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ORIGINAL CONTRIBUTIONS

Abdominal Obesity Is More Strongly Correlated with Obstructive Sleep Apnea than General Obesity in China: Results from Two Separated Observational and Longitudinal Studies

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Abstract

Background Previous studies have reported that obesity can result in or worsen obstructive sleep apnea (OSA). However, whether abdominal or general obesity indices or visceral adiposity indicators have a stronger association with OSA remains unclear.

Methods This cross-sectional study included 4344 patients who underwent polysomnography (PSG) due to suspicion of OSA. We also performed a longitudinal study on 86 patients who underwent bariatric surgery to confirm the relationship between OSA and obesity. Data on overnight PSG parameters, biochemical biomarkers, and multiple anthropometric obesity indices were collected.

Results In the cross-sectional study, waist circumference (WC) and body mass index (BMI) were independently associated with the apnea-hypopnea index (AHI) after adjusting for potential confounding factors (additional $R^2 = 0.232$, standardized beta coefficient [Beta] = 0.210; and additional $R^2 = 0.015$, Beta = 0.183, respectively). Logistic regression analysis showed similar results, as did stratified analysis of adult males aged ≤ 55 years. Restricted cubic spline (RCS) analysis revealed a linear dose-response relationship between OSA and obesity. In the longitudinal study, no significant relationship was found between remission of OSA and improvement in WC and BMI ($r = 0.252$, $p = 0.098$; and $r = 0.132$, $p = 0.395$, respectively), whereas the change in the visceral adiposity indicator (lipid accumulation calculated according to WC and fasting triglycerides) was significantly correlated with ΔAHI ($r = 0.322$, $p = 0.033$).

Conclusions Abdominal obesity, rather than general obesity, appears to play a more important role in OSA.

Keywords Abdominal obesity · Bariatric surgery · Obesity · Obstructive sleep apnea · Visceral adiposity indicator

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Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder, affecting approximately 2–4% of all middle-aged adults [1]. OSA is characterized by recurrent episodes of upper airway collapse that lead to chronic intermittent hypoxia and sleep fragmentation [1]. OSA has been linked to an increased likelihood of cardiovascular disease (CVD) [2]. The prevalence of obesity has increased rapidly over the past few decades worldwide, raising serious public health concerns due to its association with CVD and several other chronic diseases [3]. The most important risk factor for OSA is obesity, and abdominal obesity in particular [4, 5]. Bariatric surgery, which is currently the most effective treatment for morbid obesity, has been reported as a novel therapeutic treatment option for OSA [6]. The beneficial effects of bariatric surgery on OSA may be due to the change in body weight seen after bariatric surgery.

Anthropometric measurements, such as body mass index (BMI), neck circumference (NC), waist circumference (WC), and hip circumference (HC), are commonly used to assess general and abdominal obesity [7, 8]. Some studies have demonstrated that abdominal obesity is strongly associated with the abnormal fat distribution [9–11]. Abdominal obesity is strongly and positively associated with all-cause mortality, and CVD and cancer mortality, independent of BMI [12, 13]. Similarly, abdominal obesity and visceral fat accumulation are important risk factors for OSA [14–16]. However, in Chinese adults, general obesity is more strongly associated with blood pressure than abdominal obesity [8]. Obesity as indicated by BMI was the most important demographic predictor of OSA in a US population-based survey [17]. Well-designed studies are warranted to directly compare the contribution of different obesity types to OSA in the Chinese population, and to determine whether there is a causal link. Visceral adiposity indicators (VAI) are mathematical models based on anthropometric and metabolic parameters that serve as better indicators of metabolic disturbances in obese subjects [18, 19]. Emerging evidence indicates that the VAI is more sensitive to CVD and the risk of diabetes compared to BMI [20–22]. However, it is uncertain whether the VAI is superior for predicting OSA than traditional obesity measurements.

The aim of this study was to directly compare general obesity, abdominal obesity, and the visceral adiposity indicators as independent risk factors for OSA based on cross-sectional hospital data. We also performed a longitudinal study on patients who had experienced surgical weight loss to evaluate the correlation between the change in OSA and the improvement in multiple obesity measurements, which together may improve our understanding of the role of obesity in OSA.

Methods

Study Population

The Observational Population

This large-scale cross-sectional study consisted of 4344 consecutive participants who were referred to the sleep laboratory of Shanghai Jiao Tong University Affiliated Sixth People's Hospital for suspected OSA between January 2012 and January 2017. We excluded 645 patients for the following reasons: (1) aged < 18 years ($n = 75$); (2) previously treated for OSA, hypertension, dyslipidemia, diabetes, or CVD ($n = 397$); (3) presence of another systemic disease, such as respiratory disease, endocrine disease, cancer, or a psychiatric disease, or pregnancy ($n = 84$); and (4) missing data ($n = 89$). Ultimately, we used the data of 3699 participants to explore the risk factors for OSA in the cross-sectional study.

The Roux-en-Y Gastric Bypass Surgery Follow-up Population

This was a single-center study carried out in our hospital. Overweight individuals with type-2 diabetes mellitus (T2DM; 18–65 years old) were referred. A BMI of 25.0–29.9 kg/m^2 is defined as overweight and a BMI of ≥ 30 kg/m^2 is defined as obese [23]. The diagnosis of T2DM was based on the 1999 World Health Organization criteria [24]. Before roux-en-Y gastric bypass (RYGB) surgery, patients with a medical history of open abdominal surgery, serious systemic disease (i.e., heart, lung, liver, or kidney failure), type 1 diabetes, acute T2DM complications, secondary diabetes, alcoholism, drug addiction, or mental disease, and those with a relatively high surgical risk were excluded. If any patient had clinical symptoms of OSA (as evidenced by positive responses to clinical sleep-related questions, such as loud snoring, and/or experience of sleep apnea while sleeping, and/or excessive daytime sleepiness, and/or nocturnal urination or feeling of thirst in the morning), they were referred to our sleep center and evaluated by polysomnography (PSG). In total, 86 consecutive overweight patients with T2DM who underwent RYGB surgery and attended our sleep center from January 2013 to January 2015 were included in the longitudinal study. We excluded subjects who previously received or were currently undergoing therapy for OSA (e.g., continuous positive airway pressure [CPAP], oral appliance, or oropharyngeal surgery), and non-OSA cases as evidenced by the PSG data, from the RYGB surgery follow-up study. Ultimately, 50 patients were enrolled in that study. A total of 44 subjects completed the overnight PSG test before and after the RYGB surgery in the sleep center of our hospital.

