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ORIGINAL RESEARCH

The Hourly Apnea-Hypopnea Duration Better Correlates with OSA-Related Nocturnal Hypoxemia and Excessive Daytime Sleepiness Rather Than AHI

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Background: The apnea-hypopnea index (AHI) has limitations in assessing nocturnal hypoxemia and excessive daytime sleepiness (EDS) in obstructive sleep apnea (OSA) patients. This study evaluated whether hourly apnea-hypopnea duration (HAD) and mean apnea-hypopnea duration (MAD) could complement or outperform AHI.

Methods: This study included 1069 OSA patients, of whom 754 completed the Epworth Sleepiness Scale (ESS). Multivariable regression models evaluated the associations between AHI, MAD, HAD, and nocturnal hypoxemia, and standardized *Z* scores were used for comparison. The predictive ability of AHI, MAD, and HAD models for EDS was evaluated using goodness-of-fit indices, and receiver operating characteristic (ROC) curve analysis was performed using bootstrapping techniques.

Results: Nocturnal hypoxemia was observed in 317 participants (29.65%). Patients with nocturnal hypoxemia had significantly higher AHI (43.19 ± 18.41 vs 21.78 ± 14.73 events/hour, $P < 0.001$) and longer HAD (16.71 ± 7.48 vs 8.24 ± 5.40 minutes, $P < 0.001$). After adjusting for age, sex, and BMI, AHI and HAD were still significantly associated with nocturnal hypoxemia ($P < 0.05$). Standardized *Z* scores analysis revealed that HAD had the strongest association with nocturnal hypoxemia (HAD: OR = 3.69, 95% CI: 3.06−4.46, $P < 0.0001$; AHI: OR = 3.48, 95% CI: 2.90−4.18, $P < 0.0001$; MAD: OR = 1.01, 95% CI: 0.88−1.15, $P = 0.9314$) and mean SpO_2 (HAD: $\beta = -0.91$, 95% CI: −1.02−−0.79, $P < 0.0001$; AHI: $\beta = -0.85$, 95% CI: −0.97−−0.74, $P < 0.0001$; MAD: $\beta = 0.00$, 95% CI: −0.12−0.12, $P = 0.9595$), outperforming AHI and MAD. The HAD model showed the best fit for predicting EDS, with an area under the curve of 0.61 at a threshold of 5.63.

Conclusion: The HAD better correlates with OSA-related nocturnal hypoxemia and EDS rather than AHI. The duration of respiratory events warrants more investigation in clinical assessment.

Keywords: obstructive sleep apnea, hourly apnea-hypopnea duration, mean apnea-hypopnea duration, apnea-hypopnea index, nocturnal hypoxemia, excessive daytime sleepiness

Introduction

Obstructive sleep apnea (OSA) is a prevalent and highly heterogeneous disease with diverse pathophysiological features and neural regulatory mechanisms, which complicates its diagnosis and treatment.[1] The global prevalence of OSA continues to rise, but is often underestimated.[2] Approximately 1 billion people worldwide suffer from mild to severe OSA.[3]

Historically, AHI has been the main tool for diagnosing OSA and classifying its severity.[4] However, with the exploration of research in areas such as hypoxia, arousal threshold, and loop gain, the limitations of AHI have attracted increasing attention.[5–7] The index only quantifies the frequency of apnea-hypopnea events during sleep and does not accurately reflect the duration of these events.[8,9] Some studies have also described the poor performance of the AHI in many aspects, including its weak correlation with excessive daytime sleepiness (EDS) in patients with OSA and its

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potential failure to reliably predict cardiovascular disease risk.[10,11] The oversimplification of the disease by AHI is thought to be one of the reasons for the unclear effect of continuous positive airway pressure therapy on cardiovascular events in observational and randomized controlled trials.[12,13] Despite these shortcomings, no superior alternative index has been developed for widespread clinical use.

Recent studies have shown that the "hypoxia burden" indicator has significant advantages over AHI.[14] Nevertheless, it continues to fail to accurately capture the duration of respiratory events.[15] Respiratory event duration cannot be ignored, and genome-wide association studies have identified multiple genetic variants associated with respiratory event duration.[16] Shorter respiratory events have also recently been associated with mortality, have a higher heritability than AHI, and provide information about ventilatory characteristics and airway collapse that is not captured by AHI.[17–19] The sleep breathing impairment index is another newer, more comprehensive index for assessing OSA; it takes into account the duration of each obstructive event in contrast to hypoxic load and is superior to several other traditional and emerging indices in predicting cardiovascular mortality.[20]

