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Determinative sleep traits associated with dyslipidemia in obstructive sleep apnea patients

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Abstract

Background Obstructive sleep apnea (OSA) is recognized to increase the risk of dyslipidemia; however, the specific sleep traits in OSA that influence dyslipidemia are poorly understood. This study sought to determine which sleep traits are independently associated with dyslipidemia and serum lipid profiles in patients with OSA.

Methods In this cohort study, 5239 participants were included from the Sleep Heart Health Study. Further, OSA was diagnosed via polysomnography with an AHI ≥ 5 events/h. Sleep traits were assessed using polysomnographic data and questionnaires. Then, logistic regression was used to identify sleep traits that predict dyslipidemia in OSA patients. Non-linear associations between sleep traits and dyslipidemia were evaluated using restricted cubic splines. The potential mediating effect of body mass index (BMI) was also calculated. Later, linear regression analysis identified sleep traits that were independently linked to lipid levels.

Results After adjusting for confounding factors, logistic regression identified sleep latency (OR: 1.005, 95% CI: 1.002–1.009, $P=0.001$), rapid eye movement (REM) stage (OR: 0.987, 95% CI: 0.977–0.998, $P=0.022$), REM latency (OR: 1.001, 95% CI: 1.000–1.002, $P=0.027$), mean oxygen saturation (meanSpO2) (OR: 0.961, 95% CI: 0.926–0.996, $P=0.031$), percentage of time with oxygen saturation below 95% (T95) (OR: 1.003, 95% CI: 1.001–1.005, $P=0.005$), and time to fall asleep (OR: 1.004, 95% CI: 1.000–1.007, $P=0.042$) as variables independently associated with dyslipidemia. No significant non-linear associations were found (all $P>0.05$). BMI mediated the association between REM stage, meanSpO2, T95, and dyslipidemia risk. Linear regression analysis identified T95 as a consistent independent determinant of all lipid parameters. Additionally, the meanSpO2 and sleep latency were significant independent determinants of most lipid parameters.

Conclusions Sleep latency, sleep architecture, and nocturnal hypoxemia are key factors in dyslipidemia among patients with OSA. These insights suggest potential biomarkers and targeted interventions for the management of lipid-related complications of OSA.

Keywords Obstructive sleep apnea, Dyslipidemia, Sleep traits

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Background

Dysregulation of lipid metabolism is implicated in the development and progression of atherosclerosis and contributes to high cardiovascular morbidity and mortality [1]. Evidence suggests intermittent hypoxia (IH) in obstructive sleep apnea (OSA) may disrupt lipoprotein metabolism [2–5]. Although IH's role in lipid dysregulation is established, the exact mechanism by which OSA causes dyslipidemia remains has not been fully understood. Furthermore, establishing the association between OSA and dyslipidemia may be challenging because of numerous confounding factors linked to obesity [4].

Continuous positive airway pressure (CPAP) has emerged as the preferred intervention for OSA, which effectively improves the apnea-hypopnea index (AHI) and nocturnal hypoxemia. However, meta-analyses revealed that it has minimal impact on lipid metabolism, slightly improving total cholesterol (TC) levels but not affecting triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), or low-density lipoprotein cholesterol (LDL-C) [6–8], indicating no significant clinical effect on lipid metabolism [9]. Regardless of adherence, CPAP does not affect the lipid profiles of individuals with OSA [10]. These results suggest that certain dyslipidemia-related pathways in OSA may persist despite CPAP treatment. However, the specific sleep traits in OSA patients that determine abnormalities in lipid metabolism remain unclear. There is a strong belief that only severe OSA and nocturnal hypoxemia lead to lipid dysregulation. In contrast, most clinical trials attribute the negative consequences of CPAP on lipid metabolism in OSA to unchanged lifestyle factors [7] and low CPAP compliance. Further, few studies investigate the determinants of lipid abnormalities in OSA patients and design targeted clinical trials accordingly.

The pathways by which OSA affects lipid metabolism remain unclear. Animal models elucidate that intermittent hypoxemia may increase lipolysis in adipose tissues and hepatic lipid synthesis under fasting conditions and inhibit lipoprotein clearance after meals [4]. However, scant research has been done on the potential impacts of sleep architecture, sleep efficiency, sleep fragmentation, and sleep habits on lipid dysregulation. Further, understanding the associations between OSA and lipid irregularities is clinically important because they could represent modifiable factors (i.e., conduct sleep hygiene education to change sleep habits [11]). Therefore, a comprehension of lipid dysregulation is crucial for accurately assessing the effects of OSA on atherogenic dyslipidemia instead of concentrating on individual lipid levels only. Hence, the objectives of this study are to identify specific sleep traits that are independently associated with dyslipidemia in patients with OSA and to examine sleep-related factors that independently predict lipid levels in this group.

Methods

Study design and population

The data used in this analysis was acquired from the Sleep Heart Health Study (SHHS). It is a community-based longitudinal cohort study designed to investigate the association between OSA and cardiovascular comorbidities. The methodology of SHHS has been detailed in previous publications [12]. A total of 6,441 individuals aged ≥ 40 years were enrolled from 1995 to 1998 from nine large 'parent' cohorts distributed throughout the United States. Polysomnography (PSG) assessment, which follows American Academy of Sleep Medicine (AASM) guidelines, was used to calculate the AHI based on hypopneas with a desaturation of at least 4%. An AHI threshold of five or more respiratory events per hour of sleep was necessary to diagnose OSA. The SHHS complies with the principles of the Declaration of Helsinki, and ethical approval for the study protocol was granted by the institutional review boards of all involved institutions. The written informed consent from all participants was obtained prior to their involvement in the study.

Sleep traits

In this study, participants first underwent home-based overnight PSG. It monitored various physiological parameters, including both eye electrooculograms, bipolar submental electromyogram, thoracic and abdominal piezoelectric bands, nasal-oral airflow (measured by a thermocouple), finger pulse oximetry, a single lead bipolar electrocardiogram, body positioning (via a mercury gauge sensor), recording of total sleep time, and ambient light status (through a sensor affixed to the recording equipment). Comprehensive sleep traits were obtained from polysomnographic data analysis. These included AHI, AHI during REM and NREM sleep (AHI_{REM} and AHI_{NREM}), sleep latency, sleep efficiency, total sleep time, REM latency, arousal index, wake after sleep onset (WASO), average and lowest peripheral oxygen saturation (SpO2), percentage of time with SpO2 below 90% (T90) and 95% (T95), and the oxygen desaturation index (ODI). Sleep stages were quantified, including percentages of non-REM (stages 1, 2, 3) and REM sleep. The specific definitions of these sleep traits are shown in eTable S1.

