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Original Article

Oxygen desaturation index, lowest arterial oxygen saturation and time spent below 90% oxygen saturation as diagnostic markers for obstructive sleep apnea

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Abstract: Background: Obstructive sleep apnea (OSA) syndrome is associated with a high mortality, and blood oxygen indexes play an important role in evaluating this disease. The objective of this study was to explore the value of blood oxygen indexes, including minimum oxygen saturation ($LSpO_2$), oxygen reduction index (ODI) and time spent with oxygen saturation below 90% (TS 90%), as diagnostic markers for OSA syndrome. Methods: In this retrospective study, 320 patients with OSA treated in Ningbo First Hospital from June 2018 to June 2021 were included and divided into mild, moderate, and severe groups according to the severity of the condition (n = 104, 92, and 124, respectively). The blood oxygen indexes as well as the apnea-hypopnea index (AHI) were compared. The Spearman correlation analysis was performed to explore the relationship between the parameters. Receiver operating characteristic curves were generated to evaluate the diagnostic value of the blood oxygen indexes for OSA syndrome. Results: There were significant differences in body weight, body mass index, and blood pressure before and after sleep among the groups ($P < 0.05$). $LSpO_2$ levels followed a pattern with the severe group showing the lowest values, followed by the moderate group, and then the mild group, whereas ODI and TS 90% levels showed the opposite ($P < 0.05$). Spearman correlation analysis showed that AHI, ODI, TS 90% were positively correlated with severity of OSA, whereas $LSpO_2$ was negatively correlated with severity of OSA. ODI showed a high diagnostic value for OSA (area under curve (AUC) = 0.823, 95% CI: 0.730-0.917). TS 90% showed a high diagnostic value for OSA (AUC = 0.872, 95% CI: 0.794-0.950). $LSpO_2$ showed high accuracy in diagnostic value for OSA (AUC = 0.716, 95% CI: 0.596-0.835). The combination of the 3 indexes demonstrated a high diagnostic value for OSA (AUC = 0.939, 95% CI: 0.890-0.989). The diagnostic value of the combined signature was found to be significantly higher compared to the value of individual indexes ($P < 0.05$). Conclusion: The evaluation of the severity of OSA should not rely solely on a single observation index, but rather on a combination of ODI, $LSpO_2$ and TS 90%. This combined diagnostic signature can provide a more comprehensive assessment of the patient's condition and serve as an alternative diagnostic basis to ensure timely diagnosis and appropriate clinical treatment for OSA.

Keywords: Apnea hypopnea index, blood oxygen index, OSA syndrome, clinical significance

Introduction

Obstructive sleep apnea (OSA) is a condition characterized by recurrent episodes of partial or complete cessation of breathing during sleep, affecting the respiratory, cardiovascular, neurological, digestive, and endocrine system. This condition has been widely studied since the 1970s. The incidence of OSA is approximately 14% in adult men, 5% in adult women and 5-10% in children [1]. The incidence of OSA in patients with myocardial infarction is approximately 60% or higher [2]. The prevalence of OSA is 40% in patients with body mass index (BMI) exceeding 30 kg/m^2 and 60% in patients with metabolic syndrome. Epidemiological and clinical data indicate that the incidence of OSA is highly correlated with being overweight, which is an independent risk factor for OSA [3]. Type 2 diabetes can aggravate sleep disordered breathing, which is an independent risk factor for severe nocturnal hypoxia [4]. OSA occurs when the upper airway narrows or collapses intermittently during sleep, resulting in partial

or complete cessation of airflow. These repeated episodes of airway obstruction can cause interruptions in breathing and result in disrupted sleep patterns. Obesity (especially central obesity), hypertrophy of the tongue, small mandibular structure (evident among Asians), long upper airway and downward movement of the hyoid bone are key risk factors for upper airway stenosis or collapse of the upper airway. An episode of hypopnea or apnea lasts at least 10 seconds, although it can sometimes last even longer, up to 60 seconds or more. Adults with dysregulated breathing more than 5 times per hour are considered to have mild OSA. Dysregulation of breathing can be as frequent as 100 times per hour in severe cases [6]. Airway obstruction can lead to several pathophysiological conditions, such as decreased blood oxygen saturation, increased carbon dioxide, intrathoracic pressure fluctuations, sympathetic activation and frequent arousal, with hypoxemia being a key pathological factor [7, 8]. Intermittent hypoxia caused by OSA comprises a cascade of events leading to the onset and/or progression of cardiovascular disease. OSA-related hyperpnea, increased negative intrathoracic pressure and changes in arousal can exacerbate cardiovascular disease progression [9]. OSA is associated with hypercoagulable states, including an increase in thrombogenic factors such as fibrinogen and platelet activation, which further elevates the risk of cardiovascular complications [10].

