Comparison of positional and rapid eye movement-dependent sleep apnea syndromes

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Submission: 05-06-2017
Accepted: 11-08-2017

Abstract:

AIM: We aimed to compare the clinical, epidemiological, and polysomnographic features of rapid eye movement (REM)-dependent obstructive sleep apnea syndrome (OSAS) and positional OSAS which are two separate clinical entities.

METHODS: Between January 2014 and December 2015, at the Akdeniz University Medical Faculty Hospital, patients who were diagnosed REM-dependent and positional OSAS with polysomnography were retrospectively studied.

RESULTS: In this study, 1727 patients were screened consecutively. Five hundred and eighty-four patients were included in the study. Of the patients, 24.6% (140) were diagnosed with REM-dependent OSAS and 75.4% (444) were diagnosed as positional OSAS. Female predominance was found in REM-dependent OSAS ($P < 0.001$). The mean total apnea–hypopnea index (AHI), non-REM AHI, and supine AHI in REM-dependent OSAS were 14.73, 9.24, and 17.73, respectively, and these values were significantly lower when compared with positional OSAS ($P < 0.001$). Patients diagnosed with REM-dependent OSAS had a statistically significant tendency to be overweight ($P < 0.001$). For REM-dependent OSAS, total pulse rate, supine pulse rate, and REM pulse rate were statistically higher than positional OSAS ($P < 0.001$).

CONCLUSION: Positional OSAS is a clinical entity that is more common than REM-dependent OSAS. OSAS severity is higher in positional OSAS than REM-dependent OSAS. REM-dependent OSAS is observed more commonly in women.

Keywords:

Obstructive sleep apnea syndrome, positional obstructive sleep apnea syndrome, rapid eye movement-dependent obstructive sleep apnea syndrome, sleep apnea syndrome

Obstructive sleep apnea syndrome (OSAS) is a disease characterized by complete or partial obstruction of the upper respiratory tract during sleep.[1-3] Due to the recognition of different clinical features in recent years and the developments of particularly positive airway pressure (PAP) therapies, different clinical types of OSAS have been defined and appropriate treatment approaches have been identified. For today, OSAS is not a standard, single clinical condition. OSAS is considered to have variances in severity, and apnea–hypopnea index (AHI) is used to reveal severity of OSAS and influenced by several factors such as sleep state or body position.

Sleep is evaluated in two stages as rapid eye movement (REM) and non-REM (NREM). The REM stage is named after REM during this phase. This stage is classified as tonic and phasic REM. During this stage, brain activity with mixed frequency, erection, thermoregulation loss, muscle twitching, cardiorespiratory disorder, respiratory control impairment, and irregular ventilation occur. The severity of sleep apnea in NREM

Access this article online
Quick Response Code:
Website: www.thoracicmedicine.org
DOI: 10.4103/atm.ATM_184_17

How to cite this article: Uzer F, Toptas AB, Okur U, Bozkurt S, Dogrul E, Turhan M, *et al*. Comparison of positional and rapid eye movement-dependent sleep apnea syndromes. Ann Thorac Med 2018;13:42-7.

sleep is often considerably less than that observed in REM sleep.[4-5]

Body position has a strong influence on OSAS. A supine position and its associated gravitational effects on the tongue and mandible make the upper airway more collapsible, which is thought to be responsible for the worsening of OSAS compared with a nonsupine position. The mechanisms underlying positional OSAS including its interaction with upper airway collapsibility or reduced lung volume are poorly understood. Prevalence rates vary depending on the criteria defining positional OSAS. Positional OSAS accounts for a significant portion of the OSAS population, ranging from 50% to 60% of OSAS patients who present to sleep clinics and occurs more commonly in nonobese patients and patients with mild or moderate OSAS rather than severe OSAS.[3-6]

We aimed to compare the epidemiological, clinical, and polysomnographic characteristics of REM-dependent OSAS and positional OSAS, two separate clinical entities in our study.

