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Prevalence of cardiac arrhythmia in obstructive sleep apnea syndrome

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Aim: Repetitive transient activation of the parasympathetic and sympathetic systems in obstructive sleep apnea syndrome (OSAS) constitutes the basis for development of cardiac arrhythmias. We aimed to examine the prevalence of arrhythmias in OSAS.

Materials and methods: Eighty-eight patients with suspected OSAS were included in the study. Polysomnography was performed overnight in all patients. Patients with apnea-hypopnea index (AHI) < 5 were considered OSAS negative, while patients with AHI ≥ 5 were OSAS positive. Arrhythmia was defined as sinus bradycardia, sinus tachycardia, > 10/h supraventricular premature beats (SVPBs), > 10/h ventricular premature beats (VEBs), complex VPBs (bigeminal, trigeminal VEB or nonsustained VT), supraventricular tachycardia, ventricular tachycardia, > 2 s sinus arrest, second or third degree atrioventricular block and atrial fibrillation.

Results: Mean age was 47.3 ± 10.5 years; 64 were (72.7%) men, and 24 were (27.3%) women; mean body mass index was 31.1 ± 6.1 kg/m^2. Twenty-five patients were considered OSAS negative (mean AHI: 2.5 ± 1.2) and 63 patients OSAS positive (mean AHI: 40.3 ± 19.4) according to polysomnography records. Six patients in the OSAS-negative group had arrhythmia, whereas 29 patients in OSAS positive group had arrhythmia and the difference between the groups was statistically significant (P = 0.04). The prevalence of cardiac arrhythmia showed an increase parallel to the increase in AHI index in OSAS positive patients.

Conclusion: We demonstrated an increased prevalence of cardiac arrhythmia in OSAS positive patients, parallel to the increase in the severity of OSAS.

Key words: Obstructive sleep apnea syndrome, cardiac arrhythmia, polysomnography

Obstrüktif uyku apne sendromunda kardiyak aritmi görülme sıklığı

Amaç: Obstruktif uyku apnesi sendromu (OSAS)'unda tekrarlayan geçici parasempatik ve sempatik sistem aktivasyonu kardiyak aritmi gelişimi için uygun ortam oluşturmaktadır. Bu çalışma ile OSAS'lı hastalarda kardiyak aritmi sıklığını araştırmayı amaçladık.

Yöntem ve gereç: Çalışmaya OSAS şüphesi ile hastaneye başvuran 88 hasta alındı. Hastalara tüm gece polisomnografi yapıldı. Apne hipopne indeksi (AHİ) < 5 olanlar OSAS negatif, AHİ ≥ 5 olanlar ise OSAS pozitif olarak kabul edildi. AHİ ≥ 5 - < 15 arasında olan hastalara hafif derecede OSAS, ≥ 15 <30 arasında olan hastalara orta derece OSAS, AHİ ≥ 30 hastalara da ağır derece OSAS tanısı konuldu. Ritm bozukluğu olarak; sinüzal bradikardi, sinüzal taşikardi, > 10/saat supraventriküler ektopik atım (SEA), > 10/saat ventriküler ektopik atım (VEA), kompleks VEA (bigemine, trigemine VEA veya nonsustained VT), supraventriküler taşikardi (SVT), ventriküler taşikardi (VT), > 2 saniye sinuzal duraklama, ikinci veya üçüncü derece atriyoventriküler blok, atriyal fibrilasyon (AF) ritm bozukluğu olarak kabul edildi.

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Bulgular: Çalışmaya alınan 88 hastanın ortalama yaşları 47,3 ± 10.5 yıl; vücut kitle indeksi (VKİ) 31,1 ± 6,1 kg/m2; 64'ü (% 72,7) erkek, 24'ü (% 27,3) kadındı. Polisomnografi kayıtlarına göre 25 hasta OSAS negatif (ortalama AHİ 2,5 ± 1,2), 63 hasta da OSAS pozitif (ortalama AHİ 40,3 ± 19,4) olarak kabul edildi. OSAS negatif hasta grubunda 6 hastada (% 24) aritmi saptanmışken, OSAS pozitif hasta grubunda 29 hastada (% 46,8) aritmi görüldü (P = 0,04). OSAS'lı hastalarda AHI indeksindeki artışa parelel olarak aritmi sıklığında da artış saptandı.

