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The association between triglyceride glucose index and the risk of cardiovascular disease in obstructive sleep apnea

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Abstract

Purpose The triglyceride glucose (TyG) index is a dependable indicator of insulin resistance (IR), serves as a valuable biomarker for identifying obstructive sleep apnea (OSA) and predicting its comorbidities. Both OSA and the TyG index are significantly related to the incidence and development of cardiovascular disease (CVD). We focus on investigating the relationship between the TyG index and the incidence of CVD risk in OSA.

Methods The TyG index, homeostatic model assessment of IR (HOMA-IR) index, and polysomnography were assessed in 191 participants with OSA and without pre-existing CVD. To estimate the lifetime CVD risk, we employed the 'Prediction for Atherosclerotic CVD Risk in China' equation. The TyG index's association with CVD risk was scrutinized using multivariable logistic regression models, contrasting it with the HOMA-IR index. We compared the predictive power for high lifetime CVD risk of the TyG index and the HOMA-IR index using receiver-operating characteristic (ROC) curve analysis.

Results A total of 89 participants had high lifetime CVD risk. In fully adjusted model and additionally adjusted for HOMA-IR index, participants situated within the fifth quantile of the TyG index exhibited an increased lifetime CVD risk, with OR of 4.32 (95% CI, 1.19–15.67). The TyG index demonstrated significant predictive power for high lifetime CVD risk across varying severities of OSA and outperformed the HOMA-IR index, as evidenced by a larger area under the ROC curve.

Conclusion The TyG index, independent of the HOMA-IR index and obesity, was linked to an increased lifetime CVD risk. In predicting cardiovascular outcomes, the TyG index could potentially outperform the HOMA-IR index among individuals with OSA.

Keywords Obstructive sleep apnea · Cardiovascular disease · Triglyceride glucose index · Insulin resistance

Abbreviations

OSA	Obstructive sleep apnea
CVD	Cardiovascular disease
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
LAT	Low arousal threshold
PSQI	Pittsburgh Sleep Quality Index
ESS	Epworth Sleepiness Scale
OR	Odds ratio
CI	Confidence interval
ROC	Receiver-operating characteristic
AUC	The area under the curve
HbA1c	Glycosylated hemoglobin
HOMA-IR	Homeostasis model assessment of insulin resistance
IR	Insulin resistance
TyG	Triglyceride glucose
HDL-c	High-density lipoprotein cholesterol
LDL-c	Low-density lipoprotein cholesterol
PSG	Polysomnography
AHI	Apnea-hypopnea index
TST	Total sleep time
N1	Non-rapid eye movement stage 1
N2	Non-rapid eye movement stage 2
N3	Non-rapid eye movement stage 3
REM	Rapid eye movement

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$mSpO_2$	Mean values of peripheral blood oxygen saturation
$LSpO_2$	Lowest oxygen saturation by pulse oximetry
T90	The percent of time spent with SpO_2 below 90%
ODI	The oxygen desaturation index

Introduction

Obstructive sleep apnea (OSA) is a prevalent medical condition, marked by repeated episodes of hypopnea and apnea during sleep, affecting nearly 1 billion individuals globally [1]. These episodes of obstructive breathing result in arousal, sympathetic activation, and oxygen desaturation. OSA is recognized as an independent risk factor for cardiovascular disease (CVD) and a predictor of CVD-related mortality [2, 3]. Due to the heavy burden of CVD, various equations for assessing CVD risk have been developed, such as the Framingham Risk Score, the Systematic Coronary Risk Evaluation algorithm, the QRISK risk score, and the Pooled Cohort Equations for atherosclerotic CVD (ASCVD) [4]. Additionally, due to the relatively high prevalence of OSA in the Chinese population, which is often associated with different anthropometric and clinical characteristics compared to Western populations [5], and the fact that CVD is a leading cause of death in China [6], it is crucial to explore the CVD risk in the Chinese population with OSA.

However, given the genetic factors and CVD risk factors variances between Chinese and Western populations, Western CVD risk models may not be directly applicable to the Chinese population [7]. To address this, the China-PAR project (Prediction for ASCVD risk in China) was initiated, creating and validating ASCVD risk equation tailored for the Chinese population using data from various modern cohorts. In addition to major risk factors (such as age and current smoking) of CVD, this equation included waist circumference, geographic region, urbanization, and family history of CVD, which met the predefined inclusion criteria based on relative integrated discrimination improvement index of $\geq 6\%$. These factors were not included in Chinese CVD prediction models previously [8]. The equation's tailored approach allows for more accurate and relevant risk assessments, providing more accurate10-year and lifetime CVD risks predictions, and detailed risk stratifications for the Chinese population [8–10]. Moreover, The China-PAR equation has demonstrated superior predictive capabilities for CVD risk compared to its counterparts after validation [8].