Methods

In the study, patients who underwent polysomnography (PSG) at the Akdeniz University Medical Faculty Hospital between January 2014 and December 2015 and who had REM-dependent OSAS or positional OSAS were studied retrospectively. Patients were consecutively recruited. Patients with total AHI >5/h and patients older than 18 years who slept at least 4 h, 15 min for REM, 30 min for supine, and 30 min for nonsupine position were included in the study. Patients with known neurological disease, obesity hypoventilation syndrome, and overlap syndrome were excluded from the study. Sex, ages, body mass index (BMI), and comorbid diseases of the patients were noted. Polysomnographic signals recorded included mainly were electroencephalography, electro-oculogram, submental electromyogram, airflow (nasal pressure), electrocardiogram (ECG), thoracoabdominal effort, and oximetry. PSG results of all patients were manually scored according to AASM criteria.[7] Apnea was defined as a ≥90% decrease in baseline oronasal thermal sensor; and hypopnea was defined as a reduction of 50% or more in airflow by the oronasal airflow meter for 10 s or longer, accompanied by a decrease in oxygen saturation of 4% or more and arousals. The sum of apneas and hypopneas per hour of sleep period was defined as AHI. REM-dependent OSAS is defined as a condition in which REM AHI is at least twice as high as or greater than NREM AHI, with a condition of OSAS (total AHI >5) and NREM-AHI at normal limits (<5/h). Positional OSAS is defined as a condition in which supine AHI is at least twice as high as or greater than nonsupine AHI, with a condition of OSAS (total AHI >5 h) and nonsupine AHI at normal limits (<5/h). The study has been approved by the Ethics Committee of the Akdeniz University.

Statistical analysis

Results are reported as the mean ± standard deviation and categorical variables are given as percentages. The normality of distribution was confirmed by the Shapiro-Wilk's W-test. Since the Shapiro-Wilk test confirmed that all continuous variables (Age, BMI. AHI, TST, SpO2, pulse rate and etc.) were normally distributed for each study group (Positional and REM-dependent) statistical comparison of clinical data between two groups consisted of unpaired *t*-tests, whereas the chi-square/Fisher's exact tests were used for categorical variables. Analyses were performed with IBM SPSS Statistics for Windows, version 20.0 (IBM Corp. released 2013. IBM Corp., Armonk, NY, USA) software and two-tailed $P < 0.05$ was considered statistically significant.

Results

In our study, 1727 patients were screened for OSAS. Whereas 1467 patients were diagnosed as OSAS, 32 patients were excluded due to lack of file information [Figure 1]. Basic demographic characteristics of patients are given in Table 1. One hundred and fifty-two (10.36%) patients were diagnosed with REM-dependent OSAS and 464 (31.62%) patients were diagnosed as positional OSAS. Seventy-seven (25%) of REM-dependent OSAS and 88 (19.8%) of positional OSAS were female patients. In REM-dependent OSAS, statistically significant higher female predominance was detected ($P < 0.001$). The mean age of the patients was 52.27 years in REM-dependent OSAS and 50.79 years in positional OSAS. This ratio was not statistically significant ($P = 0.209$). While the mean BMI of the patients was 30.03, it was detected as 32.32 in REM-dependent OSAS and 29.31 in positional OSAS. Patients diagnosed with REM-dependent OSAS were statistically significantly more tended to be overweight ($P < 0.001$). Smoking history was 42.5% (48) and 46.4% (159) in REM-dependent and in positional

