

Factors Affecting the Correlation Between OSAS and Coronary Artery Disease and the Role of Comorbidities

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Abstract

Aim

Obstructive sleep apnea syndrome (OSAS) patients have an increased risk of hypertension, ischemic heart disease (IHD), arrhythmia, and heart failure. We aimed to investigate the incidence of ischemic heart disease in our patients with OSAS, the effect of comorbidity on the development of ischemic heart disease, and the factors affecting this in the group developing ischemic heart disease.

Methods

The records of 548 patients who underwent polysomnography (PSG) were examined, and demographic data, PSG data, presence of chronic disease, and myocardial scintigraphy findings of patients with and without OSAS were recorded. OSAS patients were also grouped with and without coronary artery disease (CAD).

Results

All patients with CAD were in the OSAS group. No significant difference was observed between the groups with or without CAD in terms of AHI staging, minimal SaO₂, heart rhythm, and myocardial scintigraphy findings. The mean SaO₂ was lower in the group with CAD. While no CAD was found in the group without comorbidity, CAD was observed in 22.1% of those with comorbidity.

Conclusion

No correlation was determined between the AHI stage and CAD. Rather than OSAS weight, the risk of CAD increases in OSAS patients in the presence of increasing age, male gender, smoking history, and comorbidity.

Keywords: Comorbidity, Coronary Artery Disease, Obstructive sleep apnea syndrome

Introduction

Obstructive sleep apnea syndrome (OSAS) is the most common breathing disorder in sleep, characterized by recurrent airway obstruction associated with narrowing of the upper airway diameter during sleep. It is estimated that 1 in 5 adults has at least mild OSAS, and 1 in 15 people has at least moderate OSAS. [1] Obstructive sleep apnea affects approximately 1-4 % of the middle-aged population, and the male/female ratio is 2:1. [2]

Flemons et al. indicated that 80 % of individuals with moderate-to-severe OSAS could remain undiagnosed and untreated. [3] Untreated OSAS has been associated with hypertension (HT), coronary artery disease (CAD), stroke, neurocognitive dysfunction, metabolic syndrome, and motor vehicle accidents. [4,5] Obesity, nasal-pharyngeal-laryngeal obstruction, race, craniofacial abnormalities, male gender, genetics, age, endocrine, neuromuscular diseases, alcohol, connective tissue diseases, analgesics, anesthetics, sedatives,

smoking, storage diseases, chronic kidney diseases are the predisposing factors for OSAS. [6] Many of these factors are also responsible for heart diseases.

OSAS is described as a cardio-metabolic disorder and is a critical risk factor for serious systemic diseases such as HT, Obesity, and diabetes. [7] In OSAS, the cardiovascular system is affected due to recurrent apneas during sleep, hypoxia, reoxygenation, hypercapnia, increased negative intrathoracic pressure, and "arousal" cycles. By activating the sympathetic nervous system, vasoconstriction, tachycardia, and acute blood pressure increase, and platelets are activated by increasing myocardial wall stress, triggering oxidative stress and systemic inflammation, and hypercoagulability and vascular endothelial damage develop. [8] As a result of these events, the risk of hypertension, ischemic heart disease (IHD), arrhythmia, and heart failure increases in OSAS patients. [9,10] As the severity of OSAS

increases, the frequency of CVD, IHD, HT, and stroke history, and arrhythmia diseases increases. [11]

However, the independent prognostic role of severe OSAS for all-cause mortality is controversial due to the presence of comorbidities [12] since comorbidities are also more common in OSAS. [13] Accompanying diseases increase with OSAS severity and aging.

Materials and Methods

The records of 548 patients who underwent polysomnography (PSG) with the preliminary diagnosis of OSAS between March 2019 and December 2021 in our hospital's sleep center were examined, and demographic data (age, weight, BMI, smoking history), PSG data, presence of chronic disease, and myocardial scintigraphy findings of patients with and without OSAS were recorded. The Declaration of Helsinki carried out our study, and approval was obtained from the local ethics committee (no:2022/51, date: 08.03.2022).

