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ORIGINAL RESEARCH

A Prediction Nomogram of Severe Obstructive Sleep Apnea in Patients with Obesity Based on the Liver Stiffness and Abdominal Visceral Adipose Tissue Quantification

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Purpose: The diagnosis of severe OSA still relies on polysomnography, which causes a strong sense of restraint in patients with obesity. However, better prediction tools for severe OSA applicable to patients with obesity have not been developed.

Patients and Methods: Relevant clinical data of 1008 patients with OSA who underwent bariatric surgery in our hospital were collected retrospectively. Patients were divided into training and test cohorts by machine learning. Univariate and multivariate logistic regression analysis was used to screen associations, including liver stiff measurement (LSM) and abdominal visceral tissue (aVAT), and to construct a severe OSA risk prediction nomogram. Then, we evaluated the effectiveness of our model and compared our model with the traditional Epworth Sleepiness Scale (ESS) model. Finally, our associations were used to explore the correlation with other indicators of OSA severity.

Results: Our study revealed that age, biological sex, BMI, LSM, aVAT, and LDL were independent risk factors for severe OSA in patients with obesity. A severe OSA risk prediction nomogram constructed by six indicators possessed high AUC (0.845), accuracy (77.6%), and relatively balanced specificity and sensitivity (72.4%, 82.8%). The Hosmer-Lemeshow test (P=0.296, 0.785), calibration curves, and DCA of the training and test cohorts suggested better calibration and more net clinical benefit. Compared with the traditional ESS model, our model had higher AUC (0.829 vs 0.545), sensitivity (78.9% vs 12.2%), PPV (77.9% vs 53.3%), and accuracy (75.4% vs 55.2%). In addition, the associations in our model were independently correlated with other indicators reflecting OSA severity.

Conclusion: We provided a simple, cheap, and non-invasive nomogram of severe OSA risk prediction for patients with obesity, which would be helpful for preventing further complications associated with severe OSA.

Plain Language Summary:

Question: Can we predict severe OSA in patients with obesity by their metabolic complications through some non-invasive examinations?

Findings: Compared with traditional questionnaires, we developed and validated a new prediction model, including liver stiffness measurement and abdominal visceral adipose tissue, to screen severe OSA in bariatric surgery candidates through non-invasive examinations, which may contribute to perioperative safety and ultimate weight loss outcomes.

Meaning: For patients with obesity who are in hospital because of metabolic disorders, it is necessary for them to be screened for possible severe OSA according to our new prediction nomogram, which is helpful for preventing further complications and perioperative risk associated with severe OSA.

Keywords: obstructive sleep apnea, obesity, liver stiffness measurement, visceral adipose tissue, nomogram

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Introduction

Obstructive Sleep Apnea (OSA) is a common sleep-breathing disorder recognized as a major public health problem.[1–3] As an important pathophysiological feature of OSA, frequent hypoxia and microarousals can cause a range of symptoms, including daytime sleepiness, fatigue, and decreased concentration, which severely affect daily life.[4,5] Several studies have found that severe OSA (AHI ≥30) is even more harmful to the health, resulting in multiple organ dysfunctions, such as cardiovascular, endocrine, and nervous system.[6–8] Therefore, early diagnosis and prompt treatment are crucial for patients with severe OSA.[3,9]

Obesity, one of the cardinal risk factors for OSA, shows a linear correlation with the incidence of severe OSA.[10,11] Moreover, abdominal visceral adipose tissue (aVAT) accumulation caused by obesity has a more severe impact on the risk of OSA, which is closely related to the decrease of total lung capacity and functional residual capacity, reduction of traction to the pharynx, and exacerbation of pharyngeal collapse.[12] Therefore, increasing literature suggests that aVAT is a critical factor in assessing OSA risk.[13–16]

A growing number of studies have demonstrated that OSA is an independent risk factor for various metabolic diseases, including nonalcoholic fatty liver disease (NAFLD).[8,13,17] Numerous investigations have revealed that OSA is closely related to the progression of NAFLD in terms of histology, radiology, and biomarkers, which may result from chronic hypoxia induced by OSA.[5,18–21] Thus, NAFLD may play a crucial role in early risk screening for OSA patients with obesity. The Liver biopsy is often used to evaluate the liver fibrosis affecting the progress of NAFLD.[21,22] However, it cannot be used for large-scale and extensive screening because of its invasiveness.[22,23] Currently, non-invasive screening tools, including transient elastography primarily based on ultrasonography and assessing the grade of liver fibrosis and steatosis by liver stiffness measurement (LSM) and controlled attenuation parameter (CAP), have been applied to diagnose liver diseases.[24,25]

Nowadays, it is widely acknowledged that Polysomnography (PSG), the gold standard for OSA diagnosis, has a high detection rate.[26] Nevertheless, due to its limitations, such as complicated operation, high cost, and poor patient compliance,[27] PSG is still not conducive to large-scale application, especially for patients with obesity, who may find it more difficult to tolerate the sense of restraint brought by the machine. As one study has shown, even in developed countries, there are still many suspected OSA patients who are under-diagnosed because of the inability to perform timely PSG tests.[28] Hence, it is necessary to develop a more acceptable detection method. Patients with OSA and obesity may be prone to have more severe liver fibrosis and aVAT accumulation.[15,16,23,29] However, no study has combined them to predict the severity of OSA in patients with obesity. Consequently, in this cross-sectional study, we incorporated a series of crucial clinical indicators, including aVAT and LSM, to construct a prediction model for severe OSA in patients with obesity and compared it with the traditional Epworth Sleepiness Scale (ESS) questionnaire, aiming to develop a more acceptable detection method for primary screening in patients with obesity suspected of severe OSA as early as possible and to prevent the further development of its complications.

Material and Methods

Study Design and Population

Our study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University [2024026K], and its procedures comply with the Declaration of Helsinki. 1544 patients who underwent bariatric surgery in the Bariatric and Metabolic Disease Surgery Center of Zhongnan Hospital of Wuhan University from September 2020 to November 2023 were initially included in our study. Then, 536 patients were excluded from our series: (1) history of OSA, (2) lack of PSG (n=307), related laboratory (n=25) and imaging examinations (n=178), (3) history of excessive alcohol consumption (n=18), (4) previous diagnosis of viral hepatitis and liver cancer (n=8). Finally, 1008 patients were enrolled in our study (Figure 1). According to machine learning, the data set was divided into a training cohort and a test cohort. Before the start of the study, all eligible participants signed an informed consent form.