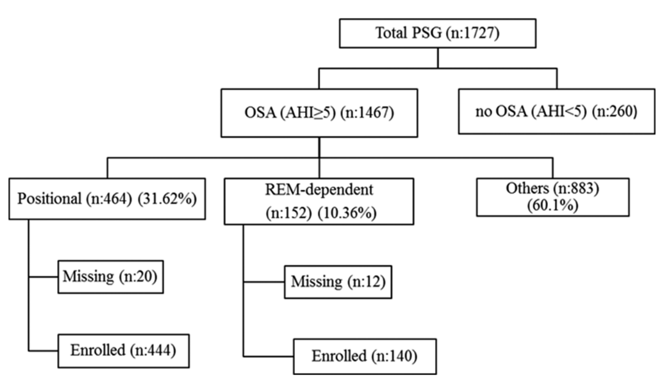

Figure 1: Distribution of patients according to diagnostic features

OSAS, respectively, and no statistically significant difference was found [Table 2]. Hypertension and diabetes mellitus were the most common comorbid conditions in both groups, and there was no statistically significant difference in the incidence of comorbid diseases between groups. The mean total AHI, NREM AHI, and supine AHI in REM-dependent OSAS were 14.73, 9.24, and 17.73, respectively, and these values were significantly lower when compared with positional OSAS ($P < 0.001$). In REM-dependent OSAS, total pulse, supine pulse, and REM pulse rates were statistically higher than positional OSAS ($P < 0.001$). Mean oxygen saturation and minimum oxygen saturation were higher in the positional OSAS (P values are P_{min} $SpO_2 = 0.002$, P_{avg} $SpO_2 = 0.001$, respectively). There was no statistically significant difference in total sleep time in both groups [Table 3]. For REM-dependent OSAS, confidence interval was 0.21–0.28, and for positional OSAS, it was 0.72–0.79.

Table 1: Basic demographic and clinical characteristics of the patients

Features	Data
Age (mean, years) (SD)	51.12 (12.16)
Sex, *n* (%)	
Male	419 (71.74)
Female	165 (28.26)
BMI (kg/m^2) (SD)	30.03 (4.83)
TST (min) (SD)	407 (60.52)
AHI (event/h) (SD)	
Total	20.16 (11.91)
Supine	39.35 (24.41)
Nonsupine	7.40 (8.44)
REM	26.29 (19.99)
Non-REM	18.63 (13.21)
SpO_2 (SD)	
Minimum	82.87 (6.38)
Mean	94.56 (2.16)
Pulse (SD)	
Total	66.42 (9.05)
Supine	66.07 (10.34)
REM	66.07 (10.32)
Smoking, *n* (%)	
Yes	207 (35.44)
No	249 (42.63)
Not reached	128 (21.91)

AHI=Apnea-hypopnea index, BMI=Body mass index, SD=Standard deviation, TST=Total sleep time, REM=Rapid eye movement, SpO_2=Oxygen saturation

Table 2: Clinical features of the patients

	REM-dependent	Positional	*P*
Age (years)			
Male	48	50	0.291
Female	56	55	0.861
All patients	52.2	50.7	0.209
BMI (kg/m^2)			
Male	31.0	29.0	0.001
Female	33.3	30.3	0.004
All patients	32.3	29.3	<0.001
Smoking history, *n* (%)			
None	65 (57.5)	184 (53.6)	0.473
Yes	48 (42.5)	159 (46.4)	
Sex, *n* (%)			
Male	63 (45)	356 (80.2)	<0.001
Female	77 (55)	88 (19.8)	

BMI=Body mass index, REM=Rapid eye movement

Discussion

The clinical and polysomnographic characteristics of positional OSAS and REM-dependent OSAS were examined in this study. There have been many studies on this subject. Positional OSAS frequency rate was high in our patient group. While some studies are line with the present study, the others are not. Studies in the literature show that the prevalence of positional OSAS is 23%–63% and REM-dependent OSAS is 10%–13%.[6,8] This variability differs according to the AHI value taken as OSAS definition. In our study, the prevalence of positional OSAS was 31.62% and REM-dependent OSAS was 10.36% when AHI >5 was taken as the OSAS definition. This rate is similar to those reported in the literature. In addition, in parallel with many studies in the literature, we found that the positional OSAS BMI was higher than the REM-dependent OSAS.[4-5]

