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Comparison of different criteria for the diagnosis of position and rapid eye movement-related obstructive sleep apnea syndrome and the value for the determination of prognosis

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Abstract:

INTRODUCTION: Determination of clinical obstructive sleep apnea syndrome (OSAS) types is important for treatment decision. In the literature, there are two different criteria for the diagnosis of position and rapid eye movement (REM) related OSAS. One of them provides the criteria that nonsupine and/or non-REM apnea-hypopnea index (AHI) below 5, the other does not. In this study, these two definitions are named as “strict definition” and “loose definition.” This study is designed to identify which definition is more beneficial to use, and the prognostic value of the definitions by using OSAS severity according to AHI. This is the first study which investigates those issues.

MATERIALS AND METHODS: This study is a retrospective cohort study. Obstructive AHI >5 of all adult patients admitted to our sleep disorders center between September 2012 and October 2014 were included to this study. The patients were grouped due to both strict and loose definitions. Patient groups were named as position related, REM related, REM + position related, pure OSAS due to loose definitions, and position dependent, aggravated by position, REM dependent, aggravated by REM, REM + position dependent, aggravated by REM + position, pure OSAS due to strict definitions. All these groups were compared for demographic and polysomnographic parameters.

RESULTS: Two hundred and eighty (73.7%) of the patients were male, 100 (26.3%) were female, with a mean age of 49.9 ± 11.6 , body mass index of 30.4 ± 5 and neck circumference of 43.2 ± 4.2 . The patients had a mean Epworth Sleepiness Scale score: 13.5 ± 7 , mean AHI: 32.3 ± 25.4 , mean arousal index: 27.1 ± 19.6 , mean peripheral capillary oxygen saturation (SpO_2): 90.6 ± 4 , and mean minimum SpO_2 : 78.7 ± 9.8 . In OSAS aggravated by REM, position, REM + position total AHI, apnea index, hypopnea index, minimum SpO_2 and desaturation percentage were all found significantly worse than REM dependent, position-dependent and REM + position-dependent OSAS patients ($P < 0.05$).

CONCLUSION: In light of current findings, when evaluated with their effect on disease severity and complications, it is useful to predict prognosis of the disease when “strict definitions” are used for position- and/or REM-related OSAS cases.

Keywords:

Diagnosis, obstructive sleep apnea syndrome, position related obstructive sleep apnea syndrome, prognosis, rapid eye movement-related obstructive sleep apnea syndrome

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Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by repeated partial or total obstruction of upper airway and desaturation during sleep. The severity of OSAS is mainly classified due to apnea-hypopnea index (AHI) as mild (AHI: 5–14), moderate (AHI: 15–30), and severe (AHI >30).^[1] Patients with OSAS may admit with systemic symptoms and results such as cardiac arrhythmia, systemic hypertension, myocardial infarction, cerebrovascular accident, pulmonary hypertension, metabolic syndrome, polycythemia, and even sudden death, whereas symptoms due to sleep disorder like snoring, witnessed apnea, excessive daytime sleepiness, cognitive disorders, and impotence.^[2-4] Punjabi *et al.* and Redline *et al.* identified that there was a positive correlation between AHI and various cardiovascular disease variables,^[5,6] so we can say that severity of OSAS is correlated with comorbidities and poor prognosis.

In the literature, the prevalence of OSAS is reported 24% in male and 9% in female adult population. Diagnosis proportion of OSAS by polysomnography (PSG) is found 4% in males and 2% in females of 30–60 years of age, when there is excessive daytime sleepiness.^[7] Sleep disorders classification is done according to American Association of Sleep Medicine (AASM).^[8] Although there are no subgroups defined for OSAS in AASM classification, rapid eye movement (REM) related, position related, both REM and position related patient groups and also patients without position and sleep stage dependence are found by several clinical studies.^[9-15] It is reported that positional OSAS is found more in younger patients and males,^[10-14] REM related OSAS is found more in younger patients and females.^[15] Risk factors, pathophysiology, and determinants of positional and REM related OSAS are not well known yet. Another question mark is about different definitions for position and REM related OSAS diagnosis. One definition has nonsupine-AHI and/or non-REM (NREM)-AHI <5 criteria, the other has not.^[9,10] These two definitions were named as “strict definition” and “loose definition” in our study. The patients were grouped due to these definitions, and also due to severity of the disease. According to our knowledge of correlation between OSAS severity and prognosis, by using comparable statistical analysis, we investigated prognostic role of the definitions and which definition was more beneficial to use. To the best of our knowledge, there is no published study on this topic.