Study participants were classified into four OSA categories based on their AHI as follows: non-OSA (AHI < 5 events/h), mild OSA (AHI 5 to < 15 events/h), moderate OSA (AHI 15 to < 30 events/h), or severe OSA (AHI ≥ 30 events/h) [13]. Additional data, such as the Epworth Sleepiness Scale (ESS) scores [14] and time to fall asleep, were extracted from sleep questionnaires.

Lipid parameters

Fasting lipid levels in terms of TG, TC, and HDL-C were measured in mg/dl. Further, LDL-C was determined using the Friedewald formula: LDL-C = TC − (HDL-C + TG/5) [15]. Dyslipidemia was defined based on serum levels exceeding or falling below the following thresholds: LDL-C ≥ 160 mg/dL, HDL-C < 40 mg/dL, TC ≥ 240 mg/dL, TG ≥ 200 mg/dL, or based on a history of lipid-lowering medication use [16]. In addition, long-term observational studies have indicated that non-HDL-cholesterol (non-HDL-C), a non-traditional lipid marker, can predict the emergence of atherosclerotic cardiovascular disease and diabetes [17, 18]. Previous studies have demonstrated that non-traditional metrics potentially provide more profound insights than conventional lipid markers by providing a more effective way to assess risk and balance pro-atherogenic and anti-atherogenic lipoproteins [19]. Hence, we also evaluated the sleep traits associated with non-traditional lipid parameters. The calculations for non-traditional lipid parameters were specified as follows [19]: Atherogenic index of plasma (AIP) = log (TG/HDL-C) [20]; non-HDL-C = TC − HDL-C [21]; atherogenic coefficient (AC) = non-HDL-C/HDL-C [22]. The detailed definitions and clinical implication of these non-traditional lipid parameters are provided in eTable S2.

Additional variables

All participants also provided detailed demographic and health-related information through questionnaires. The collected data included age, gender, race, medical history, and medication usage. Further, body mass index (BMI) was calculated based on the weight and height data collected by trained staff during the initial consultation. Participants' smoking status was categorized into three groups: current, former, and never smokers. The racial categories were specified as white, black, or other. Diabetes status was determined from parent cohort recordings. Hypertension determination was based on two to three blood pressure readings or treatment with antihypertensive drugs. Angina, stroke, myocardial infarction, and heart failure were defined through physician-reported diagnoses, verified by licensed physicians via documented medical history, ensuring data reliability.

Statistical analysis

Continuous variables are presented as either means and standard deviations (±) or medians and interquartile ranges (IQR), while categorical variables are displayed as counts and percentages. For statistical analysis, continuous data were assessed using the t-test or Kruskal-Wallis test, whereas categorical data were analyzed using the Chi-square test. eTable S3 shows the proportion of missing values for each sleep trait in OSA patients. Given only sparse missing data, complete case analyses were performed and reported throughout, with no assumptions made about missing data.

Logistic regression model was employed to investigate the relationship between OSA and dyslipidemia risk. Adjustments in these models were guided by a priori-defined directed acyclic graph (DAG) [23, 24] (eFigure S1) and included covariates age, race, gender, smoking status, and BMI. The strength of associations was evaluated using the E-value [25], which quantifies the minimum association strength that the unmeasured confounder would need to have with both the exposure and outcome to fully account for the observed association, where a higher E-value indicates that greater confounding would be necessary to invalidate the effect.

Further, to examine the specific sleep traits linked to dyslipidemia risk in OSA patients, adjusted multiple logistic regression analyses were also conducted, reporting significant E-values for sleep traits significantly associated with dyslipidemia. Also, we categorized sleep traits into quartiles to examine trends in their association with dyslipidemia using logistic regression analysis. Moreover, a restricted cubic spline model with three knots at the 10th, 50th, and 90th percentiles through the plotRCS package in R was applied to explore potential non-linear relationships between sleep traits and dyslipidemia [26]. To further evaluate the robustness of our results, we conducted a sensitivity analysis by excluding OSA patients receiving treatment with CPAP or oral appliances. Subsequently, logistic regression analyses were re-conducted to further confirm the sleep traits that significantly influence dyslipidemia.

In addition, stratified analyses were performed across different age groups (< 60 or ≥ 60 years), by sex (male or female) and BMI (< 30 or ≥ 30 kg/m^2). Furthermore, we assessed the multiplicative interactions between sleep traits and stratification factors using the likelihood ratio test, comparing the models with and without interaction terms to evaluate the interaction effects. Considering BMI as a potential mediator, we assessed the mediating effect of BMI using the "mediation" package in R.

To evaluate the predictive performance of sleep traits for dyslipidemia in OSA patients, we utilized eXtreme Gradient Boosting (XGBoost) to develop a machine-learning model. Later, Shapley Additive explanation (SHAP) values were used to assign consistent and locally precise contributions of each feature to the predictive model [27]. Also, SHAP values indicate the significance of individual features and their influence on the predictive accuracy of the model.

Additionally, multiple linear regression analysis was performed to ascertain the independent influence of sleep variables on each lipid parameter in OSA patients. All statistical analyses and computations were performed

using Anaconda Python (V3.7) and R statistical software (V4.3.2) provided by the R Foundation for Statistical Computing. Statistical significance was determined by two-tailed tests with a *P*-value threshold of < 0.05.

Results

Participant characteristics

The flow chart (eFigure S2) outlines the selection process, with a final total of 5239 participants being included in the analysis. Among the 5239 subjects, 2,632 (50.2%) were found to have dyslipidemia. Table 1 presents the baseline characteristics of the study participants. The average age of the study participants was 63.5 years, with 48.1% male and an average BMI of 28.2 kg/m². Individuals with dyslipidemia showed a higher BMI, a greater percentage of smokers, a higher prevalence of OSA, and were predominantly male than those without dyslipidemia. Regarding sleep traits, the dyslipidemia group demonstrated higher AHI, AHI_{NREM}, and AHI_{REM}, ODI, T90, T95, and arousal index. They also experienced prolonged sleep and REM latency, shorter sleep duration, reduced sleep efficiency, and lower meanSpO2 and minSpO2. Significant differences in sleep architecture were also observed between the groups. eTable S4 compares sleep traits and lipid profiles between OSA and non-OSA participants. In general, individuals with OSA exhibit elevated levels of TC, LDL-C, TG, non-HDL-C, AIP, and AC, along with reduced HDL-C compared to non-OSA participants.

