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Triglyceride-glucose index as a predictor of the risk of sarcopenia in elderly patients with OSA: a multicenter study

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Abstract

Background Given the clear association between obstructive sleep apnea (OSA) and metabolic disorders, coupled with a limited understanding of sarcopenia in patients with OSA, this study aimed to investigate the relationship between triglyceride-glucose (TyG) index and sarcopenia and in an elderly population with OSA.

Methods Multiple hematological and sleep-breathing status were meticulously recorded in the cohorts. The SARC-F scale ≥ 4 was considered indicative of probable sarcopenia. The correlations between clinical indicators and the SARC-F score were analyzed. The area under the curve (AUC) was utilized to assess the predictive ability of TyG for sarcopenia and sarcopenic obesity. Logistic regression analysis and sensitivity stratification were employed to explore the influence of TyG.

Results A total of 1,148 individuals were included, among whom the median age was 66 (62, 71). 46.3% ($n = 531$) were diagnosed with severe OSA, while 24.0% ($n = 276$) had probable sarcopenia. The SARC-F score exhibited positive correlations with TyG ($r = 0.122$, $P < 0.01$), but it was negatively correlated with mean peripheral oxygen saturation (mean SpO_2, $r = -0.157$, $P < 0.01$). The AUC for assessing sarcopenia using TyG was 65.7% (95% confidence intervals (95%CI): 61.9–69.5%. Furthermore, the cutoff value for TyG was 8.855 (sensitivity = 67.4%, specificity = 62.8%). Logistic regression and stratified sensitivity analyses, adjusted for various influencing factors, collectively revealed that TyG was a risk-related predictor of probable sarcopenia (all odds ratio > 2.0, $P < 0.05$).

Conclusions The TyG index emerges as an independent predictor of sarcopenia in patients with OSA, shedding light on the complex interplay between nighttime hypoxia and muscle health.

Keywords Obstructive sleep apnea syndrome, Triglyceride-glucose index, Sarcopenia, Polysomnography, SARC-F

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Introduction

Sarcopenia is a progressive syndrome marked by decreased muscle mass and muscle strength throughout the body and/or decreased muscle physiological function as individuals age [1]. This phenomenon increases the risk of various adverse outcomes such as falls, fractures, physical disability, and mortality. Sarcopenia is a critical predictor of all-cause mortality and hospitalization among the elderly [2]. For example, the most recent study revealed a 29% and 93% increased risk of all-cause death in elderly patients with probable and confirmed sarcopenia, respectively [3]. Findings from an approximately decade-long follow-up study suggested a direct correlation between muscle loss during weight loss and heightened cardiovascular risks; however, no significant difference was observed in cardiovascular disease risk between the group experiencing weight loss with muscle loss and those with weight gain [4]. In recent years, sarcopenia has gradually garnered increasing attention in in-depth scientific research. Its pathophysiological underlying mechanisms include imbalance in protein synthesis and decomposition, neuromuscular junction injury, satellite cell dysfunction, and so on [5].

Obstructive sleep apnea (OSA) is another potentially life-threatening disease associated with aging. It manifests as periodic episodes of diminished or interrupted ventilation mediated by upper airway collapse during sleep, leading to intermittent hypoxia, hypercapnia, and arousal. OSA is a widely prevalent global condition, with conservative estimates indicating its effect on 34% and 17% of middle-aged men and women, respectively, with even higher prevalence observed in elderly populations [6]. However, in clinical practice, the disease is frequently underdiagnosed. OSA is closely associated with several adverse health outcomes, including cardiovascular and cerebrovascular diseases, cognitive impairment, type 2 diabetes, reduced quality of life, motor vehicle accidents, and increased risk of all-cause mortality [7]. The HypnoLaus cohort study revealed a marked correlation between severe OSA and low muscle strength (OR = 2.36, 95%CI = 1.29–4.31) [8], suggesting a potential close relationship between these two conditions. The prevailing theory resolves around a key feature of OSA: intermittent hypoxia. This induces oxidative stress and triggers a robust systemic inflammatory response [9]. Within the inflammatory milieu, various pro-inflammatory cytokines exert a direct effect on nuclear factor-κB (NF-κB), p38MAPK, and JAK/STAT pathways via their corresponding receptors, thereby participating in muscle atrophy. Additionally, inflammation can indirectly induce muscle atrophy by altering the metabolic state of tissues or cells [10].