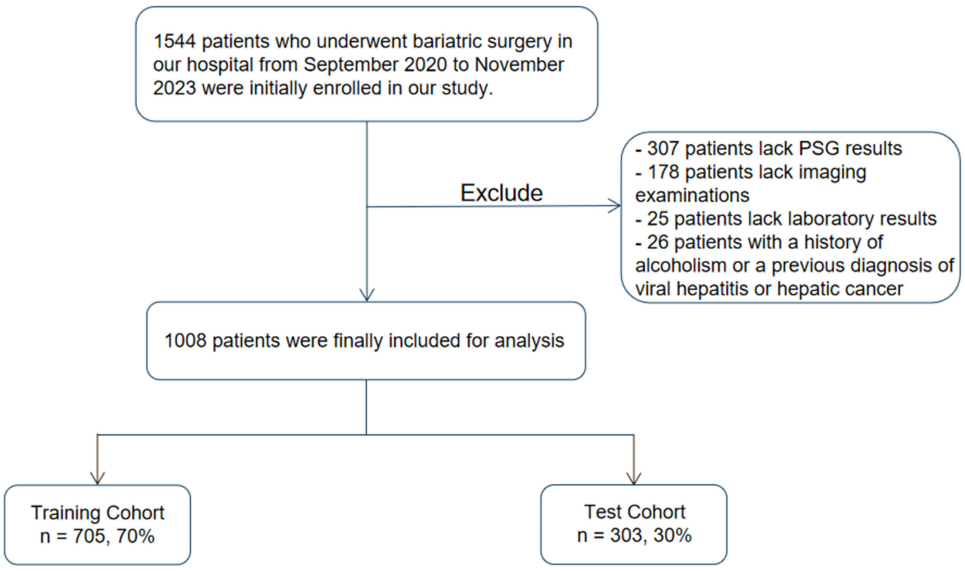

Figure 1 Study flow diagram for patient selection.

Patients' Characteristics and Laboratory Examinations

The baseline characteristics, including biological sex, age, BMI, waist circumference, comorbidity, as well as related laboratory examinations, were collected by three main researchers. The BMI was divided into obesity groups above and below class III based on a 37.4 kg/m^2 cutoff, according to the World Health Organization recommendations for Asian populations.[30] Diabetes mellitus was defined as fasting plasma glucose ≥7.0 mmol/L or two-hour postprandial plasma glucose ≥11.1 mmol/L. Hyperuricemia was defined as two fasting blood uric acid levels ≥420μmol/L, which were not measured on the same day. As for laboratory examinations, LDL ≥4.14mmol/L was considered elevated, and HOMA-IR was calculated as fasting plasma glucose × fasting insulin /22.5, with the value >1 suggesting the presence of insulin resistance.

Liver Stiffness Measurement

The liver stiffness of all patients who were asked to fast before examinations was measured by FibroScan, which is equipped with a standard M probe. An experienced nurse operated the machine and recorded the ten valid measurements.[31] The final results of LSM and CAP were the median of these ten valid measurements. Less than ten valid measurements or a ratio of interquartile range/median of LSM or CAP >0.3 were considered invalid data.[32,33] Previous research had shown that LSM >12.4 kpa suggested severe liver fibrosis or even cirrhosis, while CAP >296 dB/m suggested severe hepatic steatosis.[34] Considering that the included patients were all obese and may themselves suffer from hepatic steatosis to some extent, we took the cutoff values of LSM and CAP at 12.4 kpa and 296 dB/m.

Abdominal Visceral Adipose Tissue Quantification

We used MRI to scan the patient's abdominal fat at the L4 level, followed by the quantitative analysis of the corresponding areas through ImageJ software (Version 1.53k). The area of aVAT exhibited in cm^2 was calculated by three main researchers, and the error among the three was guaranteed to be within 10%.

Polysomnography

All patients underwent overnight PSG (within one week of LSM), which was performed at our Sleep Medicine Center. Sleep and breathing parameters were recorded by Embletta Gold software (Embla Systems, Inc., Broomfield, CO, USA) and assessed by two experienced polysomnographic technologists based on the standard criteria. The apnea hypopnea index (AHI), defined as the sum of apnea and hypopnea events per hour in sleep, was the most critical parameter of OSA

severity. Patients with AHI ≥30 could be diagnosed with severe OSA. The oxygen desaturation index (ODI) represented the 4% decrease in SpO_2 per hour during sleep. The ratio of the time of minimum oxygen saturation <90% during sleep to the total sleep time was defined as $T_{90\%}$, and the lowest oxygen saturation during sleep was expressed as SpO_{2low}. Previous studies indicated that $T_{90\%}$ >10%, SpO_{2low} <80%, and ODI >29 were strongly associated with the incidence of postoperative complications in patients who underwent general surgery.[35] Moreover, the microarousal index (MAI), an unconscious awakening during sleep, also reflected the severity of OSA to some extent.

Statistical Analysis

The pmsampsize package in R (version 4.3.1) was used to estimate the sample size for our study. The method of dividing the training set and test set was based on the Holdout validation method of random sampling by using R. The detailed steps were as follows: the dataset "data" was divided into a training set "train" and a test set "test" using the "train_test_split" function, where the test set accounted for 30% of the total data ("test_size=0.3_1008"). The randomness of the partitioning was ensured to be reproducible by setting "random_state=0". Features and labels were then extracted from the training and test sets, respectively. The Holdout validation method divided the dataset into two non-overlapping subsets, one for training the model (training set) and the other for evaluating the model (test set).

All continuous numerical variables, considered not satisfying the normal distribution through the Kolmogorov–Smirnov test, were described as median (P25, P75) and analyzed by the Mann–Whitney *U*-test. As for categorical variables, they were expressed as percentages and analyzed by Chi-square test. To ensure that the independent variables could satisfy the conditions of the binary logistic regression model, the BoxTidwell test was applied to verify that there was a linear relationship between the logit transformed values of the dependent variables and independent variables. Besides that, the variance inflation factor (VIF) was used to detect the presence of multicollinearity among independent variables. Regarding model construction, we successively used univariate and multivariate logistic regression analysis and then developed a severe OSA risk nomogram by R.

