



OPEN Triglyceride glucose-body mass index as a mediator of hypertension risk in obstructive sleep apnoea syndrome: a mediation analysis study

Liping Wang, Jingfeng Zou, Shaotian Li, Chunhui Tian, Jiajia Ran, Xin Yang, Yiting Liu, Guqiao Nie, Lei Jiang & Wen Peng

The aim of this study was to investigate whether triglyceride glucose-body mass index (TyG-BMI) plays a mediating role between obstructive sleep apnoea syndrome (OSAS) and hypertension. The study analyzed clinical data from a total of 840 OSAS patients at Wuhan Union Hospital between January 2020 to December 2023. The association between TyG-BMI and hypertension was examined using restricted cubic spline regression and logistic regression. Mediation effect analysis was conducted to explore the relationship between OSAS, TyG-BMI, and the risk of hypertension. Severe OSAS was associated with a significantly increased risk of hypertension compared to mild OSAS (OR = 1.752, $p = 0.013$). There was a positive linear relationship between TyG-BMI and the risk of hypertension (P-non-linear = 0.535). The risk of hypertension increased with increasing TyG-BMI, with a significantly higher risk of hypertension in the fourth quartile (OR = 3.407, $p < 0.001$) than in the third quartile (OR = 2.457, $p < 0.001$) and in the second quartile (OR = 1.576, $p = 0.043$). TyG-BMI mediated the association between OSAS and hypertension with a mediation effect of 41.3% ($p < 0.001$). TyG-BMI is important for assessing the risk of hypertension in patients with OSAS.

Keywords Obstructive sleep apnoea syndrome (OSAS), Triglyceride glucose-body mass index (TyG-BMI), Hypertension, Insulin resistance

Abbreviations

OSAS	Obstructive sleep apnoea syndrome
TyG-BMI	Triglyceride glucose-body mass index
TyG	Triglyceride-glucose
BMI	Body mass index
AHI	Apnoea-hypopnoea index
NLR	Neutrophil-lymphocyte ratio
ODI	Oxygen desaturation index
RCS	Restricted cubic spline
ORs	Odds Ratio
95% CI	95% confidence interval

Obstructive sleep apnoea syndrome (OSAS) is a clinical disorder characterized by recurrent apnoea and hypoventilation events during sleep, which may be complicated by nocturnal hypoxaemia. Prolonged nocturnal hypoxia leads to autonomic dysfunction, activation of oxidative stress, and chronic inflammatory responses¹. With the obesity epidemic, the prevalence of OSAS is increasing every year², but it is usually overlooked by patients and physicians because its clinical features are not clearly specific. Its main clinical manifestations are disrupted sleep structure, snoring or breath-holding at night, and daytime drowsiness. Undetected and untreated OSAS patients are highly susceptible to cardiovascular, neurological, and endocrine diseases³. Studies

General Practice Department, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Jiangnan District, Wuhan, China. email: lei_jiang@hust.edu.cn; pengwen666@sina.com

have reported that OSAS is strongly associated with a number of cardiovascular conditions, including coronary heart disease, heart failure, arrhythmias and stroke^{4–6}. Studies have shown that OSAS can increase the risk of hypertension and that positive pressure ventilation therapy has a significant clinical benefit in patients with OSAS combined with hypertension^{7,8}. Intermittent hypoxia in OSAS is independently associated with insulin resistance, and the prevalence of OSAS is significantly higher in patients with type 2 diabetes^{9,10}. Studies have revealed that the metabolic disorders associated with insulin resistance are linked to hypertension and other cardiovascular diseases¹¹.

There is an established relationship between OSAS and hypertension, but few studies have investigated the mediators of this relationship. Based on the above research evidence, the present study proposes the following hypothesis: insulin resistance may be a mediator of the association between OSAS and hypertension. The triglyceride-glucose (TyG) index is a valid and simple surrogate for insulin resistance and can be calculated using the formula $\text{Ln} [\text{triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]$ ¹². Considering that body mass index (BMI) is an independent risk factor for OSAS and hypertension, this study used the BMI-modified TyG index to investigate the value of insulin resistance in assessing hypertension risk in OSAS patients. TyG-BMI is derived by multiplying BMI by the TyG index, which several studies have shown to be superior to the TyG index in predicting insulin resistance^{13,14}. It has an excellent ability to identify patients with hypertension combined with hyperuricaemia¹⁵. Therefore, the purpose of this study was to examine the association between OSAS, TyG-BMI, and hypertension and to verify whether TyG-BMI mediates the association between OSAS and the risk of developing hypertension.