Nevertheless, more evidence is needed to support that AHI is no longer suitable as the best indicator to characterize OSA in clinical practice and research. Similarly, in the diagnosis and treatment of OSA, a combination of multiple parameters may be needed to accurately reflect the severity of the disease. One indicator that deserves further exploration is the hourly apnea-hypopnea duration (HAD), which is calculated by multiplying the number of AHI per hour by the average duration of each respiratory event during sleep.[21] This index innovatively incorporates the frequency and duration of respiratory events into the same evaluation parameter. Its calculation method is simple and easy, and it has significant cost-effectiveness advantages while ensuring clinical practical value. To date, only limited literature has been used to explore this index, resulting in insufficient progress in this field.[21] To this end, we used retrospective data from a sleep center for further exploration, and we hypothesized that the HAD better correlates with OSA-related nocturnal hypoxemia and excessive daytime sleepiness rather than AHI.

Methods

Participants

This cross-sectional study comprised patients who visited the Sleep Center, Department of Respiratory and Critical Care Medicine, Renmin Hospital of Wuhan University between March 2022 and September 2023 and received a complete home sleep apnea testing (HSAT) result. As a retrospective cross-sectional study, data for this study were collected retrospectively at specific time points. This study complies with the Declaration of Helsinki. This retrospective study design was approved by the Ethics Committee of Renmin Hospital of Wuhan University. Due to the retrospective nature of the study, the requirement for informed consent was waived, and the identities of the patients were kept anonymous.

The study comprised participants aged 18 and up who were diagnosed with OSA using HSAT and did not receive any OSA treatment. On the night of the sleep study, participants filled out a brief questionnaire that contained demographic information as well as anthropometric data. Information on smoking history, alcohol consumption, and comorbidities was collected from available medical questionnaires. Due to the retrospective nature of the study, these data were incomplete and missing values were noted in the analyses. Body mass index (BMI) was computed by dividing a participant's weight (kg) by their height squared (m^2). The American Sleep Apnea Association (AASM) defines OSA as having an AHI of $\geq$ 5 events per hour.

Exclusion criteria included: (1) age less than 18 years; (2) prior or current use of continuous positive airway pressure (CPAP) for OSA; (3) daytime or resting hypoxemia / PaO_2 < 8 kPa, or other indications for oxygen therapy; (4) severe acute exacerbation or clinically unstable medical conditions, such as hypertensive crisis, diabetic ketoacidosis, or acute cardiovascular and cerebrovascular disease; (5) other sleep disorders, such as central sleep apnea or Cheyne-Stokes breathing; (6) recorded TST less than 3 hours. A total of 1069 participants were finally recruited for analysis. At the same time, 754 of them further completed the Epworth Sleepiness Scale (ESS), and these participants were included in the subsequent analysis to further compare the predictive performance of AHI, MAD and HAD for EDS.

Sleep Studies

We used OrbSense sleep apnea monitor to assess sleep for at least 3 hours per night for each participant. The monitor was placed at the patient's bedside, no more than 100 cm away and no less than 10 cm in height. The Megasens Ultra-Wideband Biological Radar Sleep Screening Device (China) consists of a radar transmitter (OrbSense, ZG-S01D) and a pulse oximeter (ZG-P11F), both provided by Megasens Technology (Hangzhou, China).[22,23]

The parameters and efficacy of the device have been described in detail in previous studies. Our team has conducted several studies using this device.[24–27] After the next day of monitoring, the operator downloads the recorded data to a computer for processing and generates a final report. Through a proprietary algorithm, OrbSense can define all respiratory events (obstructive apnea-hypopnea events, central sleep apnea, and mixed sleep apnea). The metrics collected include the apnea-hypopnea index (AHI), mean oxygen saturation by pulse oximetry (mean SpO_2), lowest oxygen saturation by pulse oximetry ($LSpO_2$), oxygen desaturation index (ODI, defined as the number of times per hour that oxygen levels dropped ≥ 4% from baseline), the percentage of total sleep time (TST) with oxygen saturation < 90% (T90, %), the mean apnea-hypopnea durations (in seconds), sleep stage information, and TST. Radar-based sleep apnea monitors are reliable tools for screening for OSA, with sensitivity and specificity comparable to PSG or established HSAT devices.[22,23]

Sleep Studies and Sleep Breathing Parameters

The mean apnea-hypopnea duration (MAD) is defined as the average duration of apnea-hypopnea in all body positions and sleep stages. The HAD is defined as the hourly apnea-hypopnea duration, calculated using the formula: HAD (minute) = MAD (s) × AHI (events/h) / 60.[21] Participants with T90 ≥ 10% were classified as nocturnal hypoxemia.