The precise pathogenesis of sarcopenia remains incompletely understood [11]. However, biological plausibility underscores the potential relationship between sarcopenia and OSA. Both conditions involve interactions among oxidative stress, insulin resistance, and inflammation, which are simultaneously the focal points of ongoing research efforts. The triglyceride-glucose index (TyG) serves as an easy-to-calculate marker for assessing insulin resistance, calculated using the formula ln (triglyceride [mg/dL] × fasting glucose [mg/dL]/2). In recent years, some studies have proved that the index is positively correlated not only with the risk of cardiac-cerebral vascular diseases [12, 13], but with all-cause mortality [14].

Exploring the intricate relationship between nocturnal hypoxia and muscle health presents a potential avenue for clinical research aimed at developing preventive strategies. However, an uniform conclusion regarding the correlation between sarcopenia risk and the TyG index in elderly populations with OSA remains elusive. Therefore, this study aims to employ the TyG index to identify sarcopenia, with the goal of facilitating rapid screening among patients with sarcopenia. Early detection and a focus on targeted prevention and treatment strategies could help to decelerate disease progression and mitigate the risk of adverse outcomes.

Materials and methods

Study population

This was a multicenter observational study with a large sample size. From January 2015 to October 2017, the study analyzed the clinical history data of 1,148 elderly people aged ≥ 60 years, diagnosed with OSA via gold-standard nocturnal polysomnography (PSG) from the Chinese People's Liberation Army (PLA) General Hospital, Beijing Chaoyang Hospital, Peking University International Hospital, Peking University People's Hospital, the 960th Hospital of the Chinese PLA, and the Affiliated Hospital of Gansu University of Chinese Medicine. This study was conducted in strict adherence to the Declaration of Helsinki and received approval from the PLAGH Ethics Committee in China (S2022-366-01). The basic information and clinical measurement data of the patients were strictly managed and kept confidential. Informed consent was obtained from all patients or guardians.

Initially, we excluded patients with simple snoring, central sleep apnea, maxillofacial malformations, or lung disease characterized by peripheral oxygen saturation (SpO_2) < 90% under normal conditions. In this study investigating the correlation between TyG and sarcopenia, we also excluded the following: (i) individuals experiencing daily mobility challenges owing to cerebrovascular accidents, neuropathy, or trauma; (ii) those with joint damage resulting from systemic disease, (iii) people with a history of myocardial infarction, unstable angina, or severe heart failure; (iv) those diagnosed with mental

disorders or malignant tumors; (v) participants who were fully compliant with CPAP therapy; and (vi) patients with incomplete information on the consultation scale. Finally, the sample analyzed in this study comprised 1,148 elderly patients. A meta-analysis of sarcopenia in the elderly population in China revealed that the prevalence ranged from 11.22 to 22.94% [15]. Therefore, including 1,148 patients as the sample size was deemed feasible, surpassing the expected calculation size, with the allowable error δ set to 0.025.

Data collection and clinical measurements

PSG: Most participants underwent nocturnal PSG using a device manufactured by Compumedics (Melbourne, Australia). The participants were instructed to abstain from consuming tea, coffee, alcoholic beverages, and sedatives before sleep monitoring. The monitoring indices included electroencephalogram, peripheral oxygen saturation (SpO_2) (including the mean and lowest levels of SpO_2 throughout the night), oral-nasal airflow, breathing movement pattern, sleeping position, and other parameters. All indicators of PSG are automatically analyzed and manually calibrated by two specialist sleep technologists and then collated again by a senior sleep medicine physician. Respiratory events were determined according to the criteria of the American Academy of Sleep Medicine [16]. Sleep apnea was defined as a drop in the peak airflow strength signal by ≥ 90%, lasting for > 10 s. If the airflow intensity decreased by ≥ 30% for more than 10 s, accompanied by a SpO_2 decrease of ≥ 3%, it could be classified as sleep hypopnea. The severity of OSA was assessed according to the internationally recognized apnea-hypopnea index (AHI) [17], and then subgroup analysis was carried out. The severity of OSA was classified according to the AHI as mild (5 ≤ AHI < 15), moderate (15≤ AHI < 30), or severe (AHI ≥ 30). Central sleep apnea was characterized by the complete disappearance or significant weakening of chest and abdominal movements. The subjects of this study were all patients with OSA, and the number of obstructive sleep apnea events at night exceeded half of the total respiratory events.