Methods

Research population

This was a retrospective cross-sectional study. The study collected clinical data on adult OSAS patients with routine health check-ups and completed polysomnography in the General Medicine Department between January 2020 and December 2023 using the electronic medical record system of the Wuhan Union Medical College Hospital. Exclusion criteria included subjects with any of the following conditions: (1) patients whose blood counts, liver and kidney functions were outside the normal range due to long-term use of hormones, antibiotics or chemotherapy drugs. (2) patients with heart failure, kidney failure, liver failure, respiratory failure or malignant tumors. (3) Previously diagnosed hypertension due to acute or chronic renal disease, pheochromocytoma, renal artery stenosis, primary aldosteronism, Cushing's syndrome. (4) patients with missing results of any of the complete blood count, liver function tests, renal function tests, fasting blood glucose or lipid tests. In the end, a total of 840 patients with OSAS were enrolled in the analysis. This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Wuhan Union Medical College Hospital (UHCT-IEC-SOP-016-03-01), and subjects were exempted from informed consent as clinical data of all participants were analyzed retrospectively.

Basic information and laboratory measurements

General information such as age, sex, smoking history, alcohol consumption were recorded, and the history of hypertension, diabetes mellitus, and coronary heart disease was taken. Height and weight were measured and BMI was calculated. Venous blood samples were collected from patients in the fasting state and sent to the central laboratory of Wuhan Union Medical College Hospital for testing. Measurements included: white blood cells, haemoglobin, platelets, neutrophils, lymphocytes, monocytes; alanine aminotransferase, aspartate aminotransferase, creatinine, uric acid, fasting blood glucose, triglycerides and other markers. The collection of all samples and the testing of biological indicators in the blood were completed by professional technicians in the laboratory. The neutrophil-lymphocyte ratio (NLR) was calculated from the neutrophil and lymphocyte counts. The TyG index was calculated using the above formula¹² and then the TyG-BMI value was calculated.

Diagnosis of OSAS

All participants underwent polysomnographic respiratory monitoring in a quiet, comfortable sleep monitoring room. Sleep time, respiratory events, and changes in oxygen saturation during the participant's overnight sleep were recorded using a model YH-600B polysomnography monitor (BMC Medical Co., Ltd., China). Instruments were regularly quality checked and calibrated by engineers. The data obtained from the monitoring were recorded and interpreted by a sleep monitoring technician, and the results were reviewed by a sleep physician. According to the American Academy of Sleep Medicine¹⁶, apnoea is defined as the loss or significant reduction of oro-nasal airflow ($\geq 90\%$ decrease from baseline amplitude) during sleep for a duration of ≥ 10 s, and hypopnoea is defined as a decrease in oro-nasal airflow of $\geq 30\%$ from baseline, accompanied by a decrease in oxygen saturation of $\geq 3\%$, for a duration of ≥ 10 s. Sleep efficiency, apnoea-hypopnoea index (AHI), snoring, electrocardiogram, mean oxygen saturation and lowest oxygen saturation were routinely reported in the sleep apnoea monitoring results. The AHI is calculated by dividing the sum of the number of apnoeas and hypoventilations by the total sleep time. The severity of OSAS was graded according to AHI, with $5 < \text{AHI} \leq 15$ considered mild, $15 < \text{AHI} \leq 30$ considered moderate, and $\text{AHI} > 30$ considered severe. Oxygen desaturation index (ODI) was defined as the number of hourly decreases in oxygen desaturation of $\geq 3\%$ from baseline¹⁷.

Diagnosis of hypertension

Patients with previously diagnosed hypertension and new-onset hypertension diagnosed according to the 2023 ESH guidelines¹⁸.

Statistical analysis

A normality test for all continuous variables showed that the variables followed a normal distribution and were therefore described by the mean (standard deviation), and differences between groups were compared using the t-test. Categorical variables were expressed as percentages, and the chi-square test was used to compare whether the differences between groups were statistically significant. The relationship between OSAS severity and hypertension was analyzed using binary logistic regression models. The relationship between AHI and TyG-BMI was analyzed using Pearson's correlation, considering AHI and TyG-BMI as continuous variables. The study used restricted cubic spline (RCS) regression to analyze the potential non-linear relationship between TyG-BMI and risk of hypertension. Quartiles were used to divide TyG-BMI into four intervals, and multifactorial logistic regression was used to explore the association between TyG-BMI and hypertension. The variables in the multifactor logistic regression were tested for multicollinearity and the variance inflation factors (VIF) for all independent variables were less than 5. Finally, mediation analysis was used to calculate the percentage mediation effect of TyG-BMI between OSAS and hypertension, and the mediation effect was tested using the bootstrap method. The mediation effect was found to be significant when the 95% confidence interval (CI) did not include zero. Statistical analyses and graphs were performed using R 4.3.1 software for Windows. Significant results were defined as those with a two-tailed p-value less than 0.05.