For model evaluation, the area under the receiver operator characteristic (ROC) curve (AUC), specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the model were calculated by R. The consistency of the predictive model with the actual incidence of severe OSA was assessed by drawing calibration curves and performing the Hosmer–Lemeshow test. The decision curve analysis (DCA) was constructed to reflect the net benefit in making clinical decisions according to the model. What is more, the effectiveness of the model was validated by bootstrapping with 1000 resamples.

The relevant statistical results were expressed as odds ratio (OR) and 95% confidence interval (CI), and a two-tailed P <0.05 suggested that the difference was considered statistically significant.

Results

Baseline Characteristics of Patients in the Training Cohort and Test Cohort

The clinical characteristics of all patients were as follows: 496 patients were diagnosed with severe OSA. In the series of cases, the vast majority of patients were women, and the median age of all patients was 33 years old. Using the recommendations by the World Health Organization for Asian populations,[30] there were 439 patients defined as class III and higher obesity. 35.7% of patients with LSM ≥12.4 kpa, and the median area of aVAT was 173.27 cm^2. Detailed clinical information, including demographics, comorbidities, and relevant laboratory tests, was shown in Table 1, with no statistically significant differences between the training cohort and test cohort except for HOMA-IR. Based on sample size estimation, we included more samples (705 samples) than the minimum required sample size (381 samples).

Data Processing

Before developing the model, we adjusted some of the clinical data. Given that the continuous variable LDL was not linearly associated with the risk of severe OSA, we converted LDL to a categorical variable for subsequent analyses (eTable 1). In addition, AST was excluded due to multicollinearity with ALT (eTable 2).

Table 1 Baseline Characteristics of the 1008 Patients in the Training Cohort and Test Cohort

Variables	All Patients	Training Cohort	Test Cohort	*P*-Value
Biological sex, n (%)				0.646[a]
Male	239 (23.7%)	170 (24.1%)	69 (22.8%)	
Female	769 (76.3%)	535 (75.9%)	234 (77.2%)	
Age, years, median (P25–P75)	33 (28–38)	33 (28–38)	33 (28–37)	0.597[b]
BMI, n (%)				0.270[a]
≤37.4 kg/m^2	569 (56.5%)	390 (55.3%)	179 (59.1%)	
>37.4 kg/m^2	439 (43.5%)	315 (44.7%)	124 (40.9%)	
Waist circumference, cm, median (P25–P75)	115 (106–126)	115 (107–125)	115 (106–127)	0.744[b]
Comorbidity, n (%)				
Diabetes mellitus	308 (30.6%)	228 (32.3%)	80 (26.4%)	0.061[a]
Hyperuricemia	543 (53.9%)	371 (52.6%)	172 (56.8%)	0.226[a]
Polysomnography				
AHI, n (%)				0.574[a]
<30	512 (50.8%)	354 (50.2%)	158 (52.1%)	
≥30	496 (49.2%)	351 (49.8%)	145 (47.9%)	
Image examinations				
LSM, n (%)				0.798[a]
<12.4 kpa	648 (64.3%)	455 (64.6%)	193 (63.7%)	
≥12.4 kpa	360 (35.7%)	250 (35.4%)	110 (36.3%)	
CAP, n (%)				0.347[a]
≤296 dB/m	87 (8.6%)	57 (8.1%)	30 (9.9%)	
>296 dB/m	921 (91.4%)	648 (91.9%)	273 (90.1%)	
aVAT, cm^2, median (P25-P75)	173.27 (132.00–239.50)	172.93 (133.00–235.62)	174.25 (129.23–247.71)	0.695[b]
Laboratory examinations				
ALT, U/L, median (P25-P75)	34.50 (21.50–64.00)	35.00 (21.00–63.00)	34.00 (22.50–66.00)	0.373[b]
AST, U/L, median (P25-P75)	25.00 (18.00–39.00)	24.00 (17.00–39.00)	25.00 (19.00–39.00)	0.194[b]
γ-GGT, U/L, median (P25-P75)	34.00 (23.00–57.00)	34.00 (23.00–57.00)	35.00 (23.00–55.50)	0.763[b]
ALP, U/L, median (P25-P75)	77.00 (65.00–91.00)	78.00 (65.00–91.00)	77.00 (65.00–91.00)	0.994[b]
TBIL, umol/L, median (P25-P75)	12.10 (9.70–15.70)	12.00 (9.70–15.50)	12.30 (9.70–16.30)	0.364[b]
TC, mmol/L, median (P25-P75)	4.93 (4.39–5.57)	4.97 (4.41–5.60)	4.81 (4.34–5.51)	0.240[b]
TG, mmol/L, median (P25-P75)	1.69 (1.25–2.37)	1.70 (1.25–2.45)	1.67 (1.25–2.29)	0.594[b]
HDL, mmol/L, median (P25-P75)	1.06 (0.93–1.22)	1.06 (0.93–1.23)	1.06 (0.92–1.21)	0.967[b]
LDL, mmol/L, median (P25-P75)	3.18 (2.72–3.73)	3.20 (2.73–3.74)	3.13 (2.69–3.72)	0.304[b]
FFA, umol/L, median (P25-P75)	550.20 (417.50–711.80)	553.70 (415.10–714.10)	546.40 (424.10–701.90)	0.735[b]
HOMA-IR, median (P25-P75)	6.01 (4.12–9.11)	6.28 (4.20–9.60)	5.57 (3.96–8.39)	0.011[b]

Notes: [a]Chi-square test, [b]mann–Whitney *U*-test.

Abbreviations: BMI, body mass index; LSM, liver stiffness measurement; CAP, controlled attenuation parameter; aVAT, abdominal visceral adipose tissue; ALT, alanine aminotransferase; AST, aspartate aminotransferase; γ-GGT, γ-glutamyl -transpeptidase; ALP, Alkaline phosphatase; TBIL, Total bilirubin; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; FFA, free fatty acids; HOMA-IR, homeostasis model assessment insulin resistant.