Sonuç: Çalışmamızda OSAS'lı hastalarda kardiyak aritmi sıklığında artış olduğu ve OSAS'ın derecesi arttıkça aritmi sıklığının da arttığı görüldü.

Anahtar sözcükler: Obstrüktif uyku apnesi sendromu, kardiyak aritmi, polisomnografi

Introduction

Obstructive sleep apnea syndrome (OSAS) is described as a syndrome with episodes of upper airway obstruction during sleep, often accompanied by arterial oxygen desaturation (1). The prevalence of OSAS in Turkey is unknown, but worldwide prevalence is reported to be 2%-4% (2). Factors diminishing upper airway patency facilitate the development of sleep apnea syndrome are short and thick neck structure, craniofascial anomalies (such as micrognathia and retrognathia), advanced age, male sex, obesity, smoking, and use of alcohol and sedatives (3).

Major complications in patients with OSAS are of the cardiovascular system (3,4) and OSAS is an independent risk factor for cardiac mortality and morbidity. Cardiovascular disorders that coexist with OSAS include systemic arterial hypertension, coronary artery disease, congestive heart disease, cardiac arrhythmia, and pulmonary hypertension (5-7). Repetitive parasympathetic and sympathetic activation in OSAS constitute the basis of cardiac arrhythmia (8). Although cardiac arrhythmia associated with OSAS has been suggested to occur during sleep, this was not validated with large scale studies, and there is no general agreement concerning the prevalence of tachyarrhythmia and bradyarrhythmia in patients with OSAS.

Our purpose in this study was to examine the prevalence of cardiac arrhythmia in patients with or without OSAS who were admitted with the suspicion of OSAS.

Materials and methods

Patients with suspected OSAS were included in the study. An overnight polysomnography was performed using the 44 channel computerized system of *Compumedics E series*. The polysomnography procedure included 4 channels of electroencephalography (EEG), 2 channels of electrooculography (EOG), 1 channel of submental electromyography (EMG), 2 channels of EMG located on both tibialis anterior muscle, 1 channel of nasal cannula to measure oronasal airflow, 2 channels of inductive pletysmography to demonstrate thoracic and abdominal respiratory effort, 1 channel of body-position sensor to determine body position, 1 channel of finger probe to measure arterial oxihaemoglobin saturation (SpO_2), and simultaneous video recording (Figure 1).

Polysomnography including sleep stages was scored manually by a physician who was blind to the patients' information before scoring the data according to the standard criteria of American Academy of Sleep Medicine (9). Apnea was defined as the cessation of oro-nasal airflow for at least 10 s. Hypoapnea was defined as a 50% decline in oro-nasal airflow accompanied by oxygen desaturation of 4% or arousal, which is defined as awaking from sleep or passage into a superficial sleep stage.

The apnea-hypoapnea index (AHI) is the cumulative number of apnea and hypoapnea episodes in an hour. Patients with an AHI < 5 were considered OSAS-negative and AHI ≥ 5 were considered OSAS-positive. An AHI of ≥ 5 <15 represented mild OSAS, an AHI of ≥ 15 < 30 represented moderate OSAS and an AHI ≥ 30 represented severe OSAS (9,10).

Electrocardiography recordings during polysomnography were evaluated for the presence of cardiac arrhythmia. Sinus bradycardia, sinus tachycardia, > 10/h supraventricular premature beats (SVPBs), > 10/h ventricular premature beats (VPBs), complex VPBs (bigeminal, trigeminal VPB or

nonsustained VT), supraventricular tachycardia (SVT), ventricular tachycardia (VT), > 2 s sinus arrest, second or third degree atrioventricular block and atrial fibrillation (AF) were designated as cardiac arrhythmia. ECG recordings of the patients were evaluated by one separate cardiologist.