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) score was used to assess daytime sleepiness.[28] The questionnaire consists of 8 questions about how often an individual dozes off during daily activities. In this study, the Chinese version of the ESS score was used to assess daytime sleepiness in both groups of patients. Each answer was scored on a scale of 0 to 3. The ESS score ranges from 0 (never dozes off) to 24 (high chance of dozing off), with higher values indicating greater levels of daytime sleepiness or average tendency to sleep. This study has obtained a license to use the ESS (©MW Johns, 1990–1997). The Chinese version of ESS (CESS) showed good reliability in terms of language consistency and test-retest reliability, as well as acceptable internal consistency and sensitivity to clinical changes.[29]

Statistical Analysis

The study population was categorized according to the presence or absence of nocturnal hypoxemia for baseline characteristics analysis. Continuous data that are normally distributed or approximately normally distributed are presented as Mean ± SD, and the comparison between the two groups was performed with the *t*-test of two independent samples; skewedly distributed continuous data were expressed as M (Q_1, Q_3), and the rank sum test of two independent samples was used; categorical data were expressed as n (%), and the chi-square test was used. Multivariable regression analysis was performed to examine the association between sleep breathing parameters and nocturnal hypoxemia. Furthermore, the continuous variables of sleep breathing parameters were categorized to facilitate grouped regression analysis and trend tests. To facilitate the comparison of the associations between AHI, MAD, and HAD with nocturnal hypoxemia, standardized *Z* scores were calculated and included in the regression model. In sensitivity analysis, we further compared the associations between sleep breathing parameters and mean SpO_2.

To control the risk of type I error caused by multiple comparisons, the P value in the regression analysis with continuous variables as independent variables was Bonferroni-corrected (Supplementary Tables S4 and S5). The corrected P value was the original P value multiplied by the number of tests (ie, the number of independent variables), and the significance level of the confidence interval was adjusted (corrected α=0.05/number of independent variables). In addition, the variance inflation factor was used to assess multicollinearity in the linear regression model of continuous independent variables (Supplementary Figures S1-S3). The Hosmer-Lemeshow test was performed on the logistic

regression model of continuous independent variables, and the goodness of fit was assessed by comparing the observed values with the predicted values in each group (Supplementary Table S6 and Supplementary Figures S4-S6).

Finally, the coefficient of determination (R^2), Akaike information criterion (AIC), and Schwarz Bayesian information criterion (BIC) were used as goodness-of-fit indicators of the prediction model to evaluate the ability of the three models of AHI, HAD, and MAD to predict EDS. The receiver operating characteristic (ROC) curve analysis was performed by bootstrapping technique, and the area under the curve (AUC) was used as the main index to evaluate the predictive performance of the best model for EDS in OSA patients.

All analyses were performed using the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). P value of < 0.05 was considered significant by two-tailed tests.

Results

Characteristics of the Study Population

A total of 1069 participants were included in this study (Table 1), of which 317 participants (29.65%) had nocturnal hypoxemia. The mean age of the participants in the hypoxemia group was 56.91 ± 14.25 years, and the mean BMI was 26.94 ± 5.34 kg/m^2; the mean age of the participants in the non-hypoxemia group was 58.55 ± 13.41 years, and the mean BMI was 24.60 ± 4.18 kg/m^2. There was no significant difference in the mean age of the participants between the two

Table 1 Baseline Characteristics of Study Participants

Baseline Characteristics	Non-Nocturnal Hypoxemia N = 752 (70.35%)	Nocturnal Hypoxemia N = 317 (29.65%)	P-value	No. (%) Missing
Demographic characteristics				
Age (years)	58.55 ± 13.41	56.91 ± 14.25	0.080	NA
Sex, n (%)			<0.001	NA
Male	492 (65.43%)	245 (77.29%)		
Female	260 (34.57%)	72 (22.71%)		
BMI (kg/m^2)	24.60 ± 4.18	26.94 ± 5.34	<0.001	NA
Tobacco smoking, n (%)	218 (38.86%)	87 (38.33%)	0.889	281 (26.3%)
Alcohol, n (%)	124 (22.02%)	58 (25.55%)	0.287	279 (26.1%)
Hypertension, n (%)	212 (40.08%)	115 (50.22%)	0.010	311 (29.1%)
Diabetes, n (%)	67 (12.67%)	44 (19.13%)	0.021	310 (29%)
Sleep studies and sleep breathing parameters				NA
AHI (events/h)	21.78 ± 14.73	43.19 ± 18.41	<0.001	
MAD (s)	23.27 ± 3.11	23.28 ± 2.84	0.986	
HAD (minutes)	8.24 ± 5.40	16.71 ± 7.48	<0.001	
AHI (events/h)			<0.001	
5 ≤ AHI < 15	328 (43.62%)	30 (9.46%)		
15 ≤ AHI < 30	227 (30.19%)	49 (15.46%)		

(*Continued*)

Table 1 (Continued).

