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Distribution patterns of obstructive and central apnea in adults with obstructive sleep apnea-hypopnea syndrome

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Abstract

Objective: This study aimed to investigate the distribution patterns of obstructive and central apnea events in adults with obstructive sleep apnea-hypopnea syndrome (OSAHS). *Methods:* Utilizing polysomnography (PSG) data, we selected patients with a habitual snoring condition and categorized them into OSAHS and non-OSAHS groups. The OSAHS group was further stratified into mild, moderate, and severe subgroups based on disease severity. We compared the distribution of obstructive sleep apnea (OSA) and central sleep apnea (CSA) events between the groups, analyzing their correlation with the apnea-hypopnea index (AHI), age, gender, and other factors. *Results:* A total of 460 patients were enrolled for the study, 374 patients were in the OSAHS group and 86 patients in the non-OSAHS group. (1) There were statistical differences in AHI and obstructive apnea index (OAI) in all groups ($P < 0.05$), with the OSAHS group having a higher AHI and OAI than the non-OSAHS group. (2) In the OSAHS group, OAI and AHI had the highest correlation ($r = 0.884$, $P < 0.01$), and central apnea index (CAI) and AHI had the lowest correlation ($r = 0.237$, $P < 0.01$); in the non-OSAHS group, OAI and AHI had the highest correlation ($r = 0.520$, $P < 0.01$), and CAI and AHI had the lowest correlation ($r = 0.312$, $P < 0.01$). (3) In the OSAHS group, OAI was significantly correlated with the severity of patient disease ($r = 0.828$, $P < 0.01$), whereas CAI was marginally correlated with the severity of patient disease ($r = 0.235$, $P < 0.01$), but it increased as the condition became more severe.
Conclusion: Patients with OSAHS exhibited both CSA and OSA, with OAI having a significantly greater impact. OAI can serve as a valuable index for evaluating OSAHS severity, while CSA appears to be primarily influenced by the overall disease severity. Notably, patients with OSAHS had a higher CAI compared to those without OSAHS.

Keywords: Central apnea index, hypopnea index, obstructive apnea index, obstructive sleep apnea-hypopnea syndrome, polysomnography

INTRODUCTION

Obstructive sleep apnea-hypopnea syndrome (OSAHS), central sleep apnea-hypopnea syndrome (CSAHS), upper airway resistance syndrome (UARS), sleep hypoventilation syndrome (SHS), and other abnormal respiratory events that occur during sleep are referred to as sleep-related breathing disorders (SRBD).[1] The condition primarily affects the circulatory system, which causes significant harmful effect to the body and results in hypertension, cardiac disease, pulmonary arterial hypertension, and other cardiovascular diseases.[2,3] The surge of sympathetic nerve activity, nighttime hypoxia and several adverse factors associated with OSA, such as obesity, insulin resistance, and endothelial dysfunction, have been identified as potential pathogenesis of OSA-related cardiovascular complications.[4] In addition, OSAHS is also associated with neurocognitive impairment, including intelligence, memory, attention and other aspects.[5] OSAHS can also cause a series of endocrine and metabolic abnormalities, such as obesity, elevated blood sugar and insufficient secretion of growth hormone, and different endocrine diseases can also promote OSAHS

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due to their disease characteristics.[6] Currently, polysomnography (PSG) is being used in clinical settings as a diagnostic standard to reflect the sleep patterns of patients and severity of illness. It can help easily detect respiratory events, such as hypopnea, obstructive sleep apnea (OSA), and central sleep apnea (CSA), during sleep.[7]

During PSG, it has been observed that many patients exhibit a combination of both CSA and OSA, which has an impact on the clinical guidance for treatment. Failure to correctly distinguish the clinical significance of CSA and OSA may mislead the diagnosis of OSAHS. Some patients also suffer from sleep disorders such as CSA or Cheyne-Stokes respiration after elimination of obstructive respiratory events by continuous positive airway pressure.[8] However, this kind of phenomenon has not been thoroughly studied and interpreted in clinic. Therefore, the goal of this study was to analyze obstructive and central apnea events and their distribution patterns to provide evidence for clinical evaluation of the condition and guidance for treatment.