The SPSS 11.5 for Windows was used for statistical analyses. Continuous variables were expressed as mean ± SD, and categorical variables were expressed as a percentage. The Kolmogorov-Smirnov test was used to compare empirical distribution of continuous variables. Comparison of continuous variables between groups was performed using Student's t-test. The chi-square test was used for the analysis of categorical variables. The prevalence of arrhythmia in OSAS negative and positive groups were compared using the chi-square test. $P < 0.05$ was considered statistically significant.

Results

A total of 88 patients were included in the study. Mean age in the study population was 47.3 ± 10.5 years, mean body mass index (BMI) was 31.1 ± 6.1 kg/m^2, and study group consisted of 64 males (72.7%) and 24 females (27.3%). Twenty-five patients were considered OSAS-negative (mean AHI: 2.5 ± 1.2) and 63 patients OSAS positive (mean AHI: 40.3 ± 19.4) according to polysomnography records. Both groups were comparable with respect to age, sex, BMI, presence of hypertension, diabetes mellitus, hyperlipidemia, and coronary artery disease (Table 1).

Arrhythmia was found in six patients (24%) in the OSAS-negative group, whereas 29 patients (46.8%) in OSAS-positive group had cardiac arrhythmia and the difference between the groups was statistically significant (P = 0.04) (Figure 1). Arrhythmia types in OSAS-negative and -positive groups were not significantly different (Table 2). Two patients (8%) in the OSAS-negative group and 16 patients (25.4%) in the OSAS-positive group demonstrated SVPBs (P = 0.057), 2 patients (8%) in OSAS-negative group and 13 patients (20.6%) in OSAS-positive group demonstrated VPBs (P = 0.132). Sinus bradycardia and sinus arrest > 2 seconds were more common in the OSAS-positive group compared to OSAS-negative patients; however, the difference did not reach statistical significance (P = 0.45). Patients' polysomnographic records are shown in Figures 2 and 3.

There was a trend towards an increase in the prevalence of cardiac arrhythmia, parallel to an increase in the severity of OSAS (Table 3). The prevalence of arrhythmia was not statistically different between OSAS-negative and mild OSAS patients (6/25 vs 1/5; P = 0.67); however, the difference was significant when compared to patients with moderate-to-severe OSAS (6/25 vs 29/58; P = 0.024) (Figure 4).

Table 1. Characteristics of patients with OSAS negative and OSAS positive groups.

	OSAS negative group (n=25)	OSAS positive group (n=63)	P value
Age (years)	48.8 ± 10.8	46.7 ± 10.4	NS
% men	76	79,3	NS
BMI ($kg/m^{2)}$	32.8 ± 7.1	31.5 ± 5.6	NS
Hypertension	6	19	NS
Diabetes mellitus	2	6	NS
Hyperlipidemia	3	8	NS
Coronary artery disease	1	4	NS
AHI (events/hour)	2,5 ± 1.2	40.3 ± 19.4	<0.001
Wake up oxygen saturation (%)	94.0 ± 1.4	93.3 ± 2.2	NS
Mean oxygen saturation (%)	89.5 ± 0.7	89.0 ± 4.3	NS
Lowest oxygen saturation (%)	91.0 ± 0.2	74.1 ± 11.5	<0.001

OSAS: Obstructive sleep apnea syndrome, BMI: Body mass index, AHI: Apnea hypopnea index, NS: nonsignificant