Baseline Characteristics	Non-Nocturnal Hypoxemia N = 752 (70.35%)	Nocturnal Hypoxemia N = 317 (29.65%)	P-value	No. (%) Missing
AHI ≥ 30	197 (26.20%)	238 (75.08%)		
MAD (s)			0.986	
T1	219 (29.12%)	93 (29.34%)		
T2	215 (28.59%)	89 (28.08%)		
T3	318 (42.29%)	135 (42.59%)		
HAD (minutes)			<0.001	
T1	327 (43.48%)	29 (9.15%)		
T2	289 (38.43%)	67 (21.14%)		
T3	136 (18.09%)	221 (69.72%)		
Wake after sleep onset (%)	19.82 ± 11.14	17.99 ± 10.70	0.013	
REM (%)	14.88 ± 5.84	14.66 ± 6.47	0.578	
N1 + N2 (%)	39.94 ± 8.84	45.49 ± 9.76	<0.001	
N3 (%)	25.46 ± 9.51	22.03 ± 9.80	<0.001	
Mean SpO_2 (%)	94.74 ± 1.27	91.78 ± 2.15	<0.001	
$LSpO_2$ (%)	81.66 ± 5.52	66.99 ± 10.57	<0.001	
ODI (events/h)	17.37 ± 9.64	46.99 ± 21.81	<0.001	
T90 (%)	2.83 (0.82, 5.76)	18.16 (13.11, 27.01)	<0.001	
Epworth Sleepiness Scale				315 (29.5%)
ESS score > 10	80 (15.18%)	53 (23.35%)	0.007	

Notes: AHI was categorized into three levels, namely, mild 5 ≤ AHI < 15 (L1), moderate 15 ≤ AHI < 30 (L2) and severe AHI ≥ 30 (L3) according to clinical standards. The MAD (s) and HAD (min), were stratified based on tertiles and labelled as T1 through T3.

Abbreviations: BMI, body mass index; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; REM, rapid eye movement; mean SpO_2, mean oxygen saturation by pulse oximetry; $LSpO_2$, lowest oxygen saturation by pulse oximetry; ODI, oxygen desaturation index; T90, the percentage of time with oxygen saturation less than 90%; ESS, Epworth sleepiness scale.

groups (P=0.080), but the BMI of the participants in the nocturnal hypoxemia group was higher (P < 0.001). In addition, there was a difference in the sex ratio of the participants between the two groups (P < 0.001).

In terms of sleep breathing parameters, there were no significant differences in MAD, and REM sleep between the two groups (P > 0.05). It should be noted that patients in the nocturnal hypoxemia group had higher AHI, longer HAD, shorter Wake after sleep onset, longer N1+N2, and shorter N3 (P < 0.05). Significant differences were observed in mean SpO_2, $LSpO_2$, ODI, and T90 between the two groups (P < 0.05).

Sleep Breathing Parameters and Nocturnal Hypoxemia

Table 2 shows the relationship between sleep breathing parameters and nocturnal hypoxemia. In the unadjusted model 1, both AHI and HAD were associated with nocturnal hypoxemia in OSA patients, with ORs of 1.07, 95% CI: 1.06−1.08, P < 0.0001 and 1.21, 95% CI: 1.18−1.24, P < 0.0001, respectively. In adjusted model 2, the significant association between AHI and HAD and nocturnal hypoxemia remained, with ORs of 1.07, 95% CI: 1.06−1.08, P < 0.0001 and 1.20, 95% CI: 1.17−1.23, P < 0.0001, respectively. In Table 3, after categorizing MAD and HAD into tertiles and dividing AHI

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Table 2 The Association Between Sleep Breathing Parameters and Nocturnal Hypoxemia

Variables	Model 1	P-value	Model 2	P-value
	OR (95% CI)		OR (95% CI)	
AHI, events/h (continuous)	**1.07 (1.06, 1.08)**	<0.0001	**1.07 (1.06, 1.08)**	<0.0001
MAD, s (continuous)	1.00 (0.96, 1.04)	0.9856	1.00 (0.96, 1.05)	0.9314
HAD, minutes (continuous)	**1.21 (1.18, 1.24)**	<0.0001	**1.20 (1.17, 1.23)**	<0.0001

Notes: Significant results are in bold. Model 1: no covariates were adjusted. Model 2: adjusted for age, sex and BMI.
Abbreviations: BMI, body mass index; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; OR, odds ratio; CI, confidence interval.