Anthropometric and Biochemical Measurements

As a measure of general obesity, we calculated BMI as the body weight in kilograms divided by the height in meters squared (kg/m^2). Weight was categorized according to the current World Health Organization (WHO) standards, as follows: BMI < 25 kg/m^2, normal weight; 25 ≤ BMI < 30, overweight; and BMI ≥ 30 kg/m^2, obese [25]. Abdominal obesity was determined by NC, WC, or HC [7, 8]. NC was measured midway between the mid-cervical spine and mid-anterior neck to the nearest 0.5 cm, just below the laryngeal prominence if palpable. WC was measured midway between the lower costal margin and the iliac crest while the subject was standing. HC was measured as the maximum girth of the greater trochanters. Daytime blood pressure was measured after at least 5 min of rest in a sitting position using a mercury sphygmomanometer, following the American Society of Hypertension Guidelines [26], and the mean of three measurements was recorded. A fasting blood sample was collected from the antecubital vein of all participants on the morning after PSG monitoring. Serum lipid, glucose, and insulin levels were measured in

the hospital laboratory using routine procedures. Visceral adiposity indicators were calculated using previously published formulae [20–22].

Overnight PSG Parameters

Respiratory events were recorded using a laboratory-based PSG instrument (Alice 4 or 5; Respironics, Pittsburgh, PA, USA). The apnea-hypopnea index (AHI) was the number of apnea and hypopnea events per hour of sleep according to the criteria of the American Academy of Sleep Medicine. The microarousal index (MAI) was defined as the number of arousals per hour of sleep. The oxygen desaturation index (ODI) was defined as the number of times per hour of sleep that the blood oxygen level dropped by ≥ 4% from baseline. The lowest pulse oxygen saturation was the lowest oxygen saturation value recorded during sleep. An AHI ≥ 5 is defined as OSA according to the American Academy of Sleep Medicine [27].

Statistics

Data are presented as means (standard deviation, SD), medians (interquartile range), or numbers (percentages), according to whether they had a normal distribution, skewed distribution, or were categorical, respectively. Differences in baseline characteristics among subgroups were examined using the Kruskal–Wallis H-test, one-way analysis of variance, Fisher's exact test, or the $\chi 2$ test according to the data distribution. p values for linear trends across quartile groups were calculated using the polynomial linear trend test for continuous variables. Before further statistical analysis, all variables were log-transformed (natural logarithm) to approximate a normal distribution. Stepwise multivariate linear regression analyses were performed to determine the obesity indicator that best predicted the two cardinal features of OSA, which were adjusted for age, sex, fasting glucose, lipids and insulin, and lifestyle factors. The predictive value of each indicator was determined by the additional R^2 value, corresponding to the proportion of total variance in OSA that it explained; that is, the R^2 for the entire regression model minus the R^2 for a base model [28, 29]. The standardized beta coefficient (Beta) was used for each indicator in the multivariate linear regression to exclude any possible influence of differences in units [30]. We defined the fourth quartile of MAI (≥ 42) as high MAI. Then, we performed forward binary logistic regression to confirm the results of the multivariate linear regression analyses, where AHI (< or ≥ 5) and MAI (< or ≥ 42) were the dependent variables. The odds ratio (OR) and 95% confidence interval (CI) for OSA in the highest quartile of each indicator were included in binary logistic regression analysis to further determine their predictive value. In addition, we applied restricted cubic spline (RCS) transformations using R software (R Development Core Team, Vienna, Austria) to model the dose-response relationship between measurements of obesity (as continuous variables) and OSA [13]. Differences between baseline and postoperative characteristics of the participants were examined using the paired Student's t test, the Wilcoxon sign-rank test, the Kruskal–Wallis test, or the $\chi 2$ test, as appropriate. The relationship between changes in the various obesity indices, PSG parameters, and metabolic outcomes was assessed by Spearman or Pearson correlation analysis according to the data characteristics. All analyses were performed using SPSS software (ver. 20.0; SPSS Inc., Chicago, IL, USA). p values < 0.05 were considered significant.

Results

Baseline Characteristics of the Patients in the Observational and Follow-up Studies

The baseline characteristics of the 3699 patients according to BMI are shown in Table 1. According to the WHO reference value for obesity (BMI ≥ 30 kg/m^2), the percentage of the total sample with obesity was 16.70%. A higher BMI was associated with higher levels of serum lipids, fasting glucose, insulin, and indicators of visceral adiposity. As expected, the obese subjects had more severe OSA, as indexed by the AHI and MAI, and higher scores for the other sleep parameters with the exception of the proportions of rapid eye movement and N2 sleep stage.

In the follow-up study, 44 patients with OSA (18 men and 26 women aged 24–65 years) underwent RYGB surgery and their PSG test results were analyzed (Fig. S1). The interval between the two visits ranged from 5.3 to 24.7 months and the median follow-up time was 6.8 months. The RYGB surgeries were all performed by the same team. No adverse events attributable to the RYGB surgery were recorded.

The Independent Associations of General and Abdominal Obesity and Visceral Adiposity Indicators with the Cardinal Features of OSA

The relationship between obesity and the cardinal features of OSA was examined. Fasting lipids, glucose and insulin, as well as the nighttime heart rate, were included in model 2, and multivariate linear regression showed that the abdominal obesity indices of NC, WC, and HC ($\beta = 1.275$, $p = 0.000$; $\beta = 0.524$, $p = 0.000$; and $\beta = 0.115$, $p = 0.000$, respectively) were associated with OSA severity, as indexed by the AHI independent of BMI. NC and WC ($\beta = 0.562$, $p = 0.000$; and $\beta = 0.234$, $p = 0.000$, respectively) were associated with OSA severity, as indexed by the MAI independent of BMI. The additional amount of variance (additional R^2) in OSA

Table 1 The demographics characteristics and sleep parameters according to the obesity severity indexed by body mass index (BMI)