Associations and Models of Severe OSA

Firstly, we performed a univariate logistic regression analysis of possible risk factors (eTable 3), revealing that TBIL and FFA had no statistically significant differences between severe OSA and non-severe OSA groups (P=0.118 and 0.205, respectively). Subsequently, risk factors other than TBIL and FFA were included in multivariate logistic regression analyses (Table 2). The result suggested that male (P<0.001, OR 3.495, 95% CI 1.997–6.116), age (P<0.001, OR 1.103, 95% CI 1.070–1.138), BMI ≥37.4 kg/m^2 (P=0.003, OR 2.152, 95% CI 1.288–3.597), LSM ≥12.4 kpa (P=0.002, OR 1.976, 95% CI 1.295–3.015), aVAT (P<0.001, OR 1.007, 95% CI 1.004–1.011) and LDL ≥4.14 mmol/L (P=0.034, OR 2.164, 95% CI 1.061–4.416) were independent risk factors for patients with obesity combined with severe OSA.

Different combinations of these risk factors were used to analyze their efficiency and determine whether combined multifactors had more predictive value than single factors (Table 3). Although the prediction model combining the six

Table 2 General Characteristics of the Patients and Multivariate Logistic Regression Analyses for Screening Associations

Variables	Non-Severe OSA (n = 354)	Severe OSA (n = 351)	*P*-Value	OR	OR 95% CI	
Biological sex, n (%)			<0.001[a]	3.495	1.997	6.116
Male	30 (8.48%)	140 (39.89%)				
Female	324 (91.52%)	211 (60.11%)				
Age, years, median (P25-P75)	31 (26–37)	34 (30–40)	<0.001[b]	1.103	1.070	1.138
BMI, n (%)			0.003[a]	2.152	1.288	3.597
≤37.4 kg/m^2	251 (70.90%)	139 (39.60%)				
>37.4 kg/m^2	103 (29.10%)	212 (60.40%)				
Waist circumference, cm, median (P25–P75)	110 (103–120)	120 (112–129)	0.581[b]	1.006	0.984	1.029
Comorbidity, n (%)						
Diabetes mellitus	82 (23.16%)	146 (41.60%)	0.316[a]	1.258	0.803	1.971
Hyperuricemia	147 (41.53%)	224 (63.82%)	0.064[a]	1.471	0.978	2.213
Image examinations						
LSM, n (%)			0.002[a]	1.976	1.295	3.015
<12.4 kpa	281 (79.38%)	174 (49.57%)				
≥12.4 kpa	73 (20.62%)	177 (50.43%)				
CAP, n (%)			0.398[a]	1.409	0.636	3.123
≤296 dB/m	46 (12.99%)	11 (3.13%)				
>296 dB/m	308 (87.01%)	340 (96.87%)				
aVAT, cm^2, median (P25–P75)	145.66, (113.68–178.00)	217.81, (166.19–290.68)	<0.001[b]	1.007	1.004	1.011
Laboratory examinations						
ALT, U/L, median (P25-P75)	28 (18–52)	44 (26–76)	0.783[b]	1.001	0.995	1.006
γ-GGT, U/L, median (P25-P75)	29 (20–45)	41 (28–63)	0.879[b]	0.999	0.992	1.007
ALP, U/L, median (P25-P75)	75 (64–88)	80 (69–95)	0.732[b]	1.002	0.992	1.011
TC, mmol/L, median (P25-P75)	4.90 (4.35–5.36)	5.09 (4.46–5.84)	0.916[b]	1.016	0.757	1.363
TG, mmol/L, median (P25-P75)	1.53 (1.13–2.10)	1.91 (1.42–2.70)	0.971[b]	1.003	0.837	1.202
HDL, mmol/L, median (P25–P75)	1.10 (0.97–1.28)	1.02 (0.90–1.16)	0.434[b]	0.667	0.242	1.840
Elevated LDL, n (%)			0.034[a]	2.164	1.061	4.416
<4.14 mmol/L	321 (90.68%)	287 (81.77%)				
≥4.14 mmol/L	33 (9.32%)	64 (18.23%)				
HOMA-IR, median (P25-P75)	5.36 (3.54–8.08)	7.45 (5.00–10.94)	0.099[b]	1.036	0.993	1.080

Notes: [a]Chi-square test, [b]mann–Whitney *U*-test.

Abbreviations: OSA, obstructive sleep apnea; CI, confidence interval; OR, odds ratio; BMI, body mass index; LSM, liver stiffness measurement; CAP, controlled attenuation parameter; aVAT, abdominal visceral adipose tissue; ALT, alanine aminotransferase; γ-GGT, γ-glutamyl transpeptidase; ALP, Alkaline phosphatase; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA-IR, homeostasis model assessment insulin resistant.

risk factors could be more optimal in some statistical metrics, its overall efficiency was at the balanced level among all models. The model's AUC, sensitivity, specificity, PPV, NPV, and accuracy were 0.845, 72.4%, 82.8%, 80.6%, 75.1%, and 77.6%, respectively.

Construction of Risk Prediction Nomogram

To this end, we constructed simple multivariate logistic regression models based on the six statistically significant risk factors mentioned above (eTable 4). In order to make it easier for physicians to visualize the magnitude of the role of risk factors, the risk prediction nomogram was developed for use in clinical practice (Figure 2). As shown in the nomogram, each risk factor was assigned a corresponding score, and the total score obtained by summing these scores reflected the likelihood that a patient with obesity would suffer from severe OSA. If a male patient, aged 50, with BMI ≥ 37.4 kg/m^2, LSM ≥ 12.4 kpa, LDL ≥ 4.14 mmol/L, had the aVAT area of 250 cm^2, then these factors would be assigned scores of 24, 60, 13, 39, 15, and 13, respectively. The total of the above scores is 164, which indicates that the patient had a greater than 90% chance of suffering from severe OSA.

Table 3 Different Combinations of Six Associations for Severe OSA Prediction

Models	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy
Model A	0.803 (0.771–0.835)	64.7%	83.3%	79.4%	70.4%	74.0%
Model B	0.821 (0.790–0.851)	71.8%	79.9%	78.0%	74.1%	75.9%
Model C	0.834 (0.804–0.863)	70.4%	83.1%	80.5%	73.9%	76.7%
Model D	0.810 (0.779–0.842)	64.1%	85.0%	80.9%	70.5%	74.6%
Model E	0.841 (0.813–0.870)	68.4%	86.2%	83.0%	73.3%	77.3%
Model F	0.838 (0.809–0.867)	74.6%	79.4%	78.2%	75.9%	77.0%
Model G	0.827 (0.797–0.857)	72.9%	78.0%	76.6%	74.4%	75.5%
Model H	0.845 (0.817–0.873)	72.4%	82.8%	80.6%	75.1%	77.6%

Notes: Model A: combine gender, age and BMI; Model B: combine model A and LSM; Model C: combine model A and aVAT; Model D: combine model A and Elevated LDL; Model E: combine model A, LSM and aVAT; Model F: combine model A, aVAT and Elevated LDL; Model G: combine model A, LSM and Elevated LDL; Model H: combine model A, LSM, aVAT and Elevated LDL.