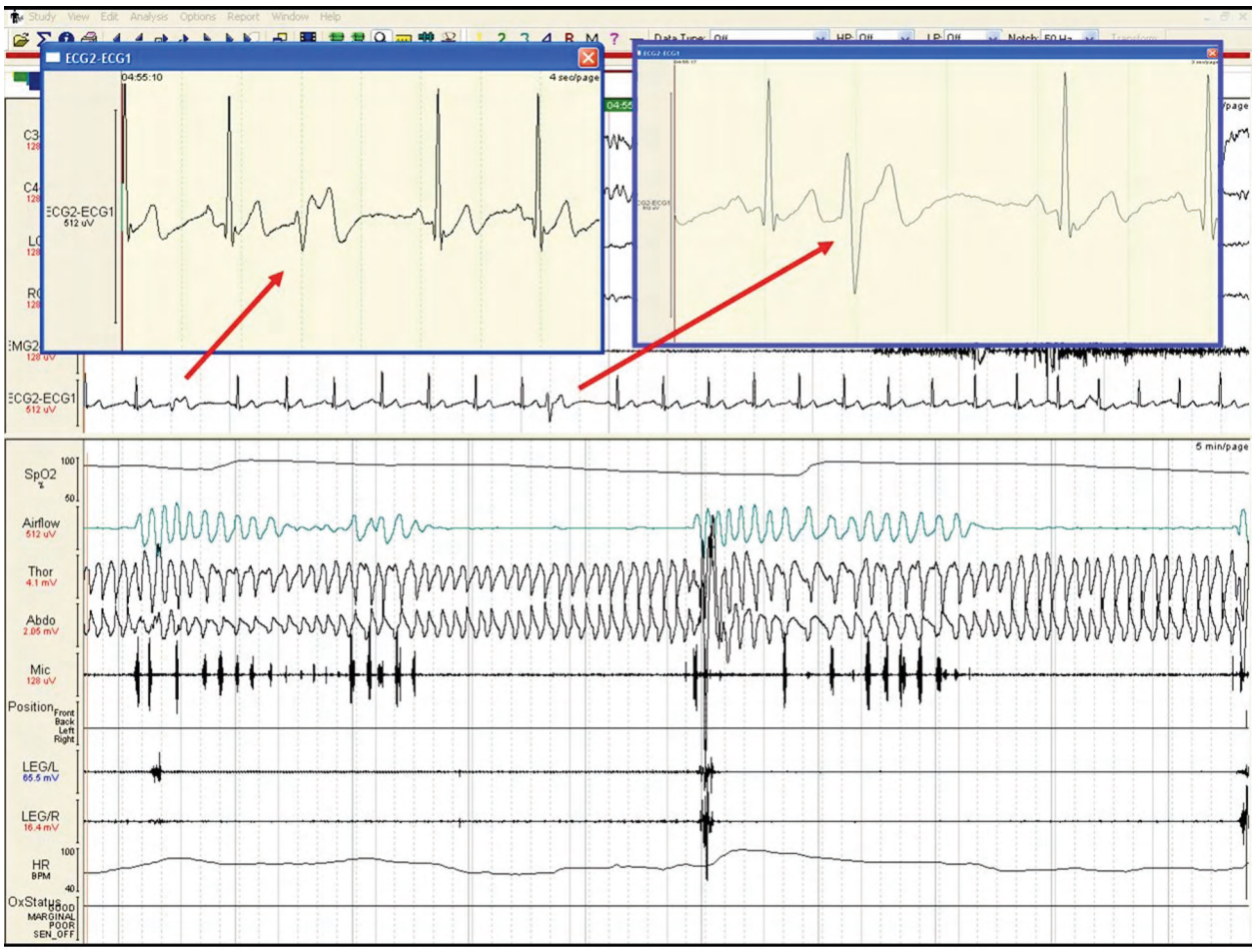

Figure 1. Segments of a patient's polysomnographic record showing epizodes of ventricular premature beats.

Table 2. Cardiac arrhythmias seen in OSAS negative and positive patients.