Clinical indicators

The age and body mass index (BMI) of individuals were recorded within 24 h of admission, along with their history of tobacco and alcohol use and common comorbidities. The situation of tobacco and alcohol included former users who were currently abstainer. Participants were instructed to refrain from staying up late or consuming alcohol for 3 days preceding the blood draw. Participants were advised to fast for nine hours before the blood draw, and the blood sample was tested for blood-related indicators. Two senior technicians in the laboratory conducted the test, reviewed the results, and issued the results. Based on the test results, further improve the relevant conversion indicators, such as the endogenous creatinine clearance (Ccr), which is calculated based on age, weight, gender and serum creatinine. Diagnosis of diabetes was based on fasting blood glucose (FBG) level ≥ 126 mg/dL, glycosylated hemoglobin (HB) A1c level ≥ 6.5%, or the use of any form of hypoglycemic therapy [18]. Hyperlipidemia was defined as a known dyslipidemia, specifically characterized by high blood concentration of total cholesterol, triglycerides, or low-density lipoprotein cholesterol (LDL-C), or by current treatment with lipid-lowering drugs [19]. Smoking and drinking tea were prohibited half an hour before blood pressure measurement. Participants were considered as hypertensive when their systolic blood pressure was ≥ 140 mmHg and/or their diastolic blood pressure was ≥ 90 mmHg. Moreover, their blood pressure was measured by experienced nursing staff while in a calm state after emptying their bladder [20]. Following assessment by a professional ultrasound doctor, the presence of a focal lesion in the carotid plaque or carotid intima-media thickness ≥ 1 mm was indicative of carotid atherosclerosis (CA) [21]. Indicators such as blood test and comorbidities were statistically analyzed as covariables.

SARC-F scale

Currently, the diagnosis of sarcopenia relies on a comprehensive assessment of muscle mass, muscle strength, and physical function [22]. Assessing muscle mass is complex, requiring methods such as computed tomography, magnetic resonance imaging, bioresistivity, and other techniques. However, utilizing these methods in evaluating sarcopenia is limited owing to concerns about radiation exposure, high cost, and inconvenience. Therefore, identifying a simple, safe, cost-effective, and efficient screening tool for sarcopenia is of significant clinical importance. The 2018 revised European Consensus recommends that muscle strength be prioritized in diagnosing sarcopenia, as it is deemed a superior predictor of adverse outcomes to muscle mass [23]. SARC-F is a rapid and simplified scale utilizing self-reported data on falls, activity, and strength for sarcopenia screening. It exhibited excellent diagnostic specificity, ranging from 93 to 99%, but its sensitivity is comparatively poor [24]. This could be attributed to the reliance of the scale on clinical symptoms, which focuses on assessing muscle function. The functional capacity assessed by the scale aligned with the diminished physical performance characteristic of severe sarcopenia, as outlined in the Asian Working Group for Sarcopenia (AWGS) expert consensus [25]. Owing to its ease of use and good validity, the SARC-F scale is a commonly recommended case-finding tool supported by evidence for its application [26]. The SARC-F scale examines five aspects: (1) Strength; (2) Assisted

walking; (3) Standing up from the chair; (4) Climbing stairs; (5) Falls. Each item has three scores: 0, 1, and 2. If the total sum of the five items is ≥ 4, predicted sarcopenia is considered (the positive screening).

Statistical analyses

Initially, the data were divided into three groups based on the TyG tripartite. Before analyzing the measurement indicators, an assessment was conducted to test for homogeneity of variance and normality. The normally distributed data were expressed as mean ± standard deviation. Skewed variables were represented by the median (interquartile range) [M(Q1, Q3)], and differences among the three groups were compared using the non-parametric Kruskal-Wallis H test. The chi-square test was used to compare unordered results in categorical data. Spearman method was applied to analyze the correlation between SARC-F score and other indicators. Subsequently, to explore the relationship between SARC-F score and TyG, sleep breathing, and other parameters, multiple linear regression was further utilized to test statistically significant data in pairwise correlation analysis. Using predicted sarcopenia (SARC-F ≥ 4) and predicted sarcopenic obesity (SO, SARC-F ≥ 4 combined with BMI ≥ 28 kg/m^2) [27] as outcome variables, the receiver operating characteristic (ROC) curves of TyG were calculated and plotted. Univariate and multifactor calibrated Logistic regression analyses were performed to explore the association between TyG and the risk of sarcopenia. Additionally, further subgroup analyses were conducted to improve the sensitivity analysis. All statistical analyses were performed using the SPSS® (version 25.0, Chicago, United States), and $P < 0.05$ was considered statistically significant.

