrospectively. In cases of a different opinion, the third cardiologist also comments on it.

The SYNTAX score is calculated by the summation of each lesion's score. All lesions with $\geq 50\%$ stenosis in a vessel ≥ 1.5 mm considered for computation of total score. Calculation details based on lesion's characteristics defined by Georgios *et al.*^[27] Gensini score is also an indicator of coronary artery involvement severity based on the location of lesion and percentage of stenosis.^[28]

Statistical analysis

Statistical analysis performed by SPSS 25. We demonstrated demographic and baseline characteristics using frequencies and Mean. We compared baseline characteristics between different groups of OSA patients using ANOVA for parametric variables and Chi-square for descriptive variables. In terms of assumption of parametric tests, a Shapiro-Wilk test (P -value >0.05) and a visual inspection of their histograms, normal Q-Q plots, and box plots showed normal distribution. Also, skewness and kurtosis Z-values between -1.96 and $+1.96$ prove this fact. SYNTAX and Gensini scores were compared between groups with the Kruskal-Wallis test because of the non-Gaussian distribution of severity and complexity of coronary artery involvement. We also adjusted confounding factors by using an extended linear regression test for investigating the relationship between the severity and complexity of coronary artery involvement with OSA risk assessed by SBQ. Assessing collinearity was performed between all of the independent factors and results show the variance inflation factor (VIF) values less than 2,

which indicated that multicollinearity wasn't problematic. In all phases of analysis, the alpha level was 5% and the *P* value <0.05 was considered significant.

Results

SYNTAX and Gensini scores analysis conducted for 135 and 145 patients, respectively, after excluding ineligible patients [Figure 1].

98 male (67.6%) and 47 female (32.4%) patients were investigated for baseline characteristics. As expected, characteristics including age, gender, BMI, and HTN history, which each of them is considered as a separate item in SBQ, were significantly different between groups of patients categorized by OSA risk. On the other hand, diabetes mellitus (DM), dyslipidemia, smoking, and family history were the same [Table 1].

22 (15.2%), 64 (44.1%), and 59 (40.7%) of the patients were low, intermediate, and high risk respectively. As expected, the prevalence of all eight SBQ items was significantly different between the three groups of OSA patients (*P*-value <0.05) [Figure 2].

Mean SYNTAX score of 135 patients was 16.38 ± 10.13 (min = 1 and max = 55). Mean Gensini score of 145 patients was 69.66 ± 57.89 (min = 1.5 and max = 272). As it's shown in Table 2, there was no statistically significant difference between mean SYNTAX and Gensini scores of low, intermediate, and high risks OSA patients.

We also analyzed further and adjusted confounding factors, including DM, dyslipidemia, smoking, and family history using an extended regression model. As demonstrated in Table 3, after adjusting, there was still no significant difference in SYNTAX and Gensini scores in different groups of OSA patients.

Discussion

Based on the study results, there is no relationship between OSA risk based on SBQ with the severity and complexity of CAD assessed by SYNTAX and Gensini scores. It means,

SBQ as a most sensitive method of screening for OSA, cannot predict the degree of coronary artery involvement in CAD patients. Except items contribute to SBQ calculation, including age, gender, BMI, and HTN, other traditional risk factors were adjusted. Internal validity of our study is concluded from multiple factors including the absence of historical and maturation factors, absence of experimental mortality (participants dropping out of the study or failure to complete protocols), high validity of testing materials which had been used, blinding circumstances and adjustment of confounding characteristics. The only limitation of internal validation of this study is the selection method of cases that were based on census sampling. In terms of external validity, the critical point here is that we studied the relationship between OSA risk assessed by SBQ with the severity and complexity of coronary involvement. This means that we had just screen patients in terms of OSA, and not diagnosing certain cases. So, our results can't be extended into the connection between OSA and CAD.