Association between OSA and dyslipidemia

The prevalence of dyslipidemia in patients with non, mild, moderate, and severe OSA was found to be 41.0%, 52.3%, 54.1%, and 60.4%, respectively (eFigure S3). Compared to non-OSA participants, OSA were statistically significantly associated with the presence of dyslipidemia after adjusting for confounding factors (OR 1.283, 95% CI 1.123–1.466, $p < 0.001$, eTable S5). Further, we applied the E-value method, which produced E = 1.52 for the estimate. The findings indicate that the detected odds ratio (OR) of 1.283 could be attributed to an unmeasured confounder associated with OSA and dyslipidemia at an OR of 1.52 each, whereas a less potent confounder would be insufficient to explain this relationship.

Furthermore, after adjusting for potential confounding factors, the presence of dyslipidemia was significantly associated with OSA at all levels of severity compared to non-OSA participants. Specifically, the ORs were 1.285 (95% CI: 1.112–1.485, $p < 0.001$) for mild OSA, 1.223 (95% CI: 1.032–1.449, $p = 0.020$) for moderate OSA, and 1.416 (95% CI: 1.155–1.736, $p < 0.001$) for severe OSA with a *P*-value for trend of 0.002 (eTable S5).

Determinative sleep traits associated with dyslipidemia in patients with OSA

Table 2 describes the association between sleep traits and dyslipidemia in OSA patients. After adjusting for confounding variables, the sleep traits were found to be independent predictors of dyslipidemia in patients with OSA as follows: sleep latency (OR: 1.005, 95% CI: 1.002–1.009, $P = 0.001$), REM stage (OR: 0.987, 95% CI: 0.977–0.998, $P = 0.022$), REM latency (OR: 1.001, 95% CI: 1.000–1.002, $P = 0.027$), meanSpO2 (OR: 0.961, 95% CI: 0.926–0.996, $P = 0.031$), T95 (OR: 1.003, 95% CI: 1.001–1.005, $P = 0.005$), and time to fall asleep (OR: 1.004, 95% CI: 1.000–1.007, $P = 0.042$). Sensitivity analysis conducted after excluding OSA patients receiving treatment with CPAP or oral appliances demonstrated the robustness of our results (eTable S6).

Figure 1 displays the associations between dyslipidemia risk and sleep latency, REM stage, REM latency, meanSpO2, T95, and time to fall asleep through the restricted cubic spline curve, and no significant non-linear associations were found (all P Non-linear >0.05). eTable S7 presents the E-values for the association between these sleep traits and dyslipidemia risk.

eTable S8 elucidates the relationship between dyslipidemia and the quartiles of various sleep traits in patients with OSA, including sleep latency, REM stage, REM latency, meanSpO2, T95, and time to fall asleep. Participants with the highest quartile for sleep latency (OR: 1.329, 95% CI: 1.101–1.606, $p = 0.003$, P-trend = 0.004) and time to fall asleep (OR: 1.256, 95% CI: 1.034–1.526, $p = 0.022$, P-trend = 0.009) demonstrated a significantly increased risk of dyslipidemia as compared to participants in the lowest quartile. In contrast, a higher meanSpO2 (OR: 0.790, 95% CI: 0.632–0.987, $p = 0.038$, P-trend = 0.014) was significantly related to a decreased risk of dyslipidemia. However, for the REM stage, REM latency, and T95, the higher quartiles did not show a significant association with dyslipidemia risk compared to the lower quartile. Nevertheless, a trend was observed for T95, with a p-trend value of 0.015.

Mediation analysis

Mediation analysis was performed to explore the mediating effect of BMI on the relationship between sleep latency, REM stage, REM latency, meanSpO2, T95, time to fall asleep, and dyslipidemia risk (Fig. 2). The results revealed that the observed associations with dyslipidemia risk were mediated through BMI by 12.0% (95% CI: 0.25–45%) for the REM stage, 48.8% (95% CI: 29.0–92.0%) for meanSpO2 and 42.1% (95% CI: 25.4–77.0%) for T95. However, BMI did not mediate the associations between sleep latency, REM latency, or time to fall asleep and dyslipidemia risk.