In middle age period, OSAS frequency in men was reported more frequently than women.[3-6,9] Female sex hormones are thought to protect women from respiratory events by increasing the genioglossus tonicity and stimulating ventilation.[4-6,8,10] However, since the atony occurs in REM sleep, female sex hormones lose their ability to affect upper airway muscles causing airway collapse.[10-12] These hormones are reduced postmenopausal; therefore, OSAS is more common in women in older ages.[3,10-12] Since women have smaller structures compared to men in the upper airways, there is more collapse in the supine position in REM.[13] Although the incidence of OSAS is normally higher in men, REM-dependent OSAS is more prevalent in women due to these reasons. O'Connor *et al*.[14] reported that REM-dependent OSAS was observed more frequent in women. In our study, in parallel with the study of O'Connor *et al*., it was found that REM-dependent OSAS is more frequent in women. It is estimated that the prevalence of OSAS increases during the advanced age period. There are studies reporting different results in the literature on the distribution of REM-dependent OSAS by age. While REM-dependent OSAS is detected in younger patients in some studies, as in our study, there are studies that have similar age in both groups.[4,15]

The definitions used to classify patients with positional and REM-dependent obstructive sleep apnea (OSA) have varied. Most of the authors consider that positional OSA

Table 3: Polysomnographic features of patients

	REM-dependent (SD)	Positional (SD)	P
Total AHI	14.73 (7.29)	21.88 (12.56)	<0.001
REM AHI	40.79 (16.82)	21.73 (18.71)	<0.001
NREM AHI	9.24 (6.90)	21.60 (13.35)	<0.001
Supine AHI	17.73 (14.15)	46.18 (22.95)	<0.001
Nonsupine AHI	9.51 (12.71)	6.74 (4.46)	0.001
Supine TST (min)	195.05 (129.50)	161.11 (95.37)	0.016
TST (min)	406.83 (65.08)	407.82 (59.08)	0.846
Minimum SpO_2	81.33 (6.94)	83.36 (6.13)	0.002
Average SpO_2	94.03 (2.54)	94.73 (2.01)	0.001
Total pulse rate	69.52 (9.97)	65.45 (8.53)	<0.001
Supine pulse rate	68,52 (13.35)	65.31 (9.08)	<0.001
REM pulse rate	69.45 (9.61)	65.34 (10.35)	<0.001

AHI=Apnea-hypopnea index, TST=Total sleep time, SD=Standard deviation, REM=Rapid eye movement, NREM=Nonrapid eye movement, SpO_2=Oxygen saturation

is present when the AHI >5/h and respiratory events occur at twice the frequency in the supine sleeping position compared to nonsupine sleeping position. There is also alternative definition of positional OSA.[16] Mador *et al*. proposed that the ratio of events in the supine position to the nonsupine positions must be greater than two to one and the AHI in the nonsupine positions must be less than 5 events/h. A commonly used diagnostic criterion for REM-dependent OSA is based on the ratio of the AHI during REM sleep to the AHI during NREM sleep, with a value of at least 2 indicating a predominance of disordered breathing during REM sleep. Mokhlesi and Punjabi proposed a new criterion to describe REM-related OSA in 2012:[17] (a) an AHI NREM of fewer than 5 events/h and (b) an AHI REM of at least 5 events/h with at least 30 min of REM sleep. Two studies also used a minimum of 10 min of REM sleep duration as a defining criterion for REM-related sleep-disordered breathing (SDB).[18,19] REM OSA was also defined as a REM AHI/NREM AHI >2 and NREM AHI <15.[20]

Clinical outcomes associated with REM-dependent and positional OSA may be different. Positional OSA is the dominant phenotype of the OSA syndrome. Supine predominant patients have been reported as subjectively more sleepy than other OSA patients.[21] Obstructive events are more severe in the supine position. In patients with severe nonpositional OSA, apnea duration and degree of oxygen desaturation are both more severe when the patients are observed in the supine sleeping position. REM-related OSA is common in women and in younger patients. While NREM sleep is associated with excessive daytime sleepiness or impaired quality of life, REM-related OSA does not have associated impairments in daytime sleep tendency or quality of life.[17] Lee *et al*. demonstrated that REM-related SDB can be associated with depressive symptoms in men.[22] Furthermore, AHI REM was positively associated with the depressive symptoms in men with REM-related SDB. Mokhlesi *et al*. showed that AHI REM ≥15/h was associated with both prevalent and incident risk of hypertension.[23]