Table 3 The Association Between Sleep Respiratory Parameters Grouped by Tertiles and Nocturnal Hypoxemia

Variables	Model 1	P-value	Model 2	P-value
	OR (95% CI)		OR (95% CI)	
AHI mild/moderate/severe				
L1	Reference		Reference	
L2	**2.36 (1.45, 3.83)**	0.0005	**2.16 (1.33, 3.52)**	0.0020
L3	**13.21 (8.69, 20.08)**	<0.0001	**10.79 (7.03, 16.58)**	<0.0001
P for trend	<0.001		<0.001	
MAD tertile				
T1	Reference		Reference	
T2	0.97 (0.69, 1.38)	0.8851	0.97 (0.67, 1.38)	0.8461
T3	1.00 (0.73, 1.37)	0.9985	1.00 (0.72, 1.39)	0.9965
P for trend	0.997		0.995	
HAD tertile				
T1	Reference		Reference	
T2	**2.61 (1.64, 4.16)**	<0.0001	**2.44 (1.53, 3.89)**	0.0002
T3	**18.32 (11.85, 28.33)**	<0.0001	**15.29 (9.76, 23.95)**	<0.0001
P for trend	<0.001		<0.001	

Notes: Significant results are in bold. AHI was categorized into three levels, namely, mild 5 ≤ AHI < 15 (L1), moderate 15 ≤ AHI < 30 (L2) and severe AHI ≥ 30 (L3) according to clinical standards. The MAD (s) and HAD (min), were stratified based on tertiles and labelled as T1 through T3. The first category of each index served as the reference. Model 1: no covariates were adjusted. Model 2: adjusted for age, sex and BMI.
Abbreviations: BMI, body mass index; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; OR, odds ratio; CI, confidence interval.

into mild (5 ≤ AHI < 15), moderate (15 ≤ AHI < 30), and severe (AHI ≥ 30), the results of model 2 showed that compared with the lowest quantile, OSA patients in the highest quantile of HAD had a 14-fold increased risk of nocturnal hypoxemia (OR: 15.29, 95% CI: 9.76–23.95, P < 0.0001), and patients in the highest quantile of AHI had a nearly 10-fold increased risk of nocturnal hypoxemia (OR: 10.79, 95% CI: 7.03–16.58, P < 0.0001).

Comparison of Z-Score of Sleep Breathing Parameters

Table 4 compares the OR values of AHI, MAD, and HAD by calculating the standardized Z-score in the logistic regression model. The analysis showed that HAD was more strongly associated with nocturnal hypoxemia in OSA patients (HAD: OR = 3.69, 95% CI: 3.06−4.46, P < 0.0001; AHI: OR = 3.48, 95% CI: 2.90−4.18, P < 0.0001; MAD: OR = 1.01, 95% CI: 0.88−1.1, P = 0.9314).

Predictive Performance of AHI, MAD, and HAD for Excessive Daytime Sleepiness

The model fitting statistics and ROC curve analysis in Tables 5 and 6 show the predictive performance of AHI, MAD, and HAD for EDS. In the unadjusted model, HAD showed the highest explanatory power (R^2 = 0.0249) and the best model fit (AIC = 689.05, BIC = 698.30), outperforming AHI (R^2 = 0.0205; AIC = 692.14, BIC = 701.40) and MAD (R^2 = 0.0020; AIC = 705.15, BIC = 714.40). After adjusting for age, gender, and BMI, HAD still maintained its advantage, with the highest R^2 value (0.0430), the lowest AIC value (682.37), and the lowest BIC value (705.49).

Further ROC curve analysis of the HAD model showed that the AUC was 0.61, the sensitivity was 0.84, the specificity was 0.35, the positive predictive value was 0.22, and the negative predictive value was 0.91 when the threshold was 5.63. Figure 1 also shows the ROC curve of HAD in predicting EDS.

Table 4 The Association Between Z-Score of Sleep Breathing Parameters and Nocturnal Hypoxemia

OR (95% CI), P-value			
Z-score	**AHI, events/h**	**MAD, s**	**HAD, minutes**
Continuous	**3.48 (2.90, 4.18)** <0.0001 (Per 1 SD increase)	1.01 (0.88, 1.15) 0.9314 (Per 1 SD increase)	**3.69 (3.06, 4.46)** <0.0001 (Per 1 SD increase)

Notes: Significant results are in bold. Adjusted for age, sex and BMI.
Abbreviations: BMI, body mass index; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; OR, odds ratio; CI, confidence interval; SD, standard deviation.