Materials and Methods

Patient selection

The study was approved on April 13, 2015, by the Clinical Researches Ethics Committee of Gazi University

with reference number 171. PSG reports of the patients who underwent full-night PSG with sleep-disordered breathing in our Sleep Disorders Center between September 2012 and October 2014 were searched. Patients who were diagnosed as OSAS due to AASM criteria were included in the study.

Polysomnographic studies

PSG was performed to patients admitted with complaints of snoring and excessive daytime sleepiness. The data from all patients were collected at our AASM-accredited sleep laboratory, all night, using a 16-channel PSG (Sensormedics Alphais Somnost system, Sensormedics, CA, USA). During recording, central and occipital electroencephalogram, bilateral electrooculogram, submental and tibial electromyogram, and electrocardiogram were used. Nasal air flow was measured by a pressure transducer. Tracheal sounds were monitored with a microphone. Thoracoabdominal belts were used in the measurement of thorax and abdomen movements. Monitoring of oxygen saturation was performed with noninvasive methods using pulse oximetry. The test was terminated after 6–8 h of recording. Rechtschaffen and Kales sleep staging and scoring criteria were used from the beginning of sleep was out of the 30-s epochs.^[16]

Patient groups

Patients were grouped due to loose definitions, then due to strict definitions. The criteria used for grouping are given in Table 1.

Statistical analysis

The data obtained in the study were evaluated using the SPSS 16.0 software (IBM SPSS Collaboration and Deployment Services Adapters). Statistical analysis results of the cases demographics, polysomnographic recording results and descriptive statistics were given as mean values accompanied by standard deviation (SD). For mean and SDs Chi-square test, for comparison of the patient groups one-way ANOVA tests were used.

Results

Three hundred and eighty patients who were diagnosed as OSAS due to their PSG results were included to the study. Two hundred and eighty (73.7%) of the patients were male, and 100 (26.3%) were female. The mean age was 49.96 ± 11.6 , the mean body mass index (BMI) was 30.41 ± 5 kg/m², the mean neck circumference was 43.24 ± 4.2 cm. Almost 28% of the patients were smoker. While determining excessive daytime sleepiness, Epworth Sleepiness Questionnaire was performed by all patients and the mean score was 13.48 ± 7 . The most common comorbidities among patients were upper airway diseases, hypertension, gastroesophageal reflux

Table 1: Criteria used for loose and strict definitions

Definition	Criteria
Loose definitions	
Position-related OSAS	Supine AHI >2x nonsupine AHI
REM-related OSAS	REM AHI >2x NREM AHI
REM + position-related OSAS	Supine AHI >2x nonsupine AHI + REM AHI >2x NREM AHI
Pure OSAS	OSAS patients without conditions above
Strict definitions	
Position dependent OSAS	Supine AHI >2x nonsupine AHI and nonsupine AHI <5
OSAS aggravated by position	Supine AHI >2x nonsupine AHI and nonsupine AHI ≥5
REM dependent OSAS	REM AHI >2x NREM AHI and NREM AHI <5
OSAS aggravated by REM	REM AHI >2x NREM AHI and NREM AHI ≥5
REM+position dependent OSAS	Supine AHI >2x nonsupine AHI and nonsupine AHI <5 + REM AHI >2x NREM AHI and NREM AHI <5
OSAS aggravated by REM + position	Supine AHI >2x nonsupine AHI and nonsupine AHI ≥5 + REM AHI >2x NREM AHI and NREM AHI ≥5
Pure OSAS	OSAS patients without conditions above

REM: Rapid eye movement, AHI: Apnea-hypopnea index, OSAS: Obstructive sleep apnea syndrome, NREM: Non-REM

disease, and type 2 diabetes mellitus. 39.4% of the patients had severe, 33.2% had moderate, and 27.4% had mild OSAS. When polysomnographic parameters were analyzed, the mean arousal index was 27.08 ± 19.9 , mean apnea index was 21.98 ± 24.8 , mean total AHI was 32.35 ± 25.4 , mean SpO₂ was $\%90.67 \pm 4$, and minimum SpO₂ was $\%78.71 \pm 9.8$ [Table 2].

Distribution of the patients due to loose and strict definitions is given in Table 3.

When the patients were grouped due to strict definitions, number of males was higher in all groups except REM dependent and REM + position-dependent OSAS groups ($P = 0.042$).

Means of weight, BMI, neck circumference, Epworth Sleepiness Scale (ESS) score, arousal index, total AHI, REM-AHI, supine-AHI and desaturation percentage were found higher, and means of stage N3 percentage and REM percentage were found lower in pure OSAS group ($P < 0.05$) [Table 4].