METHODS

Respondents

Five hundred patients with a snoring habit who sought treatment at Beijing Jishuitan Hospital affiliated to Capital Medical University from May 2019 to May 2021, were retrospectively examined. Medical history, and basic information, including age, gender, height, and weight, of these patients, were recorded. Relevant physical examination and routine otolaryngology examination was done before recording signs and symptoms.

Exclusion criteria were: (1) patients with other sleep disorders, such as insomnia and periodic limb movement disorder; (2) patients with depression, anxiety, schizophrenia, and other mental disorders; (3) patients with severe heart, lung, liver and kidney insufficiency; (4) patients with sleep-disordered breathing due to thyroid dysfunction, apituitarism, acromegaly (gigantism), narcolepsy, myasthenia gravis, recurrent laryngeal nerve paralyses and other special causes; (5) patients with alcohol dependency or long-term use of sedative hypnotics, anti-depressant drugs, anti-anxiety drugs, and other psychiatric medication; (6) patients not receiving OSAHS-related treatment, including ventilator therapy, surgery (e.g., palatopharyngoplasty, nasal surgery expansion, maxilla and mandible surgery) or oral appliance treatment. The flow chart of the screening process is shown in Figure 1.

Polysomnography

Patients were monitored at the hospital using the Polysomnography System (COMPUMEDICS, Australia) during the night for more than 7 hours. Items and parameters monitored included electroencephalogram (EEG), electrooculogram (EOG), submental electromyogram (EMG), oronasal airflow, thoraco-abdominal range of motion, arterial oxygen saturation (SaO_2), electrocardiogram (ECG), and others. The monitoring results were automatically analyzed by a machine and corrected by an assigned professional. The final indicators included apnea hypopnea index (AHI), obstructive apnea index (OAI), central apnea index (CAI), as well as sleep-related parameters such as SaO_2. The respiratory events were scored in accordance with the Manual for the Scoring of Sleep and Associated Events designated by American Academy of Sleep Medicine (AASM) in 2012. OSA was defined as a reduction in airflow by more than 90% of the baseline for at least 10s with effort to breathe. Obstructive hypopnea was an abnormal respiratory event characterized by a reduction of at least 30% in thoracoabdominal movement or airflow, for at least 10 s and with more than 4% of blood oxygen saturation reduction, when compared to the baseline. CSA was defined as a reduction in airflow by more than 90% of the baseline for at least 10s, accompanied by loss of thoracoabdominal movement. The severity of OSAHS was classified based on the AHI values in PSG monitoring results; specifically, OSAHS with 5 to 15 times per hour was mild, with 15 to 30 times per hour was moderate, and with 30 times per hour was severe.

Statistical methods

The data of enrolled patients was statistically analyzed using SPSS22.0 statistical software (SPSS Inc., Chicago, IL). Measurement data with a normal distribution are expressed as mean ± standard deviation and compared between groups using the independent sample *t*-test. Measurement data with abnormal distribution are expressed as median (Q1, Q3), and compared between groups using the Kruskal-Wallis H test. Enumerated data was compared between groups using the chi-squared test. The correlation of measured data between the two groups was analyzed using the Spearman's correlation analysis. Receiver operating characteristic (ROC) curve analysis was conducted, and the area under ROC curve (AUC) and Youden's index was calculated to show the