Extensive evidence indicates that OSA and CVD have a bidirectional relationship, influenced by factors such as intermittent hypoxia, sympathetic activation, inflammatory responses, and insulin resistance (IR) [11, 12]. Different mechanisms may predominate in specific comorbidities. For example, sympathetic activation is associated with the development of hypertension [13]; swings in intrathoracic pressure, inflammation, and oxidative stress are linked to the development of atherosclerosis, coronary artery disease, and heart failure [14]. Conversely, studies indicated that blood pressure fluctuations can affect upper airway tone, as evidenced by inhibitory changes on electromyogram [15]. Additionally, heart failure can lead to fluid accumulation and redistribution during sleep, increasing the likelihood of upper airway collapse [16]. Regarding IR, numerous studies have suggested that it is a more pivotal contributor to cardiometabolic complications than hyperglycemia [17]. Even in the absence of diabetes, individuals with IR are predisposed to an increased risk of CVD [18, 19], making the measurement of IR in OSA patients vital for predicting CVD events [20]. The homeostatic model assessment for IR (HOMA-IR) index is highly sensitive and specific and is extensively used in both research and clinical practice to estimate the severity of IR [21, 22]. Currently, the triglyceride glucose (TyG) index, calculated from fasting triglyceride and glucose levels, has become a dependable alternative marker for IR. It has proven to be effective in assessing the risk of adverse CVD events and has outperformed the HOMA-IR index, showing significant correlation with the hyperinsulinemic-euglycemic clamp technique [23–26]. Moreover, several studies have indicated that a higher TyG index is linked to an increased OSA risk [27, 28]. Therefore, given the relationship between the TyG index and OSA risk, as well as its contribution to CVD risk, early risk stratification for patients with OSA is particularly important. This not only aids in the prevention of CVD occurrence but also provides a basis for developing personalized treatment plans.

Up to now, numerous studies have established that elevated TyG index is linked to a higher risk of both OSA and CVD [27, 29]. However, the precise relationship between the TyG index and CVD risk in OSA patients remains underexplored. In this study, we aimed to elucidate the connection between lifetime CVD risk and the TyG index in OSA patients. Additionally, we compare the efficacy of the TyG index and the HOMA-IR index in predicting lifetime CVD risk across varying severities of OSA.

Methods

Participants

This study utilized data from the sleep center of Peking Union Medical College Hospital (PUMCH). After completing the overnight polysomnography (PSG), patients aged

18 to 60 with OSA were enrolled. We excluded participants who: (1) had an AHI of < 5/h; (2) had pre-existing CVD before enrollment, such as coronary heart disease, arrhythmia, and heart failure; (3) lacked data for the TyG index or the HOMA-IR index; (4) had recently received treatment for OSA, such as continuous positive airway pressure; (5) had uncontrolled nervous system diseases and cardiovascular diseases, such as Parkinson's disease and acute kidney failure; (6) had total sleep time (TST) < 4 h (TST < 4 h was defined as poor sleep [30], and extremely short sleep duration may underestimate the frequency of relevant events, leading to potential biases in the results. Insufficient sleep can significantly affect physiological parameters and health outcomes [31]. Additionally, previous studies have consistently excluded participants with TST < 4 h to maintain data integrity and ensure comparability [32, 33].); (7) had poor quality PSG data. (8) were treated with insulin (because HOMA-IR index requires the inclusion of insulin levels for its calculation, and the use of exogenous insulin can significantly interfere with the accurate assessment of insulin resistance, distorting the HOMA-IR values [21, 34]. Additionally, the utility of the HOMA-IR index is limited in individuals undergoing insulin treatment [22].).

This study adhered with the principles outlined in the Declaration of Helsinki. It received approval from the ethics committee of PUMCH (JS-3573), and all participants provided written informed consent.

Data collection

We collected demographic data from all participants, including age, sex, body mass index (BMI), neck circumference, waist circumference, smoking and drinking status, and diseases history. After a 10-minute rest, seated blood pressure was measured three times consecutively on the nondominant arm with a 1-minute interval in the morning. All participants were also asked to complete the Epworth Sleepiness Scale (ESS) questionnaire and Pittsburgh Sleep Quality Index (PSQI). Blood examinations were conducted to measure serum lipid profiles, glycosylated hemoglobin (HbA1c), fasting insulin, and fasting blood glucose (FBG) using standard procedure. According to previous studies [21, 26], the TyG index and the HOMA-IR index were calculated using the formulas, respectively: ln (fasting triglycerides [mg/dL] × FBG [mg/dL]/2) and (fasting insulin [IU/mL] × FBG [mmol/L]/22.5).

The China-PAR project, used for determining lifetime and 10-year CVD risk, incorporates factors such as age, smoking status, waist circumference, history of hypertension and diabetes mellitus, geographic region, urbanization, and family history of ASCVD, systolic and diastolic blood pressure, total cholesterol, and high-density lipoprotein cholesterol [8, 9]. A lifetime CVD risk of 32.8% or higher was categorized as high risk [9].