The risk of death in patients with OSA was predicted using several parameters. The findings demonstrated that nocturnal hypoxemia was an independent risk factor for the prediction of sudden cardiac death. Previous results revealed that OSA could cause sudden cardiac-related death [11]. Myocardial infarction patients presenting with OSA have a higher risk of major adverse cardiac events than those without OSA [12]. A multivariate analysis after adjusting for multiple variables demonstrated that the lowest nocturnal oxygen saturation less than 90% was the main cause of respiratory failure [13]. Clinically, polysomnography (PSG) is commonly used to assess the severity of OSA. In China, the main diagnostic strategies typically involve the apnea-hypopnea index (AHI) and blood oxygen saturation ($LSpO_2$) measurements obtained from PSG. OSA severity is determined using the AHI, which only determines the frequency of apneas and hypopneas per hour of sleep, without considering the duration or amplitude. Moreover, AHI does not accurately reflect the pathophysiology or severity of hypoxia [14]. Patients with the same AHI may exhibit variations in clinical symptoms and complications [15]. $LSpO_2$ cannot accurately determine the frequency and duration of nocturnal hypoxemia. It can only provide information on instantaneous blood oxygen saturation levels. AHI is not correlated with the degree of hypoxemia, whereas the degree of hypoxia in some patients is weakly correlated with severe OSA [16]. Nocturnal hypoxemia in patients with OSA is used to determine the indexes that are useful for estimating nocturnal hypoxemia. The time spent with oxygen saturation below 90% (TS 90%) is an objective parameter that can be easily obtained from PSG. In recent studies, TS 90% has been used as an assessment parameter to determine the degree of hypoxia in Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS), as it has been found to be positively correlated to the duration and severity of hypoxia. Therefore, the aim of the present study was to explore the value of blood oxygen indexes in predicting the severity of OSA. At the same time, we sought to explore the diagnostic value of blood oxygen index $LSpO_2$, oxygen reduction index (ODI) and TS 90% for OSA syndrome.

Patients and methods

Basic patient information

A total of 320 patients with OSA admitted to Ningbo First Hospital from June 2018 to June 2021 were retrospectively included in this study as a research group. The control group consisted of 320 non-OSA individuals who underwent physical examinations during the same period. In the control group, there were 173 men and 147 women, with ages ranging from 36 to 69 years and an average age of 45.91±3.54 years. In the research group, there were 186 men and 134 women, with ages ranging from 35 to 70 years and an average age of 45.68±3.64 years. The blood oxygen indexes and AHI of the two groups were compared. The patients were assigned into mild (n = 104), moderate (n = 92) and severe groups (n = 124) based on their disease severity. No significant differences were found in age and sex between groups ($P > 0.05$). The study was

approved by the Medical Ethics Association of Ningbo First Hospital.

Inclusion criteria: patients who met the diagnostic criteria of OSA based on the guidelines for the diagnosis and treatment of OSA [17]; patients with age over 14 years old; patients who did not take drugs affecting their mental health and nervous system within 3 months; patients who exhibited sleep efficiency more than 60% after over 7 hours of monitoring and recording. The patients were required to not consume alcohol, tea and caffeine 24 hours before monitoring.

Exclusion criteria: patients with a history of neuromuscular diseases or upper airway tumors that affected the local anatomical structure of the upper respiratory tract; patients diagnosed with other diseases that could cause hypoxia; patients with severe mental diseases that may affect treatment compliance.

The OSA severity scale [18], formulated by the American Sleep Medical Association (AASM) in 1999, defined OSA as having an average of 5 or more apnea and hypopnea episodes per hour during 7 hours of sleep. The severity is classified as mild with a score of $5 \leq AHI < 15$ points, moderate with a score of $15 \leq AHI < 30$ points, and severe with a AHI score ≥ 30 points.

Methods

All subjects were monitored using an American Embla N7000 PSG system (CFDA: 20142212-212) after the admission. The AHI, pulse oxygen saturation (SpO_2), $LSpO_2$, ODI and TS 90% were recorded. TS 90% is a common indicator in PSG data, representing the percentage of time during the entire night that SpO_2 falls below 90%. Patient data were analyzed by SPSS22.0 software and manually according to the latest interpretation guidelines of AASM.

Observation index

General information was collected from the participants, including name, age, sex, height, weight, history of hypertension, type 2 diabetes, etc. (1) Secondary indicators included age, sex, height, and weight. Patients were instructed to remove their shoes and wear only their underwear, and to maintain an upright position while looking straight ahead during the measurement of height and weight. All physical parameters were measured twice to obtain an average value. (2) Primary indicators were history of hypertension and type 2 diabetes.

Statistical analysis

Data processing was carried out using SPSS v24.0 statistical software. Data with normal distribution were expressed as mean ± standard deviation. An independent sample t test was adopted for comparison of the sample mean of variables with normal distribution. Count data were presented as n (%), and the χ^2 test was used to analyzed the data. Spearman correlation analysis method was used for correlation analysis. The diagnostic values of the blood indexes (ODI, TS 90% and $LSpO_2$) were evaluated by receiver operating characteristic (ROC) curves. The area under curve (AUC) was used for indicating the diagnostic value. $AUC > 0.5$ indicated a low diagnostic value, $0.7 < AUC \leq 0.9$ indicated a moderate diagnostic value, and $AUC > 0.9$ indicated a high diagnostic value. $P < 0.05$ was considered a statistical difference.

Results

Comparison of general data

There was no significant difference in height and disease history between the two groups ($P > 0.05$, **Table 1**). The body weight, BMI, blood pressure before and after sleep were higher in the research group than those in the control group ($P < 0.05$).

Blood oxygen indexes and AHI

The AHI, ODI and TS 90% in the research group were higher than those in the control group. The $LSpO_2$ level was significantly lower in the research group than that in the control group ($P < 0.05$). There were significant differences in the blood oxygen indexes and AHI between patients with OSA and the healthy subjects ($P < 0.05$). See **Table 2**.