Results

General clinical characteristics

The OSAS patients were divided into hypertensive and non-hypertensive groups, a total of 573 (68.21%) had hypertension and 267 (31.79%) in the non-hypertensive group. Table 1 showed that the hypertensive group was older, had more overweight and obesity, diabetes and coronary heart disease; higher levels of neutrophils, NLR, uric acid, fasting glucose, AHI, ODI and TyG-BMI; and had lower mean oxygen saturation and lowest oxygen saturation. Variables that differed between the two groups were included in the regression model to be analyzed. Table 2 showed that age, TyG-BMI, uric acid, diabetes and coronary heart disease were risk factors for the development of hypertension in patients with OSAS.

Multifactorial logistic regression analysis of OSAS severity and hypertension

OSAS was categorized into mild, moderate and severe according to AHI values and three logistic regression models were constructed in Table 3, with OSAS severity as the independent variable and the presence of hypertension as the dependent variable. Compared with mild OSAS as reference, model 1 found a significantly increased risk of hypertension in patients with severe OSAS (OR = 1.667, 95% CI: 1.138–2.442, $p = 0.009$); models 2 and 3 progressively included adjustments for the remaining confounders and finally found that this risk remained (OR = 1.752, 95% CI: 1.125–2.728, $p = 0.013$).

Correlation analysis between AHI and TyG index, BMI, TyG-BMI

Pearson's correlation analysis of AHI with TyG index, BMI and TyG-BMI found that TyG-BMI ($r = 0.573$, $p < 0.001$) was more closely correlated with AHI compared to TyG index ($r = 0.004$, $p = 0.002$) and BMI ($r = 0.051$, $p < 0.001$). This indicated that BMI combined with the TyG index is more strongly associated with the severity of OSAS and may be more meaningful in assessing the disease.

RCS regression analysis of TyG-BMI and risk of hypertension

The study used RCS regression to analyze the potential non-linear relationship between TyG-BMI and hypertension. The results are shown in Fig. 1, where TyG-BMI was linearly and positively associated with the risk of hypertension (P -non-linear = 0.535).

Logistic regression analysis of TyG-BMI and risk of hypertension

The relationship between TyG-BMI levels and the risk of hypertension was assessed using logistic regression models and the results are presented in Table 4. TyG-BMI was divided into four levels from Q1 to Q4 from low to high using the quartile method, and Q1 was used as the reference level. The results showed that in model 1 without adjustment for confounders, the risk of hypertension was significantly increased when TyG-BMI was at the Q3 and Q4 levels, and the risk of hypertension was significantly higher at the Q4 level (OR = 2.859, 95% CI: 1.864–4.385, $p < 0.001$) than at the Q3 level (OR = 2.144, 95% CI: 1.423–3.230, $p < 0.001$). Model 2 adjusted initially for some of the confounders, and model 3 further adjusted for the remaining confounders based on model 2, finding that the increasing trend in this risk persisted. The ORs at the Q2, Q3 and Q4 levels in model 3 were 1.576 (95% CI: 1.015–2.445, $p = 0.043$), 2.457 (95% CI: 1.527–3.954, $p < 0.001$) and 3.407 (95% CI: 2.001–5.802, $p < 0.001$), respectively.

Mediation analyses

In this study, mediation analysis was used to investigate the mediating effect of TyG-BMI and NLR in the association between OSAS and hypertension. The results are shown in Fig. 2. In mediation analysis, the sum of the average direct effect and the average causal mediation effect is the total effect, and the average causal mediation effect divided by the total effect is the mediation ratio. Figure 2A showed that after adjustment for the risk factors of age, uric acid, diabetes and coronary heart disease, this mediation ratio was 41.3% (95% CI: 0.184–1.050, $p < 0.001$). The study was analyzed with the NLR as a mediator, no significant mediation effect was observed as the confidence interval for the mediation effect contained zero (Fig. 2B).