Overnight PSG

All participants attended overnight PSGs (Embla N7000, Natus Medical Incorporated, Orlando, FL, USA) from 11 p.m. to 6 a.m. in our sleep center. All PSG data were recorded and analyzed by experienced sleep technologist using the standard criteria recommended by the American Academy of Sleep Medicine. OSA diagnosis was based on the International Classification of Sleep Disorders-Third Edition [35]. Non-OSA, mild OSA, moderate OSA, and severe OSA were defined as an AHI of < 5/h, 5–15/h, 15–30/h, and ≥ 30/h, respectively. Additionally, we scored non-rapid eye movement (N1, N2, N3) sleep, rapid eye movement (REM) sleep, sleep efficiency, TST, the oxygen desaturation index (ODI), mean oxygen saturation by pulse oximetry ($mSpO_2$), lowest oxygen saturation by pulse oximetry ($LSpO_2$), the percent of time spent with SpO_2 below 90% (T90), and arousals. ODI was calculated by dividing the total number of ≥ 3% SpO_2 drop per hour. The arousal index was calculated as the total number of arousals episodes per hour of electroencephalographic sleep. The low arousal threshold (LAT) and score were referenced to a previous study [36].

Statistical analysis

Continuous variables were presented as mean ± standard deviation if they followed a normal distribution, or as median (P25, P75) if they did not. Categorical variables were presented as numbers (percentage). The Kolmogorov-Smirnov test was used to assess the normality of variable distributions. For comparing continuous variables, we used the independent samples t-test and Mann-Whitney U test, while the chi-squared test and Fisher's exact test were employed for categorical variables. The relationship between the TyG index and high lifetime CVD risk was evaluated using multivariate logistic regression across five adjusted models. Variables included in the China-PAR were not included for adjusting. Established roles of the TyG index and the HOMA-IR index in predicting CVD risk and their widespread use as surrogate markers for insulin resistance, as well as both indices have been proven to be associated with increased CVD risk in various populations [23, 37]. Moreover, evidence suggested that the TyG index is outperforms the HOMA-IR index in predicting CVD incidence in the general population, and it is also a more affordable and convenient alternative [34, 38, 39]. Thus, we assessed the overall performance of the TyG index and the HOMA-IR index for predicting high lifetime CVD risk in OSA patients by calculating the area under the receiver-operating characteristic

(ROC) curve (AUC). This provides a comprehensive understanding of how these indices perform in identifying individuals at high risk for cardiovascular events. The optimal cut-off points were identified as the points on the curve with the highest sensitivity and specificity. All statistical analyses were performed using SPSS software version 26 (IBM Corporation, Armonk, NY, United States). A two-sided P-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 240 participants with suspected OSA underwent overnight PSG, and 191 eligible participants were included in the analysis after excluding those who met the exclusion criteria (Fig. 1). Among the participants, 140 (73.30%) had moderate-to-severe OSA, 89 (46.60%) had high lifetime CVD risk. The included participants had a median age of 45 years, a median BMI of 27.10 kg/m^2, a median TyG index of 6.11, and a median HOMA-IR index of 2.96. The baseline characteristics of participants across different lifetime CVD risk groups were shown in Table 1. It indicated that the high lifetime CVD risk group had significantly larger neck circumference, higher PSQI scores and BMI, and higher TyG index and HOMA-IR index, compared to the low lifetime CVD risk group, in addition to the characteristics included in the China-PAR prediction equation.

PSG characteristics

Table 2 presented the primary PSG characteristics of participants with different lifetime CVD risks. Participants with high lifetime CVD risk appeared to have a higher frequency of respiratory events (38.75/h vs. 26.95/h, $P = 0.086$) and reduced time in REM and slow wave sleep. Moreover, these individuals experienced more severe nocturnal hypoxia, as