Table 5 Comparison of Model Fit Statistics for AHI, MAD, and HAD in Predicting EDS: Unadjusted and Adjusted Analyses

Variables	**R^2**	**AIC**	**BIC**
Unadjusted			
AHI	0.0204988	692.1443	701.3951
MAD	0.0019842	705.1517	714.4024
HAD	0.0249035	689.0498	698.3006
Adjusted			
AHI	0.0405094	684.0859	707.2129
MAD	0.0351654	687.8403	710.9673
HAD	0.0429570	682.3663	705.4933

Abbreviations: R^2, Coefficient of determination; AIC, Akaike's Information Criterion; BIC, Bayesian Information Criterion; BMI, body mass index; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; EDS, excessive daytime sleepiness. Adjusted model adjusted for age, sex, and BMI.

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Table 6 ROC Curve Analysis AUC and Diagnostic Performance Metrics

ROC Area (AUC)	Threshold	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
0.61	5.63	0.84	0.35	0.22	0.91

Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve.

Sensitivity Analysis

In sensitivity analysis, we also compared the associations between different sleep breathing parameters and mean SpO_2 in patients with OSA. Supplementary Table S1 shows that in the unadjusted model 1, both AHI and HAD showed a significant correlation with mean SpO_2, with β values of −0.05, 95% CI: −0.06−−0.05, P < 0.0001 and −0.14, 95% CI: −0.15−−0.12, P < 0.0001, respectively. The link between mean SpO_2 and both AHI and HAD remained significant in model 2, which was adjusted for age, sex, and BMI. The respective β values for AHI and HAD were −0.05, 95% CI: −0.05 to −0.04, P<0.0001 and −0.13, 95% CI: −0.14 to −0.11, P < 0.0001. Supplementary Table S2 shows the results of quantile regression analysis with the lowest quantile as the reference after stratifying MAD and HAD into tertiles and AHI into mild (5 ≤ AHI < 15), moderate (15 ≤ AHI < 30), and severe (AHI ≥ 30). Upon controlling for covariates, different patterns emerged. In model 2, AHI remained statistically significant only in L3 (β: −1.43, 95% CI: −1.71−−1.14, P < 0.0001). In contrast, HAD was statistically significant in the T2-T3 quantiles. Compared with the lowest quantile of HAD level, T1, the highest quantile of HAD level, T3, was associated with a 1.64-unit decrease in mean SpO_2 (β = −1.64, 95% CI: −1.94−−1.35, P < 0.0001). Mean SpO_2 decreased with increasing AHI and HAD quantile levels compared with the lowest quantile of AHI and HAD (P for trend < 0.001). In addition, no statistically significant association was found between MAD and mean SpO_2 (P > 0.05).

Supplementary Table S3 compared the β values of MAD, HAD, and AHI by calculating the Z-score in the linear regression model. The analysis showed that HAD had a stronger association with the mean SpO_2 in OSA patients (HAD: β = −0.91, 95% CI: −1.02−−0.79, P < 0.0001; AHI: β = −0.85, 95% CI: −0.97−−0.74, P < 0.0001; MAD: β = 0.00, 95% CI: −0.12−0.12, P = 0.9595).