Characteristics	Non-hypertension (n = 267)	Hypertension (n = 573)	P
Age (years)	52.06 (9.64)	55.90 (10.24)	< 0.001
Sex, n (%)			0.695
Female	34 (12.70)	66 (11.50)	
Male	233 (87.30)	507(88.50)	
BMI (kg /m ²), n (%)			< 0.001
BMI < 18.5	1 (0.40)	2 (0.30)	
18.5 ≤ BMI < 24	78 (29.20)	91 (15.90)	
24.0 ≤ BMI < 28	133 (33.80)	261 (45.50)	
BMI ≥ 28	55 (20.60)	219 (38.20)	
WBC (× 10 ⁹ /L)	5.95 (1.67)	6.11 (1.71)	0.183
Haemoglobin (g/L)	141.72 (16.05)	142.47 (15.18)	0.512
Platelet (× 10 ⁹ /L)	212.79 (52.19)	207.71 (54.22)	0.201
Neutrophil (× 10 ⁹ /L)	3.54 (3.18)	3.56 (1.28)	0.903
Lymphocyte (× 10 ⁹ /L)	1.95 (0.59)	1.90 (0.69)	0.28
Monocyte (× 10 ⁹ /L)	0.42 (0.16)	0.44 (0.16)	0.055
NLR	1.90 (1.63)	2.03(1.05)	0.004
ALT(U/L)	32.37 (27.36)	32.14 (22.34)	0.898
AST(U/L)	25.03 (10.25)	25.87 (13.76)	0.379
Creatinine(μmol/L)	72.78 (23.53)	75.42 (23.63)	0.132
Uric acid(μmol/L)	373.00 (81.98)	394.89 (98.59)	0.002
FPG (mmol/L)	5.41 (1.23)	5.84 (1.70)	< 0.001
Triglyceride(mmol/L)	2.36 (2.60)	2.90 (15.95)	0.587
HDL-C(mmol/L)	1.07 (0.32)	1.04 (0.39)	0.284
LDL-C(mmol/L)	2.70 (0.80)	2.60 (1.04)	0.15
TyG	8.92 (0.74)	9.00 (0.78)	0.166
TyG-BMI	230.86 (38.41)	245.68 (40.39)	< 0.001
Sleep efficiency (%)	76.82 (16.18)	76.98 (17.25)	0.895
AHI	29.99 (19.12)	33.78 (19.67)	0.009
Lowest SpO ₂ (%)	79.30 (9.29)	77.05 (11.34)	0.005
Mean SpO ₂ (%)	94.91 (1.97)	94.50 (2.50)	0.019
ODI	23.56 (19.32)	26.64 (20.16)	0.037
Smoking, n (%)	120 (44.90)	236 (41.20)	0.305
Alcohol, n (%)	92 (34.50)	238 (41.50)	0.05
Diabetes, n (%)	54 (20.20)	240 (41.90)	< 0.001
CHD, n (%)	37 (13.90)	164 (28.60)	< 0.001

Table 1. General clinical characteristics of the participants. Abbreviations: BMI, body mass index; WBC, white blood cell; NLR, neutrophil–lymphocyte ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride–glucose index; TyG-BMI, Triglyceride glucose–body mass index; AHI, apnea–hypopnea index; SpO₂, Oxygen Saturation; ODI, oxygen desaturation index; CHD, coronary heart disease.

Discussion

The findings of this study indicated a strong association between OSAS, TyG-BMI and the risk of hypertension. The risk of hypertension was significantly higher in patients with severe OSAS than in those with mild OSAS, and the severity of OSAS was positively correlated with TyG-BMI. Additionally, the risk of hypertension in patients with OSAS also increased with increasing TyG-BMI. Mediation analysis confirmed that the risk of hypertension in patients with OSAS was partially mediated by TyG-BMI, with a mediation effect of 41.3%. NLR is a novel inflammatory marker¹⁹, but the study did not tentatively find a mediating role for NLR in the association between OSAS and hypertension risk. Perhaps future studies could explore the role of other inflammatory markers in the relationship between OSAS and hypertension. This suggests that insulin resistance may explain some of the pathological mechanisms underlying the development of hypertension in OSAS.

Numerous studies have confirmed the strong association between OSAS and hypertension, and there is a clear dose-dependent relationship between the degree of hypoxia in OSAS and the severity of hypertensive disease²⁰. Repeated intermittent hypoxia during sleep is the main pathological feature of OSAS. Hypoxia induces the production of inflammatory factors such as interleukin-6 and tumor necrosis factor-alpha in adipose tissue, which promotes the conversion of adipocytes to a pro-inflammatory phenotype, leading to adipose tissue

Variable	Univariable analysis			Multivariable analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.040	1.024–1.056	<0.001	1.051	1.032–1.070	<0.001
TyG-BMI	1.010	1.006–1.014	<0.001	1.011	1.006–1.016	<0.001
Diabetes	2.843	2.020–4.001	<0.001	2.161	1.432–3.260	<0.001
CHD	2.493	1.685–3.687	<0.001	1.85	1.215–2.815	0.004
Uric acid	1.003	1.001–1.004	0.002	1.002	1.001–1.004	0.012
FPG	1.234	1.099–1.385	<0.001	0.985	0.862–1.125	0.819
AHI	1.010	1.003–1.018	0.009	1.014	1.000–1.028	0.058
Lowest SpO ₂	0.979	0.965–0.964	0.005	0.988	0.968–1.009	0.264
Mean SpO ₂	0.913	0.846–0.985	0.019	0.985	0.906–1.009	0.725
ODI	1.008	1.000–1.016	0.038	0.987	0.906–1.071	0.118
NLR	1.130	0.958–1.333	0.147	1.036	0.972–1.175	0.589

Table 2. Logistic regression analysis of risk factors for hypertension in OSAS patients. Abbreviations: TyG-BMI, Triglyceride glucose-body mass index; CHD, coronary heart disease; FPG, fasting plasma glucose; AHI, apnea-hypopnea index; SpO₂, Oxygen Saturation; ODI, oxygen desaturation index; NLR, neutrophil-lymphocyte ratio.