	Normal weight BMI < 25	Over weight BMI ≥ 25	Obesity BM ≥ 30	*p* value	P for linear trend
	n = 1312	*n* = 1769	*n* = 618		
Demographics					
Age years	42.84 (13.44)	43.98 (11.61)	42.24 (11.73)	0.000	0.315
Male *n* (%)	923 (70.4)	1514 (85.6)	504 (81.6)	0.000	0.000
BMI kg/m^2	22.7 (1.8)	27.25 (1.38)	32.76 (2.87)	0.000	0.000
NC cm	36.63 (3.06)	40.11 (2.83)	43.04 (3.25)	0.000	0.000
WC cm	86.3 (8.24)	97.31 (6.48)	109.06 (10.2)	0.000	0.000
HC cm	95.28 (7.54)	101.54 (9.2)	109.14 (15.65)	0.000	0.000
WHR	0.9 (0.06)	0.95 (0.05)	0.99 (0.06)	0.000	0.000
TyG	8.51 (0.65)	8.96 (0.63)	9.15 (0.63)	0.000	0.000
VAI	2.22 (2.56)	3.35 (3.67)	3.73 (3.65)	0.000	0.000
LAP	37.24 (37.8)	72.82 (65.06)	105.53 (80.43)	0.000	0.000
Biochemistry assays					
TC mmol/L	4.57 (0.99)	4.84 (1.94)	4.86 (0.94)	0.000	0.000
TG mmol/L	1.49 (1.25)	2.16 (1.8)	2.34 (1.78)	0.000	0.000
HDL-C mmol/L	1.16 (0.29)	1.03 (0.23)	1.01 (0.2)	0.000	0.000
LDL-C mmol/L	2.86 (0.88)	3.03 (1.12)	3.09 (0.81)	0.000	0.000
apoA-I g/L(reviewer #3, comment #3)	1.14 (0.24)	1.08 (0.24)	0.99 (0.37)	0.000	0.000
apoB g/L	0.78 (0.19)	0.84 (0.21)	0.79 (0.31)	0.000	0.277
apoE mg/L	4.23 (1.55)	4.79 (2.57)	4.75 (3.26)	0.000	0.000
Lp (a) g/L	14.27 (18.65)	12.05 (14.85)	9.5 (11.04)	0.000	0.000
Fasting glucose mmol/L	5.16 (1.04)	5.56 (1.23)	6.18 (1.78)	0.000	0.000
Fasting insulin μU/L	8.64 (6.23)	13.82 (8.88)	20.34 (13.4)	0.000	0.000
SBP	122.26 (13.69)	126.71 (13.94)	131.09 (15.14)	0.000	0.000
DBP	77.69 (9.42)	81.42 (10.25)	84.43 (11.26)	0.000	0.000
Sleep parameters					
AHI	19.68 (21.13)	39.53 (26.39)	53.51 (27.74)	0.000	0.000
MAI	23.59 (16.32)	32.78 (20.72)	38.78 (22.57)	0.000	0.000
ODI	18.98 (21.11)	40.54 (27.05)	56.79 (29.05)	0.000	0.000
ESS	6.54 (5.32)	8.83 (5.72)	10.42 (6.32)	0.000	0.000
REM (%SPT) (reviewer #3, comment #3)	10.6 (6.1)	10.62 (6.07)	9.83 (5.7)	0.013	0.009
N1(%SPT)	16.24 (11.29)	18.7 (12.73)	21.68 (14.23)	0.000	0.000
N2(%SPT)	46.97 (15.37)	48.08 (15.52)	48.25 (15.22)	0.091	0.089
N3(%SPT)	13.07 (9.34)	11.47 (9.16)	10.73 (9.11)	0.000	0.000
WAKE(%SPT)	11.6 (13.42)	9.46 (11.2)	8.06 (9.6)	0.000	0.000
Night heart rate	69.7 (10.5)	72.1 (10.3)	74.64 (10.64)	0.000	0.000
Lifestyle history					
Current smoker *n* (%)	358 (27.3)	798 (45.1)	285 (46.1)	0.000	0.000
Alcohol drinker *n* (%)	466 (35.5)	816 (46.1)	268 (43.4)	0.000	0.000

The data are presented as means (SD) and categorical data as the number (percentage). Differences in the baseline characteristics among the subgroups were examined using a Kruskal–Wallis H test or $\chi 2$ tests according to the characteristics of the data distribution. *BMI*, body mass index; *NC*, neck circumference; *WC*, waist circumference; *HC*, hip circumference; *WHR*, waist hip rate; *SBP*, systolic blood pressure; *SDP*, diastolic blood pressure; *TC*, total cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *apo*, apolipoprotein; *Lp(a)*, lipoprotein(a); *AHI*, apnea-hypopnea index; *MAI*, microarousal index; *ODI*, oxygen desaturation index; *ESS*, Epworth Sleepiness Scale; *REM*, rapid eye movement; *LAP*, lipid accumulation product; *VAI*, visceral adiposity index; *TyG*, triglycerides and glucose index

explained by the abdominal obesity measurements ranged from 0.002 to 0.232 for the AHI and from 0.088 to 0.096 for the MAI, over and above the BMI, and WC was the strongest predictor in both cases. In model 2, the Beta value of WC was higher than that of BMI for predicting the AHI and MAI (Beta of WC for AHI = 0.210; Beta of BMI for AHI = 0.183; Beta of

WC for MAI = 0.128; and Beta of WC for MAI = 0.072). In contrast, the variance in OSA explained by the log values of the visceral adiposity indicators and BMI was comparable (Table 2).

The results of direct comparison of the ORs and 95% CIs for the obesity measurement quartiles in the binary forward logistic regression models are presented in Table 3. After adjusting for age, smoking status, alcohol use, fasting glucose, and lipids, WC, NC, LAP, and TyG were strongly associated with OSA, whereas the VAI and HC were not associated with AHI ≥ 5 or MAI ≥ 42. WC showed a stronger association with OSA than any of the general obesity indices. The OR (highest vs. lowest quartile) of the association of WC with AHI ≥ 5 was 3.625 (95% CI 2.208, 5.951), and that with MAI ≥ 42 was 2.526 (95% CI 1.633, 3.283). The OR of the association of WC with AHI ≥ 5 per SD increase was 1.735 (95% CI 1.370, 1.951), and that for MAI ≥ 42 was 1.473 (95% CI 1.193, 1.582). The OR of the association of BMI with AHI ≥ 5 and MAI ≥ 42 was 1.412 (95% CI 1.350, 1.925) and 1.225 (95% CI 1.073, 1.398), respectively. The models showed that WC was consistently superior to BMI for predicting the AHI and MAI. There was no indication that the visceral adiposity indicators were superior to general obesity (i.e., BMI) for predicting AHI and MAI. In stratified analyses, WC was a better predictor than BMI of both AHI ≥ 5 and MAI ≥ 42 than BMI in younger subjects (< 55 years), and in men. The OR (highest vs. lowest quartile) of the associations of WC and BMI with AHI ≥ 5 was 3.797 (95% CI 2.216, 6.505) and 2.406 (95% CI 1.455, 3.980), respectively, in patients aged < 55 years; in men, the respective ORs were 3.610 (95% CI 2.046, 6.369) and 3.154 (95% CI 1.724, 5.769). Similar associations were generally observed for MAI ≥ 42 and for the per SD increase analyses.