Inclusion criteria consisted of patients over 18 years of age, those with symptoms of OSAS (snoring and witnessed apnea and excessive daytime sleepiness), those who had not been diagnosed and treated for OSAS before, and who had not been diagnosed with other sleep disorders back.

Patients who did not meet these criteria were excluded. Besides, patients whose sleep efficiency was below 60% in PSG examination and who had other sleep disorders (central sleep apnea syndrome, sleep-related movement disorders, parasomnias, insomnia) were also omitted.

The diagnosis of OSAS was made using in-laboratory polysomnographic studies (EMBLA S4500). PSG included 6-channel electroencephalography, electrooculography, submental electromyography, anterior tibialis electromyography on both sides, electrocardiography, finger pulse oximetry, dual thoracoabdominal RIP (respiratory inductance plethysmography) belts (for thoracic and abdominal movements), airflow (nasal pressure gauge), the oronasal thermal sensor (thermistor) and digital microphone for snoring detection. PSG recordings were analyzed by a physician experienced in sleep disorders using RemLogic Recordings v.3.2.1. Scoring of sleep and respiratory events was performed according to the standard criteria of the American Academy of Sleep Medicine. [17]

Apnea was defined as a decrease in airflow for more than 10 seconds, more than 90 % of the baseline level. Hypopnea was determined as a

[14,15] There are also studies indicating no relationship between any level of OSAS and coronary heart disease. [16]

The present study aimed to investigate the incidence of ischemic heart diseases in our patients with OSAS, the impact of comorbidity on the development of ischemic heart disease, and the factors affecting this in the group developing ischemic heart disease.

decrease in oxygen saturation of more than 3% with a reduction in airflow for more than 10 seconds, more than 30 % of the basal level, or ending with arousal. [17] Apnea-hypopnea index (AHI) was defined as the total number of apnea and hypopnea events per hour. AHI= 5-14.9 was classified as 'mild OSAS,' AHI=15-29.9 as 'moderate OSAS,' and AHI $\geq$ 30 as 'severe OSAS.' Those with AHI < 5 and diagnosed with simple snoring were described as the non-OSA (control) group. Comorbidities were grouped as congestive heart failure (CHF), cerebrovascular accident (CVE), asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), hypertension (HT), heart valve diseases, chronic kidney failure (CKF), arrhythmia, hypothyroidism, malignancies, and dyslipidemia. The group without comorbidity was formed by patients who did not have these diseases. The diagnosis of CAD was made based on the result of myocardial scintigraphy, a documented myocardial infarction, percutaneous coronary angioplasty, coronary artery bypass grafting, or electrocardiographic evidence of myocardial infarction.

Statistics: The analysis of the data obtained as a result of the research was performed in the statistical package program (IBM SPSS Inc., version 20, Chicago, IL). Descriptive statistical methods (frequency, arithmetic mean, standard deviation, median, minimum, maximum, and crosstabs) were used. Kolmogorov-Smirnov examined compliance with the normal distribution. The arithmetic means of the groups with normal distribution were compared, and the Independent Sample t-test was used for two independent groups. A comparison of 2 dependent groups was performed with Paired Sample t-test. The Mann-Whitney U test compared two groups by comparing the medians of the groups that did not show normal distribution. A comparison of 2 dependent groups was made with the Wilcoxon test. Chi-square and Fisher exact tests examined the association between categorical variables. The statistical significance level was accepted as $p < 0.05$.

Results

The mean age in the OSAS group was 48.8 ± 12 years, while the control group consisted of younger patients (40.1 ± 14.5) ($p < 0.001$). There was male predominance in the OSAS group ($p: 0.018$). There was no significant difference between OSAS and control groups regarding smoking history, BMI, and comorbidity. Mean oxygen

saturation (SaO₂) and minimum SaO₂ values were lower in the OSAS group ($p < 0.001$) (**Table 1**). While there was no significant difference between heart rhythm and myocardial scintigraphy results, all patients with CAD were in the OSAS group ($p: 0.037$) (**Table 1**).