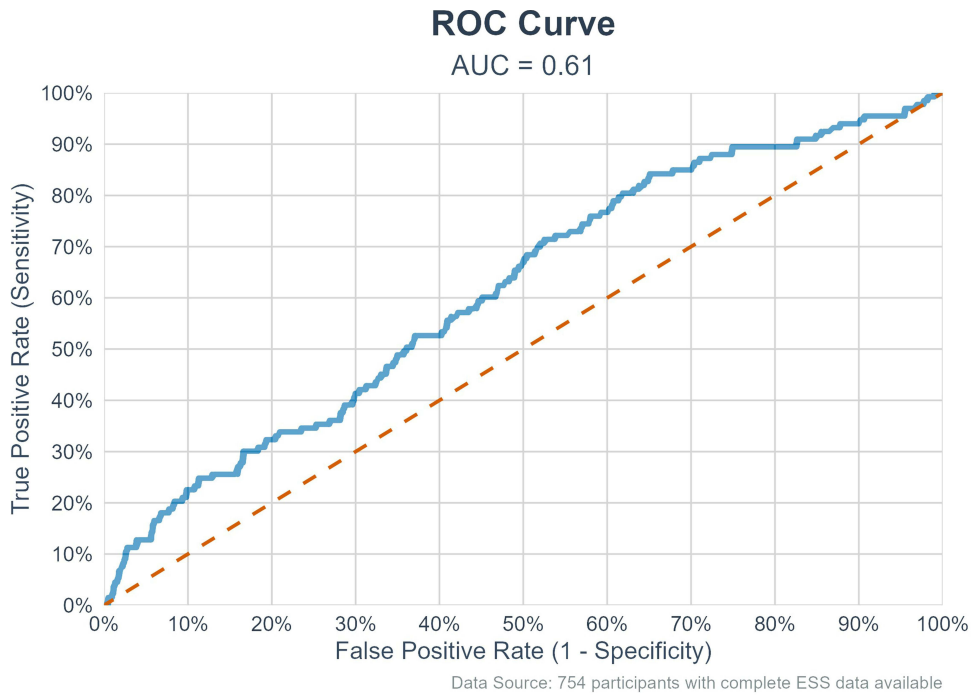

Figure 1 ROC curve analyses for the prediction of EDS.
Abbreviations: ROC, receiver operating characteristic; EDS, excessive daytime sleepiness.

Discussion

This cross-sectional study of 1069 patients with OSA showed that HAD was more strongly associated with nocturnal hypoxemia and mean SpO_2 than AHI and was not affected by confounding factors. Each 1-minute increase in HAD was associated with a 20% increased risk of hypoxemia and a 13% decrease in SpO_2. Patients in the highest tertile of HAD had a 14-fold increased risk of hypoxemia and a 1.64-unit decrease in SpO_2 compared with those in the lowest tertile. Quantile regression showed that HAD remained significant in the T2-T3 quantiles of SpO_2, whereas AHI was significant only in L3. The HAD model had superior predictive performance for EDS (AUC = 0.61, sensitivity = 0.84, and specificity = 0.35 at a threshold of 5.63), suggesting that it may be a more reliable but modest predictor than AHI or MAD.

Traditionally, AHI has been the gold standard for diagnosing and classifying OSA severity. Limited studies have been conducted on the duration of respiratory events in OSA, which may be attributed to the dominant role of AHI in diagnosis and severity assessment.[30–32] However, increasing evidence suggests that the duration of apnea and hypopnea events may significantly affect the pathophysiology of OSA. Patients with similar AHI severity may experience distinct cardiovascular disease burdens associated with the disease.[30,32] The physiological consequences of respiratory events can vary greatly depending on their duration; for example, a 10-second apnea event will have significantly different consequences than one that lasts tens of seconds.[33] These differences may affect the hemodynamic response, physiological changes, and complications associated with OSA. Longer duration respiratory events may result in more severe oxygen desaturation, thereby exacerbating the burden of hypoxia. At the same time, recent studies have also shown that even short respiratory events might negatively impact the physiological and clinical outcomes of OSA, potentially serving as predictors of death in both men and women.[17] The precise mechanisms are not fully understood, but short respiratory events may indicate a diminished arousal threshold, resulting in heightened ventilatory instability and amplified autonomic nervous system responses, which correlate with sleep fragmentation and elevated sympathetic tone.[17]

OSA causes a range of nocturnal and daytime symptoms, especially pronounced daytime sleepiness, which can significantly affect quality of life. In severe OSA, patients who report subjective sleepiness (ESS $\geq$ 16) have higher AHI compared with those without sleepiness (ESS $\leq$ 10).[34] However, the correlation between AHI and daytime sleepiness remains controversial.[35–37] In our study, the HAD model had the best goodness of fit in predicting EDS in OSA patients. This difference may be attributed to the fact that AHI only considers the frequency of events when measuring OSA severity. This emphasizes the clinical significance of considering the duration of respiratory events when evaluating OSA-related symptoms. As an indicator of sleep fragmentation and intermittent hypoxemia, the duration of respiratory events is easily available but relatively understudied compared with the above indicators.[38] Nevertheless, we acknowledge the importance of AHI. Polysomnography generates a large amount of data, and although AHI is a focus, other parameters such as the duration of respiratory events must not be overlooked.