Results

Descriptive statistics via TyG stratification

From a total of 1,290 patients, 1,148 eligible elderly individuals with OSA were included in the final sample assessed. The median age was 66 years, and 38.7% ($n = 444$) of the subjects were female. Of these, 46.3% ($n = 531$) had severe OSA, and 24.0% ($n = 276$) had probable sarcopenia. All participants were categorized into three groups based on the TyG tripartite (Supplementary Fig. 1 and Table 1). Since the TyG was determined based on triglyceride and fasting blood-glucose, there were significant differences in the distribution of hyperlipidemia and diabetes mellitus (both $P < 0.05$). Regarding sleep-related indicators, the lower the TyG index of the group, the lower the levels of AHI and T90, while the higher the Lowest SpO_2 level. However, no statistically significant difference was observed in the proportion of varying severity among all groups ($P > 0.05$). Age and BMI levels also varied across the tertiles. Additionally, the blood indicators, such as creatinine, Ccr, HDL-C, and HB, showed variations between the groups (all $P < 0.05$). However, no significant differences were observed among the tertiles regarding total bilirubin, LDL-C, uric acid, γ-GT, and alcohol consumption (all $P > 0.05$). The proportions of patients with hypertension, predicted sarcopenia, and predicted SO were greater in the higher TyG group ($P < 0.05$).

Correlation analyses between SARC-F score and clinical indices

Table 2 shows that in the entire participant cohorts, the SARC-F score exhibited positive correlations with age, T90, Longest time of apnea, and TyG ($r = 0.566$, 0.078, 0.110, and 0.122, respectively; all $P < 0.01$). In contrast, the score showed negative correlations with Ccr, hemoglobin, and mean peripheral oxygen saturation (mean SpO_2, r = -0.258, -0.088, and −0.157, respectively; $P < 0.01$. Figure 1). No significant relationships were observed between the SARC-F score and BMI, uric acid, creatinine, or AHI (all $P > 0.05$).

The statistically relevant indicators mentioned above maintained their association with the SARC-F score in approximately the same direction across various subgroup analyses. However, in the male subgroup, the marked positive association between BMI and the SARC-F score was observed (r = -0.115), while the association between T90 and score was weakened. In the female subgroup, positive associations between AHI and T90 with the score were underlined ($r = 0.101$ and 0.237, respectively). Among patients with AHI < 15, SARC-F showed a positive correlation with T90 ($r = 0.148$) and a negative correlation with mean SpO_2 (r = -0.266), while no significant correlation was observed with TyG ($P > 0.05$). Conversely, in the group with AHI ≥ 15, we observed an inverse correlation between mean SpO_2 and the score (r = -0.120) and a direct correlation between TyG and it ($r = 0.154$). However, no consistent statistically significant association was observed between SARC-F scores and age, T90, and mean SpO_2 across different age subgroups. Table 2 shows the relationships between examination indexes and SARC-F score, revealing that regardless of the subgroup, Ccr consistently maintained a negative correlation with the score.

Following the pairwise correlation analysis, we conducted a multiple linear regression analysis. The results showed a positive association between SARC-F score and TyG, age, as well as AHI level, while an inverse association was observed with mean SpO_2 (all $P < 0.05$). No significant relationship was found between Ccr and the score ($P > 0.05$). The five factors (Table 3) collectively accounted for 45.9% of the variations in the SARC-F score. Meanwhile, it was observed that TyG could predict certain changes in the score. After further excluding