Table 1: Evaluation of demographic and polysomnographic data, the cardiac status of OSAS, and control group

	OSAS(n:507)	Control (n:41)	Total patients (n: 548)	p-value
Age	48.8 ±12	40.1 ± 14.5	48.1± 12.4	0.000
Gender				0.018
Female	146 (88.5 %)	19 (11.5 %)	165 (30.1 %)	
Male	361 (94.3 %)	22 (5.7 %)	383 (69.9 %)	
Non-smoker	58 (92.1 %)	5 (7.9 %)	63 (11.5 %)	0.675
Ex-smoker	40 (93 %)	3 (7 %)	43 (7.8 %)	
Smoker	71 (95.9 %)	3 (4.1 %)	74 (13.5 %)	
BMI kg/m2	39.7± 7.1	35.9 ± 3.5	39.4 ± 7	0.371
Comorbidity				0.371
Yes	222 (93.7 %)	15 (6.3 %)	237 (43.2 %)	
No	285 (91.6 %)	26 (8.4 %)	311 (56.8 %)	
Mean SaO2	92.7(75.8-98.9)	94.9(90.6-97.9)	92.8(75.8-98.9)	0.000
Min SaO2	82 (50-92)	90 (85-95)	83 (50-95)	0.000
Cardiac rhythm/min	69 (47-108)	67 (55-95)	69 (47-108)	0.151
Presence of CAD	49 (100 %)	0 (0 %)	49 (8.9 %)	0.037
Myocardial scintigraphy				0.718
Normal	38 (92.7 %)	3 (7.3 %)	41 (7.5 %)	
Ischemic	8 (100 %)	0 (0 %)	8 (1.5 %)	

BMI: body mass index, SaO2: oxygen saturation, CAD: coronary artery disease

While the mean age was 58.2±10.3 years in the group with CAD in OSAS patients, it was 47.8±11.7 in the group without CAD ($p < 0.001$). There was male predominance in the CAD group. While 14 % of OSAS patients were smokers, 11.4 % were non-smokers, and 7.9 % were ex-smokers, the smoking history of the rest could not be reached. There was CAD in 30 of the ex-smokers ($p < 0.001$). Although BMI could not be determined in all patients, the difference between the group with and without CAD was not statistically significant. There was no significant difference between the groups

with or without CAD in terms of AHI staging, minimal SaO2, heart rhythm, and myocardial scintigraphy findings. The mean SaO2 was lower in the group with CAD ($p:0.008$). While no CAD was found in the group without comorbidity, CAD was observed in 22.1 % of those with comorbidity ($p < 0.001$) (**Table 2**).

The results of the myocardial scintigraphy of 49 patients were accessed. 7 (87.5 %) of 8 patients with ischemia were in the CAD group. However, it was not considered statistically significant since it did not meet the test's assumptions.

Table 2: Evaluation of demographic and polysomnographic data and cardiac status of OSAS patients when classified according to the presence of CAD

	with CAD (n: 49)	without CAD (n: 458)	Total patients (n: 507)	p-value
Age	58.2± 10.3	47.8± 11.7	48.8 ± 12	0.000
Gender				0.002
Female	5 (3.4 %)	141 (96.6 %)	146 (28.8 %)	
Male	44 (12.2 %)	317 (87.8 %)	361 (71.2 %)	
Non-smoker	7 (12.1 %)	51 (87.9 %)	58 (11.4 %)	0.000
Ex-smoker	12 (30 %)	28 (70 %)	40 (7.9 %)	
Smoker	8 (11.3 %)	63 (88.7 %)	71 (14 %)	
BMI kg/m2	40±0	39.7± 7.5	39.4 ± 7(n:38)	0.624
Comorbidity				0.000
Yes	49(22.1%)	173 (77.9 %)	222(43.8 %)	
No	0 (0 %)	285(100 %)	285 (56.2 %)	