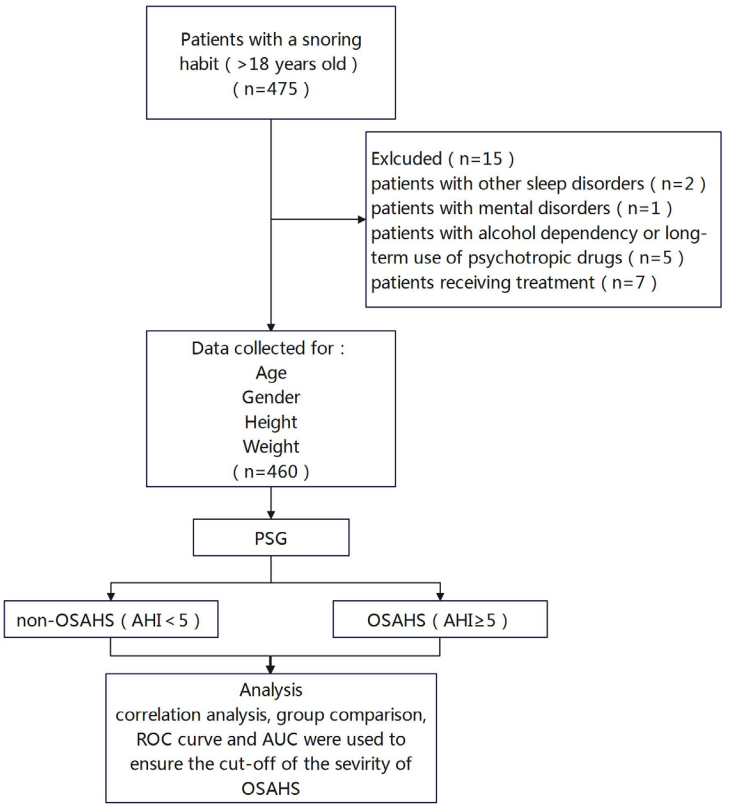

Figure 1. The flow chart of the screening process.

significantly present. Statistical differences were indicated by $P < 0.05$.

RESULTS

A total of 460 patients with habitual snoring were enrolled after being screened in accordance with the exclusion criteria, and the OSAHS and non-OSAHS group were divided based on PSG results. The age range of these patients was 39.3 ± 10.8 years, with 374 patients in the OSAHS group and 86 patients in the non-OSAHS group, including 387 males (84.1%) and 73 females (15.9%). There was no significant difference in age and gender between the two groups. Specific parameters are shown in Table 1.

Analysis of differences in respiratory events between the two groups

There were statistical differences in AHI, lowest oxygen saturation ($LSaO_2$), OAI, and CAI between the OSAHS and non-OSAHS group, ($P < 0.05$). Specific parameters are shown in Table 2.

Distribution pattern of respiratory events in the two groups

OAI and CAI respiratory events were seen in combination in 239 patients (63.9%) with OSAHS and 16 patients (18.6%) with non-OSAHS.

Correlation analysis between respiratory events in the two groups

Based on the results of the Spearman's correlation analysis, in the OSAHS group, OAI was highly positively correlated with AHI ($r = 0.884$, $P < 0.01$); CAI had a low correlation with AHI ($r = 0.237$, $P < 0.01$), but they were significantly positively correlated with each other; OAI ($r = -0.177$, $P < 0.01$) and CAI ($r = -0.183$, $P < 0.01$) were negatively correlated with gender; CAI was positively correlated with age ($r = -0.105$, $P < 0.05$), and OAI was not. In the non-OSAHS group, there was a high correlation between OAI and AHI ($r = 0.520$, $P < 0.01$); CAI had a low correlation with AHI ($r = 0.312$, $P < 0.01$), but they were significantly positively correlated with each other. There was no correlation between respiratory events and gender and age (Figure 2 and Table 3).