Blood oxygen indexes in different severity groups

The levels of AHI, ODI and TS 90% followed a pattern with the severe group showing the highest, followed by the moderate group, and then

Table 1. Basic and clinical data of patients

Group	Control Group (n = 320)	Research Group (n = 320)	t/χ^2	P
Height (cm)	168.18±3.54	168.49±3.42	1.126	0.235
Body weight (kg)	84.95±4.31	94.59±4.42	27.933	< 0.001
BMI (kg/m^2)	27.45±3.31	30.85±3.36	12.895	< 0.001
Before going to bed				
Diastolic pressure (mmHg)	114.83±4.53	125.83±4.53	30.175	< 0.001
Systolic blood pressure (mmHg)	71.94±3.66	83.19±3.54	39.522	< 0.001
After sleep				
Diastolic pressure (mmHg)	120.59±3.43	128.96±4.22	27.532	< 0.001
Systolic blood pressure (mmHg)	78.94±3.31	84.93±2.66	25.233	< 0.001
Past disease				
high blood pressure	241 (75.31)	248 (77.50)	0.424	0.463
diabetes	231 (72.19)	239 (74.69)	0.512	0.438

Abbreviations: BMI, Body Mass Index.

Table 2. The blood oxygen indexes and AHI ($\bar{x} \pm s$) of the study subjects

Group	Control Group (n = 320)	Research Group (n = 320)	t	P
AHI (time/h)	1.35±1.21	25.93±2.31	168.614	< 0.001
$LSpO_2$ (%)	89.95±3.42	82.95±4.53	22.061	< 0.001
ODI (time/h)	1.28±0.64	20.93±4.12	84.360	< 0.001
TS 90% (%)	0.18±0.06	16.26±1.21	234.733	< 0.001

Abbreviations: AHI, apnea-hypopnea index; $LSpO_2$, the lowest peripheral oxygen saturation; ODI, oxygen desaturation index; Ts 90%, time spent below 90% oxygen saturation.

Table 3. The blood oxygen indexes and AHI in patients with different severities of OSA ($\bar{x} \pm s$)

Group	Mild group (n = 104)	Moderate group (n = 92)	Severe group (n = 124)	F	P
$LSpO_2$ (%)	89.49±3.31	83.59±4.42	73.94±9.03	172.829	< 0.001
ODI (time/h)	9.91±2.31	18.49±3.31	54.96±13.42	878.873	< 0.001
TS 90% (%)	29.58±6.42	31.84±6.34	34.38±5.87	17.117	< 0.001

Abbreviations: $LSpO_2$, the lowest peripheral oxygen saturation; ODI, oxygen desaturation index; Ts 90%, time spent below 90% oxygen saturation.

Table 4. Relationship between blood oxygen indexes and AHI of patients with varying severity of OSA

Index	r	P
$LSpO_2$	-0.923	< 0.001
ODI	0.646	< 0.001
TS 90%	0.682	< 0.001

Abbreviations: $LSpO_2$, the lowest peripheral oxygen saturation; ODI, oxygen desaturation index; Ts 90%, time spent below 90% oxygen saturation.

the mild group, and the level of $LSpO_2$ exhibited the opposite. There were significant differences in blood oxygen indexes and AHI among patients with different severity of OSA (P < 0.05). See **Table 3**.

Relationship between blood oxygen indexes and severity of OSA

Spearman correlation analysis showed that AHI, ODI, TS 90% were positively correlated with the severity of OSA. On the contrary, $LSpO_2$ was negatively correlated with the severity of OSA (P < 0.05). See **Table 4**.

ROC curve of the diagnostic value of the blood oxygen indexes

ROC curves were generated to evaluate the diagnostic value of ODI (AUC = 0.823, 95% CI = 0.730-0.917), TS 90% (AUC = 0.872, 95% CI = 0.794-0.950), $LSpO_2$ (AUC = 0.716, 95% CI = 0.596-0.835), and the combination of the three