Based on previous studies, OSA has been identified as a provoking factor for developing various cardiovascular events. But, playing a role as an independent factor for CAD is still controversial. Numerous observational studies showed definite OSA diagnosed by PSG was associated with an increased risk of myocardial infarction, revascularization procedures, or cardiovascular death.^[29] The same results were achieved by Gottlieb *et al.* in the male gender population under 70 years old ages.^[16] Improved outcomes in terms of coronary events in OSA cases managed by continuous positive airway pressure (CPAP) or upper airway surgery, is another confirming evidence that shows this connection.^[17] Interestingly, OSA had been proved to be associated with the subclinical coronary disease as estimated by coronary artery calcium scoring measured by electron-beam computed tomography (EBCT). Also, the calcification degree correlates with the increasing severity of OSA.^[18]

On the other hand, according to meta-analysis done by Loke *et al.* link between OSA and CAD is limited to studies with predominantly male gender population (Odds ratio [OR]: 1.92; 95% CI, 1.06–3.48), but in both

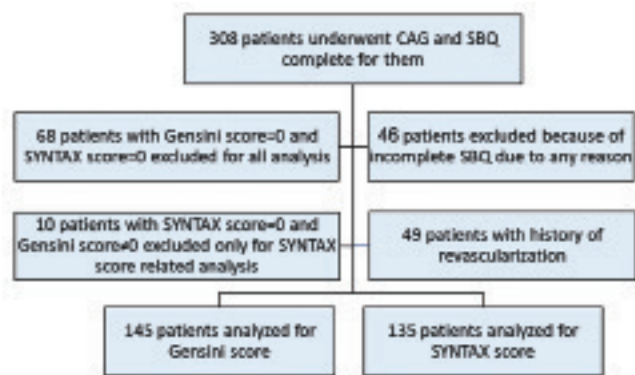


Figure 1: Patients' flowchart. Study population-based on inclusion and exclusion criteria

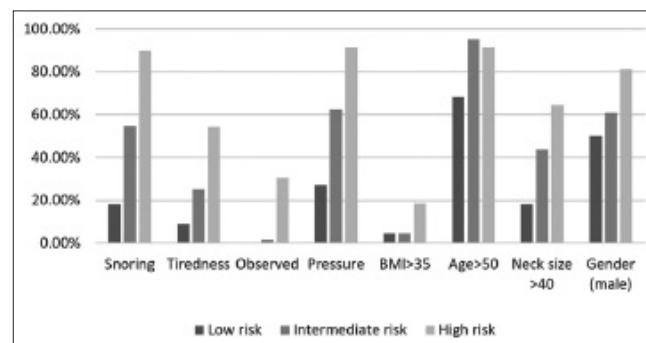


Figure 2: STOP-BANG questionnaire

Table 1: Baseline and angiographic characteristics

Variable	Total n (%)	OSA ^{**} risk			P	
		Low	Intermediate	High		
Age (y), mean±SD * (95% CI [†])	62.72±10.99	55.77±11.22 (50.80-60.75)	63.33±10.05 (60.82-65.84)	64.66±11.05 (61.78-67.54)	0.004	
BMI (kg/m ²), mean±SD (95% CI [†])	28.75±5.05	26.95±5.47 (24.52-29.38)	27.84±4.21 (26.78-28.89)	30.42±5.31 (29.03-31.80)	0.003	
Gender	Male	98 (67.6%)	11 (50%)	39 (60.9%)	48 (81.4%)	0.009
	Female	47 (32.4%)	11 (50%)	25 (39.1%)	11 (18.6%)	
Comorbidities	DM [‡]	57 (39.3%)	6 (27.3%)	22 (34.4%)	29 (49.2%)	0.112
	HTN [§]	100 (69%)	6 (27.3%)	40 (62.5%)	54 (91.5%)	<0.001
	Dyslipidemia	71 (49%)	9 (40.9%)	30 (46.9%)	32 (54.2%)	0.512
Current smoker	32 (22.1%)	5 (22.7%)	13 (20.3%)	14 (23.7%)	0.898	
Positive family history	45 (31%)	5 (22.7%)	22 (34.4%)	18 (30.5%)	0.591	
Target vessel	LMCA	8 (5.5%)	2 (9.1%)	3 (4.7%)	3 (5.1%)	0.781
	LAD [¶]	120 (82.8%)	15 (68.2%)	55 (85.9%)	50 (84.7%)	0.143
	LCX ^{**}	89 (61.4%)	11 (50%)	39 (60.9%)	39 (66.1%)	0.414
	RCA ^{††}	97 (66.9%)	15 (68.2%)	41 (64.1%)	41 (69.5%)	0.807
Number of diseased vessels	0	10 (6.9%)	3 (13.6%)	2 (3.1%)	5 (8.5%)	0.218
	1	28 (19.3%)	6 (27.3%)	15 (23.4%)	7 (11.9%)	
	2	43 (29.7%)	4 (18.2%)	21 (32.8%)	18 (30.5%)	
	3	64 (44.1%)	9 (40.9%)	26 (40.6%)	29 (49.2%)	
Dominancy	Right	122 (84.1%)	19 (86.4%)	56 (87.5%)	47 (79.7%)	0.747
	Left	18 (12.4%)	3 (13.6%)	6 (9.4%)	9 (15.3%)	
	Balanced	5 (3.4%)	0 (0%)	2 (3.1%)	3 (5.1%)	