BMI and REM + supine AHI mean values were found significantly lower in position-dependent group ($P < 0.001$). REM dependent group and the group aggravated by REM + position had significantly lower height, neck circumference, ESS, apnea index, hypopnea index and total AHI values than the other OSAS groups ($P < 0.05$). Arousal index ($P = 0.003$), desaturation percentage and supine-AHI means were found lowest in REM-dependent OSAS group ($P < 0.001$).

When the patients were grouped due to strict definitions, comorbidity and smoking history did not have significant difference among patient groups, but we recognized was that severity class of patient groups might change depending on the definition used. When

strict definitions were used, REM-dependent and REM + position-dependent OSAS groups were classified as mild according to mean AHI values while there was no mild OSAS group when loose definitions were used. Distribution of both strict and loose defined groups due to OSAS severity is shown at Figure 1.

Discussion

Because it is underdiagnosed and has mortal complications, OSAS is a serious public health problem. Determination of OSAS type is important as well as the diagnosis of OSAS for treatment modality decision. Position dependence prevalence has been reported 9%–60% in different studies.^[17] It is considered that this variability is a result of small sample size of these studies. Similar with literature, we found position-related OSAS as 37.9%, position-dependent OSAS 26.5% and OSAS aggravated by position as 17.9%.

REM related OSAS prevalence shows variability from 10% to 36% in clinical studies.^[18-21] In our study, it was found 11.8% when loose definition was used, REM-dependent OSAS prevalence was found 4.5% when strict definition was used. These rates are quite different from the literature data. But it is known that REM related OSAS is more common in female OSAS population, and in our study, only quarter of the patients were female. Also, other studies used different definition criteria for REM related OSAS. These could explain the difference of our result.^[22,23]

In older studies, patient populations with position-related and position-dependent OSAS were younger and male dominant, and had lower BMI^[7,10-14,18,24-26] One study has reported that position related group was more sleepy than other OSAS patients while the other study found it less.^[10,25] Mador *et al.* have reported

Table 2: Polysomnographic parameters of the patients

	Mean±SD*
Total sleep time (min)	331.82±58.8
Sleep latency (min)	18.26±17.9
Sleep efficiency (%)	78.18±11.8
Stage N3 sleep (%)	19.28±9.9
REM sleep (%)	18.64±6.4
Arousal index (/h)	27.08±19.6
Apnea index (/h)	21.98±24.8
Hypopnea index (/h)	10.52±8.4
Total AHI (/h)	32.36±25.4
REM-AHI (/h)	38.77±25.9
Supine-AHI (/h)	44.44±27.8
REM + supine AHI (/h)	45.82±31.4
Awake SpO ₂ (%)	95.66±1.9
Mean SpO ₂ (%)	90.67±4
Minimum SpO ₂ (%)	78.71±9.8
Desaturation percentage (%)	28.48±31.7

*Chi-square test is used for mean±SD. SD: Standard deviation, REM: Rapid eye movement, AHI: Apnea-hypopnea index

Table 3: Distribution of the patients due to loose and strict definitions

	Percentage (n=x)
Loose definitions	
Position related OSAS	37.9 (n=144)
REM related OSAS	11.8 (n=45)
REM + position related OSAS	24.7 (n=94)
Pure OSAS	25.5 (n=97)
Total	100 (n=380)
Strict definitions	
Position-dependent OSAS	26.5 (n=101)
OSAS aggravated by position	17.9 (n=68)
REM-dependent OSAS	4.5 (n=17)
OSAS aggravated by REM	8.1 (n=31)
REM + position-dependent OSAS	6.8 (n=26)
OSAS aggravated by REM + position	10.5 (n=40)
Pure OSAS	25.5 (n=97)
Total	100 (n=380)

OSAS: Obstructive sleep apnea syndrome, REM: Rapid eye movement

that position-dependent OSAS patients did not show difference in age, gender, height, weight, BMI and ESS.^[24] Like this study, we did not find any difference of weight, BMI, ESS, total AHI and SpO₂ value in position-dependent OSAS group. Similar to others, in our study position related OSAS was found more common in male patients ($P = 0.01$, 42.1%). But contrary to them, when we grouped the patients according to their ages, position related OSAS was found more common in patients older than 50 years (44.1% vs. 31.4%) ($P = 0.049$).