Table 1: The demographic distribution in groups

	Total Number (cases)	Gender (cases)		Age (years)	
		Male (%)	Female (%)	Mean (SD)	Range
OSAHS	374	315 (83.2%)	59 (15.8%)	39.9 (10.9)	18-65
Non-OSAHS	86	72 (83.7%)	14 (16.3%)	36.5 (9.9)	18-65
P value		0.908		0.067	

OSAHS: obstructive sleep apnea hyponea syndrome

Correlation analysis between respiratory events and disease severity in OSAHS group

The OSAHS group consisted of 107 patients with mild (28.6%), 90 patients with moderate (24.1%), and 177 patients with severe symptoms (47.3%). Spearman's correlation analysis results showed that OAI had high correlation ($r = 0.828$, $P < 0.01$) and CAI had low correlation with the severity of patient disease ($r = 0.235$, $P < 0.01$). As OSAHS progressed to a more severe state, OAI and CAI increased in the patients (Table 4).

ROC curve analysis showed that the AUC value of OAI predicting OSAHS severity was 0.958, while the Youden's index peaked at 0.719 when the OAI was 12.5. The AUC of CAI predicting OSAHS severity was 0.608, and the Youden's index peaked at 0.187 when CAI was 0.95 (Figure 3).

DISCUSSIONS

OSAHS refers to the apnea or hypopnea condition caused by upper airway obstruction or collapse during sleep, resulting in a series of physiological processes such as hypoxemia, hypercapnia, and sleep structure disorder, with an incidence of about 2~4%.[9] CSAHS is a class of sleep breathing disorders mainly characterized by apnea caused by loss of breathing effort during sleep. CSAHS has a significantly lower incidence, but a higher risk for cardiovascular and cerebrovascular disorders due to the apnea that results from a reduced respiratory effort during sleep. Apnea without respiratory drive, reduced oronasal airflow, decreased respiratory capacity and thoraco-abdominal breathing movement are all symptoms of CSA. Complicated factors, including unstable respiratory drive are considered the primary cause of CSA. After a regular sleep cycle, patients with CSA experience a loss of subjective behavioral control over breathing, and more pronounced abnormalities of the metabolic control system, which exacerbate hypopnea and hypercapnia, leading to central hypopnea and central apnea.[10-12]

Several studies have demonstrated the significance of differentiating between OSA and CSA, which are closely correlated with each other, while investigating OSAHS. The most accurate techniques are typically thought to be esophageal pressure monitoring and diaphragm EMG monitoring.[13,14] In the case of OSA, respiratory central drive and respiratory effort contribute to increased esophageal pressure until the airflow is restored; in the case of CSA, esophageal pressure disappears with the loss of respiratory central drive, leaving only minor fluctuations consistent with the heart rate.[15] The techniques of recording respiratory movements with a thoraco-abdominal girdle and recording oronasal flow with oronasal heat sensor signals are used for identification as

Table 2: Differences in AHI, OAI, and CAI between groups

	OAI	CAI	AHI	$LSaO_2$
OSAHS	8.6 (2.9, 25.5)	0.2 (0, 0.7)	27.8 (13.8, 54.5)	80 (71, 85)
Non-OSAHS	0.1 (0, 0.4)	0 (0, 0.1)	1.7 (0.9, 3.1)	90 (86, 92)
χ^2 value	367.83	69.56	419.07	212.52
P value	<0.01	<0.01	<0.01	<0.01

AHI: apnea hypopnea index; OAI: obstructive apnea index; CAI: central apnea index; OSAHS: obstructive sleep apnea hyponea syndrome