Table 1 General characteristics of the study participants

Characteristic	Total (*N* = 5239)	Dyslipidemia (*N* = 2632)	Non-dyslipidemia (*N* = 2607)	*P* value
Age, years	63.5 ± 11.1	63.5 ± 10.6	63.4 ± 11.6	0.630
Males, N (%)	2520 (48.1)	1451 (55.1)	1069 (41.0)	< 0.001
BMI, kg/m^2	28.2 ± 5.1	28.9 ± 4.9	27.4 ± 5.1	< 0.001
Race, N (%)				
White	4462 (85.2)	2288 (86.9)	2174 (83.4)	< 0.001
Black	447 (8.5)	170 (6.5)	277 (10.6)	
Other	330 (6.3)	174 (6.6)	156 (6.0)	
Smoking status, N (%)				
Never	2473 (47.2)	1153 (43.8)	1320 (50.6)	< 0.001
Former	2263 (43.2)	1189 (45.2)	1074 (41.2)	
Current	503 (9.6)	290 (11.0)	213 (8.2)	
OSA, N (%)	3652 (69.7)	1982 (75.3)	1670 (64.1)	< 0.001
Diabetes, N (%)	376 (7.2)	238 (9.0)	138 (5.3)	< 0.001
Hypertension, N (%)	2273 (43.4)	1295 (49.2)	978 (37.5)	< 0.001
Angina, N (%)	381 (7.3)	267 (10.1)	114 (4.4)	< 0.001
Heart Failure, N (%)	89 (1.7)	53 (2.0)	36 (1.4)	0.071
Myocardial infarction, N (%)	332 (6.3)	225 (8.5)	107 (4.1)	< 0.001
Stroke, N (%)	174 (3.3)	99 (3.8)	75 (2.9)	0.203
Sleep traits				
AHI, events/h	9.6 [4.0, 19.9]	11.0 [5.1, 22.1]	8.1 [3.2, 17.7]	< 0.001
$AHI_{NREM,}$ events/h	5.9 [1.9, 15.6]	7.4 [2.6, 18.1]	4.6 [1.5, 13.1]	< 0.001
AHI_{REM}, events/h	16.3 [6.3, 32.8]	18.2 [7.9, 35.6]	14.3 [5.0, 29.3]	< 0.001
Sleep latency, min	7.5 [0.0, 20.0]	8.5 [0.0, 21.0]	6.5 [0.0, 18.0]	< 0.001
Total sleep time, min	360.0 ± 64.3	356.9 ± 65.0	363.0 ± 63.4	0.001
Sleep efficiency, %	85.2 [77.8, 90.5]	84.7 [77.3, 90.0]	85.6 [78.3, 90.7]	< 0.001
REM stage, %	19.8 ± 6.3	19.6 ± 6.4	20.1 ± 6.1	0.003
NREM1 stage, %	4.5 [2.8, 7.0]	4.7 [2.8, 7.3]	4.4 [2.7, 6.7]	< 0.001
NREM2 stage, %	56.6 ± 11.6	56.9 ± 11.7	56.2 ± 11.5	0.017
NREM3 stage, %	17.5 [9.0, 25.5]	16.9 [8.8, 25.1]	17.9 [9.5, 25.9]	0.021
REM latency, min	72.0 [54.0, 102.8]	73.5 [54.0, 105.5]	70.5 [53.5, 101.0]	0.025
Arousal index, events/h	16.8 [12.1, 23.7]	17.6 [12.6, 24.8]	16.1 [11.5, 22.5]	< 0.001
WASO, min	49.5 [29.5, 82.0]	50.5 [30.5, 82.6]	48.5 [29.0, 81.0]	0.074
MeanSpO2, %	94.8 [93.5, 95.9]	94.5 [93.2, 95.6]	95.0 [93.8, 96.2]	< 0.001
MinSpO2, %	87.0 [83.0, 90.0]	86.0 [83.0, 89.0]	87.0 [84.0, 90.0]	< 0.001
ODI, events/h	8.8 [4.3, 16.7]	10.1 [4.9, 18.7]	7.8 [3.8, 15.1]	< 0.001
T90, %	0.2 [0.0, 1.9]	0.3 [0.0, 2.4]	0.1 [0.0, 1.1]	< 0.001
T95, %	38.3 [8.5, 76.6]	47.4 [14.0, 81.8]	28.5 [5.1, 69.7]	< 0.001
ESS	7.0 [4.0, 11.0]	7.0 [5.0, 11.0]	7.0 [4.0, 10.0]	0.097
Time to fall asleep, min	15.0 [5.0, 20.0]	15.0 [7.0, 20.0]	13.0 [5.0, 20.0]	0.121
Lipid profile				
TC, mg/dl	205.0 [182.0, 230.0]	224.0 [190.0, 249.2]	196.0 [177.0, 213.0]	< 0.001
LDL-C, mg/dl	125.2 [104.0, 147.9]	139.6 [110.0, 166.0]	117.6 [100.0, 134.2]	< 0.001
HDL-C, mg/dl	48.0 [39.0, 59.0]	39.0 [34.0, 51.0]	54.0 [47.0, 64.0]	< 0.001
TG, mg/dl	125.0 [88.0, 180.0]	169.0 [116.8, 234.0]	100.0 [74.5, 132.0]	< 0.001
Non-HDL-C, mg/dl	154.0 [131.0, 180.0]	177.0 [149.0, 200.0]	139.0 [119.0, 156.0]	< 0.001
AIP	0.9 [0.5, 1.4]	1.4 [1.0, 1.8]	0.6 [0.2, 0.9]	< 0.001
AC	3.2 [2.4, 4.3]	4.2 [3.3, 5.2]	2.5 [1.9, 3.1]	< 0.001

Abbreviations: BMI = body mass index; OSA = Obstructive sleep apnea; AHI = apnea-hypopnea index; REM = rapid eye movement; NREM = non-REM sleep; AHI_{NREM} = apnea-hypopnea index during NREM sleep; AHI_{REM} = apnea-hypopnea index during REM sleep; WASO = wake after sleep onset; MeanSpO2 = nocturnal mean oxygen saturation; MinSpO2 = lowest nocturnal oxygen saturation; ODI = oxygen desaturation index; T90 = Percent total sleep duration with below 90% oxygen saturation; T95 = Percent total sleep duration with below 95% oxygen saturation; ESS = Epworth sleepiness scale; TC = total cholesterol; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglycerides; Non-HDL-C = Non-high-density lipoprotein cholesterol; AIP = Atherogenic index of plasma; AC = Atherogenic coefficient

Table 2 Determinative sleep traits associated with dyslipidemia in OSA patients

Sleep traits	Bivariate analysis		Multivariate analysis	
	Crude odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)†	*P* value
AHI, events/h	1.008(1.003,1.012)	<0.001		
AHI_{NREM}, events/h	1.009(1.005,1.014)	<0.001		
AHI_{REM}, events/h	1.004(1.001,1.008)	0.019		
Sleep latency, min	1.005(1.002,1.009)	0.002	1.005(1.002,1.009)	0.001
Total sleep time, min	0.999(0.998,1)	0.239		
Sleep efficiency, %	0.997(0.991,1.003)	0.289		
REM stage, %	0.988(0.978,0.999)	0.029	0.987(0.977,0.998)	0.022
NREM1 stage, %	1.019(1.003,1.035)	0.023		
NREM2 stage, %	1.003(0.997,1.009)	0.281		
NREM3 stage, %	0.998(0.992,1.004)	0.482		
REM latency, min	1.001(1,1.002)	0.036	1.001(1.000,1.002)	0.027
Arousal index, events/h	1.009(1.003,1.015)	0.003		
WASO, min	1(0.998,1.001)	0.875		
MeanSpO2, %	0.914(0.883,0.945)	<0.001	0.961(0.926,0.996)	0.031
MinSpO2, %	0.991(0.981,1.001)	0.091		
ODI, events/h	1.01(1.005,1.015)	<0.001		
T90, %	1.007(1.002,1.014)	0.014		
T95, %	1.006(1.004,1.008)	<0.001	1.003(1.001,1.005)	0.005
ESS	1.007(0.992,1.022)	0.388		
Time to fall asleep, min	1.001(0.998,1.005)	0.483	1.004(1.000,1.007)	0.042