	OSAS negative group (n = 25)	OSAS positive group (n = 63)	P value
>10/h SVPBs	2	16	NS
>10/h VPBs	2	13	NS
Complex VPBs	1	5	NS
SVT	0	4	NS
VT	0	0	NS
>2 s pause	1	6	NS
Sinusal tachycardia	2	13	NS
Sinusal bradycardia	0	2	NS
Atrial fibrillation	0	3	NS
2nd degree AV block	0	1	NS
3rd degree AV block	0	1	NS

SVPBs= supraventricular premature beats, VPBs= ventricular premature beats, SVT= supraventricular tachycardia, VT= ventricular tachycardia, AV block= atrioventricular block

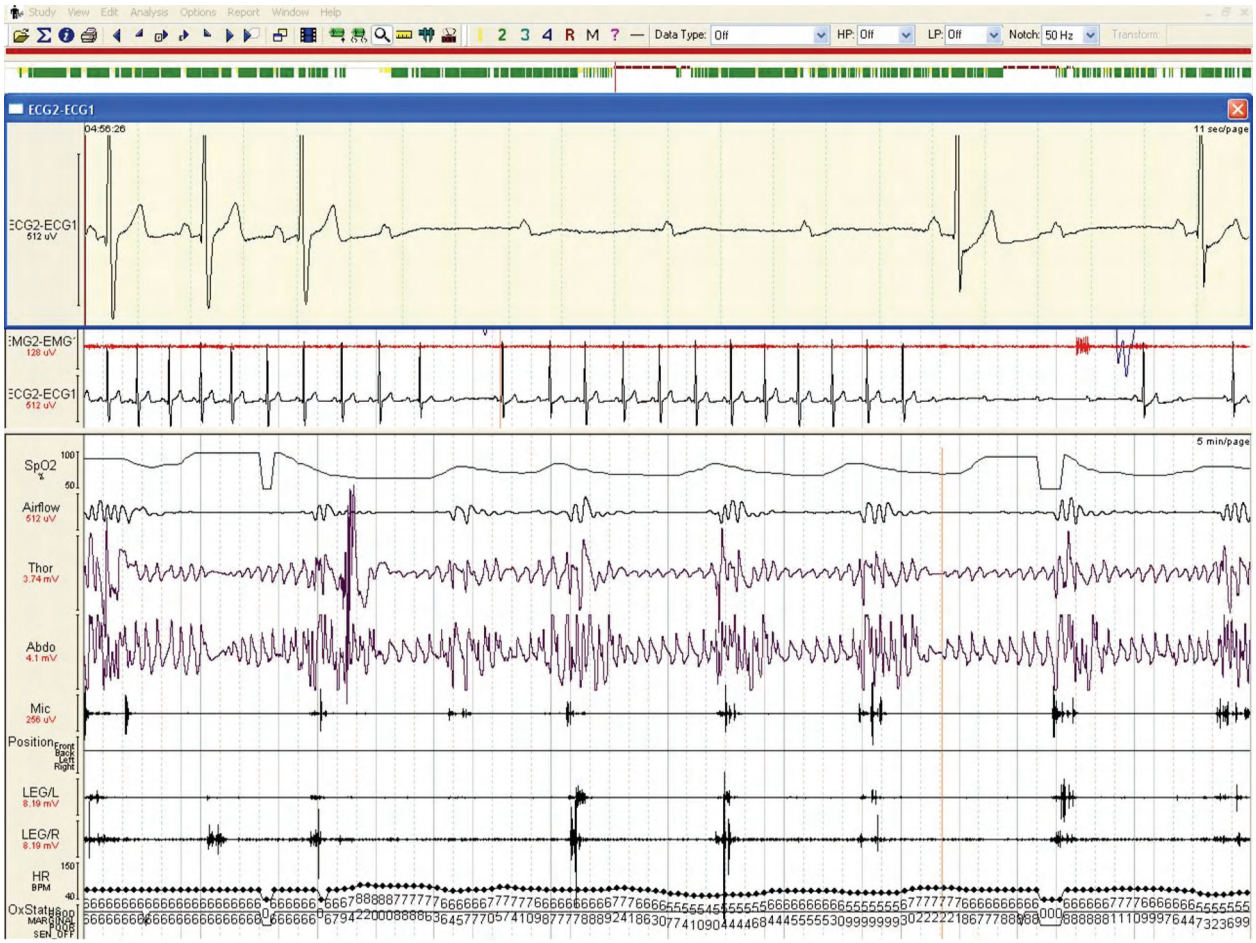

Figure 2. Segments of a patient's polysomnographic record showing epizodes of third degree atrioventricular block