In REM sleep stage medullary sensitivity to hypoxia and hypercapnia decreases, therefore respiratory events occur more commonly at this stage.^[20,22] However, there are studies that found no difference in AHI between REM

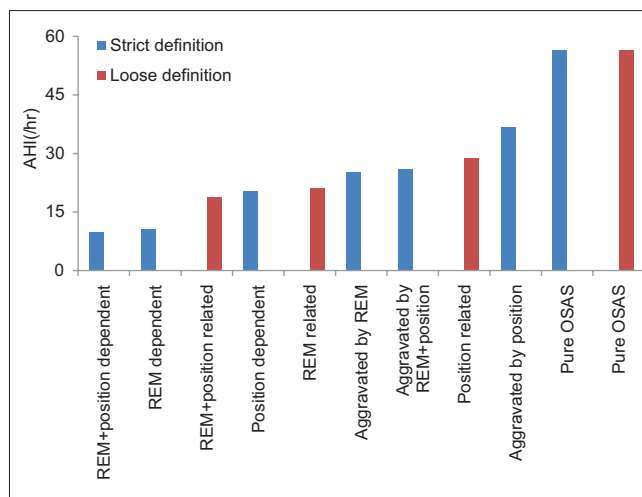


Figure 1: Distribution of all groups due to obstructive sleep apnea syndrome severity*. *Mean apnea-hypopnea index values of the groups are used to classify as mild (apnea-hypopnea index: 5–14), moderate (apnea-hypopnea index: 15–30) and severe obstructive sleep apnea syndrome (apnea-hypopnea index >30)

and NREM sleep.^[27,28] When SpO₂ values of sleep stages are compared, variability of SpO₂ tends to be bigger and minimum SpO₂ lower at REM stage.^[29,30] Most of the studies report that REM related OSAS is more common in younger patients, females, children and mild-moderate OSAS^[18-20,22,31] Punjabi *et al.* have not found correlation between REM related OSAS and excessive daytime sleepiness,^[32] while two others have found.^[19,33] Gupta *et al.* have not found difference in REM-AHI and desaturation index between two groups, and have found the groups similar according to demographic parameters.^[34] In our study, as expected, we found REM-AHI value higher in REM related OSAS group, but no difference was found in other polysomnographic and demographic parameters.

Demographic and polysomnographic properties of REM + position-dependent OSAS patients have been investigated firstly in the study of Joosten *et al.* They found age and BMI were lower with more male patients than REM related group, and higher age and BMI with more female patients than position related group. But no difference except lower total AHI in REM + position dependent group was found when they compared all three groups REM + position dependent (named as “overlapping” in their study), REM predominant, supine predominant.^[25] In our study, in REM + position-dependent group, height ($P = 0.041$), neck circumference ($P = 0.026$), sleepiness ($P = 0.022$), apnea-hypopnea indices ($P < 0.001$) were found significantly lowest. Besides, female predominancy was found highest in both REM dependent and REM + position-dependent group among all patient groups ($P = 0.042$). Therefore it is considered that REM + position-dependent OSAS is a different phenotype defining less sleepy, female and mild cases with short height and slim neck.

Table 4: Comparison of demographic parameters of patient groups due to strict definitions (mean±standard deviation)