Abbreviations: OSA = obstructive sleep apnea; AHI = apnea-hypopnea index; REM = rapid eye movement; NREM = non-REM sleep; AHI_{NREM} = apnea-hypopnea index during NREM sleep; AHI_{REM} = apnea-hypopnea index during REM sleep; WASO = wake after sleep onset; MeanSpO2 = nocturnal mean oxygen saturation; MinSpO2 = lowest nocturnal oxygen saturation; ODI = oxygen desaturation index; T90 = percent total sleep duration with below 90% oxygen saturation; T95 = percent total sleep duration with below 95% oxygen saturation; ESS = Epworth sleepiness scale

† Based on the directed acyclic graph, the following covariates were adjusted: age (years), sex (male/female), race (white, black, and other races), smoking status (never/previous/current smoker), and BMI (continuous, kg/m^2)

Subgroup analysis

eFigure S4 displays the results of the subgroup analysis. Significant correlations were observed between dyslipidemia risk and several sleep traits: sleep latency, REM stage, T95, and time to fall asleep for participants ≥ 60 years. While for those < 60 years, only sleep latency was significantly associated with dyslipidemia. Moreover, gender-specific analyses revealed that sleep latency significantly impacts dyslipidemia risk in females, whereas meanSpO2 showed a marginally significant association in males. Among participants with a BMI < 30 kg/m^2, strong associations were found between dyslipidemia risk and sleep latency, meanSpO2, T95, and time to fall asleep. Conversely, among the group with a BMI ≥ 30 kg/m^2, only sleep latency and REM stage demonstrated a significant link to dyslipidemia risk.

The effect of T95 on dyslipidemia risk was more evident in participants with a BMI < 30 kg/m^2 (P-interaction = 0.041). Similarly, the influence of the time to fall asleep on dyslipidemia risk was significantly stronger in participants aged ≥ 60 years and those with a BMI < 30 kg/m^2 (P-interaction < 0.05).

Sleep traits importance assessment

The analysis concerning the importance of various sleep traits in the prediction model was conducted using the XGboost algorithm and SHAP values. The results revealed that meanSpO2 played a relatively significant role (see eFigure S5).

Determinants of lipid levels in OSA patients

Table 3 presents the determinants of lipid levels in OSA patients. TC levels were influenced by various factors, including AHI, AHI_{NREM}, ODI, meanSpO2, minSpO2, T95, REM stage, and REM latency. LDL-C levels were specifically associated with T95, whereas HDL-C was independently influenced by meanSpO2, T95, NREM1, sleep latency, and time to fall asleep. Also, TG levels were independently affected by AHI_{NREM}, ODI, meanSpO2, T90, T95, and sleep latency.

Further, for novel lipid parameters, non-HDL-C was influenced by AHI, AHI_{NREM}, meanSpO2, ODI, T95, REM stage, REM latency, and sleep latency. The AIP determinants included meanSpO2, T95, sleep latency, and time to fall asleep. The AC was determined by AHI, AHI_{NREM}, ODI, meanSpO2, T95, NREM1, NREM3, and sleep latency.

Overall, T95 has emerged as a consistent independent determinant of all the lipid parameters. Further, meanSpO2 and sleep latency were significantly independent determinants of most lipid parameters.

Discussion

In the present study, we have performed a community-based cross-sectional analysis to establish the association between specific sleep traits and dyslipidemia in patients with OSA. Our research demonstrates an independent association between OSA and dyslipidemia, which is evident even in mild cases of OSA. Sleep latency, REM stage, REM latency, meanSpO2, T95, and time to fall asleep are the primary determinants of dyslipidemia in patients with OSA. Furthermore, our analysis reveals that BMI is a mediating factor for interconnecting REM stage,