Abbreviations: OSA, obstructive sleep apnea; CI, confidence interval; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; BMI, body mass index; LSM, liver stiffness measurement; aVAT, abdominal adipose tissue; LDL, low density lipoprotein.

Model Evaluation

As for the training cohort, the AUC was 0.845 (95% CI 0.817–0.873) (Figure 3A), and the model had a high goodness of fit according to Hosmer–Lemeshow test (P=0.296). The calibration curve revealed high agreement between the predicted and actual probability of occurrence of severe OSA in patients with obesity (Figure 4A). The DCA indicated that our

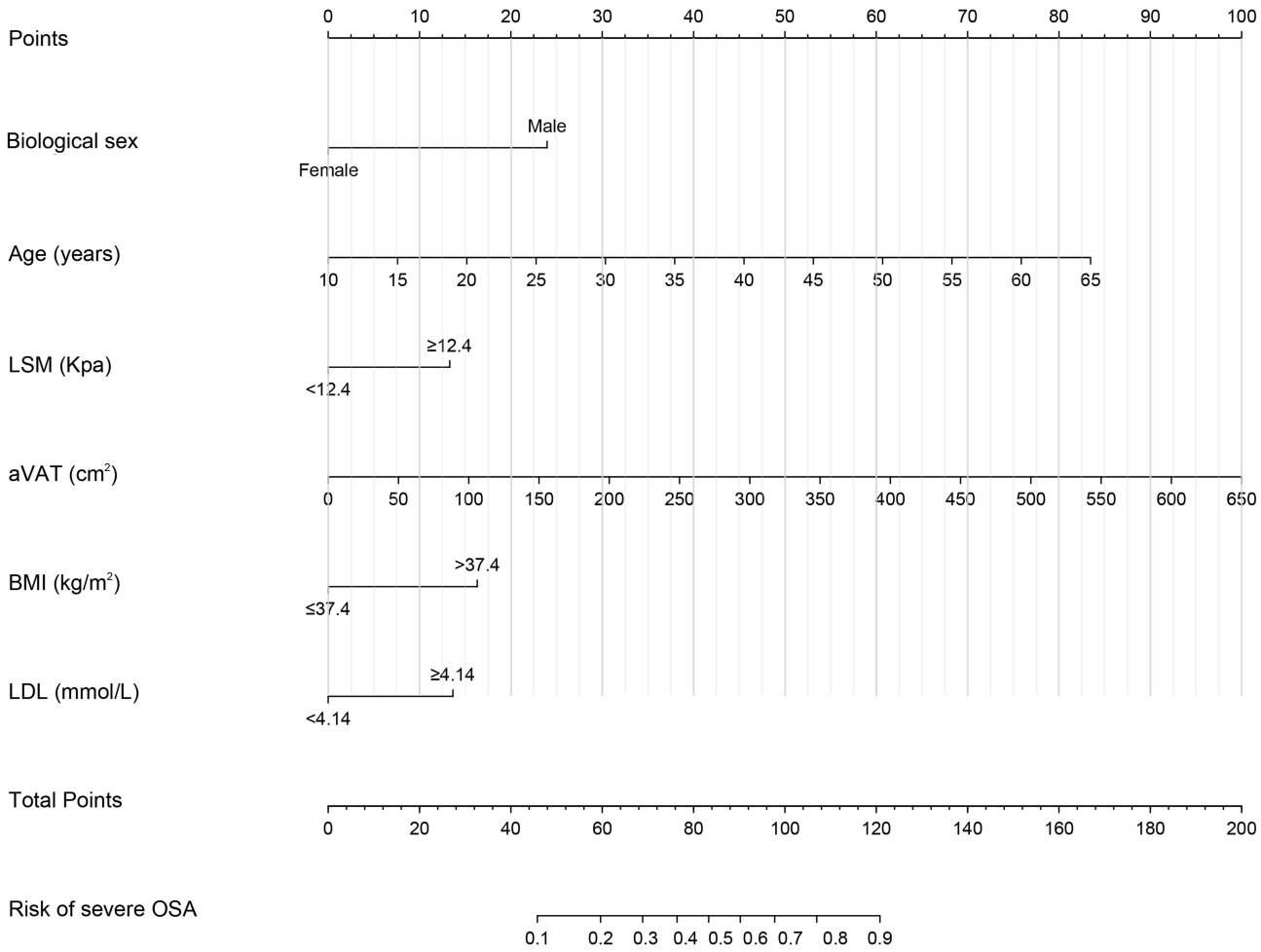

Figure 2 A severe OSA risk prediction nomogram.