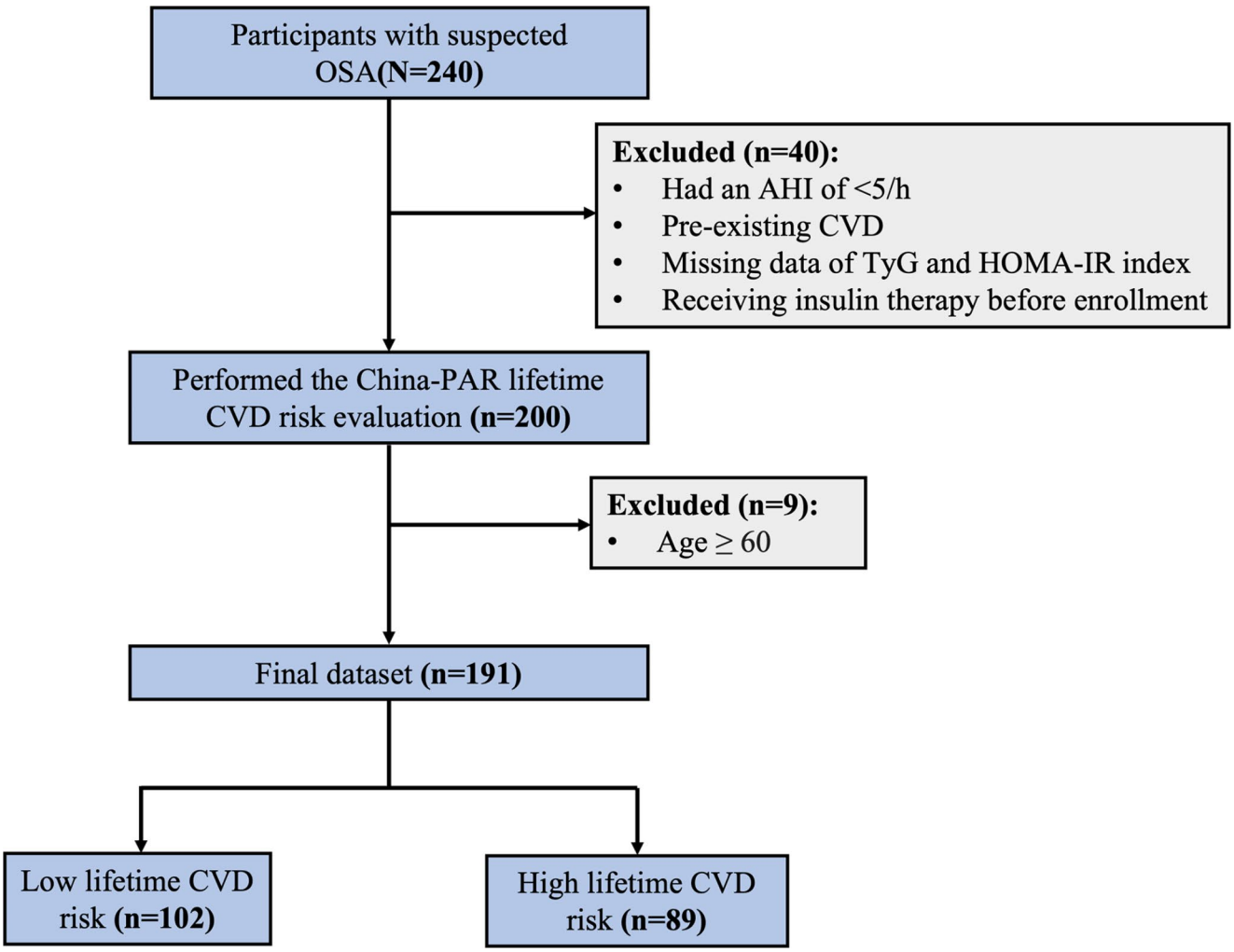

Fig. 1 Flow chart of study. Abbreviations: OSA, obstructive sleep apnea; CVD, cardiovascular disease; HOMA-IR, homeostasis model assessment of insulin resistance; TyG, triglyceride glucose; China-PAR, Prediction for ASCVD Risk in China

Table 1 Baseline characteristics between groups with different lifetime CVD risk

Variables	Low lifetime CVD risk ($N=102$)	High lifetime CVD risk ($N=89$)	P
Age, y*	46.00 (36.75, 53.00)	44.00 (35.00, 52.00)	0.311
Male, n (%)*	93 (91.20%)	80 (89.90%)	0.761
Cigarettes smoking, n (%)*	37 (36.30%)	56 (62.90%)	< 0.001
Alcohol, n (%)	53 (52.00%)	59 (66.30%)	0.045
HTN, n (%)*	23 (22.50%)	48 (53.90%)	< 0.001
DM, n (%)*	12 (10.30%)	32 (34.40%)	< 0.001
Systolic blood pressure, mmHg*	127.00 (116.75, 133.00)	138.50 (132.25, 146.75)	< 0.001
Diastolic blood pressure, mmHg*	83.90 ± 9.38	92.66 ± 10.63	< 0.001
BMI, kg/m^2	26.61 (24.45, 28.41)	27.71 (25.48 (30.11)	0.003
Neck circumference, cm	40.00 (37.75, 41.63)	40.25 (39.00, 43.00)	0.003
Waist Circumference, cm*	96.75 (90.00, 102.00)	99.00 (94.13 (105.00)	0.011
EES	11.00 (7.75, 15.00)	13.00 (8.00, 16.00)	0.245
PSQI	7.00 (4.00, 9.00)	8.00 (7.00, 11.00)	< 0.001
10-year CVD risk, %	2.70 (1.50, 5.03)	8.30 (3.43, 13.68)	< 0.001
Lifetime CVD risk, %	24.35 (19.40, 28.93)	41.60 (36.12, 51.33)	< 0.001
TC, mmol/L*	4.84 ± 0.96	5.14 ± 1.29	0.066
TG, mmol/L	1.53 (1.21, 2.10)	2.37 (1.48 (3.06)	< 0.001
HDL-c, mmol/L*	1.11 (0.96, 1.25)	0.96 (0.84, 1.08)	< 0.001
LDL-c, mmol/L	2.30 ± 0.87	3.25 ± 1.10	0.077
FBG, mmol/L	5.50 (5.10, 6.20)	6.10 (5.40, 6.90)	< 0.001
Insulin levels, μIU/ml	10.85 (7.70, 14.78)	13.55 (8.33, 18.85)	0.009
HbA1c, %	5.45 (5.20, 5.80)	5.80 (5.40, 6.48)	< 0.001
HOMA-IR index	2.66 (1.78, 4.02)	3.84 (2.32, 5.96)	0.001
TyG index	5.90 (5.66, 6.24)	6.44 (6.07, 7.12)	< 0.001
Moderate-to-severe OSA, n (%)	76 (74.50%)	64 (71.90%)	0.685