*SD: Standard deviation; [†] CI: Confidence interval; [‡]DM: Diabetes mellitus; [§]HTN: Hypertension; ^{||}LMCA: Left main coronary artery; [¶]LAD: Left anterior descending artery; ^{**}LCX: Left circumflex artery; ^{††}RCA: Right coronary artery; ^{**}OSA: Obstructive sleep apnea

Table 2: SYNTAX and Gensini scores

Variables	OSA risk						P
	Low		Intermediate		High		
	Mean (95% CI*)	Median	Mean (95% CI*)	Median	Mean (95% CI*)	Median	
SYNTAX score	17.15±13.67 (10.56-23.74)	14.00	15.67±9.78 (13.19-18.16)	14.00	16.93±9.21 (14.42-19.45)	15.75	0.754
Gensini score	66.4±70.75 (35.04-97.77)	40.00	66.21±55.05 (52.45-79.96)	58.50	74.61±56.33 (59.93-89.3)	64.00	0.697

*CI: Confidence interval

Table 3: SYNTAX and Gensini scores (extended regression models)

OSA* risk	SYNTAX score				Gensini score			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	B (95% CI)	P	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
Low risk	Reference	0.767	Reference	0.805	Reference	0.756	Reference	0.728
Intermediate risk	-0.09 (-0.421, 0.241)	0.593	-0.089 (-0.421, 0.242)	0.597	-0.003(-0.458, 0.452)	0.99	0.014 (-0.443, 0.472)	0.951
High risk	-0.013 (-0.35, 0.324)	0.940	-0.024 (-0.365, 0.316)	0.888	0.117 (-0.343, 0.576)	0.619	0.139 (-0.329, 0.607)	0.561

*OSA: Obstructive sleep apnea; [†]B: Regression coefficient; [‡]CI: Confidence interval

sex together, nonsignificant relation concluded (OR: 1.56; 95% CI, 0.83–2.91).^[19] Similarly, Wang *et al.* and Dong *et al.* mentioned moderate to severe OSA in comparison with the reference group, although, results in higher rates of stroke and all-cause mortality did not significantly increase the rates of coronary events.^[20,21]

Effective risk stratification and highlighting treatment strategies despite low costs is the ultimate goal of a screening tool. SBQ questionnaires, as a screening tool, had been widely studied about sensitivity and predictive

value for OSA case detection.^[24,25] Still, there is not enough evidence trying to detect the benefits of this method to predict cardiovascular events. Correia *et al.* investigated the use of the Berlin questionnaire for predicting coronary events in patients with unstable angina or NSTEMI. Results showed a higher prevalence of mortality, non-fatal MI, and refractory angina in groups of patients with a higher risk of OSA assessed by the Berlin questionnaire.^[30] Explanation of this difference with our results is about the difference in the population of studies and screening tools (SBQ vs.

Berlin questionnaire). Also, in this study, clinical endpoints, including mortality, etc. had been studied, but we had investigated the severity and complexity of coronary involvement. And the main difference. Hayashi *et al.* conducted another study that is somehow different from our study results. In 59 patients, which show that there is a relation between nocturnal oxygen desaturation (NOD) from SDB and the severity of coronary involvement based on the Gensini score.^[31] Various OSA identification tools (SBQ vs. NOD) and small sample size are the reasons that explain the differences in results.

Further studies with a definitive diagnosis of OSA and a larger sample size are recommended for more precise investigation in terms of the relationship between OSA and CAD.

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Conflicts of interest

There are no conflicts of interest.

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