Obesity is a factor very closely associated with the presence of OSAS.[1,3,12] There has been a rapid increase in the incidence of obesity in recent years and is accepted as the most important predisposing factor of OSAS. In our study, BMI was higher in REM-dependent OSAS than positional OSAS. This proportion was statistically significant. There are studies in the literature showing that there is no difference between two groups as well as studies reporting that the BMI of the positional OSAS is low, as in our study.[6,13,15]

Heart rhythm variability is frequently detected in ECG obtained during PSG records of patients with OSAS. Bradyarrhythmias in the early stages of apnea and tachycardia with waking up after apnea episode can occur.[24,25] In the study of Guilleminault *et al*., sinus arrest was seen in 10% of patients with OSAS and second-degree atrioventricular block in 5%.[25] In our study, total heart rate of patients was significantly higher in REM-dependent OSAS than positional OSAS. In studies, severe OSAS, morbid obesity, and severity of oxygen desaturation have been detected as independent risk factors for heart block development during apnea.[24] In our study, similar with literature, total heart rate was lower in positional OSAS than REM-dependent OSAS.

As expected, apnea and hypopnea event was occurred most frequently in the supine position in patients with positional OSAS. In the REM-dependent OSAS, the AHI value was detected to be high in the supine position. Side-lying position may provide some relief in two patient groups either. There was no significant difference in nonsupine AHI in both groups. In many studies, it was shown that nonsupine sleeping position decreases AHI below 10–20 in 75%–89% of patients with diagnosis of positional OSAS.[26,27] In some studies, the duration of supine sleep was higher in REM-dependent OSAS, whereas it was similar in both groups in our study.

OSAS is a complex and heterogeneous disorder. Phenotyping can improve prognostication, understanding of mechanisms, and also personalized treatments. Recent data suggest that patients may respond differently to non-PAP treatments depending on their pathophysiologic characteristics such as arousal propensity or ventilatory sensitivity.[28] Currently, the best way to treat positional or REM-dependent OSAS is unknown. Positional therapy such as waistband or tennis ball technique is an effective method to treat these patients on the short-term, but long-term compliance is low.[29] More comfortable device such as vibrating devices might be more useful in the treatment of positional OSAS.[29] Chami *et al*. showed that in the absence of NREM SDB, REM SDB is not associated with sleepiness, impaired health-related quality of life, or sleep disruption.[30] As the effects of REM SDB are unknown, whether REM SDB should be treated in the absence of non-REM SDB remains undetermined.

Our study has some limitations. Although a large cohort of consecutive patients were included this study, there may be a selection bias since only symptomatic patients were being referred for testing. This may limit the validity and generalizability of our results. The prevalence of positional and REM-dependent OSAS in our study is not true reflection of the burden of OSAS phenotypes in our region; it only reflects a sleep clinic prevalence. In this study, we used minimum threshold values for REM-dependent and positional OSAS. If we were used greater threshold values, such as 30-minute REM sleep time or 1-h supine sleep time, prevalence rates would have been decreased. Because of its retrospective design, we were unable to reach results of clinical features such as snoring, witnessed apnea, neck circumference before many patients diagnosed with OSAS, and inability to reach results of Epworth sleepiness scale are other limitations of the present study.

Conclusion

Positional OSAS is a clinical entity that is more common than REM-dependent OSAS. OSAS severity is higher in positional OSAS. REM-dependent OSAS is more commonly seen in women. Patients diagnosed with REM-dependent OSAS tend to be more obese compared to patients with positional OSAS. When clinicians being determine OSA severity and choose between treatment methods, they should take consider not only sleeping stage but also sleep position.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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