The Dose-Response Relationship Between Multiple Anthropometric Obesity Measurements and OSA Risk

A previous study showed a non-linear relationship between obesity and all-cause mortality in the general population [31]. We used the dose-response model between the obesity measurements and OSA after adjusting for age, sex, smoking, and drinking status, fasting lipid, glucose, and insulin levels, and nighttime heart rate. The shapes of the dose-response curves are shown in Fig. 1 A–H. OSA was defined by an AHI (AHI ≥ 5) according to the diagnostic criteria and MAI value in the highest quartile. Notably, the risk of OSA increased linearly with the values of the obesity indices. Spline regression showed a linear association of general and abdominal obesity measurements with OSA (AHI ≥ 5 and MAI ≥ 42), and the values did not significantly depart from linearity ($p > 0.05$). The RCS results confirmed that the associations in the linear and logistic regression models were linear.

Bariatric Surgery Follow-up Results

To further delineate the relationship between obesity and OSA, patients were followed-up after the bariatric surgery to determine the impact of weight loss on OSA. Spearman's rank correlation analysis showed that the preoperative BMI, NC, WC, and HC in all 44 patients were 30.79 ± 0.54 kg/m^2, 39.60 ± 0.44 cm, 105.05 ± 1.45 cm, and 108.07 ± 1.3 cm, respectively, and were significantly correlated with the AHI at baseline ($r = 0.342$, $p = 0.023$; $r = 0.300$, $p = 0.048$; $r = 0.416$, $p = 0.005$; and $r = 0.335$, $p = 0.026$, respectively). After the follow-up period, nocturnal oxygen parameters, i.e., the AHI and ODI, changed significantly ($p \leq 0.001$). However, the arousal index did not show a significant change ($p = 0.633$ although daytime sleepiness declined significantly ($p < 0.001$) (Table 4)). No significant relationships were observed between the postoperative obesity indices and postoperative OSA severity, nor between the change in AHI and the improvement in multiple obesity indices and fasting glucose and lipid levels (ΔAHI vs. ΔWC $r = 0.252$, $p = 0.098$; ΔAHI vs ΔBMI $r = 0.132$, $p = 0.395$), but the change in the AHI was correlated with the ΔLAP ($r = 0.322$, $p = 0.033$) (Table 5). There was no significant correlation between the change in the AHI and improvement in multiple obesity indices in the male and female subgroups (data not shown).

Discussion

Both abdominal obesity and general obesity had an independent linear association with OSA. Importantly, abdominal obesity may play a greater role in OSA, particularly in men aged < 55 years. The longitudinal study revealed that the response to bariatric surgery of patients with OSA was heterogeneous, and was mainly governed by a change in both abdominal obesity and lipid levels rather than one or other of these parameters alone, which supported the results of the cross-sectional study.

An increase in abdominal soft tissue, previously cited as a major predisposing factor for OSA, exerts a more significant influence on OSA than does general obesity [16]. Similarly, male patients with OSA had a greater amount of CT-determined visceral adipose tissue in the abdomen than a group of BMI-matched men without OSA [32]. Our results were consistent with those of Terence et al. [14]. However, an Italian study reported that neck fat mass had a stronger independent correlation with the AHI in obese patients with OSA compared to obese patients without OSA [33]. A Turkish study conflicted with ours, reporting that NC contributed to metabolic syndrome and OSA over and above WC [7]. This difference may be due to differences in the ethnicity of the study populations. A previous study showed a U-shaped

Table 2 The stepwise multivariate linear regression model for predicting AHI and MAI

	AHI						MAI					
	Model 1			Model 2			Model 1			Model 2		
Predictors	β(SE) (reviewer #3, comment #3)	Additional R2	Beta	β(SE)	Additional R2	Beta	β(SE)	Additional R2	Beta	β(SE)	Additional R2	Beta
General obesity versus abdominal obesity												
BMI vs. NC												
BMI	1.983 (0.140)***	0.041	0.280	1.683 (0.144)***	0.041	0.238	0.748 (0.114)***	0.007	0.144	0.557 (0.117)***	0.007	0.107
NC	1.492 (0.168)***	0.212	0.202	1.275 (0.168)***	0.212	0.172	0.705 (0.136)***	0.096	0.130	0.562 (0.136)***	0.096	0.103
BMI vs. WC												
BMI	1.550 (0.170)***	0.014	0.219	1.294 (0.171)***	0.015	0.183	0.545 (0.136)***	0.005	0.105	0.374 (0.138)***	0.005	0.072
WC	0.596 (0.061)***	0.232	0.239	0.524 (0.061)***	0.232	0.210	0.277 (0.049)***	0.088	0.151	0.234 (0.049)***	0.088	0.128
BMI vs. HC												
BMI	2.694 (0.119)***	0.207	0.381	2.188 (0.128)***	0.207	0.309	1.148 (0.084)***	0.070	0.221	0.852 (0.093)***	0.070	0.164
HC	0.098 (0.040)***	0.001	0.039	0.115 (0.040)***	0.002	0.046	NS	NS	NS	NS	NS	NS
General obesity versus visceral adiposity indicators												
BMI vs. TyG												
BMI	2.503 (0.110)***	0.207	0.354	2.225 (0.118)***	0.206	0.314	0.933 (0.089)***	0.070	0.179	0.772 (0.095)***	0.070	0.149
TyG	5.428 (0.630)***	0.020	0.134	4.598 (0.639)***	0.020	0.114	3.589 (0.505)**	0.014	0.121	3.013 (0.517)***	0.014	0.101
BMI vs. VAI												
BMI	2.721 (0.105)***	0.207	0.384	2.352 (0.115)***	0.207	0.332	1.080 (0.085)***	0.070	0.208	0.850 (0.093)***	0.070	0.163
VAI	0.769 (0.118)***	0.009	0.093	NS	NS	NS	0.482 (0.095)***	0.007	0.080	0.690 (0.283)***	0.007	0.114
BMI vs. LAP												
BMI	2.469 (0.111)***	0.207	0.349	1.949 (0.136)***	0.207	0.275	0.909 (0.090)***	0.070	0.175	0.727 (0.096)***	0.070	0.140
LAP	0.058 (0.007)***	0.019	0.136	0.117 (0.021)***	0.019	0.273	0.039 (0.005)***	0.014	0.122	0.035 (0.005)***	0.014	0.110