OSAS	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
	Model 1		Model 2		Model 3	
Mild	Reference		Reference		Reference	
Moderate	1.240 (0.830–1.852)	0.294	1.150 (0.757–1.748)	0.512	1.207 (0.781–1.866)	0.398
Severe	1.667 (1.138–2.442)	0.009	1.651 (1.105–2.467)	0.014	1.752 (1.125–2.728)	0.013

Table 3. Logistic regression models of the relationship between OSAS severity and hypertension. Model 1: crude model; Model 2: Adjusted for age, sex, smoking history, alcohol consumption history, white blood cell, haemoglobin, platelet, neutrophil, lymphocyte and monocyte counts; Model 3: Adjusted for age, sex, smoking, alcohol, white blood cells, haemoglobin, platelets, neutrophils, lymphocytes, monocytes, alanine aminotransferase, aspartate aminotransferase, creatinine, uric acid, fasting glucose, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, sleep efficiency, diabetes, and coronary heart disease.

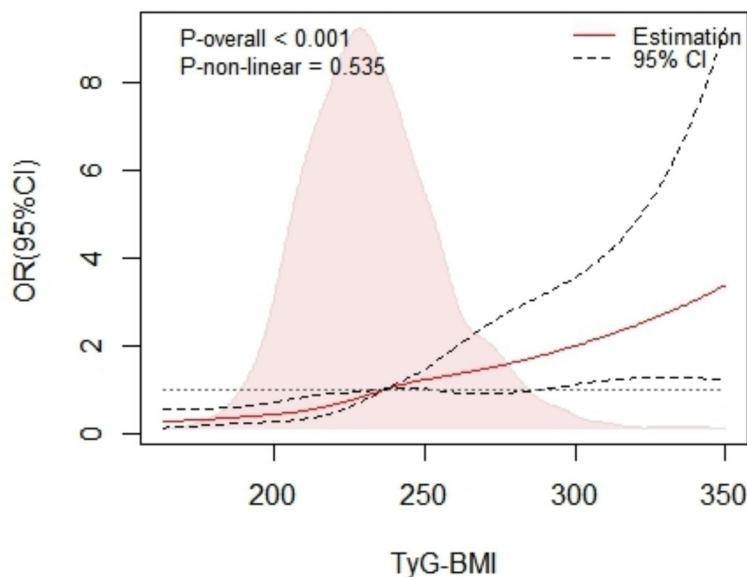


Fig. 1. Restricted cubic spline plot between TyG-BMI and OR (95% CI) of hypertension.

TyG-BMI	Hypertension (yes/no)	OR (95%CI)		OR (95%CI)		OR (95%CI)	
		Model 1	P	Model 2	P	Model 3	P
Q1	118/92	Reference		Reference		Reference	
Q2	136/74	1.433 (0.967-2.123)	0.073	1.606 (1.057-2.442)	0.027	1.576 (1.015-2.445)	0.043
Q3	154/56	2.144 (1.423-3.230)	< 0.001	2.673 (1.712-4.172)	< 0.001	2.457 (1.527-3.954)	< 0.001
Q4	165/45	2.859 (1.864-4.385)	< 0.001	4.225 (2.603-6.859)	< 0.001	3.407 (2.001-5.802)	< 0.001

Table 4. Logistic regression analysis of TyG-BMI and hypertension Model 1: crude model; Model 2: Adjusted for sex, age, smoking history, alcohol consumption history, white blood cell, haemoglobin, platelet, neutrophil, lymphocyte and monocyte counts; Model 3: Adjusted for sex, age, smoking, alcohol, white blood cells, haemoglobin, platelets, neutrophils, lymphocytes, monocytes, alanine aminotransferase, aspartate aminotransferase, creatinine, uric acid, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, sleep efficiency, diabetes, and coronary heart disease