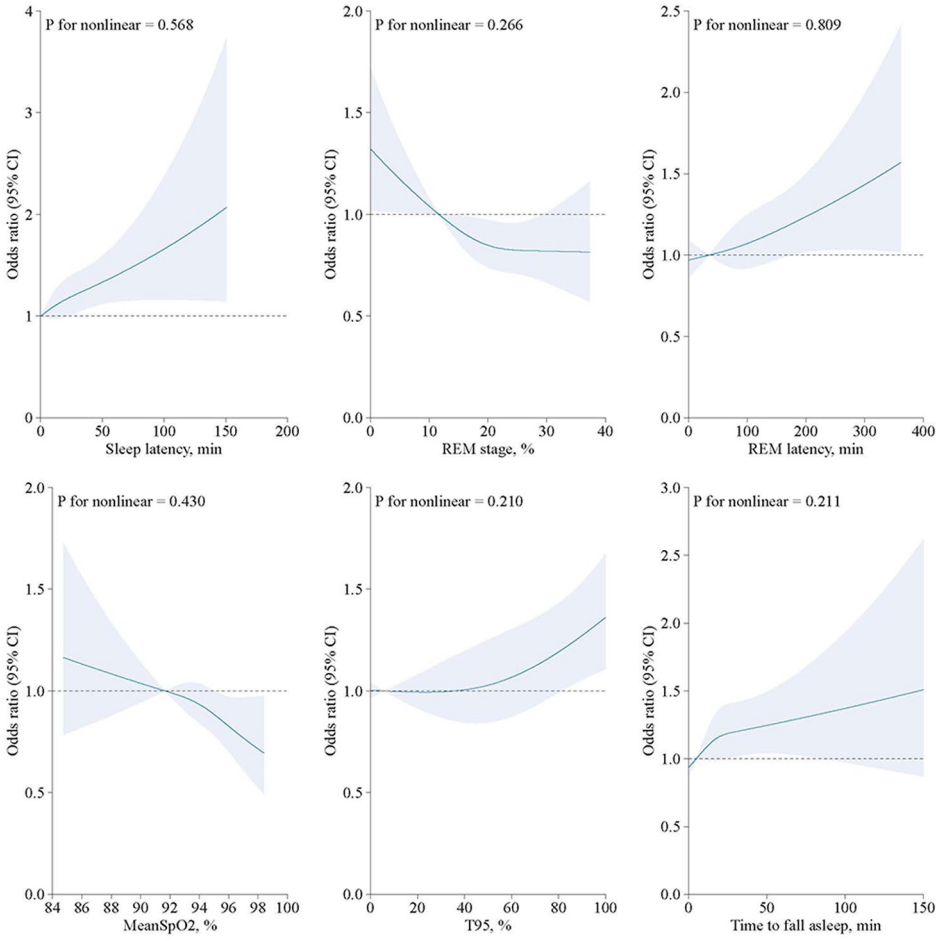

Fig. 1 Restricted cubic spline of the relationship between dyslipidemia and sleep latency, REM stage, REM latency, meanSpO2, T95, and time to fall asleep. Potential non-linear relationships were examined using restricted cubic splines (with 3 knots at the 10th, 50th, and 90th percentiles) with odds ratios (ORs) based on logistic regression models. The dashed line represents the OR of 1. ORs were adjusted for age (years), sex (male/female), race (white, black, and other races), smoking status (never/previous/current smoker), and BMI (continuous, kg/m^2). Abbreviations: REM = rapid eye movement; MeanSpO2 = nocturnal mean oxygen saturation; T95 = percent total sleep duration with below 95% oxygen saturation

meanSpO2, T95, and dyslipidemia. On the other hand, our findings also demonstrate that traditional and novel lipid levels depend upon several parameters, including the AHI, nocturnal hypoxemia, sleep architecture, and sleep latency. Notably, the T95 has emerged as a consistent independent determinant across all the lipid parameters. Furthermore, meanSpO2 and sleep latency were also found to be significant independent determinants for most of the lipid parameters.

The observed higher prevalence of dyslipidemia in OSA patients compared to non-OSA individuals corroborates with earlier findings [3, 4, 28]. The relationship between OSA and dyslipidemia is also in good agreement with Mendelian randomization [29]. However, earlier studies have predominantly linked dyslipidemia with severe cases of OSA [5]. Contrary to these findings, the patient subgroup analysis in our study reveals that even a mild case of OSA is associated with dyslipidemia, highlighting the necessity for lipid screening and management. This distinction stresses a significant shift in understanding the spectrum of OSA-related lipid abnormalities.

In terms of nocturnal hypoxemia, dyslipidemia strongly correlates with meanSpO2 and T95, akin to findings from the Brazilian Longitudinal Study of Adult Health [30]. However, it shows no dependency on minSpO2 and T90. Thus, the meanSpO2 level reflects a more accurate impact of nocturnal hypoxemia compared to the minimum values recorded. Further, compared to T95, T90 does not appear to be a sensitive hypoxia index for reflecting dyslipidemia, which may be attributed to the relatively mild hypoxia condition observed in the community-dwelling OSA patients, as evidenced by a median T90 value of 0.2. Therefore, the present study identifies T95 as a sensitive indicator that has been overlooked previously in the literature and, for the first time, establishes its association with dyslipidemia and lipid levels.