* Indicates the variables included in the China-PAR equation. Abbreviations: CVD, cardiovascular disease; OSA, obstructive sleep apnea; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; TC, total cholesterol; TG, triglyceride; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; TyG, triglyceride glucose

indicated by ODI (33.45/h vs. 22.50/h, $P=0.007$). Additionally, PSG characteristics according to mild and moderate-to-severe OSA groups were shown in Table S1 in the supplementary material. Patients with severer OSA exhibited more severe nocturnal hypoxia, an increased proportion of N2, a higher prevalence of LAT, and a reduced proportion of N3.

Association between the TyG index and high lifetime CVD risk

We assessed the relationship between the TyG index quantiles and high lifetime CVD risk using multivariate logistic regression analysis, as detailed in Table 3. To achieve better adjustments, we gradually incorporated variables with $P<0.1$ between different lifetime CVD risk groups into the logistic regression model. Participants situated within the fourth and fifth quantiles of the TyG index demonstrated a higher proportion of high lifetime CVD risk with unadjusted odds ratio (OR) of 3.73 (95% confidence interval [CI], 1.41–9.87) and 6.48 (95% CI, 2.36–17.83), respectively. After we gradually adjusted for BMI, neck circumference, PSQI and alcohol using (Model 1), sleep structures (Model 2), ODI and AHI (Model 3), and insulin levels, FBG levels, low-density lipoprotein cholesterol, and HbA1c levels (Model 4), the association between the highest quantile of the TyG index and high lifetime CVD risk remained significant in Model 4 (OR, 3.97 [95% CI, 1.12–14.09]). Moreover, after additionally adjusting for the HOMA-IR index (Model 5), the highest quantile of the TyG index also showed a positive association with high lifetime CVD risk, with an OR of 4.32 (95% CI, 1.19–15.67).

The abilities of the TyG index and the HOMA-IR index for predicting high lifetime CVD risk

We conducted the ROC curve analysis for mild OSA and moderate-to-severe OSA to predict the high lifetime CVD risk, with the results presented in Fig. 2, respectively. Table 4 displayed the optimal cut-off values for the TyG index and the HOMA-IR index, achieving the best balance between sensitivity and specificity in predicting high lifetime CVD risk, along with AUC statistics. In both groups,

Table 2 Polysomnographic characteristics between groups with different lifetime CVD risk

Variables	Low lifetime CVD risk ($N=102$)	High lifetime CVD risk ($N=89$)	P
TST, min	405.30 (362.90, 441.00)	404.50 (351.00, 440.35)	0.667
AHI, /h	26.95 (14.33, 49.13)	38.75 (14.55, 64.73)	0.086
Obstructive apnea, /h	14.20 (5.30, 36.83)	22.15 (7.25, 47.73)	0.105
Central apnea, /h	0.10 (0.00, 0.40)	0.00 (0.00, 0.30)	0.554
Mixed apnea, /h	0.20 (0.00, 2.23)	0.30 (0.00, 1.73)	0.995
Apnea, /h	16.20 (5.85, 39.78)	25.10 (7.78, 59.03)	0.111
Hypopnea, /h	5.80 (2.10, 10.95)	5.85 (2.18, 12.65)	0.621
N1, %	7.60 (4.38, 14.63)	9.45 (5.75, 15.78)	0.139
N2, %	43.80 (36.08, 57.85)	54.05 (42.53, 68.25)	0.001
N3, %	24.15 (12.68, 34.80)	17.25 (5.88, 28.03)	0.005
REM, %	16.39 ± 6.23	14.24 ± 6.27	0.019
REM-AHI, /h	37.30 (14.60, 55.60)	50.15 (16.15, 63.55)	0.122
SE, %	90.90 (82.88, 96.30)	90.90 (80.23, 95.75)	0.709
$mSpO_2$, %	96.00 (94.38, 97.50)	95.90 (93.48, 97.40)	0.502
$LSpO_2$, %	85.00 (79.75, 88.00)	82.00 (74.00, 88.00)	0.275
T90, %	0.35 (0.00, 2.45)	1.30 (0.00, 8.23)	0.120
ODI, /h	22.50 (11.28, 41.53)	33.45 (11.70, 63.33)	0.007
Arousal index	1.08 (0.59, 1.66)	0.94 (00.54, 1.59)	0.441
LAT score	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	0.177
LAT, n (%)	47 (46.10%)	34 (38.20%)	0.272