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

Model 1 was adjusted for age (continuous variables), sex (categorized variables), and smoking and drinking status (categorized variables)

Model 2 was adjusted for all the variables in model 1 plus TG (continuous variable), LDL-C (continuous variable), HDL-C (continuous variable), fasting glucose (continuous variable), fasting insulin (continuous variable), night heart rate (continuous variables), and systolic and diastolic BP (continuous variables)

β, unstandardized beta coefficients; *SE*, standard error; *Beta*, standardized beta coefficients; *NS*, no significant; *AHI*, apnea–hypopnea index; *MAI*, microarousal index; *BMI*, body mass index; *NC*, neck circumference; *WC*, waist circumference; *HC*, hip circumference; *LAP*, lipid accumulation product; *VAI*, visceral adiposity index; *TyG*, triglycerides and glucose index; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *BP*, blood pressure; *OSA*, obstructive sleep apnea

Table 3 Binary logistic regression model for the best predictor of OSA

	OR(Q2)	OR(Q3)	AHI OR(Q4)	Each SD Increase	P for Linear Trend	OR(Q2)	OR(Q3)	MAI OR(Q4)	Each SD Increase	P for Linear Trend
General obesity versus abdominal obesity										
BMI vs. NC					(reviewer #3, comment #3)					
BMI	1.449 (1.140, 1.841)**	2.183 (1.867, 3.428)***	3.964 (2.654, 5.922)***	1.775 (1.523, 2.069)***	0.000	1.375 (1.042, 1.815)*	1.734 (1.301, 2.311)***	2.232 (1.636, 3.046)***	1.373 (1.230, 1.532)***	0.000
NC	1.127 (0.886, 1.423)*	1.350 (1.034, 1.762)***	1.724 (1.240, 2.397)***	1.608 (1.359, 1.903)***	0.000	1.095 (0.813, 1.476)	1.519 (1.11, 2.078)**	1.75 (1.245, 2.461)**	1.214 (1.071, 1.377)**	0.000
BMI vs. WC†										
BMI	1.269 (0.988, 1.630)	1.862 (1.330, 2.605)***	2.725 (1.706, 4.352)***	1.412 (1.350, 1.925)***	0.000	1.279 (0.959, 1.706)	1.535 (1.126, 2.093)**	1.831 (1.301, 2.579)**	1.225 (1.073, 1.398)**	0.000
WC	1.766 (1.364, 2.286)***	3.157 (2.194, 4.543)***	3.625 (2.208, 5.951)***	1.735 (1.370, 1.951)***	0.000	1.424 (1.066, 1.901)*	1.767 (1.289, 2.422)***	2.526 (1.633, 3.283)***	1.473 (1.193, 1.582)***	0.000
BMI vs. HC										
BMI	1.498 (1.144, 1.882)**	2.855 (2.069, 3.940)***	5.294 (3.424, 8.185)***	2.249 (1.981, 2.554)***	0.000	1.526 (1.171, 1.987)**	2.175 (1.683, 2.810)***	3.144 (2.433, 4.062)***	1.536 (1.414, 1.669)***	0.000
HC	1.385 (1.078, 1.780)*	1.408 (1.034, 1.916)*	1.451 (0.976, 2.1555)	NS	0.020	NS	NS	NS	NS	NS
General obesity versus visceral adiposity indicators										
BMI vs. TyG										
BMI	1.643 (1.300, 2.077)***	3.524 (2.654, 4.678)***	6.831 (4.798, 9.726)***	2.188 (1.924, 2.488)***	0.000	1.486 (1.138, 1.942)**	2.156 (1.663, 2.795)***	3.180 (2.449, 4.128)***	1.487 (1.365, 1.619)***	0.000
TyG	1.846 (1.443, 2.362)***	2.001 (1.528, 2.620)***	2.989 (2.182, 4.096)***	1.406 (1.239, 1.596)***	0.000	1.147 (0.892, 1.476)	1.305 (1.017, 1.675)*	1.560 (1.217, 2)***	1.238 (1.137, 1.348)***	0.000
BMI vs. VAI										
BMI	1.655 (1.309, 2.091)***	3.441 (2.589, 4.574)***	6.662 (4.670, 9.504)***	2.249 (1.981, 2.554)***	0.000	1.466 (1.123, 1.914)**	2.124 (1.640, 2.750)***	3.151 (2.434, 4.081)***	1.539 (1.416, 1.671)***	0.000
VAI	NS	NS	NS	NS	NS	1.208 (0.943, 1.546)	1.388 (1.087, 1.774)**	1.711 (1.341, 2.182)***	1.197 (1.111, 1.289)***	0.000
BMI vs. LAP										
BMI	1.451 (1.140, 1.846)**	2.700 (2.003, 3.639)***	4.537 (3.103, 6.635)***	1.863 (1.592, 2.179)***	0.000	1.440 (1.095, 1.894)**	1.970 (1.505, 2.604)***	2.734 (2.057, 3.633)***	1.476 (1.355, 1.608)***	0.000
LAP	1.982 (1.546, 2.541)***	2.428 (1.813, 3.251)***	3.895 (2.675, 5.672)***	3.373 (1.938, 5.870)***	0.000	1.020 (0.781, 1.332)	1.411 (1.078, 1.846)*	1.693 (1.287, 2.228)***	1.248 (1.154, 1.349)***	0.000
Stratified analyses										
Age stratification†										
WC (age ≤ 55)	1.741 (1.317, 2.301)***	3.208 (2.161, 4.762)***	3.797 (2.216, 6.505)***	1.647 (1.351, 2.007)***	0.000	1.428 (1.034, 1.973)*	1.791 (1.254, 2.558)**	2.426 (1.634, 3.602)***	2.182 (1.594, 2.988)***	0.000
BMI (age ≤ 55)					0.000					0.005