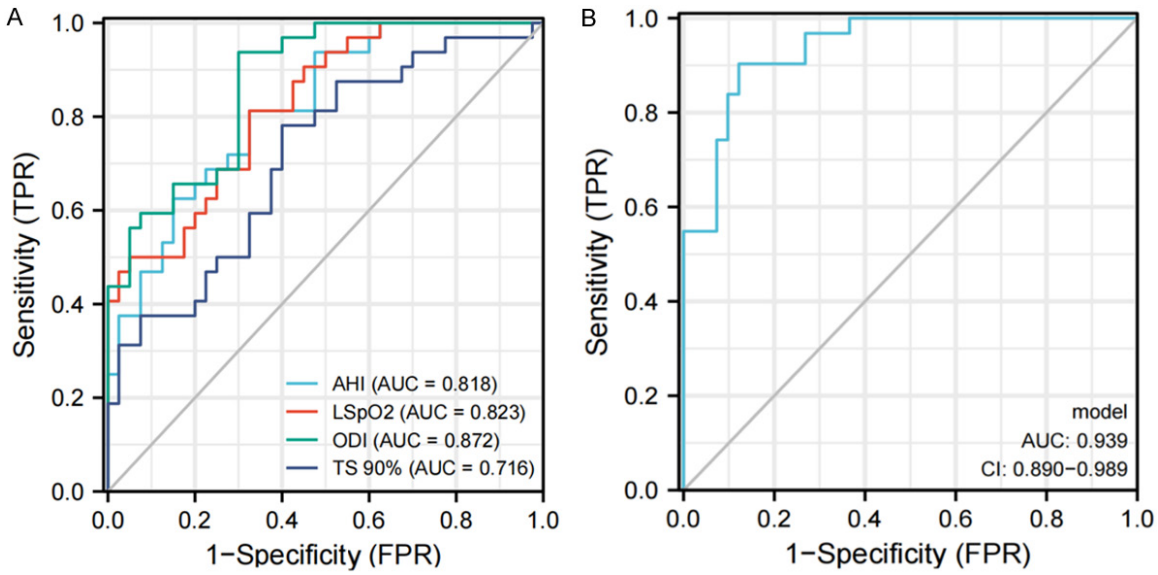

Figure 1. ROC curve of the diagnostic value of the blood oxygen indexes. A: ROC curve of the diagnostic value of ODI, TS 90% and $LSpO_2$ for OSA. B: ROC curve of the combination of blood oxygen indexes for diagnosing OSA. LSpO2, the lowest peripheral oxygen saturation; ODI, oxygen desaturation index; TS 90%, time spent below 90% oxygen saturation. Obstructive sleep apnea (OSA).

Table 5. Partial ROC related data for each predictive variable under their respective optimal cut-off values

Predictive variable	Cut-off value	sensitivity	Specificity degree	Positive predictive value	Negative predictive value	Yoden index
AHI	1.542	0.812	0.675	0.667	0.818	0.488
$LSpO_2$	1.263	0.812	0.675	0.667	0.818	0.488
ODI	1.728	0.938	0.700	0.714	0.933	0.637
TS 90%	1.552	0.781	0.600	0.610	0.774	0.381
Combination	0.039	0.903	0.878	0.848	0.923	0.781

Abbreviations: AHI, apnea-hypopnea index; $LSpO_2$, the lowest peripheral oxygen saturation; ODI, oxygen desaturation index; Ts 90%, time spent below 90% oxygen saturation.

indexes (AUC = 0.939, 95% CI = 0.890-0.989) ($P < 0.05$) for OSA. The AUC value of the combined signature was found to be higher compared to the value of the individual indexes ($P < 0.05$). The results are presented in **Figure 1A**, **1B** and **Table 5**.

Discussion

OSA is one of the main clinical pathogenic factors of sudden cardiac death. It is characterized by upper airway collapse during sleep. Chronic intermittent hypoxia, sleep fragmentation, and inflammatory activation are the main pathophysiological mechanisms of OSA [19]. The common clinical manifestations of OSA include loud snoring, apnea observed by others, sleep interruption, and drowsiness [20]. The condition is also associated with mental and neurological symptoms such as loss of attention, lack of concentration, irritability, anxiety and depression [21]. Recent studies have reported that about 425 million people aged between 30 and 69 worldwide have moderate to severe OSAHS [22]. A higher prevalence of mental illness is observed among men than among women (about 49.7% versus 23.4%), with a male-to-female ratio of 2:1 to 4:1 [23]. Currently, AHI is the most commonly used parameter in PSG data. AHI has been widely used in OSA research for nearly 40 years. OSA scores have been used to diagnose and determine the severity of OSA. However, the OSA scores do not accurately reflect clinical manifestations

and long-term prognoses. Therefore, some scholars have raised questions about the scientific and statistical characteristics of AHI as a gold standard for the diagnosis of OSA. Recent studies have identified significant physiological changes in patients with OSA between day and night, but the AHI did not capture these changes [24]. Besides, AHI does not accurately predict the prognosis of OSA associated conditions, such as cardiovascular diseases and continuous positive airway pressure [25]. In addition, studies have shown that relying solely on the AHI is insufficient for accurately assessing the severity of OSA. Anthropometric measurements and the nocturnal hypoxemia markers should also be evaluated [26]. AHI is a dependent variable of OSA, but is not the preferred indicator for studying the possible outcomes of OSA, such as drowsiness, stroke, hypertension and death [27]. Previous studies have explored diagnostic methods that are more effective in predicting the prognosis of OSA [28, 29]. Identification of prognostic features of diseases facilitates risk stratification and exploration of interventions for specific physiological disorders. Therefore, studies should be conducted to explore whether other characteristics of OSA can be used to predict the OSA-associated morbidity and mortality and provide insight into the underlying pathophysiological differences that may affect the outcomes [30]. Studies have reported the limitations of AHI [31]. It is not effective for predicting the duration of respiratory events, which is as vital as apnea and hypopnea, when assessing the severity of OSA. A longer apnea time is associated with more severe hypoxemia. A longer apnea time is associated with poor long-term and short-term prognosis [32]. The decrease in oxygen caused by apnea is highly correlated with time, area and depth compared with hypopnea. Prolonged duration of respiratory events can lead to prolonged time and area of hypoxia, prolonged apnea time, and increased severity of related hypoxia. Apnea should be attributed a higher weightage when evaluating the severity of cardiovascular events in OSA [33].