To our knowledge, only one other study has explored the advantages of HAD in predicting hypoxemia in OSA patients.[21] Ma et al reported that HAD had the best adaptability for hypoxemia. In their prediction model, the area under the curve value for predicting hypoxemia was 0.95 in both the training and validation sets. However, unlike our study, Ma et al defined hypoxemia as a pulse $SpO_2 < 90\%$ measured by a pulse oximeter, while our study defined nocturnal hypoxemia as T90 $\geq$ 10%. Although both SpO_2 and T90 are important indicators for assessing hypoxemia, they reflect different dimensions. SpO_2 provides blood oxygen saturation status, which can reflect the oxygenation during sleep, but it may not fully represent the rapid fluctuations in blood oxygen saturation that may occur, especially during frequent apnea or hypoventilation events.[39] In contrast, the T90 index reflects the proportion of time a patient experiences hypoxemia during sleep and is an important indicator of health.[40] The higher the T90, the longer the duration of hypoxemia, which can better represent the severity and impact, and is particularly useful for assessing potential complications of cardiopulmonary function.[41–43]

Strengths and Limitations

Our study has some strengths and limitations. The main strengths include the large sample size for cross-sectional analysis, adjustment for potential confounders (age, sex, and BMI), and exclusion of patients with severe cardiopulmonary disease, daytime or resting hypoxemia, or requiring oxygen therapy, which enhances the robustness of the model. In addition, converting AHI, HAD, and MAD to standardized Z-score for correlation analysis allows for

a more detailed comparison of the relationship between different sleep breathing parameters and nocturnal hypoxemia.

However, several limitations should be acknowledged. The single-center design may introduce regional bias, which may limit the generalizability of the study results. The lack of long-term follow-up data does not allow the assessment of the effect of HAD on cardiovascular and cerebrovascular events. Furthermore, the HSAT device used in this study also has certain limitations, especially in terms of the accuracy of sleep staging, arousal detection, and sleep structure analysis, which is lower compared with PSG. The device also cannot distinguish AHI and HAD values between REM and NREM sleep stages, nor can it distinguish the duration of respiratory events in these stages. The assessment of sleepiness is also limited by the lack of objective measures (eg, multiple sleep latency test). In addition, the retrospective design limits the systematic collection of a detailed medication history, including sedatives (eg, benzodiazepines, hypnotics) or opioids, which may affect the severity of nocturnal hypoxemia and sleep apnea. Similarly, due to the retrospective nature of this study, incomplete data on smoking history, alcohol consumption, and comorbidities are inevitable.

Finally, although our study found several statistically significant differences, it is important to emphasize that statistical significance does not necessarily have clinical relevance. Future studies are warranted to further explore the clinical relevance of these findings. It would be interesting and meaningful to investigate other sleep parameters that better reflect nocturnal hypoxemia and to deepen our understanding of the pathophysiology of OSA and nocturnal hypoxemia.

Conclusions

Our results highlight the importance of HAD in the correlation between OSA-related nocturnal hypoxemia and EDS. The ability of the HAD to capture both the number and duration of respiratory events makes it a valuable complement to the AHI. These findings contribute to a better understanding of the impact of respiratory event duration on OSA-related outcomes and highlight the need to integrate the HAD into clinical assessment and diagnostic models.

Abbreviations

AASM, the American Academy of Sleep Medicine; HSAT, home sleep apnea testing; OSA, obstructive sleep apnea; AHI, apnea–hypopnea index; MAD, mean apnea–hypopnea duration; HAD, hourly apnea–hypopnea duration; Mean SpO_2, mean oxygen saturation by pulse oximetry; $LSpO_2$, lowest oxygen saturation by pulse oximetry; BMI, body mass index; R^2, Coefficient of determination; AIC, Akaike's Information Criterion; BIC, Bayesian Information Criterion; ROC, receiver operating characteristic; AUC, area under the curve.

Data Sharing Statement

Data is available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This retrospective study design was approved by the Ethics Committee of Renmin Hospital of Wuhan University. As this study was retrospective and involved only retrospective analysis of anonymized medical records, posed no additional risks to participants, and did not involve direct interaction with patients, the hospital's Institutional Review Board waived the requirement for written informed consent. All patient data were anonymized and handled in accordance with the hospital's confidentiality agreement to ensure privacy and were used only for the purpose of this study.

Patient and Public Involvement

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

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Author Contributions

Y.W. - Conceptualization, Methodology, Writing - original draft. W.Y. - Writing - review & editing, Data curation. B.Z. - Data curation, Formal analysis. Y.W., W.Y., B.Z., J.Z., Y.H., and M.W. - Data curation. K.H. - Supervision, Methodology, Writing - review & editing. All authors made contributions to the conception, design, and data collection of the study, as well as to the drafting, writing, and revision of the manuscript. All authors agreed to submit the article to Nature and Science of Sleep, approved the final version of the manuscript, and agree to be accountable for its content.

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Disclosure

The authors declare that they have no competing interests.

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