Table 3 (continued)

	AHI					MAI				
	OR(Q2)	OR(Q3)	OR(Q4)	Each SD Increase	P for Linear Trend	OR(Q2)	OR(Q3)	OR(Q4)	Each SD Increase	P for Linear Trend
	1.228 (0.932, 1.616)	1.805 (1.254, 2.599)**	2.406 (1.455, 3.980)***	1.557 (1.283, 1.879)***		1.281 (0.923, 1.778)	1.615 (1.136, 2.296)**	1.690 (1.144, 2.497)**	1.212 (1.043, 1.408)***	
WC (age > 55)	2.111 (1.125, 3.960)*	5.105 (2.356, 11.059***	8.364 (3.169, 22.075)***	NS	0.027	NS	NS	NS	NS	NS
BMI (age > 55)	NS	NS	NS	2.680 (1.924, 3.773)***	NS	1.493 (0.860, 2.593)	1.616 (0.911, 2.866)	3.602 (2.094, 6.198)***	1.582 (1.307, 1.914)***	0.000
Sex stratification†										
WC (men)	1.886 (1.389, 2.559)***	3.983 (2.582, 6.143)***	3.610 (2.046, 6.369)***	1.911 (1.520, 2.401)***	0.000	1.304 (0.948, 1.793)	1.663 (1.176, 2.351)**	2.247 (1.535, 3.290)***	1.305 (1.116, 1.524)***	0.000
BMI (men)	1.327 (0.977, 1.804)	1.714 (1.147, 2.561)**	3.154 (1.724, 5.769)***	1.624 (1.293, 2.039)***	0.000	1.260 (0.921, 1.724)	1.595 (1.140, 2.231)**	1.863 (1.285, 2.701)**	1.297 (1.108, 1.513)**	0.000
WC (female)	1.523 (0.931, 2.494)	2.013 (1.021, 3.966)*	5.879 (2.039, 16.953)**	1.284 (0.980, 1.683)*	0.001	2.945 (1.566, 5.537)**	3.505 (1.826, 6.729)***	5.276 (2.848, 9.774)***	1.639 (1.363, 1.971)***	0.000
BMI (female)	1.020 (0.644, 1.615)	2.573 (1.340, 4.942)**	2.241 (1.054, 4.762)*	1.587 (1.206, 2.089)**	0.045	NS	NS	NS	NS	NS

The data are presented as the odds ratio (OR) (95%CI). We performed forward binary logistic regression. Q2, Q3, and Q4 are the second, third, fourth quartile; *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

The ORs from quartile 1 (Ref) to quartile 4 for general obesity versus abdominal obesity or general obesity versus visceral adiposity indicators were adjusted for age (continuous variables), sex (categorized variables), smoking and drinking status (categorized variables), LDL-C (quartile), HDL-C (quartile), TG (quartile), fasting glucose (quartile), blood pressure (quartile), fasting insulin (quartile), and night heart rate (quartile)

The ORs per SD increase for general obesity vs. abdominal obesity or general obesity vs. visceral adiposity indicators were adjusted for age (standardized), sex (categorized variables), smoking and drinking status (categorized variables), LDL-C (standardized), HDL-C (standardized), TG (standardized), fasting glucose (standardized), blood pressure (standardized), fasting insulin (standardized), and night heart rate (standardized)

†ORs in stratified analyses were adjusted for BMI vs. WC adjusted by possible factors above except the stratified factor

NS, no significant; *BMI*, body mass index; *NC*, neck circumference; *WC*, waist circumference; *HC*, hip circumference; *LAP*, lipid accumulation product; *VAI*, visceral adiposity index; *TyG*, triglycerides and glucose index; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *OSA*, obstructive sleep apnea