The gold standard test for the diagnosis of OSA is nocturnal PSG. AHI only determines the number of times a subject has hypopnea and apnea per hour, but it does not indicate the severity or duration of intermittent nocturnal hypoxia. OSAHS patients with the same AHI value may have diverse clinical symptoms and cardiovascular risks, markedly affecting the symptoms and outcomes of the disease. Excessive daytime sleepiness (EDS) is associated with a higher nocturnal oxygen saturation index and longer apnea duration. Although no significant difference was observed in AHI between the study group and the controls, a correlation between arousal index and overall sleep structure was revealed by a previous study [34]. Hypoxia duration is determined by TS 90%. TS 90% was proposed to be an objective index to evaluate the condition of patients with OSAHS [35] and believed to be the best indicator for nocturnal hypoxia [36]. A study conducted in China reported the clinical utility of TS 90% as an evaluation parameter for chronic intermittent hypoxia (CIH) in patients with OSAHS, revealing a correlation between TS 90% and AHI. Sleepiness on the Epworth scale was higher than $LSpO_2$ after adjusting BMI and other factors associated with cardiovascular risk. The evaluation of OSAHS severity should consider a combination of variables, including AHI, as well as other parameters such as TS 90% and ODI, which reflect nocturnal CIH, rather than relying solely on AHI alone [37]. Previous findings showed that TS 90% was highly correlated with AHI and the total duration of apnea ($r = 0.770$ and 0.776, respectively) [38]. AHI has been widely used to evaluate the severity of OSA for many years, but some studies reported that AHI was not a reliable predictor of surgical prognosis in some patients [39]. A previous study was conducted on 119 patients with OSA who had undergone velopharyngeal surgery, including repair uvulopalatopharyngoplasty, uvula-sparing and dilated velopharyngoplasty [40]. The results showed that TS 90% was an independent predictor of the prognosis of patients. In the current study, the results indicated that TS 90% was a more accurate prognostic indicator for surgery than AHI. This is possibly because TS 90% reflects the severity of intermittent hypoxia during sleep, which may be attributed to unstable respiratory control and respiratory chemoreceptors. Reduced sensitivity is associated with impaired pharyngeal dilator function [41], so TS 90% can also be used to predict subjects eligible for surgery. The present study showed that TS 90% increased with the aggravation of OSA, especially in patients with moderate to severe OSA. This

indicated that the increase of TS 90% was resulted from the aggravation of OSA. Additionally, the increase of TS 90% may represent the severity of OSA. A blood oxygen saturation of less than 90% is considered harmful to the human body.

The ODI represents the decreasing frequency of oxygen saturation ≥ 3% per hour. Our results showed that AHI and ODI were consistent in reflecting the severity of OSA. This indicates that ODI is also a reliable parameter to evaluate the condition of OSA. Pulse oxygen saturation measurement is a noninvasive and continuous method that can effectively reflect the SpO_2 level of human body. The SpO_2 level of healthy people is usually over 90%, and several physical and chemical factors can compromise the SpO_2 level. Notably, factors that reduce pulsatile blood flow, such as cold stimulation, sympathetic nerve excitement, shock, and arteriosclerosis, can affect the accuracy SpO_2 level detection [42]. Currently, $LSpO_2$, ODI and TS 90% are commonly used to evaluate the severity of hypoxia in OSAHS patients during sleep. $LSpO_2$ is the most widely used parameter but it only reflects the maximum extent of nocturnal oxygen saturation decline. On the contrary, ODI and TS 90% reflect the frequency and duration of nocturnal oxygen saturation decline, respectively, but cannot be used independently to evaluate the degree of hypoxia in OSAHS patients [43]. $LSpO_2$ is used to evaluate human hypoxia caused by one or several apneas in OSA patients during night sleep, whereas TS 90% is used to evaluate hypoxia during the any type of sleep [44].

Spearman correlation analysis in this study demonstrated that AHI, ODI, TS 90% were positively correlated with OSA, whereas $LSpO_2$ was negatively correlated with OSA. AHI is considered an accurate diagnostic marker of OSA. ODI could accurately predict OSA. TS 90% showed high accuracy as a diagnostic predictor of OSA. $LSpO_2$ is a potential diagnostic predictor of OSA. The combination of these parameters showed a high accuracy in diagnostic value for OSA, significantly higher than that of the individual indexes. Previous research has shown a positive correlation between AHI and ODI [45]. ODI is a reliable predictor of AHI, with ODI values greater than 5, 15 and 30 being good predictors of AHI values greater than 5, 15 and 30, respectively. Studies report that ODI > 10 exhibits a high sensitivity (93%) and a reliable specificity (75%) in detecting moderate and severe sleep disordered breathing, thus it can be used for the diagnosis of moderate and severe OSAHS [46]. The present study exhibited that the increase of AHI and the decrease of $LSpO_2$ at night were correlated with severity of OSAHS. However, TS 90% and ODI showed stronger correlation with AHI than $LSpO_2$, indicating that TS 90% and ODI can better reflect the severity of hypoxia in patients with OSAHS. Therefore, ODI and TS 90% can be used to evaluate the severity of nocturnal hypoxemia. The blood oxygen indexes consider the number of times of apnea and hypopnea and the duration of respiratory events in patients with OSA. This partially makes up for the limitation of AHI and evaluates respiratory disorders throughout the night, thus contributing to a more comprehensive diagnosis and severity grading of OSA [47-49]. The 2011 edition of the guidelines for diagnosis and treatment of OSAHS indicates that AHI and hypoxemia are significantly different clinically [50], but there is no correlation analysis conducted between them in the guidelines. The degree of hypoxia in some patients with severe OSA is low, but the level of hypoxia is high in some patients with mild and moderate OSA. AHI can be affected by the structural dysregulation of the upper airway, which is significantly correlated with the severity of OSAHS. Previous findings indicate that frequent distinction between AHI and hypoxemia may be attributed in part to the difference in pulmonary diffusion function and the decrease in ventilation/perfusion ratio [51]. However, due to the limited sample size included in this study, subsequent clinical studies and systematic evaluation with large sample data are required.