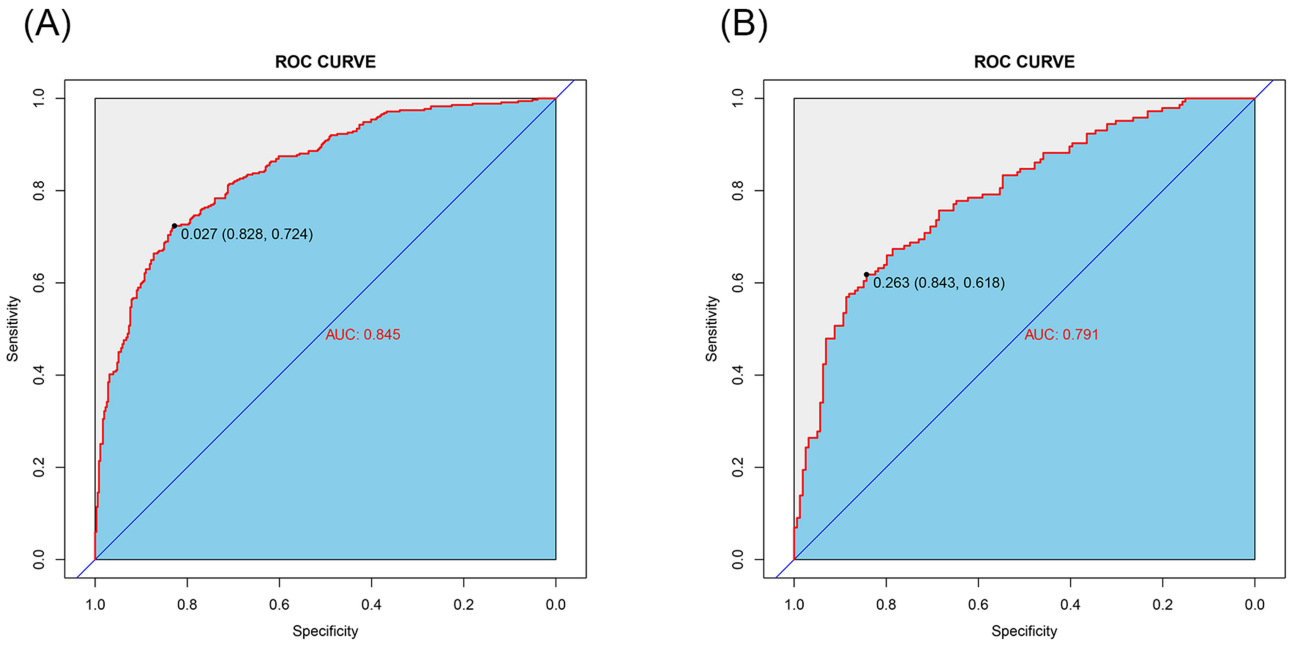

Figure 3 ROC curves of the training cohort (**A**) and test cohort (**B**).

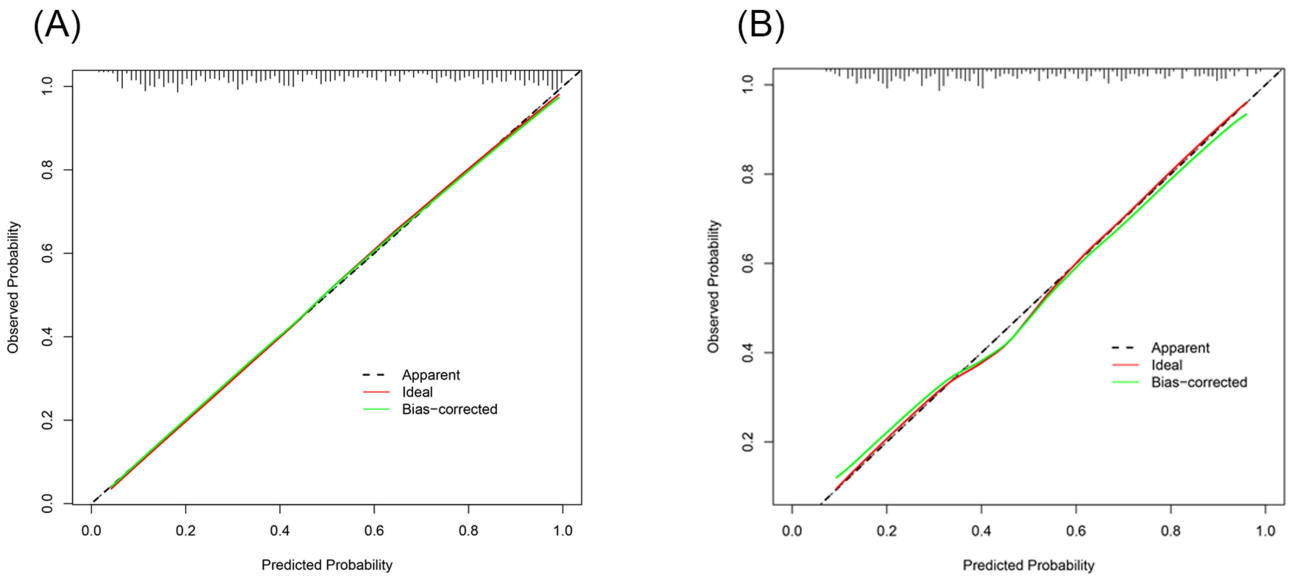

Figure 4 The calibration curves of the training cohort (**A**) and test cohort (**B**).

predictive model led to better net clinical benefits for patients (Figure 5A). In the test cohort, the AUC was 0.791 (95% CI 0.741–0.842) (Figure 3B), and the Hosmer–Lemeshow test suggested that the model had high goodness of fit (P=0.785). Furthermore, the calibration curve (Figure 4B) and DCA (Figure 5B) had well outcomes similar to the training cohort.

Comparison with the ESS

Epworth Sleep Scale, a classic screening tool to assess daytime sleepiness, can also be used to screen for OSA, even though its efficiency is not optimal. The ESS score >16 tends to represent severe OSA.[36] Hence, 183 patients with ESS scores were included to construct the ESS model and our new model (Table 4) (Figure 6A and B). The AUC, sensitivity,