AHI				
Low	6 (5.3 %)	108 (94.7 %)	114 (23.7 %)	0.167
Moderate	8 (7.6 %)	97 (92.4 %)	105 (21.8 %)	
Severe	29 (11.1 %)	233(88.9 %)	262 (54.5 %)	
Mean SaO2	91.4 (85.4-97.5)	92.7 (75.8-98.9)	92.7 (75.8-98.9)	0.008
Min SaO2	80.5 (50-89)	81.9 (50-92)	81.7 (50-92)	0.217
Cardiac rhythm/min	67 (51-93)	69.1 (47-108)	68.9 (47-108)	0.140
Myocardial scin.				0.000*
Normal	10 (26.3 %)	28 (73.7 %)	38 (7.5 %)	
Ischemia	7 (87.5 %)	1 (12.5 %)	8 (1.6 %)	

* Does not meet the assumptions of the chi-square test. BMI: body mass index, SaO2: arterial oxygen saturation, AHI: apnea-hypopnea index

Discussion

Studies have indicated that cardiovascular diseases increase in OSAS patients compared to the control group. [11] In our research, while there was no CAD in the control group, it was observed in all of the patients in the OSAS group. CAD was observed in the subgroup of OSAS patients with comorbidities, yet there was no CAD in the group without comorbidities. According to this result, we can conclude that 'OSAS is a risk factor for CAD in the presence of comorbid diseases. This result supports studies demonstrating no relationship between OSAS and coronary heart disease levels. [16]

Male gender and age [18], predisposing factors for OSAS, are also risk factors for comorbid diseases. Therefore, comorbidities are also more common in OSAS. [13] However, while there was no difference in comorbidity between OSAS and the control group in our study, the patients in the OSAS group were older and male-dominated. Anatomical and histopathological changes in the pharynx due to aging cause an increase in collapse (elastic tissue loss) in the upper airways, so the prevalence of OSAS increases with age. [19] In OSAS patients, the mean age was higher in the group with CAD than in the group without CAD, with a male predominance.

Smoking, comorbidity, and increased BMI increase the risk of CAD. Our study determined no significant differences between OSAS and the control group regarding these variables. While 14 % of OSAS patients were smokers, 11.4 % were non-smokers, and 7.9 % were ex-smokers, the smoking history of the rest could not be reached. CAD was present in 30 % of ex-smokers ($p < 0.001$). In our study, the difference in BMI was not statistically significant between the group with and without CAD. However, this result is controversial since the number of patients we have BMI information was low. It was reported that the prevalence of OSAS in patients with BMI >30 ranged from 40 % to 60 %. While Obesity is a risk factor for OSAS, if OSAS is not treated, the patient's weight increases. [20]

Patients with OSAS experience intermittent hypoxia and reoxygenation due to apnea/arousal cycles. Persistent hypoxia can lead to oxidative stress and activation of the systemic inflammatory response, with increases in the general blood antioxidant activity and the production of cytokines such as tumor necrosis factor- α and interleukin-6. [21] These changes affect endothelial function and may lead to OSAS-related hypercoagulability, atherosclerosis, and cardiovascular disorders due to increased platelet activity, plasma fibrinogen levels, and decreased fibrinolytic capacity. [22,24] Increased sympathetic activity, activation of the renin-angiotensin system, and metabolic disorder are also effective in developing cardiovascular disease. [25,27] We concluded that mean SaO2 and minimum SaO2 were lower in the OSAS group and only tell SaO2 was lower in the group with CAD. While the bradycardia rate was higher in OSAS patients compared to the control group, and the bradycardia deepened as the OSAS stage increased [11], no significant difference was detected between the OSAS group and the control group in terms of heart rhythm.

An increase of 10 events per hour in AHI was associated with a 9-36 % higher CVD risk. [28,29] An increased risk of cardiovascular disease has been demonstrated in moderate-severe OSAS rather than mild OSAS. [30] However, our study determined no correlation between the AHI stage and CAD. Rather than OSAS weight, the risk of CAD increases in OSAS patients in the presence of increasing age, male gender, smoking history, and comorbidity.

Although it is a retrospective and single-center study, smoking history and deficiencies in our BMI information are our limitations, the results we obtained are sufficient to remind us that the development of cardiovascular diseases in OSAS patients with comorbidities should not be overlooked.

Conclusion

We concluded that the risk of CAD increases in the presence of comorbidity in patients with OSAS; therefore, close cardiac monitoring of comorbid groups is essential.

Disclosures

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