In summary, relying solely on a single index may be insufficient for accurately assessing the severity of OSA. IN addition to AHI, ODI, $LSpO_2$ and TS 90% indexes should be combined for the comprehensive evaluation of the disease severity. These indexes serve as an auxiliary diagnostic basis for exploring treatment strategies for OSA.

Disclosure of conflict of interest

None.

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References

[1] Won C, Bogan RK, Doghramji K, Ojile J, Bujanover S, Hyman DL, Hewett KA and Thomas R. In-office communication about excessive daytime sleepiness associated with treated obstructive sleep apnea: insights from an ethnographic study of physician-patient visits. Sleep Sci Pract 2022; 6: 696-699.

[2] Li C, Kou YF, DeMarcantonio MA, Heubi CH, Fleck R, Kandil A, Smith DF and Ishman SL. Sleep endoscopy and cine magnetic resonance imaging evaluation of children with persistent obstructive sleep apnea. Otolaryngol Head Neck Surg 2023; 168: 848-855.

[3] Christou EE, Kostikas K, Asproudis C, Zafeiropoulos P, Stefaniotou M and Asproudis I. Retinal microcirculation characteristics in obstructive sleep apnea/hypopnea syndrome evaluated by OCT-angiography: a literature review. Int Ophthalmol 2022; 42: 3977-3991.

[4] Rubio E, Levey EJ, Rondon MB, Friedman L, Sanchez SE, Williams MA and Gelaye B. Poor sleep quality and obstructive sleep apnea are associated with maternal mood, and anxiety disorders in pregnancy. Matern Child Health J 2022; 26: 1540-1548.

[5] Steffen A, Moritz FJ, König IR, Suurna MV and Brüggemann N. Electric field aspects in hypoglossal nerve stimulation for obstructive sleep apnea: a bilateral electrophysiological evaluation of unilateral electrode configuration changes. J Sleep Res 2023; 32: e13592.

[6] Jonassen TM, Bjorvatn B, Saxvig IW, Eagan TM and Lehmann S. Clinical information predicting severe obstructive sleep apnea: a cross-sectional study of patients waiting for sleep diagnostics. Respir Med 2022; 197: 106860.

[7] Kajiyama T, Komori M, Hiyama M, Kobayashi T and Hyodo M. Changes during medical treatments before adenotonsillectomy in children with obstructive sleep apnea. Auris Nasus Larynx 2022; 49: 625-633.

[8] Wojeck BS, Inzucchi SE, Neeland IJ, Mancuso JP, Frederich R, Masiukiewicz U, Cater NB, McGuire DK, Cannon CP and Yaggi HK. Ertugliflozin and incident obstructive sleep apnea: an analysis from the VERTIS CV trial. Sleep Breath 2022; [Epub ahead of print].

[9] Bommineni VL, Erus G, Doshi J, Singh A, Keenan BT, Schwab RJ, Wiemken A and Davatzikos C. Automatic segmentation and quantification of upper airway anatomic risk factors for obstructive sleep apnea on unprocessed magnetic resonance images. Acad Radiol 2023; 30: 421-430.

[10] Xu J, Li Q, Xu CY, Mao S, Jin JJ, Gu W, Shi Y, Zou CF and Ye L. Obstructive sleep apnea aggravates neuroinflammation and pyroptosis in early brain injury following subarachnoid hemorrhage via ASC/HIF-1α pathway. Neural Regen Res 2022; 17: 2537-2543.

[11] Bouzerda A. Cardiovascular risk and obstructive sleep apnea. Pan Afr Med J 2018; 29: 47.

[12] da Silva RP, Martinez D, Uribe Ramos JM, Martins EF, Tedesco-Silva LM, Lopez P and Cadore EL. The effects of resistance exercise on obstructive sleep apnea severity and body water content in older adults: a randomized controlled trial. Sleep Med 2022; 95: 37-46.

[13] Valik JK, Mellhammar L, Sundén-Cullberg J, Ward L, Unge C, Dalianis H, Henriksson A, Strålin K, Linder A and Nauclér P. Peripheral oxygen saturation facilitates assessment of respiratory dysfunction in the sequential organ failure assessment score with implications for the sepsis-3 criteria. Crit Care Med 2022; 50: e272-e283.

[14] Monna F, Ben Messaoud R, Navarro N, Baillieul S, Sanchez L, Loiodice C, Tamisier R, Joyeux-Faure M and Pépin JL. Machine learning and geometric morphometrics to predict obstructive sleep apnea from 3D craniofacial scans. Sleep Med 2022; 95: 76-83.

[15] Ashraf W, Jacobson N, Popplewell N and Moussavi Z. Fluid-structure interaction modelling of the upper airway with and without obstructive sleep apnea: a review. Med Biol Eng Comput 2022; 60: 1827-1849.

[16] Judson MA, Tiwari A and Gemoets DE. The relationship of obesity and OSA to the development of sarcoidosis: a large retrospective case-control US veterans administration analysis. Chest 2022; 162: 1086-1092.