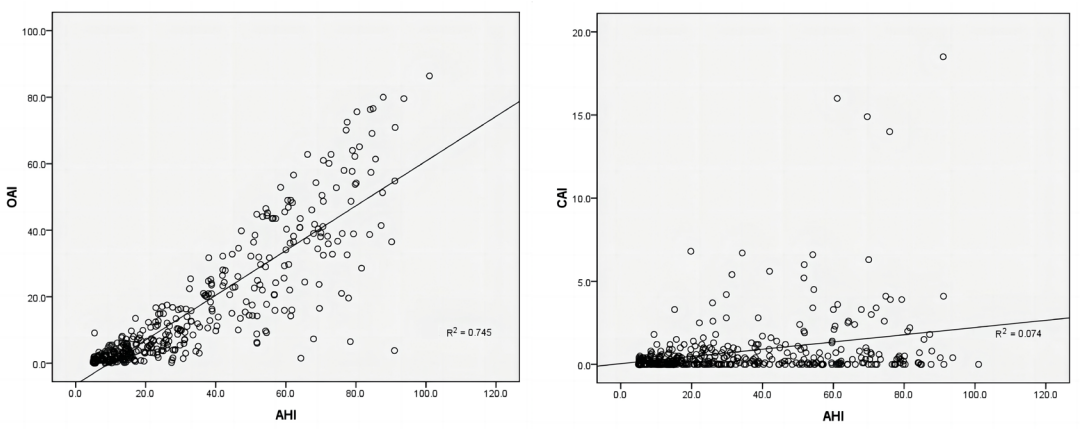

Figure 2. Scatter diagram of correlation between OAI, CAI, and AHI in the OSAHS group.

these are less intrusive and do not affect the sleep quality of patients.

Additionally, some studies suggest that nasal congestion and other upper airway obstruction factors may contribute to altered sleep breathing patterns, which may result in central and obstructive apnea. Ventilation is controlled by neurological, behavioral and metabolic drives in wakefulness, and by metabolic control during sleep, specifically, arterial carbon dioxide as the primary stimulus for both unstable ventilation and OSA.[16] Some patients with idiopathic CSA have similar clinical manifestations as those patients with OSA. In other studies, OSA treated by techniques such as continuous positive airway pressure, oral appliance, and maxillofacial surgery also resulted in intermittent or chronic central apnea or hypopnea.[17] Bradyarrhythmia induced by OSAHS may further aggravate the pulmonary circulation congestion at night, and indirectly impair cardiac function, resulting in CSA.[18] Hence, the effect of CSA and OSA on SRBD should receive equal attention.

The results showed that patients with OSAHS had a significantly higher CAI than patients with non-OSAHS, and by the way, the proportion of patients with concurrent OAI and CAI in OSAHS group was significantly higher than non-OSAHS group, indicating that CSA may also be one of the contributors of OSA, and that arousals and sleep fragmentation may be the mechanism by which OSA is induced.

The results also showed that CAI increased in frequency as OSAHS severity increased, but patients did not exhibit obvious contributors of OSA, indicating that OSA increased in frequency as OSAHS severity increased, and that OSAHS was also a contributor of OSA. OAI and AHI are also factors that promote the increase in CAI.

The results of this study revealed that patients in the OSAHS group had a higher CAI than patients in the non-OSAHS group; among them the CAI in patients with moderate and severe OSAHS was higher than in patients with mild OSAHS and showed an increasing trend ($P < 0.001$). This finding indicated that the severity of OSAHS was related to the severity of OSA. However, the CAI of patients with severe OSAHS was lower than in patients with moderate OSAHS, however, this mechanism is unclear and needs to be further studied.

It should be noted that as this was a retrospective study, additional follow-up studies and more diverse samples are needed. Additionally, there were no follow-up observations of PSG after the upper airway obstruction was relieved. Only the thoraco-abdominal girdle and oronasal airflow were used to qualitatively and quantitatively

Table 3: Correlation analysis on respiratory events and AHI between the two groups

	OSAHS group		Non-OSAHS group	
	Spearman's coefficient	**P value**	**Spearman's coefficient**	**P value**
OAI	0.884	<0.01	0.520	<0.01
CAI	0.237	<0.01	0.312	<0.01

AHI: apnea hypopnea index; OSAHS: obstructive sleep apnea hyponea syndrome;
OAI: obstructive apnea index; CAI: central apnea index