Abbreviations: CVD, cardiovascular disease; TST, total sleep time; AHI, apnea-hypopnea index; N1, non-rapid eye movement stage 1; N2, non-rapid eye movement stage 2; N3, non-rapid eye movement stage 3; REM, rapid eye movement; SE, sleep efficiency; $mSpO_2$, mean values of peripheral blood oxygen saturation; $LSpO_2$, lowest oxygen saturation by pulse oximetry; T90, percent of time spent with SpO_2 below 90%; ODI, oxygen desaturation index; LAT, low arousal threshold

Table 3 Associations between the TyG index and high lifetime CVD risk in participants with OSA

TyG index Quantiles	Model 0 OR (95%CI)	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)	Model 4 OR (95%CI)	Model 5 OR (95%CI)
Q1	1	1	1	1	1	1
Q2	0.52 (0.18, 1.50)	0.39 (0.12, 1.26)	0.37 (0.11, 1.25)	0.39 (0.12, 1.30)	0.32 (0.09, 1.17)	0.33 (0.92, 1.20)
Q3	1.27 (0.48, 3.39)	0.75 (0.25, 2.21)	0.79 (0.26, 2.35)	0.78 (0.26, 2.33)	0.73 (0.22, 2.41)	0.75 (0.23, 2.46)
Q4	3.73 (1.41, 9.87)**	2.10 (0.71, 6.24)	2.36 (0.76, 7.34)	2.37 (0.75, 7.46)	1.84 (0.54, 6.25)	2.01 (0.58, 6.97)
Q5	6.48 (2.36, 17.83)**	4.19 (1.40, 12.55)*	4.67 (1.45, 15.05)*	4.56 (1.41, 14.72)*	3.97 (1.12, 14.09)*	4.32 (1.19, 15.67)*

*$P<0.05$, **$P<0.01$. Model 0 was unadjusted; Model 1: adjusted for BMI, neck circumference, PSQI and alcohol using; Model 2: adjusted for N2, N3, REM plus all covariates in Model 1; Model 3: adjusted for ODI and AHI plus all covariates in Model 2; Model 4: adjusted for insulin, HbA1c, FBG, LDL-c plus all covariates in Model 3; Model 5: adjusted for HOMA-IR plus all covariates in Model 4. Abbreviations: CVD, cardiovascular disease; OSA, obstructive sleep apnea; BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; N2, non-rapid eye movement stage 2; N3, non-rapid eye movement stage 3; REM, rapid eye movement; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; LDL-c, low-density lipoprotein cholesterol; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; TyG, triglyceride glucose

the AUC value for the TyG index was significantly greater than that for the HOMA-IR index ($p<0.05$).

Discussion

This cross-sectional study revealed that elevated TyG index was consistently linked to an increased lifetime CVD risk, independent of obesity and the HOMA-IR index in adults with OSA. Furthermore, the TyG index has been proven to be a valuable tool for predicting CVD outcomes in OSA patients and outperformed the HOMA-IR index.

Previous studies predominantly reported a link between OSA and an elevated risk of CVD incidence, progression, and mortality [2, 3, 40, 41]. However, this association has been met with some contention in the literature [42, 43]. In this current study, we additionally demonstrated that individuals with OSA ($N=191$) had a higher lifetime CVD risk compared to those without OSA ($N=18$) (32.20% vs. 28.20%, $P=0.059$, data not shown). Previous studies suggested that intermittent hypoxia, sympathetic activation, inflammatory disturbances, and hemodynamic changes could be the reasons for the increased CVD risk in OSA [11, 44].