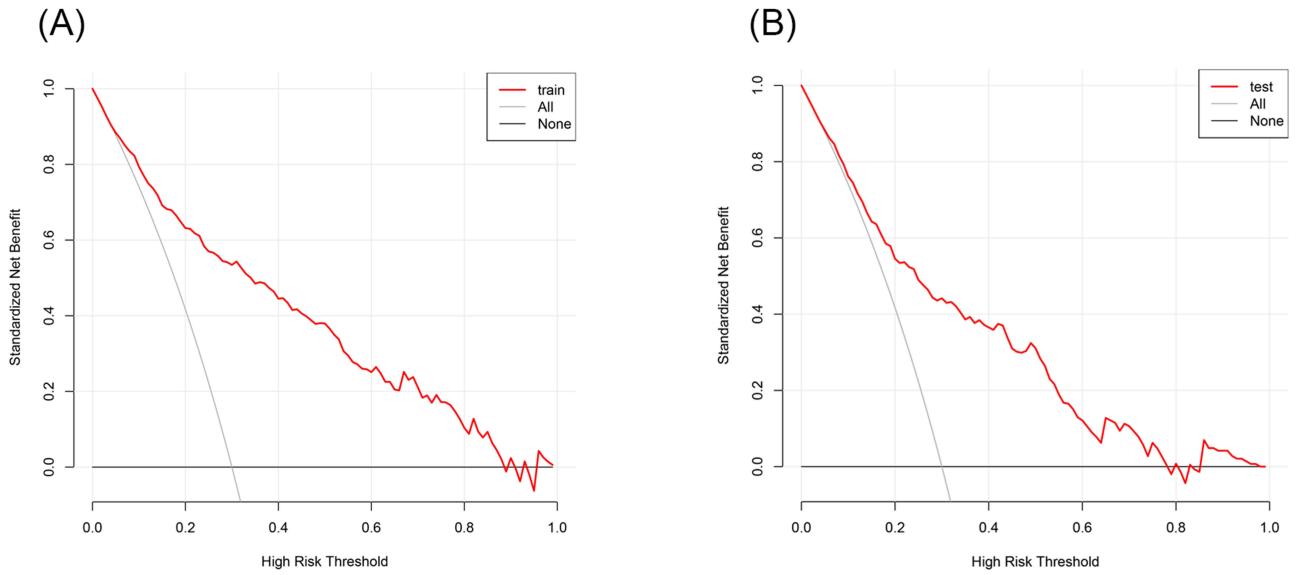

Figure 5 The decision curve analysis of the training cohort (**A**) and test cohort (**B**).

specificity, PPV, NPV, and accuracy of the ESS model and our new model were 0.545, 12.2%, 96.8%, 78.6%, 53.3%, 55.2% vs 0.829, 78.9%, 72.0%, 73.2%, 77.9%, 75.4%. Although our new model was not as good as the ESS model in terms of specificity and PPV, its overall efficiency was still much better than the ESS model.

The Relationship Between Associations and Other Indicators of OSA Severity

Although the gold standard for determining the severity of OSA is AHI, some of the respiratory parameters, including ODI, $SpO2_{Low}$, and $T_{90\%}$, as well as the sleep parameters, including MAI, also reflect the severity of OSA to some extent. Therefore, we performed a multivariate logistic regression analysis of the above six associations with these four indicators of OSA severity (Table 5). With the exception of LDL, the other five associations were independent risk factors for each of these four indicators of OSA severity, which revealed that the associations of our model were universally applicable to predicting the occurrence of severe OSA.

Discussion

In our study, 49.2% of patients were accidentally diagnosed with severe OSA when they decided to undergo bariatric surgery. This means that the vast majority of people with obesity in China are not aware that they may suffer from severe OSA. Considering the lack of accessibility of PSG globally, we included cheap, convenient, and noninvasive associations such as LSM and aVAT to construct a prediction model for severe OSA in patients with obesity and a more intuitive nomogram for clinical application. Overall, our model has better performance, goodness of fit, and more clinical benefit.

In fact, this is the first study to combine LSM and aVAT to predict severe OSA, although previous studies have analyzed the correlation between these two associations and OSA separately.[23,37,38] In our study, we included six associations, including LSM and aVAT area, to predict severe OSA in patients with obesity. Then, we constructed the

Table 4 Comparison of the Effectiveness of Two Models in Predicting Severe OSA

Model Characteristics	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
ESS (n = 183)	0.545 (0.506–0.583)	12.2% (5.5%–19.0%)	96.8% (93.2%–100%)	78.6% (57.1%–100%)	53.3% (45.7%–60.8%)	55.2% (54.9%–55.5%)
The new model (n = 183)	0.829 (0.770–0.887)	78.9% (70.5%–87.3%)	72.0% (62.9%–81.2%)	73.2% (64.4%–82.0%)	77.9% (69.1%–86.7%)	75.4% (75.2%–75.6%)

Abbreviations: OSA, obstructive sleep apnea; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value.

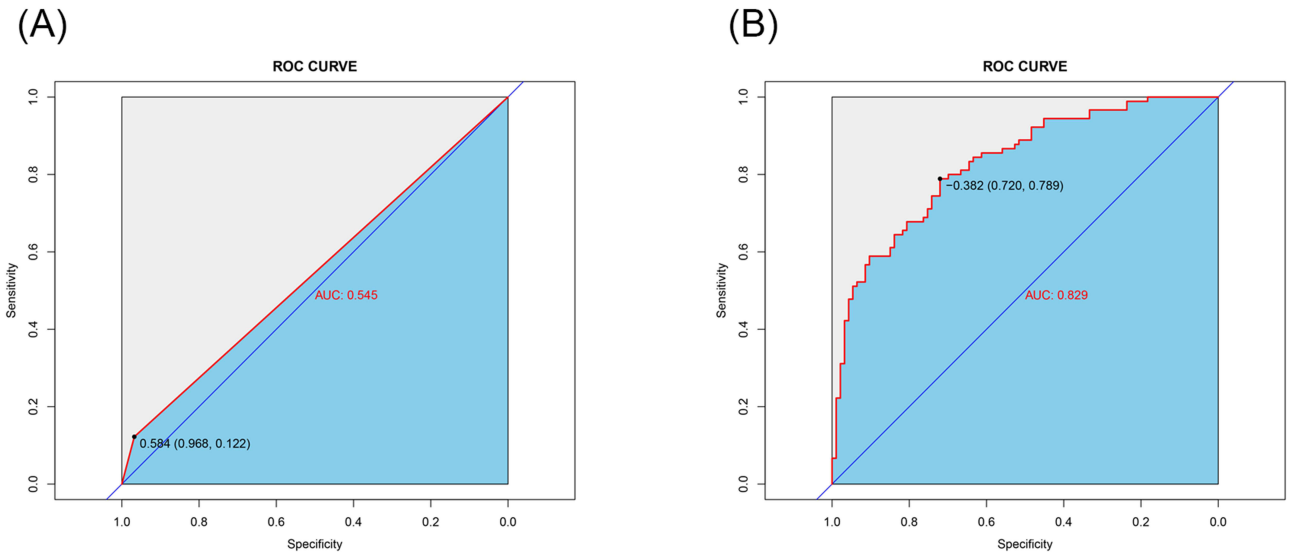

Figure 6 ROC curves of the ESS model (**A**) and our model (**B**).

model with different combinations of these six associations. Although the final model, including biological sex, age, BMI, LSM, aVAT, and LDL, was not optimal in terms of sensitivity, specificity, PPV and NPV, the overall effectiveness was relatively stable (AUC: 0.845, Accuracy: 77.6%), which was better than a previous study that applied liver stiffness associations including HSI and CAP alone to predict OSA (AUC: 0.75).[39] In our model, due to the lack of appropriate categorization criteria, aVAT and age were not converted into categorical variables, which led to their low OR (1.009 and 1.093, respectively). However, this did not mean that these two associations were of less clinical significance. The risk for severe OSA would increase by approximately 50% for every 5-year increase in age or 50 cm^2 increase in aVAT area. Meanwhile, we constructed a severe OSA prediction nomogram for clinical application and found the high AUC (0.845), better calibration, and more net clinical benefits of the risk prediction nomogram. Moreover, our internal validation data similarly reflected good model effectiveness and clinical decision value.