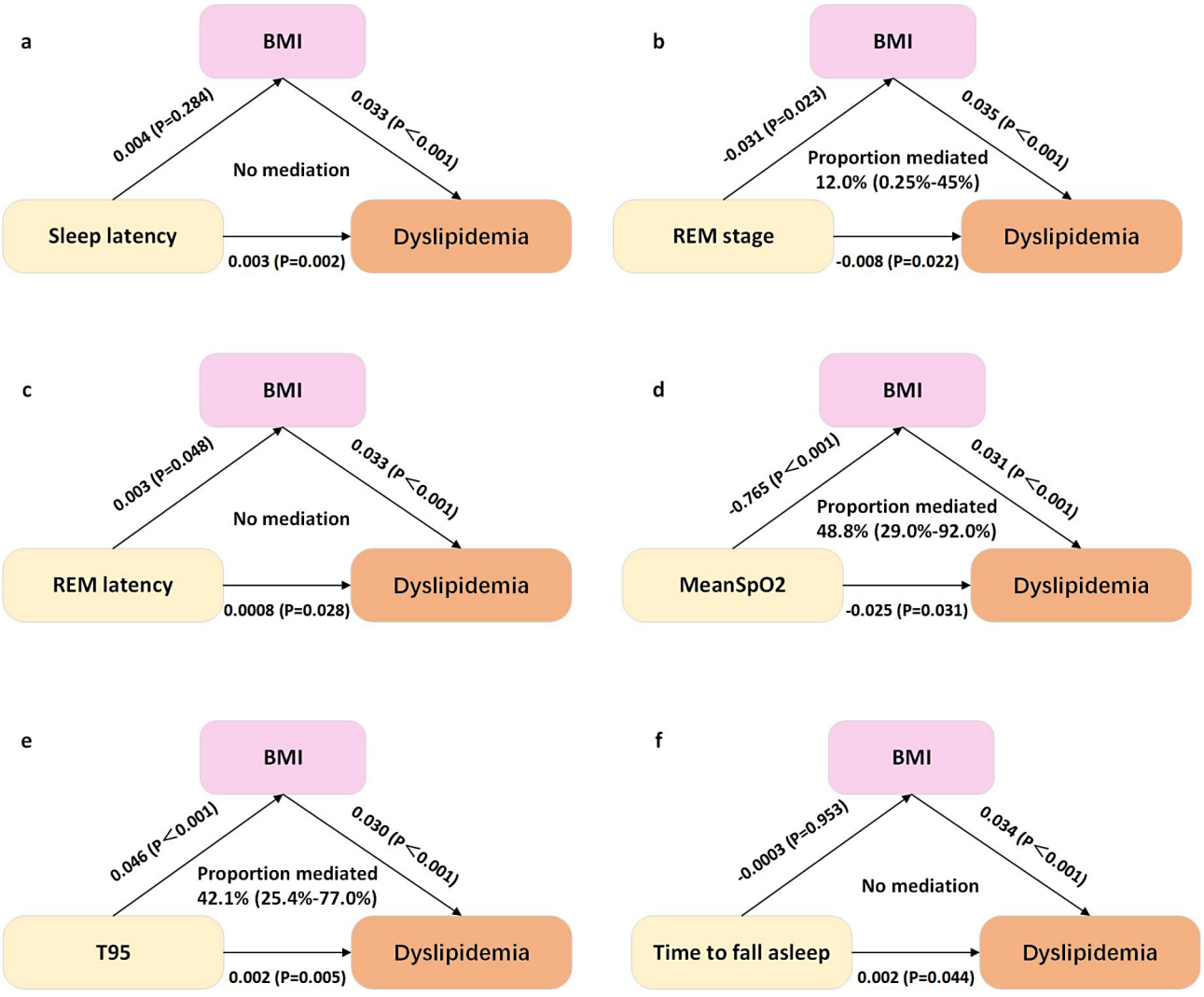

Fig. 2 The mediating effect of BMI on the relationship between sleep latency, REM stage, REM latency, meanSpO2, T95, time to fall asleep, and dyslipidemia in patients with OSA. Abbreviations: BMI = body mass index; OSA = Obstructive sleep apnea; REM = rapid eye movement; MeanSpO2 = nocturnal mean oxygen saturation; T95 = percent total sleep duration with below 95% oxygen saturation

Regarding the underlying mechanisms, it appears that intermittent hypoxia condition enhances lipolysis in adipose tissues and hepatic biosynthesis while concurrently delaying the clearance of lipoproteins after meals [4].

The relationship between insomnia and dyslipidemia is still contentious. Zhan et al. [31] have reported that women experiencing insomnia symptoms three or more times a week have a 25% increased likelihood of elevated total cholesterol level compared to women without insomnia symptoms. However, two other studies have found no association between sleep latency or insomnia symptoms and dyslipidemia [4, 5]. In contrast, our findings indicate a significant positive correlation between dyslipidemia risk and PSG-based sleep latency and patient-reported sleep onset time. The possible mechanism may be ascribed to the impact of prolonged sleep latency on neuroendocrine regulation in patients with OSA. An extended sleep onset period could enhance the sympathetic nervous system activity, which in turn affects the adipocyte function. Consequently, this alteration may increase the levels of circulating free fatty acids, which are subsequently transported to the liver, accelerating the synthesis of triglycerides and cholesterol. These findings emphasize the significance of considering the impact of sleep latency in the management of dyslipidemia in patients with OSA, alongside the prescription of CPAP. Also, efforts should be made to minimize the sleep latency period to enhance the treatment efficacy.

Very few studies have investigated the relationship between the sleep stages and dyslipidemia. Previous findings suggest that the duration of the NREM3 stage and the latency of REM sleep have inverse and independent

Table 3 Independent predictors of lipid indices in the multivariate linear regression analysis

	β	SE	95% CI for B		*P* value	*R*-squared	Adjusted *R*-squared
			Lower limit	Upper limit			
TC, mg/dl							
AHI, events/h	0.102	0.041	0.022	0.181	0.012	0.056	0.054
$AHI_{NREM,}$ events/h	0.112	0.041	0.032	0.192	0.006	0.055	0.053
ODI, events/h	0.124	0.047	0.031	0.217	0.009	0.056	0.054
MeanSpO2, %	-0.818	0.324	-1.454	-0.183	0.012	0.056	0.054
MinSpO2, %	-0.215	0.099	-0.409	-0.02	0.031	0.056	0.054
T95, %	0.063	0.02	0.023	0.102	0.002	0.057	0.055
REM stage, %	-0.239	0.1	-0.435	-0.043	0.017	0.055	0.052
REM latency, min	0.028	0.011	0.008	0.049	0.007	0.057	0.054
LDL-C, mg/dl							
T95, %	0.038	0.019	0.001	0.075	0.044	0.017	0.015
HDL-C, mg/dl							
MeanSpO2, %	0.246	0.115	0.021	0.472	0.032	0.228	0.226
T95, %	-0.026	0.007	-0.04	-0.012	<0.001	0.230	0.228
NREM1, %	0.118	0.055	0.01	0.226	0.033	0.229	0.227
Sleep latency, min	-0.028	0.011	-0.049	-0.007	0.009	0.228	0.226
Time to fall asleep, min	-0.023	0.011	-0.046	-0.001	0.040	0.229	0.227
TG, mg/dl							
$AHI_{NREM,}$ events/h	0.254	0.114	0.031	0.476	0.026	0.064	0.061
ODI, events/h	0.321	0.131	0.064	0.578	0.014	0.065	0.062
MeanSpO2, %	-3.66	0.897	-5.418	-1.902	<0.001	0.067	0.065
T90, %	0.301	0.152	0.003	0.599	0.048	0.064	0.062
T95, %	0.253	0.056	0.144	0.363	<0.001	0.068	0.066
Sleep latency, min	0.22	0.083	0.057	0.383	0.008	0.065	0.063
Non-HDL-C							
AHI, events/h	0.094	0.041	0.013	0.176	0.023	0.053	0.051
$AHI_{NREM,}$ events/h	0.113	0.041	0.032	0.195	0.006	0.052	0.049
MeanSpO2, %	-1.065	0.331	-1.713	-0.416	0.001	0.055	0.052
ODI, events/h	0.126	0.048	0.031	0.22	0.009	0.054	0.051
T95, %	0.089	0.021	0.049	0.129	<0.001	0.057	0.055
REM stage, %	-0.228	0.102	-0.428	-0.028	0.025	0.051	0.049
REM latency, min	0.028	0.011	0.007	0.05	0.008	0.054	0.052
Sleep latency, min	0.08	0.031	0.02	0.141	0.009	0.054	0.052
AIP							
MeanSpO2, %	-0.026	0.006	-0.038	-0.015	<0.001	0.144	0.142
T95, %	0.002	0	0.001	0.003	<0.001	0.147	0.145
Sleep latency, min	0.002	0.001	0.001	0.003	<0.001	0.143	0.141
Time to fall asleep, min	0.001	0.001	0	0.003	0.02	0.143	0.14
AC							
AHI, events/h	0.004	0.002	0	0.007	0.023	0.146	0.144
$AHI_{NREM,}$ events/h	0.005	0.002	0.002	0.008	0.002	0.145	0.143
ODI, events/h	0.005	0.002	0.002	0.009	0.006	0.146	0.144
MeanSpO2, %	-0.047	0.013	-0.072	-0.022	<0.001	0.148	0.145
T95, %	0.004	0.001	0.003	0.006	<0.001	0.152	0.149
NREM1, %	-0.013	0.006	-0.025	-0.001	0.034	0.144	0.142
NREM3, %	0.005	0.002	0	0.009	0.045	0.144	0.142
Sleep latency, min	0.003	0.001	0.001	0.006	0.005	0.146	0.144