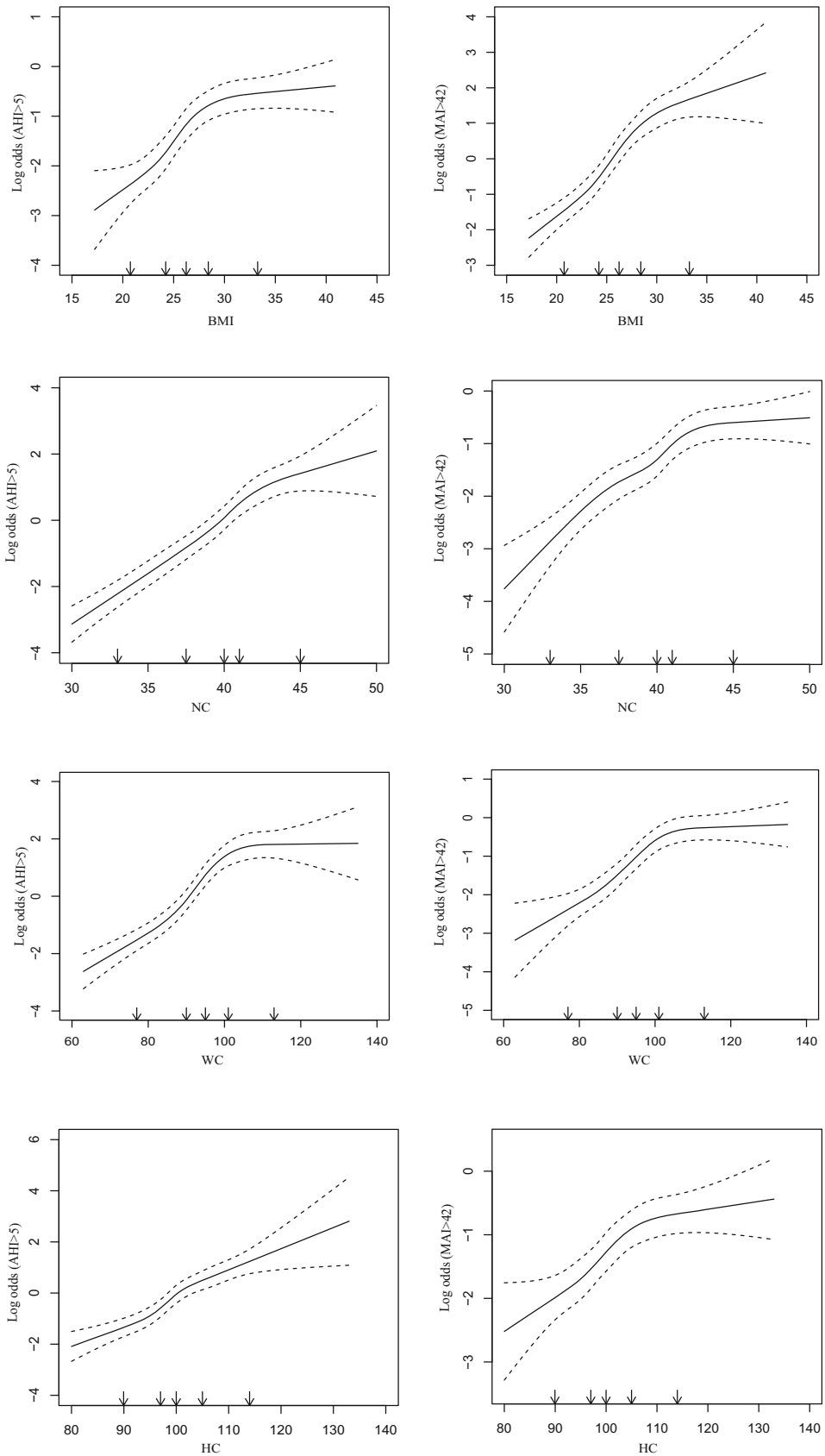

Fig. 1 Restricted cubic spline regression of the dose response correlation patterns between obstructive sleep apnea (OSA) (AHI ≥ 5 and MAI ≥ 42) and the severity of general or abdominal obesity. The x-axis represents the continuous values of the body mass index (BMI), neck circumference (NC), waist circumference (WC), and hip circumference (HC). The left y-axis represents the log odds of OSA for each obesity index

relationship between obesity and all-cause mortality in the general population [31]; in contrast, our hospital-based study of a heavier Chinese OSA population revealed a right-skewed curve. Our data indicate that obesity and OSA have a linear relationship. However, how abdominal obesity affects OSA risk is poorly understood, but the relationship is thought to involve fat accumulation in the upper airway [34]. Preliminary evidence suggests that tongue adiposity may parallel ectopic fat accumulation elsewhere, with positive associations between abdominal subcutaneous and visceral adipose tissue and tongue fat being noted in obese subjects [35]. Although there are several other potential mechanisms that support a relationship between abdominal obesity and OSA, well-designed studies need to be conducted on this complex issue [4].

A previous study using dual-energy absorptiometry supported sex differences in the association between OSA severity and anthropometric measures [29]. Lee et al. reported that obesity accounts for significant differences in the variability of AHI according to age [36]. These findings support the results of our stratified analyses and indicate that glucose homeostasis and energy balance are regulated differently according to age and sex [37].

The effect of bariatric surgery on LAP may explain the role of abdominal obesity in OSA, where LAP is based on WC and the fasting concentration of circulating TGs [22]. The LAP may be a more sensitive marker of the efficacy of bariatric surgery for treating obesity than either WC or fasting lipid alone. However, in this study, there was no direct relationship between weight loss and improvement in the AHI, albeit this was in line with the results of previous prospective reports [38, 39]. Changes in fat distribution and improvement in central obesity following surgical weight loss may partly explain changes in the severity of OSA after bariatric surgery. However, the follow-up duration in one study may have been too short to unequivocally determine the reason for obesity

Table 4 Comparison of the data associated with anthropometric characteristics and polysomnography variables before and after RYGB surgery

Characteristic	Preoperative (SD)	Postoperative (SD)	Mean difference (95%CI)	*p* value
Preoperative characteristics				
Weight kg	85.63 (13.45)	67.91 (10.71)	17.72 (15.26 to 20.18)	0.000 (reviewer #3, comment #3)
BMI kg/m^2	30.9 (3.42)	24.27 (2.6)	6.4 (5.48 to 7.31)	0.000
NC cm	39.6 (2.89)	35.16 (3.38)	4.44 (3.64 to 5.24)	0.000
WC cm	105.05 (9.64)	87.83 (9.09)	17.22 (14.81 to 19.62)	0.000
HC cm	108.07 (8.64)	95.48 (6.74)	12.59 (10.7 to 14.48)	0.000
SBP	136.45 (17.27)	120.37 (13.04)	15.65 (9.39 to 21.9)	0.000
DBP	85.24 (11.79)	76.46 (8.62)	8.79 (4.01 to 13.57)	0.001
TC mmol/L	5.02 (0.97)	4.31 (0.97)	0.71 (0.44 to 0.99)	0.000
TG mmol/L	2.27 (1.43)	1.17 (0.4)	1.1 (0.64 to 1.57)	0.000
HDL-C mmol/L	1.05 (0.24)	1.2 (0.27)	− 0.15 (− 0.23 to − 0.07)	0.001
LDL-C mmol/L	2.95 (0.83)	2.43 (0.75)	0.53 (0.23 to 0.82)	0.001
Fasting glucose mmol/L	8.25 (2.46)	5.73 (1.18)	2.52 (1.87 to 3.17)	0.000
Fasting insulin μU/L	20.63 (17.2)	7.33 (4.87)	13.31 (8.8 to 17.81)	0.000
TYG	9.40 (0.60)	8.51 (0.45)	0.89 (0.68 to 1.1)	0.000
VAI	4.37 (3.98)	2.06 (1.09)	2.32 (1.14 to 3.5)	0.000
LAP	103.72 (80.83)	31.5 (20.7)	72.22 (47.18 to 97.25)	0.000
Sleep parameters				
AHI	22.44 (17.84)	7.07 (9.43)	15.37 (10.44 to 20.29)	0.000
MAI	19.39 (14)	18.29 (13.37)	1.1 (− 3.53 to 5.73)	0.633
ODI	25.43 (18.65)	6.37 (9.01)	19.05 (14.25 to 23.86)	0.000
ESS	6.82 (4.68)	3.09 (2.85)	3.73 (2.42 to 5.04)	0.000