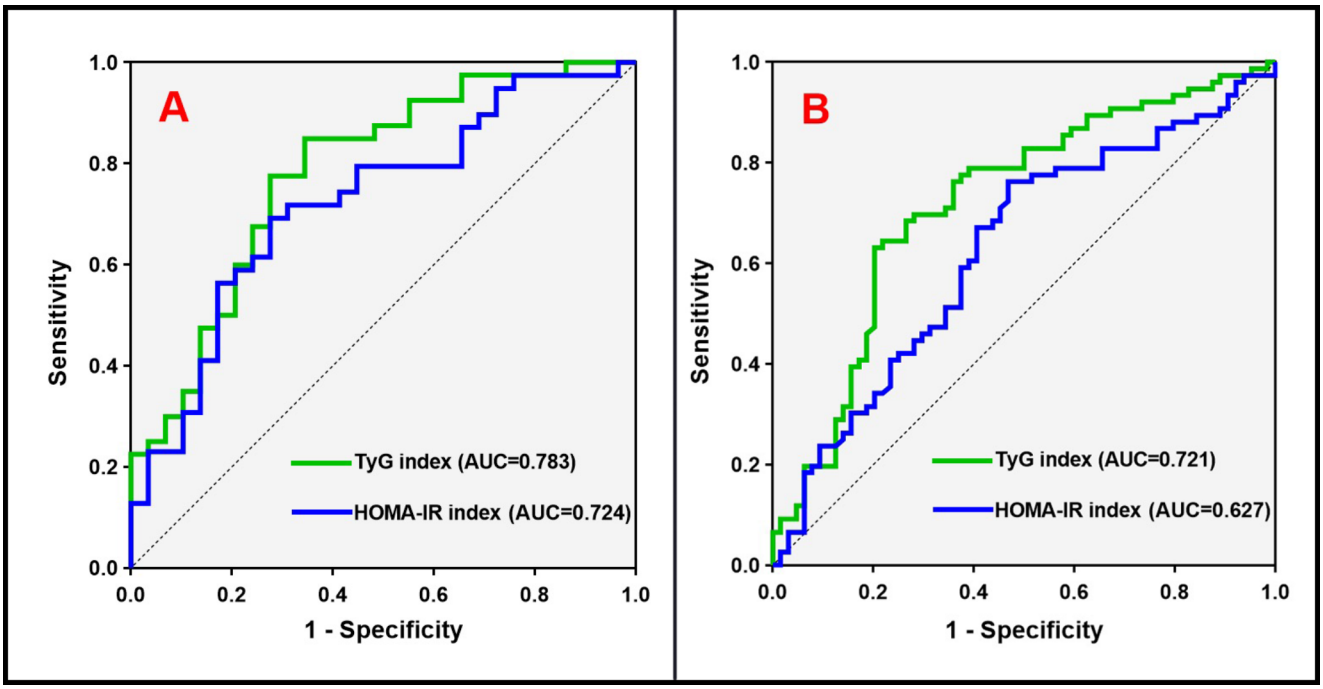

Fig. 2 ROC curves to predict CVD outcomes by the HOMA-IR and the TyG index in individuals with **(A)** mild OSA and **(B)** moderate-to-severe OSA. Abbreviations: OSA, obstructive sleep apnea; CVD, cardiovascular disease; HOMA-IR, homeostasis model assessment of insulin resistance; TyG, triglyceride glucose; ROC, receiver-operating-characteristic

Table 4 The cut-off points and AUC of the TyG index and the HOMA-IR index by severity of OSA for predicting high lifetime CVD risk

OSA severity	Index	Sensitivity	Specificity	Cut-off point	AUC	*P*
mild OSA	HOMA-IR	0.724	0.692	2.881	0.724	0.002
	TyG	0.655	0.846	6.181	0.783	< 0.001
moderate-to-severe OSA	HOMA-IR	0.531	0.763	3.720	0.627	0.008
	TyG	0.797	0.632	6.039	0.721	< 0.001

Abbreviations: CVD, cardiovascular disease; OSA, obstructive sleep apnea; AUC, the area under the curve; HOMA-IR, homeostasis model assessment of insulin resistance; TyG, triglyceride glucose

IR is well-recognized as a major risk factor contributing to the increased incidence and mortality associated with hypertension, coronary artery disease, and stroke, with hyperglycemia, inflammation, oxidative stress, and lipid metabolism disturbances as the key underlying mechanisms [38, 39, 45]. While the HOMA-IR index is commonly employed to measure IR, its utility is limited in individuals undergoing insulin treatment or those with non-functioning beta cells [22]. Additionally, directly measuring serum insulin levels is costly and often unavailable in many cities within developing countries, making the HOMA-IR index difficult to obtain. Consequently, the TyG index has been introduced as a more affordable and convenient alternative [34].

As an effective surrogate marker for IR, the TyG index has been increasingly linked to the development and prognosis of CVD. Previous studies have indicated that the TyG index is significantly associated with cardiovascular outcomes, such as heart failure [46], atrial fibrillation [47], coronary artery disease [48], stroke [49], arterial stiffness [50], peripheral artery disease [51], and even composite heart diseases [52]. Given the relationship between OSA and the TyG index, several studies have shown that the TyG index could be a valuable biomarker for diagnosing OSA and predicting its comorbidities, even in patients without any other metabolic risk factors [27, 28, 53]. Additionally, composite lipid indices including adiposity index, atherogenic index of plasma, and lipid accumulation product possess valuable diagnostic and prognostic capabilities in OSA [54]. Our findings further underscore this point, revealing a higher TyG index in individuals with OSA compared to those without OSA (6.11 vs. 5.73, $P = 0.008$, data not shown), highlighting the metabolic dysregulation present in these individuals.