Adjustment for age (years), sex (male/female), race (white, black, and other races), smoking status (never/previous/current smoker), BMI (continuous, kg/m^2), and lipid-lowering medications (yes, or no)

Abbreviations: TC = total cholesterol; AHI = apnea-hypopnea index; AHI_{NREM} = apnea-hypopnea index during NREM sleep; ODI = oxygen desaturation index; MeanSpO2 = nocturnal mean oxygen saturation; MinSpO2 = lowest nocturnal oxygen saturation; T95 = percent total sleep duration with below 95% oxygen saturation; REM = rapid eye movement; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; NREM = non-REM sleep; TG = triglycerides; T90 = percent total sleep duration with below 90% oxygen saturation; Non-HDL-C = non-high-density lipoprotein cholesterol; AIP = atherogenic index of plasma; AC = atherogenic coefficient

correlations with TC and LDL-C levels [32]. Contrary to these findings, the present study demonstrates a positive relationship between REM latency and dyslipidemia while a negative correlation with the REM stage. This might be attributed to the influence of REM sleep on hormone production, such as cortisol and growth hormone, which in turn affects lipid metabolism [32].

The mediation analysis highlights the role of BMI as a mediator in the relationship between sleep traits and dyslipidemia. This finding suggests that BMI partially explains how sleep traits influence lipid profiles. Specifically, meanSpO2, T95, and REM percentage may affect dyslipidemia risk through their impact on BMI, revealing the intertwined nature of obesity, metabolic alterations, and OSA. Understanding BMI's mediating role underscores the importance of integrated approaches that address hypoxemia, sleep architecture disturbance, and weight management in reducing dyslipidemia risk among OSA patients. This mechanistic insight has important clinical implications, as demonstrated by a prior study [33] showing that combining effective weight loss strategies with CPAP therapy significantly reduces serum triglyceride levels compared to CPAP alone. These findings suggest that comprehensive treatment approaches incorporating both sleep improvement and weight management may be more effective than addressing either component alone. Future research should explore targeted interventions that simultaneously improve sleep traits and manage BMI to enhance cardiovascular health outcomes.

Strengths and limitations

The main strength of this study lies in its large sample size, which improves the reliability of the results regarding the association between sleep traits and dyslipidemia in patients with OSA. Additionally, this research is the first to systematically examine the connection between specific sleep traits and dyslipidemia in a community-based group of OSA patients. By identifying modifiable sleep traits associated with dyslipidemia, the study offers important insights for creating targeted interventions. These findings advocate for incorporating sleep improvement into OSA management strategies, emphasizing the potential to reduce metabolic risks related to the disorder through customized sleep interventions.

However, this study has several limitations. First, given the cross-sectional study design, reverse causality cannot be excluded. Future longitudinal observational studies, or experimental studies targeting sleep traits, are necessary to confirm the causal relationship between sleep traits and dyslipidemia in OSA patients. Second, the reliance on single-point measurements for both sleep traits and lipid profiles may not fully capture long-term or fluctuating patterns in sleep or lipid metabolism, given the variability in sleep traits [34, 35] and the sensitivity of lipid levels to dietary and medication influences. Future studies should consider implementing dynamic monitoring of both sleep traits and lipid profiles, while evaluating the impact of multiple-night PSG monitoring and sleep trait variability on dyslipidemia. Third, dietary habit may influence both sleep traits and lipid metabolism, and the DAG identifies it as a potential confounder. Due to the lack of dietary data, we are unable to adjust for this factor, and we recommend that future studies incorporate dietary assessments for a more comprehensive analysis. Fourth, dyslipidemia was defined as the presence of abnormal lipid concentrations or the use of lipid-lowering medication. Lipid-lowering medications might also be prescribed for conditions unrelated to dyslipidemia, such as neurological or anti-inflammatory purposes, potentially introducing bias. Future studies should aim to distinguish the underlying indications for lipid-lowering medication use to more accurately assess the burden of dyslipidemia. Lastly, while the community-based nature is a strength, concurrently, it poses a limitation as the specific population demographics and geographic location may not represent other populations [36], particularly those with different healthcare systems, environmental factors, and genetic backgrounds that could affect sleep traits and lipid profiles. Future studies should include more diverse populations to validate these findings.

In conclusion, our study provides preliminary evidence for the role of sleep latency, sleep architecture, and nocturnal hypoxemia in dyslipidemia among OSA patients. These findings suggest potential therapeutic targets beyond traditional CPAP therapy, including sleep hygiene optimization and enhanced monitoring of nocturnal oxygen saturation, which may help manage dyslipidemia in OSA patients. Nevertheless, further research is needed to validate these sleep traits as clinical markers for dyslipidemia risk assessment and intervention strategies in OSA management.

Abbreviations

OSA	Obstructive sleep apnea
BMI	Body mass index
REM	Rapid eye movement
T95	Percentage of time with oxygen saturation below 95%
IH	Intermittent hypoxia
CPAP	Continuous positive airway pressure
TC	Total cholesterol
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
SHHS	Sleep Heart Health Study
PSG	Polysomnography
T90	Percentage of time with SpO2 below 90%
ODI	Oxygen desaturation index
ESS	Epworth sleepiness scale
Non-HDL-C	Non-high-density lipoprotein cholesterol
AIP	Atherogenic index of plasma
AC	Atherogenic coefficient

DAG	Directed acyclic graph
XGBoost	eXtreme Gradient Boosting
SHAP	Shapley Additive explanation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03480-9.

Supplementary Material 1

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Author contributions
WLL: conceptualization, methodology, writing – original draft. GP: methodology, review. GXL: methodology, writing – review & editing, supervision.

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Data availability
The data utilized in this research are publicly available through the [Sleep Heart Health Study (SHHS)] at https://sleepdata.org/datasets/shhs.

Declarations

Ethics approval and consent to participate
Participants in the SHHS study gave written informed consent, and the study protocols were approved by the ethical review boards at the respective institutions.

Consent for publication
Not applicable.

Clinical trial number
Not applicable.

Competing interests
The authors declare no competing interests.

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