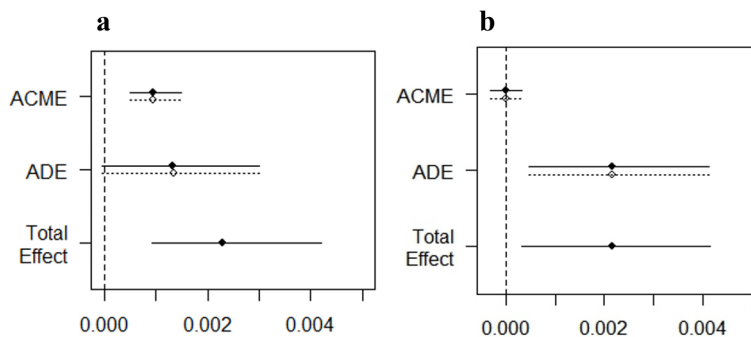


Fig. 2. The study presented total effects, average causal mediation effects (ACME) and average direct effects (ADE). (A) and (B) show mediation effect plots for TyG-BMI and NLR as mediators, respectively. Models were adjusted for risk factors.

dysfunction and insulin resistance^{9,21}. Hypoxia is an independent risk factor for exacerbating the adipose tissue inflammatory response in patients with OSAS²². Rats exposed to intermittent hypoxia have increased levels of liver cytokines, inflammatory factor activity and insulin resistance index²³. Intermittent hypoxia accelerates insulin resistance through specific microRNA upregulation of selenoprotein P levels in human hepatocytes²⁴. In addition, intermittent hypoxia may mediate insulin resistance by increasing the secretion of myokines and myonectin²⁵. In summary, intermittent hypoxia induces insulin resistance by affecting the expression and secretion of adipokines, hepatocytokines, muscle factors and other inflammatory factors.

Insulin resistance is an important risk factor for the development of hypertension^{26,27}, and the cause of hypertensive disorders due to insulin resistance is mainly related to abnormal activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system^{28,29}, as well as a decrease in insulin-mediated production of NO, which has a vasodilatory effect³⁰. Various metabolic disorders caused by insulin resistance are also high-risk factors for cardiovascular disease³¹. In conclusion, the results of many previous studies support the findings of this study.

The TyG index is a classic indicator of insulin resistance, and the TyG-BMI, as a derivative of the TyG index, has been shown in most previous studies to have a significantly higher predictive power for insulin resistance than the TyG index^{14,32,33}. The strong correlation between obesity and insulin resistance could explain these study results. In this study, considering that obesity is an independent risk factor for both OSAS and hypertension, the modified TyG index based on BMI was used as an indicator of insulin resistance and evaluated for its association with both OSAS and hypertension, and the results showed that this combined index is important for assessing the risk of hypertension in OSAS patients. The study results support the application of TyG-BMI values in clinical practice to assess the risk of hypertension in patients with OSAS and to prevent the development of hypertension by controlling body weight, fasting blood glucose and triglyceride levels. Due to the high cost of polysomnographic testing and the low specificity of the clinical presentation of OSAS, this has led to an increased rate of underdiagnosis in patients with OSAS, and the OSAS population is highly susceptible to neglect. However, the metabolic abnormalities associated with OSAS predispose individuals to the development of cardiovascular disease, making the management of this population extremely important. Monitoring and control of body weight and simple biological indicators to reduce the incidence of complications such as hypertension, is very beneficial in the management of chronic diseases. The significance of controlling these indicators should be widely publicized in the daily health education of OSAS patients in order to reduce the risk of developing hypertension.

This study has the following strengths: firstly, there are few studies on the mediators of the association between OSAS and hypertension risk, and exploring the intrinsic link between the two diseases through mediation analyses is the main innovation of this study. Second, the study used the BMI-modified TyG index as a surrogate indicator of insulin resistance, which provided a more comprehensive assessment of the risk of developing hypertension in OSAS by taking into account the additional risk factor of obesity in addition to fasting plasma glucose and triglyceride levels. Finally, compared to some studies that used patients with suspected OSAS who were screened out by snoring or portable home sleep monitors as the study population, this study used the gold standard method of polysomnographic monitoring to diagnose OSAS, which improved diagnostic accuracy and was more rigorous in terms of study design.

Some shortcomings of this study should be noted. Due to the limitations of a cross-sectional study, this study could not establish a causal relationship between OSAS and hypertension. The study was unable to collect information on participants' dietary preferences, lifestyle and exercise habits, and other information related to hypertension. Finally, this is a single-center study, which lacks a sufficiently large sample size to be representative of the general population and has some limitations in terms of the generalisability of the results. Further cytological and molecular studies are needed to investigate the pathological mechanisms of insulin resistance in the effects of OSAS on hypertension and to reveal the causal relationship between the two diseases. At the same time, multicenter studies with large samples should be conducted to broaden the applicability of the results.