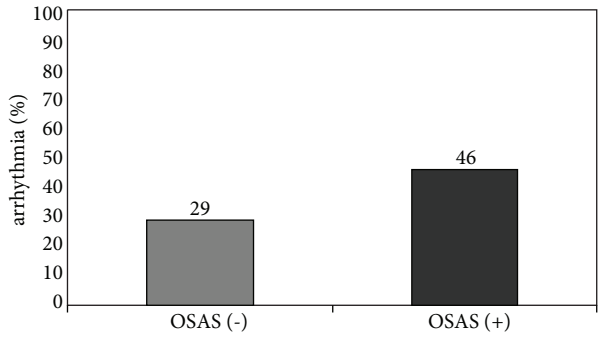

Figure 3. Frequency of cardiac arrhythmia in OSAS negative and OSAS positive groups (6/25 versus 29/63; P = 0.041).

One patient in the mild OSAS group and 29 patients in the severe OSAS group demonstrated cardiac arrhythmia (P = 0.2), indicating no statistical difference between the 2 groups.

Discussion

The underlying mechanism in obstructive sleep apnea syndrome is the collapse of the pharyngeal wall (1). The patency of upper airway is determined by the balance between collapsing intraluminal negative pressure during inspiration and dilator muscle activity. Complete or partial collapse occurs during inspiration when the balance has changed in favor of collapsing forces, resulting in insufficient ventilation during sleep. This causes a decline in oxygen concentration and an increase in carbon dioxide concentration of the blood (11). At the critical level of hypoxemia and hypercapnia, an increase in muscle tone is achieved by arousal or inspiration returns, by changing body position. Elimination of sympathetic inhibition by hypoxia and hypercapnia during the

Table 3. Cardiac arrhythmia frequency in OSAS negative and OSAS positive groups.

	Non OSAS (AHI < 5)	Mild OSAS (AHI 5-15)	Moderate-severe OSAS (AHI > 15)	Severe OSAS (AHI > 30)	Very severe OSAS (AHI > 45)
Number of cases	25	5	58	16	25
Arrhythmia (+)	6	1	29	5	17

	Mild OSAS	Moderate-severe	Severe OSAS	Very severe OSAS
Non OSAS	P = 0.671	P = 0.024	P = 0.016	P = 0.01

OSAS: Obstructive sleep apnea syndrome

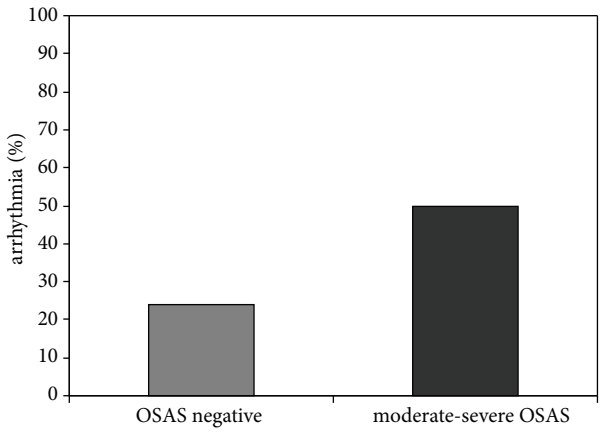

Figure 4. Frequency of cardiac arrhythmia in OSAS negative and moderate-severe OSAS groups (6/5 versus 29/58; P = 0.024).

early phases of apnea, and increased intrathoracic negative pressure caused by forced inspiration in response to obstructed airways stimulate N. Vagus, whereas hypoxemia induces the activity of carotid body, which together produce bradyarrhythmia with a transient increase in parasympathetic activity. Arousal following apnea episode and re-establishing respiration through cortical centers causes sympathetic discharge and decrease in vagal tone. Therefore, a marked increase in heart rate and blood pressure is observed just after the apnea episode (12,13).