	Position dependent OSAS	OSAS aggravated by position	REM dependent OSAS	OSAS aggravated by REM	REM + position-dependent OSAS	OSAS aggravated by REM + position	Pure OSAS	P*
Age	50.8±11.4	51.19±11.8	48.66±11.2	49.22±13.9	48.84±9	46.45±10.7	50.41±11.9	0.311
Height (cm)	171.6±8.2	172.6±8.6	166.3±10.7	170.3±11.2	166.23±8.1	170.02±8.6	171.22±10.1	0.041
Weight (kg)	83.9±13.2	89.58±17.4	86.06±14.6	90.93±14.7	84.96±14.9	91.27±13.4	94.13±17.6	0.01
BMI (kg/m ²)	28.43±4.2	29.55±4	31.04±4.2	31.21±7.2	30.67±4.5	31.64±4.7	32.18±5.4	<0.001
Neck circumference (cm)	41.59±2.9	41.46±3.8	41±5.5	42.95±4	41±4.7	44.12±4	44.92±4.2	0.026
ESS	11.52±6.1	13.35±7.3	10.5±7.8	12.93±7.4	10.36±6.8	13.73±7.6	16.2±6.2	0.022
Total sleep time (min)	336.39±55.8	328.5±61.22	351.16±56.7	328.06±70.3	338.73±50.8	340.86±53.9	322.03±60.3	0.607
Sleep latency (min)	19.32±16.5	18.53±18.6	11.13±9.2	18.83±16.4	23.17±22.8	17.42±19.2	16.75±18.2	0.271
Sleep efficiency (%)	78.65±10.4	77.75±11.3	81.33±8.5	74.56±18.5	79.23±10	79.1±11.2	78.13±11.8	0.973
Stage N3 (%)	22.73±8.4	17.2±8.1	25.64±6.6	21.38±8	24.8±7.7	24.42±8	11.87±10	<0.001
REM (%)	19.56±5	18.19±6.4	21.84±5.8	19.79±6.6	21.98±6.5	18.33±6.5	16.31±6.8	<0.001
Arousal index (/h)	25.76±12.1	28.54±19.5	17.05±6.7	22.05±14.3	20.54±8.3	23.17±14.7	34.07±28.7	0.003
Apnea index (/h)	11.9±12.7	25.34±17.3	4.99±3.7	11.76±8.1	4.91±4.7	13.76±10.4	44.3±34.3	<0.001
Hypopnea index (/h)	8.49±4.5	11.47±7.7	5.18±2.9	13.72±7	4.99±2.9	12.18±5.4	12.65±12.7	<0.001
Total AHI (/h)	20.45±12.3	36.83±17.2	10.17±3.8	24.93±8.8	9.91±4.1	25.95±10.1	56.45±33.2	<0.001
REM-AHI (/h)	22.89±19.8	31.32±22.5	36.77±15.6	55.92±19.7	33.3±19	54.32±19.2	50.19±28.5	<0.001
Supine-AHI (/h)	39.02±19.4	57.65±24.5	10.9±5.5	27.46±12.9	17.09±7.4	41.09±16.8	60.57±33.9	<0.001
REM + supine AHI (/h)	36.49±28.2	43.94±34.9	40.96±21.9	52.26±25.8	44.46±18.4	60.36±33.3	49.69±34.1	0.003
Awake SpO ₂ (%)	96±1.5	95.54±1.7	96.07±1.2	95.51±1.9	95.88±2.7	95.62±1.6	95.34±12.7	0.2
Mean SpO ₂ (%)	92.29±2	90.52±2.9	92.73±0.9	90.74±3	92.11±3.6	91.22±2.4	88.1±2.3	<0.001
Minimum SpO ₂ (%)	82.77±5.9	78.78±9	84.2±5.8	77.22±9.3	82.15±8	78.07±7.6	73.38±12.5	<0.001
Desaturation (%)	14.53±20.4	30.58±30.5	4.61±5.8	34.62±22.5	15.9±26.7	23.56±23.4	49.05±36.6	<0.001

*P<0.05 is accepted as statistical significance, One-way ANOVA is used to compare the groups. OSAS: Obstructive sleep apnea syndrome, REM: Rapid eye movement, BMI: Body mass index, ESS: Epworth sleepiness scale, AHI: Apnea-hypopnea index

There are not many data about pure OSAS in the literature. We named the OSAS patients dependent from position and sleep stage as pure OSAS in the study. In pure OSAS group weight ($P = 0.02$), BMI ($P < 0.001$), neck circumference ($P = 0.007$), ESS ($P = 0.006$), arousal index ($P < 0.001$), total AHI ($P < 0.001$), apnea index ($P < 0.001$) and desaturation percentage ($P < 0.001$) were found significantly higher than other patient groups. Moreover, N3 sleep stage percentage, REM sleep stage percentage, mean and minimum SpO₂ were found lower ($P < 0.001$). In the literature we found only one study on this patient group, Joosten *et al.* have named this group as intermittent OSAS, and they have found total AHI higher in this group like our study.^[25] According to our statistical results patients with pure OSAS had higher neck circumference, worse oxygenation, they were more weighty, more sleepy and more severe.

When we grouped our patients due to strict definitions there were no difference in age, total sleep time, sleep latency, sleep efficiency, awake SpO₂, smoking and comorbidity status between the groups.

As shown before, several significant differences were found. However, we had some more important clinical outcomes among them. In OSAS groups aggravated by

REM, supine position and REM + position; total AHI, apnea index, hypopnea index, minimum SpO₂ and desaturation percentage were worse than REM dependent, position dependent, REM + position-dependent groups ($P < 0.005$). REM + position-dependent OSAS appeared as a new OSAS phenotype. Another remarkable result was that severity class of patient groups might change depending on the definition used.

Conclusion

When evaluated with its effect on disease severity and complications, these outcomes make us think that it is useful to predict prognosis of the disease when "strict definitions" are used for position- and/or REM-related OSAS cases.

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Conflicts of interest

There are no conflicts of interest.

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