Conclusions

TyG-BMI plays an important mediating role between OSAS and the risk of hypertension, suggesting that 41.3% of the risk of hypertension in OSAS patients is attributable to insulin resistance. Chronic intermittent hypoxia in OSAS patients induces insulin resistance, which promotes abnormal activation of vascular tone regulation systems. The study supports the use of TyG-BMI as an important tool to assess hypertension risk in OSAS populations.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Received: 26 May 2024; Accepted: 14 October 2024

Published online: 29 October 2024

References

1. Lv, R. et al. Pathophysiological mechanisms and therapeutic approaches in obstructive sleep apnea syndrome. *Signal Transduct. Target Ther.* **8**, 218. <https://doi.org/10.1038/s41392-023-01496-3> (2023).
2. Heinzer, R. et al. Prevalence of sleep-disordered breathing in the general population: The HypnoLaus study. *Lancet Respir. Med.* **3**, 310–318. [https://doi.org/10.1016/s2213-2600\(15\)00043-0](https://doi.org/10.1016/s2213-2600(15)00043-0) (2015).
3. Lévy, P. et al. Obstructive sleep apnoea syndrome. *Nat. Rev. Dis. Primers* **1**, 15015. <https://doi.org/10.1038/nrdp.2015.15> (2015).
4. Somers, V. K. et al. Sleep apnea and cardiovascular disease: An American Heart Association/American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing. *J. Am. Coll. Cardiol.* **52**, 686–717. <https://doi.org/10.1016/j.jacc.2008.05.002> (2008).
5. Redline, S., Azarbarzin, A. & Peker, Y. Obstructive sleep apnoea heterogeneity and cardiovascular disease. *Nat. Rev. Cardiol.* **20**, 560–573. <https://doi.org/10.1038/s41569-023-00846-6> (2023).
6. Yaggi, H. K. et al. Obstructive sleep apnea as a risk factor for stroke and death. *N. Engl. J. Med.* **353**, 2034–2041. <https://doi.org/10.1056/NEJMoa043104> (2005).
7. Peppard, P. E., Young, T., Palta, M. & Skatrud, J. Prospective study of the association between sleep-disordered breathing and hypertension. *N. Engl. J. Med.* **342**, 1378–1384. <https://doi.org/10.1056/nejm200005113421901> (2000).
8. Schein, A. S., Kerkhoff, A. C., Coronel, C. C., Plentz, R. D. & Sbruzzi, G. Continuous positive airway pressure reduces blood pressure in patients with obstructive sleep apnea; A systematic review and meta-analysis with 1000 patients. *J. Hypertens.* **32**, 1762–1773. <https://doi.org/10.1097/hjh.0000000000000250> (2014).
9. Ota, H. et al. Relationship between intermittent hypoxia and type 2 diabetes in sleep apnea syndrome. *Int. J. Mol. Sci.* **20**, <https://doi.org/10.3390/ijms20194756> (2019).
10. Martínez Cerón, E., Casitas Mateos, R. & García-Río, F. Sleep apnea-hypopnea syndrome and type 2 diabetes. A reciprocal relationship?. *Arch. Bronconeumol.* **51**, 128–139 (2015).
11. da Silva, A. A. et al. Role of hyperinsulinemia and insulin resistance in hypertension: Metabolic syndrome revisited. *Can. J. Cardiol.* **36**, 671–682. <https://doi.org/10.1016/j.cjca.2020.02.066> (2020).
12. da Silva, A. et al. Triglyceride-glucose index is associated with symptomatic coronary artery disease in patients in secondary care. *Cardiovasc. Diabetol.* **18**, 89. <https://doi.org/10.1186/s12933-019-0893-2> (2019).
13. Lim, J., Kim, J., Koo, S. H. & Kwon, G. C. Comparison of triglyceride glucose index, and related parameters to predict insulin resistance in Korean adults: An analysis of the 2007–2010 Korean National Health and Nutrition Examination Survey. *PLoS One* **14**, e0212963. <https://doi.org/10.1371/journal.pone.0212963> (2019).
14. Er, L. K. et al. Triglyceride glucose-body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. *PLoS One* **11**, e0149731. <https://doi.org/10.1371/journal.pone.0149731> (2016).
15. Li, Y. et al. Insulin resistance surrogates predict hypertension plus hyperuricemia. *J. Diabetes Investig.* **12**, 2046–2053. <https://doi.org/10.1111/jdi.13573> (2021).
16. Qaseem, A. et al. Management of obstructive sleep apnea in adults: A clinical practice guideline from the American College of Physicians. *Ann. Intern. Med.* **159**, 471–483. <https://doi.org/10.7326/0003-4819-159-7-201310010-00704> (2013).
17. Sateia, M. J. International classification of sleep disorders-third edition: Highlights and modifications. *Chest* **146**, 1387–1394. <https://doi.org/10.1378/chest.14-0970> (2014).
18. Mancia, G. et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J. Hypertens.* **41**, 1874–2071. <https://doi.org/10.1097/hjh.00000000000003480> (2023).
19. Lux, D. et al. The association of neutrophil-lymphocyte ratio and lymphocyte-monocyte ratio with 3-month clinical outcome after mechanical thrombectomy following stroke. *J. Neuroinflamm.* **17**, 60. <https://doi.org/10.1186/s12974-020-01739-y> (2020).