[17] The Chinese Medical Association, the Journal of the Chinese Medical Association, the General Medicine Branch of the Chinese Medical Association, the Sleep Respiratory Disorders Group of the Respiratory Society of the Chinese Medical Association, the editorial Committee of the Chinese Journal of General Practitioners of the Chinese Medical Association, expert group for compiling guidelines for primary diagnosis and treatment of respiratory diseases. Guidelines for primary diagnosis and treatment of adult OSA (2018). Chinese Journal of General Practitioners 2019; 18: 21-29.

[18] Fang Y, Su J, Zhao C, Meng Y, Wei B, Zhang B, Huang Y, Dai L and Ouyang S. Association between nontraditional lipid profiles and the se-

verity of obstructive sleep apnea: a retrospective study. J Clin Lab Anal 2022; e24499.
[19] Bonsignore MR. Obesity and obstructive sleep apnea. Handb Exp Pharmacol 2022; 274: 181-201.
[20] Shao C, Wang H, He Y, Yu B and Zhao H. Clinical phenotype of obstructive sleep apnea in older adults: a hospital-based retrospective study in China. Ir J Med Sci 2023; [Epub ahead of print].
[21] Solanki N, Jurel SK, Singh BP and Chand P. Response to the letter to the editor regarding Solanki et al. "Evaluation of mandibular advancement device placement based on levels of TNF-alpha in participants with obstructive sleep apnea: a clinical study". J Prosthet Dent 2022; 128: 119.
[22] Schweitzer PK, Maynard JP, Wylie PE, Emsellem HA and Sands SA. Efficacy of atomoxetine plus oxybutynin in the treatment of obstructive sleep apnea with moderate pharyngeal collapsibility. Sleep Breath 2022; 13: 1-9.
[23] Puri S, Kissane D, Panza G, Lin HS and Mateika JH. Loop gain is increased and the arousal threshold is decreased in caucasian compared to African American males with OSA. FASEB J 2022; 36: 494-496.
[24] Amorim MR, Wang X, Pho H, Bevans-Fonti S, Anokye-Danso F, Escobar J, Dergacheva O, Branco LGS, Mendelowitz D and Polotsky VY. Activation of leptin-receptor-expressing neurons in the dorsomedial hypothalamus increases hypercapcnic ventilatory response and relieves OSA in obese mice. FASEB J 2022; 36: 193-196.
[25] Puri S, Kissane D, Panza G, Lin HS and Mateika JH. Repeated exposure to mild intermittent hypoxia mitigates the severity of OSA, reduces blood pressure and improves microvascular function and walking endurance in adults with OSA for 4-8 weeks post therapy. FASEB J 2022; 36: 581-585.
[26] Dündar Y, Saylam G, Tatar EÇ, Özdek A, Korkmaz H, Fırat H and Ardıç S. Does AHI value enough for evaluating the obstructive sleep apnea severity? Indian J Otolaryngol Head Neck Surg 2015; 67 Suppl 1: 16-20.
[27] Peng YJ, Su XY, Wang B, Mathews T, Nanduri J and Prabhakar NR. Olfactory receptor78 participates in carotid body-dependent sympathetic activation and hypertension in murine models of OSA. FASEB J 2022; 36: 193-195.
[28] Panza G, Kissane D, Puri S, Lin HS and Mateika J. 15-days of therapeutic mild intermittent hypoxia improves cardiovascular, upper airway and motor limb function in participants with motor incomplete spinal cord injury and severe OSA. FASEB J 2022; 36: 494-496.
[29] Sharma N, Power G, Soares RN, Ramirez-Perez FI, Khalyfa A, Gozal D, Martinez-Lemus LA, Manrique-Acevedo C and Padilla J. Intermittent hypoxia promotes the development of abdominal aortic aneurysm in male mice. FASEB J 2022; 36: 194-196.
[30] Santos RR, Silva TM, Silva LEV, Eckeli AL, Salgado HC and Fazan R. Correlation between heart rate variability and polysomnography-derived scores of severities for OSA. FASEB J 2022; 36: 393-398.
[31] Barbero E, Mañas E, Bikdeli B, García-Ortega A, Oscullo G, García-Sánchez A, Durán D, Retegui A, Rodríguez C, Cano-Pumarega I, Martinez-Garcia MÁ and Jimenez D. Untreated obstructive sleep apnea and cardiovascular outcomes in patients with acute symptomatic pulmonary embolism. Thromb Res 2022; 214: 87-92.
[32] Su X, Han J, Gao Y, He Z, Zhao Z, Lin J, Guo J, Chen K, Gao Y and Liu L. Correlation of obstructive sleep apnea with components of metabolic syndrome and implications for long-term adverse cardiovascular risk in elderly patients. Nan Fang Yi Ke Da Xue Xue Bao 2021; 41: 1592-1599.
[33] Grote L, Sommermeyer D, Ficker J, Randerath W, Penzel T, Fietze I, Sanner B, Hedner J and Schneider H. REM sleep imposes a vascular load in COPD patients independent of sleep apnea. COPD 2017; 14: 565-572.
[34] Jaritos VR, Vanegas E, Facundo Nogueira J, Leiva Agüero S, Giovini V, Rey de Castro J, Rodríguez Reyes Y, Luis Carrillo Alduenda J, Torres Gittaim P, Romero Z, Terán Pérez G, Angélica Bazurto M, Sarfraz A, Sarfraz Z, José Farfán Bajaña M, Mautong H, Felix M and Cherrez-Ojeda I. Frequency of use and preferences for information and communication technologies in patients with sleep apnea: a multicenter, multinational, observational cross-sectional survey study. Int J Med Inform 2022; 162: 104760.
[35] Sajnani R, Karapetian E, Golla A, Tsui I and Sarraf D. Peripheral retinal neovascularization in a patient with obstructive sleep apnea. Am J Ophthalmol Case Rep 2022; 26: 101498.
[36] Romero J, Gianni C, Natale A and Di Biase L. What is the appropriate lesion set for ablation in patients with persistent atrial fibrillation. Curr Treat Options Cardiovasc Med 2017; 19: 35.
[37] Fransson AMC, Isacsson G and Nohlert E. The outcome of oral appliance therapy on position-dependent obstructive sleep apnea: a multicenter randomized controlled trial. Am J Orthod Dentofacial Orthop 2022; 162: 386-393.
[38] Silva MDS, Poyares D, Silva LO, Souza KM, Andersen ML, Ohayon MM, Tufik S and Piove-