Cyclic variation of heart rate is the most commonly observed arrhythmia associated with OSAS (8) in which bradycardia in the early phases of apnea episode is followed by tachycardia when respiration is resumed. Bradycardia begins with the onset of apnea, which is proportional to the degree of hypoxemia. Bradycardia associated with OSAS is caused by vagal activity and recovers after atropine administration. Furthermore, electrophysiological studies have not indicated an abnormal finding (14,15).

Data about the prevalence of cardiac arrhythmia in patients with OSAS is controversial. Studies investigating the relationship between oxygen desaturation and arrhythmias in patients with obstructive sleep apnea syndrome indicated that supraventricular brady- and tachyarrhythmias are more often caused by the activation of autonomic nervous system, whereas ventricular arrhythmias are related with hypoxemia (7,13). Decreased oxygen saturation below 60% corresponds to an increase in the prevalence of ventricular arrhythmia.

Sinus bradycardia and sinus arrest are the most common types of arrhythmia (16,17). Guilleminault et al. (17) reported rates of 10% sinus arrest and 5% 2nd degree AV block among 400 patients with OSAS. In our study the rates of sinus arrest and 2nd or 3rd degree AV block were 9.5% and 3.2% respectively. Flemons et al. (16) did not report a significant difference between OSAS-negative and -positive patients. Roche et al. (18) examined 147 patients with suspected OSAS, in which they reported comparable rates of congestive heart failure, history of myocardial infarction, hypertension, and ventricular arrhythmia in OSAS-positive and -negative patients, but higher rates of nocturnal paroxysmal asystole among OSAS-positive patients (10.6% vs. 1.2%) (P < 0.01) and increasing prevelance of bradycardia and sinus arrest episodes with the increasing severity of the disease.

All bradycardia episodes have been reported in patients with severe OSAS (AHI > 30) in which arterial oxygen desaturation has been observed. Hoffstein and Mateika (19) reported higher prevalence of arrhythmia in patients with severe OSAS. In our study, the prevalence of arrhythmia was significantly different between OSAS-positive and -negative patients (6/25 vs. 29/63; P = 0.041). Severe OSAS, morbid obesity, REM sleep, severity of oxygen desaturation during apnea episode are independent risk factors for the occurrence of heart block during apnea episode (14). In our study the prevalence of arrhythmia was higher among patients with moderate-severe OSAS, which increased in proportional to AHI.

The relation between OSAS and ventricular arrhythmia remains controversial. Autonomic over-activity and trigger activation have been implicated in the development of ventricular arrhythmias associated with OSAS (20). OSAS-positive patients with ventricular arrhythmia represent evidences for sympathetic over-activation and autonomic dysfunction caused by compromised baroreceptor activity. The prevalence rates of VT and VPB are reported to be 3%-13% and 20%-67% respectively (17,21). It is likely that the prevalence of ventricular arrhythmia is related to the severity of OSAS and oxygen desaturation. Lown et al. (22) noted an increase in the prevalence of VF during REM sleep and suggested a relation with the sympathetic over activation. In our study the prevalence rates of VPB and complex VPB in OSAS positive patients were 20.6% and 7.9% respectively. We did not note VT in our patients.

Arrhythmias in OSAS-positive patients mostly occur secondary to OSAS. Electrophysiological studies have failed to demonstrate conduction disturbances which could explain the appearance of arrhythmias (23).

Our limitation was by comparing OSAS-positive patients with those admitted with the suspicion of OSAS and validated to have an AHI < 5 in polysomnography recordings. Patients were not compared with healthy controls free of symptoms associated with OSAS.

In conclusion, we determined a significant relation between OSAS and the prevalence of cardiac arrhythmia. OSAS should be kept in mind as the etiologic factor particularly in those representing nocturnal arrhythmia. Large-scale controlled trials are needed to examine the relation between OSAS and each type of cardiac arrhythmia in detail.

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