One study explored the relationship between the TyG index and incident CVD in patients with OSA. The results showed that the incidence of myocardial infarction was correlated with the TyG index-waist circumference in patients

with hypertension and OSA, but it did not evaluate the predictive efficacy against the HOMA-IR index [55]. This current study, which focuses on individuals with OSA, supports the positive correlation between the TyG index and lifetime CVD risk. Several previous studies have indicated that the TyG index outperforms the HOMA-IR index in predicting the development and outcomes of CVD in the general population [34, 38]. Aligning with these insights, our findings also demonstrate enhanced predictive performance of the TyG index for CVD outcomes across varying severities of OSA. The potential mechanism for superiority of the TyG index could be that it combines two risk factors for CVD, lipid-related and glucose-related factors, providing a more comprehensive assessment of metabolic health, whereas the HOMA-IR index only includes fasting glucose and insulin levels. Hyperglycemia may trigger inflammation and oxidative stress, leading to systemic lipid disturbances such as increased TG (triglyceride), especially the TG-rich Apolipoprotein B-containing remnants within the coronary wall, which may be related to the pathogenesis of atherosclerosis [56]. IR can induce an increased production of glycosylated products and free radicals, leading to nitric oxide (NO) inactivation [57]. The abnormal secretion of NO and overproduction of reactive oxidative stress related to IR damage the vascular endothelium, resulting abnormal coronary microcirculation, which is associated with CVD [34].

The clinical utility of our findings includes considering the TyG index as a convenient and superior marker of IR in OSA patients with high lifetime CVD risk. Given the limitations of common markers like the HOMA-IR index, such as the complexity and higher cost of measurement, the TyG index proves to be a cost-effective and reliable alternative. It shows high sensitivity (96.5%) and specificity (85.0%) for IR compared to the gold standard, the euglycemic-hyperinsulinaemia clamp test [26, 34]. Previous studies have shown that the TyG index outperforms the HOMA-IR index in predicting CVD and metabolic disease in the general population [34, 38, 58]. The TyG index's higher sensitivity to metabolic changes allows for earlier identification of patients at high CVD risk and better stratification of OSA patients based on their CVD risk. This enables healthcare providers to implement preventive measures and interventions sooner and develop more personalized treatment plans, potentially reducing the incidence of cardiovascular events in OSA patients. For instance, OSA patients with higher TyG index may benefit from more aggressive lipid-lowering therapies and glucose control. Additionally, the use of the TyG index facilitates a more integrated care approach, addressing both metabolic and cardiovascular health. This holistic approach is crucial for OSA patients, as the interplay between metabolic disorders and cardiovascular risk factors can significantly impact patient outcomes [34]. This study demonstrates the significant association between the TyG index and high lifetime CVD risk in OSA patients, highlighting its better predictive ability compared to the HOMA-IR index. However, the impact of the TyG index on CVD prognosis in OSA patients remains explored. Thus, further research is needed to address this gap.

This current study represents some strengths. The TyG index, being a more cost-effective measure, could be considered as an essential tool for the early detection of CVD in clinical practice. Additionally, assessing the TyG index may provide a basis for selecting appropriate OSA interventions or treatments to improve IR in this at-risk population, thereby enhancing their CVD outcomes. This study acknowledges several limitations. Firstly, this is a cross-sectional study conducted at a single center with a relatively small sample size, predominantly consisting of male patients. Secondly, we excluded individuals with pre-existing CVD based on their self-reported data, lacking clinical validation. Thirdly, the primary outcome relied on indirect measures from the China-PAR prediction equation, which has yet to be validated in OSA populations and are limited to ASCVD events. The robustness of this association is yet to be determined for other cardiovascular comorbidities in long-term prospective studies. Fourthly, the China-PAR equation is specifically developed and validated in a Chinese population and its risk factors are tailored to the genetic, environmental, and lifestyle characteristics prevalent in China. As a result, the generalizability of our findings to populations outside of China may be impacted. Finally, this equation's maximum age limit of 60 years, making it uncertain if our conclusions apply to those older than this age range.

Conclusion

Individuals with an increased TyG index are linked to higher lifetime CVD risk independent of obesity and even the HOMA-IR index. Regardless of the severity of OSA, the AUC for the TyG index is consistently higher than that for the HOMA-IR index, suggesting that the TyG index is more effective in predicting CVD risk compared to the HOMA-IR index.

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Data availability The datasets used and/or analyzed during the current

study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval This study protocol was approved by the ethics committees of PUMCH (JS-3573), and informed consent for involvement in the study was obtained from each participant.

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

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