Table 5 The Relationship Between Our Associations and Other Indicators of OSA Severity

Variables	ODI > 30		SpO_{2Low} < 80%		T_{90}% > 10%		MAI > 21.4	
	P-Value	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value	OR (95% CI)
Biological sex	<0.001[a]	3.494 (2.186–5.584)	<0.001	2.959 (1.838–4.764)	<0.001[a]	3.941 (2.514–6.177)	<0.001[a]	3.400 (2.142–5.399)
Age	<0.001[b]	1.060 (1.033–1.088)	<0.001	1.056 (1.030–1.083)	0.002	1.040 (1.014–1.068)	<0.001	1.074 (1.048–1.101)
BMI	<0.001[a]	2.536 (1.699–3.787)	<0.001	2.510 (1.709–3.688)	<0.001[a]	3.147 (2.089–4.740)	0.009[a]	1.656 (1.135–2.417)
LSM	0.002[a]	1.846 (1.247–2.731)	0.013	1.625 (1.107–2.386)	0.018[a]	1.611 (1.084–2.395)	0.008[a]	1.659 (1.142–2.411)
aVAT	<0.001[b]	1.009 (1.006–1.012)	<0.001	1.008 (1.005–1.011)	<0.001[b]	1.008 (1.005–1.011)	<0.001[b]	1.005 (1.002–1.007)
Elevated LDL	0.078[a]	1.593 (0.949–2.672)	0.105	1.516 (0.917–2.507)	0.409[a]	1.215 (0.735–2.130)	0.022[a]	1.764 (1.085–2.867)

Notes: [a]Chi-square test, [b]mann–Whitney *U*-test.

Abbreviations: OSA, obstructive sleep apnea; CI, confidence interval; OR, odds ratio; ODI, oxygen desaturation index; T_{90}%, the percentage of total recording sleep time with oxygen saturation<90%; MAI, microarousal index; SpO_{2Low}, minimum oxygen saturation; BMI, body mass index; LSM, liver stiffness measurement; aVAT, abdominal visceral adipose tissue; LDL, low-density lipoprotein.

Table 6 Literature on the Prediction of Severe OSA by the STOP-BANG Questionnaire

Literature	Year	Cases	AUC	Sensitivity	Specificity
Chiu et al[40]	2017	15,503	/	93%	35%
Zheng et al[41]	2022	1671	0.712	86%	35%
Hwang et al[42]	2022	6419	0.630	90%	27%
Waseem et al[43]	2021	666	0.756	96%	18%
Singh et al[44]	2022	200	0.760	91%	36%
Tan et al[45]	2016	242	0.682	69%	67%
Sangkum et al[46]	2017	208	0.776	98%	9%
Luo et al[47]	2014	212	0.751	98%	18%
Nagappa et al[48]	2015	3175	0.720	96%	25%

Abbreviations: OSA, obstructive sleep apnea; AUC, area under the curve.

Although the ESS questionnaire is considered one of the traditional tools for screening for OSA, its effectiveness could be more satisfactory.[36] In our study, clinical information on 183 patients with ESS scores was collected to compare the ESS questionnaire with our new model. As a result, our new model was much better at predicting severe OSA than the traditional ESS model (AUC: 0.829 and 0.545, sensitivity: 78.9% and 12.2%, NPV: 77.9% and 53.3%, Accuracy: 75.4% vs 55.2%). Moreover, several studies about predicting severe OSA using the STOP-BANG questionnaire were listed in Table 6.[40–48] High sensitivity (85.7%–98.3%) and low specificity (9.4%–67.1%) were reported in these studies, which indicates that many non-severe OSA patients were misdiagnosed. In contrast, while we did not directly compare our model to the STOP-BANG questionnaire, our model had a more balanced sensitivity (72.4%) and specificity (82.8%) than the results reported in the literature. The AUC of our model (0.845) is also better than that of the STOP-BANG questionnaire reported in the literature (0.630–0.776).

In addition to AHI, other respiratory parameters, including ODI, $T_{90\%}$, SpO_{2low}, as well as related sleep indicators such as MAI, can likewise reflect the severity of OSA. We analyzed the correlation between the six selected associations and these parameters. The results revealed that associations for constructing the new model, except LDL, were independently correlated with the above parameters reflecting the severity of OSA. LDL was independently associated with MAI (P=0.022), but its difference with ODI, $T_{90\%}$, and SpO_{2low} was not significant (P=0.078, 0.409, 0.105, respectively), which might be related to the absence of an optimal cutoff value for the different respiratory parameters. So, we were reasonably confident that our model was well suited to predicting the severity of OSA.

Nevertheless, our study has some limitations. First, considering the large night-to-night variability in PSG results, single-night PSG tests may have some bias. Secondly, there are so few patients with ESS scores (183 patients), and no STOP-BANG questionnaire data are collected in our series. Thirdly, our model lacks external validation, which may impact model generalizability. Moreover, regarding the assessment of logistic regression assumptions, there is a risk of overfitting in our model because 6 variables are included in the model with 496 severe OSA cases. A common rule of thumb is that logistic regression models should be fit with a minimum of 10 outcome events per predictor variable (EPV) to avoid overfitting. Last but not least, it is difficult to avoid some inherent bias in a retrospective study. Therefore, in future studies, we will work with other medical centers to recruit more patients for prospective studies to further verify the effectiveness of the model. Meanwhile, we will evaluate the ESS and STOP-BANG questionnaire in future recruited patients to compare with our model. If possible, we will also perform multiple-night PSG tests on patients to avoid bias in single-night PSG tests.

Conclusion

In conclusion, we provided a new risk prediction nomogram of severe OSA in patients with obesity, which was characterized by simple, cheap, non-invasive and well-balanced sensitivity and specificity. To the best of our knowledge, our model was the first to be constructed by combining associations such as LSM and aVAT, which was beneficial for patients with obesity who might suffer from severe OSA.

Ethics Statements

Our study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University [2024026K].

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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