Table 4: Comparison of respiratory events between groups

		OAI	CAI	AHI	$LSaO_2$
OSAHS	Mild	1.5 (0.8, 3.4)	0.1 (0, 0.3)	9.7 (6.6, 13)	85 (82, 88)
	Moderate	5.6 (3.2, 9.7)	0.25 (0, 0.9)	22.2 (17.8, 26)	82 (78, 86)
	Severe	28.1 (15.9, 43.5)	0.3 (0, 1.2)	56.4 (41.9, 79.5)	74 (65, 80)
Non-OSAHS		0.1 (0, 0.4)	0 (0, 0.1)	1.7 (0.9, 3.1)	90 (86, 92)
χ^2 value		367.826	69.552	419.065	212.519
P value		<0.01	<0.01	<0.01	<0.01

OAI: obstructive apnea index; CAI: central apnea index; AHI: apnea hypopnea index; OSAHS: obstructive sleep apnea hyponea syndrome

analyze the respiratory central drive due to non-compliance of patients for invasive procedures, which may lead to an overestimation of the incidence of CSA events although esophageal pressure monitoring is recommended for the diagnosis of CSA as it is the standard reference measurement for OSA hypopnea.

In conclusion, observation of the distribution characteristics of OSA in adults with OSAHS led to the following conclusions: Patients with OSAHS had a significantly higher CAI than patients without OSAHS; patients with OSAHS developed both CSA and OSA, but OAI had a greater impact; the severity of the disease was the primary cause of CSA; both CAI and OAI could be used as indices to evaluate the severity of OSAHS; hypopnea was primarily manifested in patients without OSAHS; and OAI was a factor for the severity of OSAHS.

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DISCLOSURE

Ethics: The study was approved by Ethics Committee of the Beijing Jishuitan Hospital. Written informed consent was obtained from all participants.

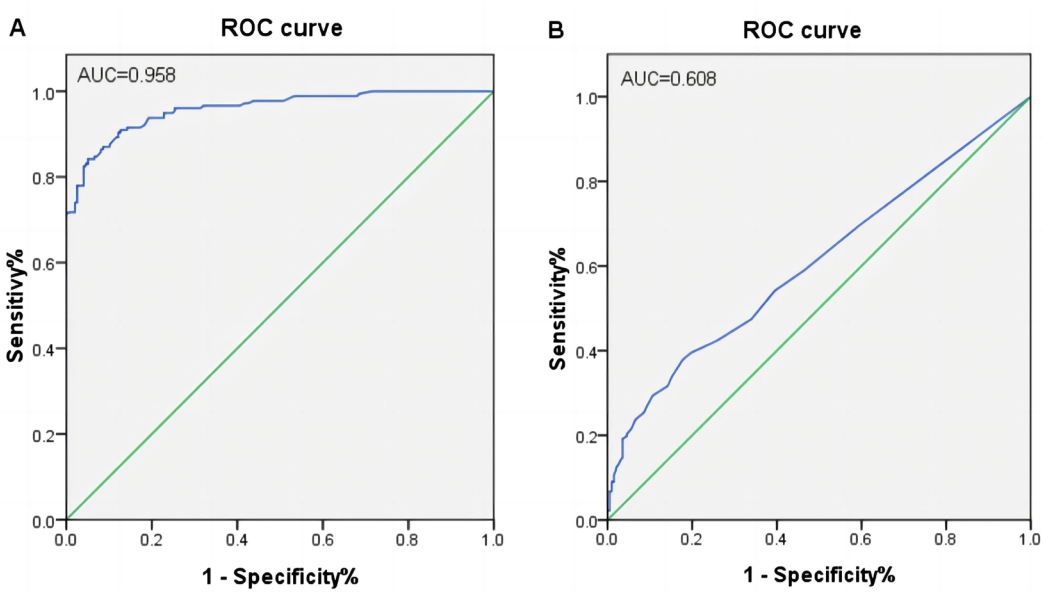

Figure 3. Illustrations of ROC curves for the OSAHS severity with OAI and CAI. Results concern the OAI and severity (A), CAI and severity (B).

Data availability: All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Conflict of interest: None

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