zan RD. Associations of the severity of obstructive sleep apnea with age-related comorbidities: a population-based study. Front Neurol 2022; 13: 802554.
[39] Pépin JL, Raymond N, Lacaze O, Aisenberg N, Forcioli J, Bonte E, Bourdin A, Launois S, Tamisier R and Molinari N. Heat-moulded versus custom-made mandibular advancement devices for obstructive sleep apnoea: a randomised non-inferiority trial. Thorax 2019; 74: 667-674.
[40] Davanian A, Williamson L, Taylor C, Harrover A, Bollinger K, Chaudhary B, Taskar V, Lee TJ, Liu Y, Chen Q and Marcus DM. Optical coherence tomography angiography and Humphrey visual field in patients with obstructive sleep apnea. J Clin Sleep Med 2022; 18: 2133-2142.
[41] Fernandes M, Chiaravalloti A, Manfredi N, Placidi F, Nuccetelli M, Izzi F, Camedda R, Bernardini S, Schillaci O, Mercuri NB and Liguori C. Nocturnal hypoxia and sleep fragmentation may drive neurodegenerative processes: the compared effects of obstructive sleep apnea syndrome and periodic limb movement disorder on Alzheimer's disease biomarkers. J Alzheimers Dis 2022; 88: 127-139.
[42] Spicuzza L, Mancuso S, Campisi R and Vancheri C. Sleep quality and mental health during the COVID-19 pandemic in patients with severe obstructive sleep apnea. J Patient Rep Outcomes 2022; 6: 46.
[43] Kucuktepe U, Selcuk OT, Ellidag HY, Aydenizoz D, Selcuk NT, Eyigor H, Renda L, Osma U and Yilmaz MD. Serum hepcidin and paraoxonase levels in patients with severe, moderate, and mild obstructive sleep apnea hypopnea syndrome (OSAS): a comparison between OSAS patients and simple snoring patients. Cranio 2022; [Epub ahead of print].
[44] Wu Y, Jia Y, Ning X, Xu Z and Rosen D. Detection of pediatric obstructive sleep apnea using a multilayer perceptron model based on single-channel oxygen saturation or clinical features. Methods 2022; 204: 361-367.
[45] Al Mortadi N, Khassawneh B, Khasawneh L, Alzoubi O and Alzoubi KH. Berlin and Epworth surveys to predict obstructive sleep apnea for adults on biomimetic oral appliance therapy: a nonrandomized clinical trial. Int J Dent 2022; 2022: 5283406.
[46] Ali Khan I. Role of adenotonsillectomy and tonsillectomy in children with down syndrome who develop obstructive sleep apnea by obesity as a risk factor. Int J Pediatr 2022; 2022: 8074094.
[47] Younes MK, Beaudin AE, Raneri JK, Gerardy BJ and Hanly PJ. Adherence index: sleep depth and nocturnal hypoventilation predict long-term adherence with positive airway pressure therapy in severe obstructive sleep apnea. J Clin Sleep Med 2022; 18: 1933-1944.
[48] Honaker SM, Gopalkrishnan A, Brann M, Wiehe S, Clark AA and Chung A. "It made all the difference": a qualitative study of parental experiences with pediatric obstructive sleep apnea detection. J Clin Sleep Med 2022; 18: 1921-1931.
[49] Namen AM, Forest D, Saha AK, Xiang KR, Younger K, Maurer S, Ahmad Z, Chatterjee AB, O'Donovan C, Sy A, Peters SP and Haponik EF. DOISNORE50: a perioperative sleep questionnaire predictive of obstructive sleep apnea and postoperative medical emergency team activation. A learning health system approach to sleep questionnaire development and screening. J Clin Sleep Med 2022; 18: 1909-1919.
[50] Burns-Mullett C and Zhang Y. STOP-bang screening for obstructive sleep apnea in preoperative patients: a quality improvement project. J Perianesth Nurs 2022; 37: 601-606.
[51] Mashaqi S, Kallamadi R, Matta A, Quan SF, Patel SI, Combs D, Estep L, Lee-Iannotti J, Smith C, Parthasarathy S and Gozal D. Obstructive sleep apnea as a risk factor for COVID-19 severity-the gut microbiome as a common player mediating systemic inflammation via gut barrier dysfunction. Cells 2022; 11: 1569.