The data are presented as means (SD), and the difference was means (95% CI). Differences in the baseline and the postoperative were examined using a paired Student's *t* test, the Wilcoxon signed rank test, the Kruskal–Wallis test, or the $\chi 2$ test, as appropriate. $^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ (reviewer #3, comment #3)

BMI, body mass index; *NC*, neck circumference; *WC*, waist circumference; *HC*, hip circumference; *SBP*, systolic blood pressure; *SDP*, diastolic blood pressure; *TC*, total cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *AHI*, apnea-hypopnea index; *MAI*, microarousal index; *ODI*, oxygen desaturation index; *ESS*, Epworth Sleepiness Scale; *LAP*, lipid accumulation product; *VAI*, visceral adiposity index; *TyG*, triglycerides and glucose index

Table 5 The correlation between the changes in OSA and obesity measurements in the follow-up study

		AHI change	BMI change	NC change	WC change	HC change	FG change	IN change	TC change	TG change	HDL change	LDL change	TYG change	VAI change	LAP change
AHI change	R	1	0.132	0.033	0.252	0.212	−0.079	−0.063	−0.063	0.258	−0.019	−0.293	0.081	0.205	0.322*
	Sig.		0.395	0.831	0.098	0.167	0.608	0.687	0.686	0.091	0.902	0.054	0.603	0.182	0.033
BMI change	R		1	0.507**	0.537**	0.289	−0.091	−0.234	−0.292	−0.007	−0.323*	−0.111	0.011	−0.090	0.051
	Sig.			0.000	0.000	0.057	0.556	0.125	0.055	0.964	0.032	0.472	0.942	0.561	0.742
NC change	R			1	0.761**	0.488**	−0.019	−0.208	−0.207	−0.340*	−0.518**	0.194	−0.169	−0.277	−0.284
	Sig.				0.000	0.001	0.901	0.175	0.178	0.024	0.000	0.206	0.273	0.068	0.061
WC change	R				1	0.655**	−0.163	−0.282	−0.355*	−0.030	−0.584**	−0.123	−0.034	0.036	0.113
	Sig.					0.000	0.291	0.064	0.018	0.846	0.000	0.428	0.827	0.817	0.465
HC change	R					1	−0.105	−0.158	−0.109	−0.020	−0.298*	−0.046	−0.003	0.060	0.097
	Sig.						0.499	0.305	0.482	0.898	0.050	0.767	0.987	0.701	0.529
FG change	R						1	−0.227	0.142	0.049	0.043	0.083	0.482**	0.046	−0.023
	Sig.							0.139	0.358	0.753	0.781	0.590	0.001	0.765	0.885
IN change	R							1	0.152	0.086	0.009	0.077	−0.023	0.115	0.001
	Sig.								0.324	0.578	0.956	0.619	0.882	0.456	0.997
TC change	R								1	0.068	0.605**	0.622**	0.203	0.036	−0.021
	Sig.									0.662	0.000	0.000	0.186	0.816	0.891
TG change	R									1	0.063	−0.608**	0.773**	0.950**	0.954**
	Sig.										0.684	0.000	0.000	0.000	0.000
HDL change	R										1	0.125	−0.016	−0.056	0.025
	Sig.											0.418	0.916	0.720	0.874
LDL change	R											1	−0.253	−0.595**	−0.673**
	Sig.												0.097	0.000	0.000
TYG change	R												1	0.727**	0.658**
	Sig.													0.000	0.000
VAI change	R													1	0.936**
	Sig.														0.000
LAP change	R														1
	Sig.														

The correlation was examined using Spearman test or Pearson test according to the characteristics of the data

R, correlation coefficient; *BMI*, body mass index; *NC*, neck circumference; *WC*, waist circumference; *HC*, hip circumference; *TC*, total cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *FG*, fasting glucose; *IN*, insulin; *AHI*, apnea-hypopnea index; *LAP*, lipid accumulation product; *VAI*, visceral adiposity index; *TyG*, triglycerides and glucose index

status changes [39]. Furthermore, other factors may also contribute to variability in the AHI, in addition to weight loss, such as alterations in the neurohumoral and metabolic-inflammatory milieu, vagal manipulation, reduced gastric size, anatomical gut rearrangement/altered flow of nutrients, and defects in neuromuscular responses to mechanical loads [6, 40, 41]. The beneficial effects of weight loss after bariatric surgery may break the vicious cycle between OSA and obesity [6, 38].

From a clinical perspective, our study indicates that not only increased body weight, but also the type of obesity, plays an important role in the development of OSA. OSA therapy should be tailored based on the obesity type, especially abdominal obesity, to eliminate OSA and treat CVD [12]. WC was a better predictor of sleep apnea than BMI, suggesting that WC may have more utility for evaluating the therapeutic effect of weight loss on OSA. Effective treatments that focus on abdominal obesity in OSA are important, such as bariatric surgery. However, more studies are warranted to precisely determine the pathophysiology of obesity in patients with OSA.

Some limitations of our hospital-based, cross-sectional study should be discussed. First, although we adjusted for several common confounders, other factors such as exercise and dietary habits were not considered. Second, the relatively small sample size and the short-term follow-up without control group may have resulted in inadequate statistical power to detect a significant correlation between the change in OSA and obesity. However, these limitations did not negate the overall value of our study. Further studies are required to identify the mechanisms underlying the association between OSA and obesity.

Conclusion

WC, as an indicator of abdominal obesity, was more strongly associated with the likelihood of OSA than was general obesity (i.e., BMI). RYGB surgery to reduce weight loss may be an effective treatment for obese patients with OSA and T2DM. Improvement in OSA was significantly associated with a change in LAP, indicating that high levels of fasting lipids and abdominal obesity were responsible for OSA. These results suggest that abdominal obesity may play a more important role in OSA than general obesity.

Authors' Contributions Prof. Shankai Yin, Jian Guan, and Hongliang Yi had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Study design: Xiaolong Zhao, Jian Guan, Hongliang Yi, and Shankai Yin; data collection: Huajun Xu, Yupu Liu, Yingjun Qian; statistical analysis: Huajun Xu; manuscript draft: Xiaolong Zhao, Jian Guan, Hongliang Yi, and Shankai Yin.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

Ethical Approval This study was approved by the Internal Review Board of the Institutional Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth Hospital and was conducted in accordance with the Declaration of Helsinki.

Informed Consent Informed consent was obtained from all participants included in the study

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