20. Sanders, M. H. Article reviewed: Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *Sleep Med.* **1**, 327–328. [https://doi.org/10.1016/s1389-9457\(00\)00060-5](https://doi.org/10.1016/s1389-9457(00)00060-5) (2000).
21. Ryan, S. *et al.* Adipose tissue as a key player in obstructive sleep apnoea. *Eur. Respir. Rev.* **28**, <https://doi.org/10.1183/16000617.0006-2019> (2019).
22. Thorn, C. E. *et al.* Adipose tissue is influenced by hypoxia of obstructive sleep apnea syndrome independent of obesity. *Diabetes Metab.* **43**, 240–247. <https://doi.org/10.1016/j.diabet.2016.12.002> (2017).
23. Briançon-Marjollet, A. *et al.* Intermittent hypoxia in obese Zucker rats: Cardiometabolic and inflammatory effects. *Exp. Physiol.* **101**, 1432–1442. <https://doi.org/10.1113/ep085783> (2016).
24. Uchiyama, T. *et al.* Up-regulation of selenoprotein P and HIP/PAP mRNAs in hepatocytes by intermittent hypoxia via down-regulation of miR-203. *Biochem. Biophys. Res. Commun.* **481**, 130–137. <https://doi.org/10.1016/j.bbrep.2017.07.005> (2017).
25. Takasawa, S. *et al.* Upregulation of IL-8, osteonectin, and myonectin mRNAs by intermittent hypoxia via OCT1- and NRF2-mediated mechanisms in skeletal muscle cells. *J. Cell Mol. Med.* **26**, 6019–6031. <https://doi.org/10.1111/jcmm.17618> (2022).
26. Sasaki, N. *et al.* Adipose tissue insulin resistance predicts the incidence of hypertension: The Hiroshima Study on Glucose Metabolism and Cardiovascular Diseases. *Hypertens. Res.* **45**, 1763–1771. <https://doi.org/10.1038/s41440-022-00987-0> (2022).
27. Sung, K. C., Lim, S. & Rosenson, R. S. Hyperinsulinemia and homeostasis model assessment of insulin resistance as predictors of hypertension: A 5-year follow-up study of Korean sample. *Am. J. Hypertens.* **24**, 1041–1045. <https://doi.org/10.1038/ajh.2011.89> (2011).
28. Reaven, G. M., Lithell, H. & Landsberg, L. Hypertension and associated metabolic abnormalities—the role of insulin resistance and the sympathoadrenal system. *N. Engl. J. Med.* **334**, 374–381. <https://doi.org/10.1056/nejm199602083340607> (1996).
29. Jia, G. & Sowers, J. R. Hypertension in diabetes: An update of basic mechanisms and clinical disease. *Hypertension* **78**, 1197–1205. <https://doi.org/10.1161/hypertensionaha.121.17981> (2021).
30. Hill, M. A. *et al.* Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism* **119**, 154766. <https://doi.org/10.1016/j.metabol.2021.154766> (2021).
31. Alizargar, J., Bai, C. H., Hsieh, N. C. & Wu, S. V. Use of the triglyceride-glucose index (TyG) in cardiovascular disease patients. *Cardiovasc. Diabetol.* **19**, 8. <https://doi.org/10.1186/s12933-019-0982-2> (2020).
32. Wang, R., Dai, L., Zhong, Y. & Xie, G. Usefulness of the triglyceride glucose-body mass index in evaluating nonalcoholic fatty liver disease: Insights from a general population. *Lipids Health Dis.* **20**, 77. <https://doi.org/10.1186/s12944-021-01506-9> (2021).
33. Li, N. *et al.* Value of the triglyceride glucose index combined with body mass index in identifying non-alcoholic fatty liver disease in patients with type 2 diabetes. *BMC Endocr. Disord.* **22**, 101. <https://doi.org/10.1186/s12902-022-00993-w> (2022).

Acknowledgements

We would like to express our sincere gratitude to all the members of the research team and all the participants who took part in this study.

Author contributions

LW was responsible for study design, statistical software operation, data analysis, and manuscript writing. LW, JZ, SL and CT were involved in project management and data collection. JR, XY, YL were involved in data collection and verification. GN reviewed and revised the manuscript. LJ and WP supervised the research project and guided the methodological and conceptual components.

Funding

No funding.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Wuhan Union Medical College Hospital (UHCT-IEC-SOP-016-03-01) and informed consent was waived.

Consent for publication

Not applicable.

Additional information

Correspondence and requests for materials should be addressed to L.J. or W.P.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

© The Author(s) 2024