Table 1 Characteristics of older patients with OSA by TyG stratum

	Total (n = 1148)	*quartile 1 (n = 383)*	quartile 2 *(n = 383)*	*quartile 3 (n = 382)*	*P* value
TyG [a, b,c]	8.78(8.45, 9.15)	8.28(8.06, 8.45)	8.78(8.67, 8.90)	9.29(9.15, 9.58)	< 0.001
Sleep-related indicators					
AHI, events/h [b]	27.70(15.40, 45.60)	25.90(14.95, 41.15)	28.30(15.65, 47.05)	28.90(16.40, 50.10)	0.024
T90, % [a]	3.62(0.59, 15.69)	2.59(0.46, 11.89)	4.50(0.73, 17.89)	4.03(0.66, 16.75)	0.006
Mean time of apnea, sec	22.2(19.6, 25.4)	22.7(19.4, 26.0)	22.2(19.6, 25.4)	22.0(19.7, 25.0)	0.300
Longest time of apnea, sec [b, c]	52.2(33.6, 76.8)	56.0(35.0, 76.3)	52.9(35.7, 79.0)	49.1(29.5, 73.8)	0.019
Mean SpO_2, %	93.4(91.9, 95.0)	93.9(92.0, 95.0)	91.3(93.0, 95.0)	93.7(91.9, 95.0)	0.187
Lowest SpO_2, % [a]	80.0(72.0, 85.0)	81.0(73.0, 85.5)	79.0(71.0, 84.0)	80.0(72.0, 85.0)	0.018
Severity of OSA, n (%)					0.311
Mild OSA	269(23.4)	96(25.1)	88(23.0)	85(22.3)	
Moderate OSA	348(30.3)	127(33.2)	109(28.5)	112(29.3)	
Severe OSA	531(46.3)	160(41.8)	186(48.6)	185(48.4)	
Clinical Indicators					
Age, years [a, b]	66.0(62.0, 71.0)	67.0(63.0, 72.0)	65.0(62.0, 71.0)	65.0(62.0, 70.0)	0.001
BMI, kg/m^2 [a, b]	26.51(24.08, 29.04)	25.78(23.53, 28.15)	26.83(24.23, 29.41)	26.64(24.31, 29.38)	< 0.001
TBil, μmol/L	10.5(8.3, 13.6)	10.7(8.3, 14.3)	10.2(8.2, 13.2)	10.5(8.3, 13.6)	0.141
DBil, μmol/L	3.4(2.8, 4.4)	3.5(2.8, 4.6)	3.4(2.7, 4.4)	3.4(2.9, 4.3)	0.444
HDL-C, mmol/L [b]	1.10(0.90, 1.36)	1.07(0.86, 1.33)	1.10(0.91, 1.31)	1.12(0.92, 1.49)	0.004
LDL-C, mmol/L	2.42(1.91, 3.00)	2.41(1.92, 2.98)	2.41(1.91, 3.02)	2.44(1.89, 3.02)	0.941
creatinine, μmol/L [b, c]	71.0(61.0, 83.7)	71.0(61.0, 81.6)	74.0(64.1, 87.8)	69.2(58.9, 82.6)	0.001
Ccr, % [b, c]	84.45 ± 28.71	79.91(63.47, 98.40)	83.17(66.50, 102.10)	90.75(71.68, 105.13)	< 0.001
uric acid, μmol/L	340.0(284.6, 390.8)	332.0(285.6, 388.5)	354.6(299.0, 389.0)	341.2(279.0, 400.5)	0.087
γ-GT, u/L	26.0(19.8, 33.0)	26.3(19.9, 33.0)	27.1(20.1, 35.9)	27.1(19.5, 37.0)	0.204
HB, g/L [a]	138.0(127.5, 147.0)	137.0(123.5, 147.0)	139.0(129.0, 148.0)	137.0(129.0, 146.5)	0.002
Classification index					
Female, n (%) [b]	444(38.7)	132(34.5)	143(37.3)	169(44.2)	0.017
Diabetes, n (%) [a, b]	281(24.5)	62(16.2)	100(26.1)	119(31.2)	< 0.001
Hyperlipidemia, n (%) [b, c]	316(27.5)	71(18.5)	91(23.8)	154(40.3)	< 0.001
Hypertension, n (%) [a, b]	736(64.1)	221(57.7)	259(67.6)	256(67.0)	0.006
CA, n (%)	269(23.4)	99(25.8)	84(21.9)	86(22.5)	0.385
Smoking, n (%) [b, c]	264(23.0)	105(27.4)	104(27.2)	55(14.4)	< 0.001
Drinking, n (%)	129(11.2)	44(11.5)	50(13.1)	35(9.2)	0.230
Evaluation index					
SARC-F [b, c]	1(0, 3)	1(0, 2)	0(0, 3)	1(0, 4)	< 0.001
Predicted Sarcopenia, n (%)[a, b,c]	276(24.0)	55(14.4)	78(20.4)	143(37.4)	< 0.001
Predicted SO, n (%)[a, b]	96(8.4)	16(4.2)	32(8.4)	48(12.6)	< 0.001

AHI: apnea-hypopnea index; T90: the proportion of time corresponding to pulse oxygen saturation less than 90% in total sleep time; SpO_2: peripheral oxygen saturation; BMI: body mass index; TBil: total bilirubin; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Ccr: creatinine clearance rate; γ-GT: γ-glutamyltranspeptidase; HB: hemoglobin; CA: carotid atherosclerosis; SO: sarcopenic obesity

[a]: the difference between 1–2 was statistically significant; [b]: the difference between 1–3 was statistically significant; [c]: the difference between 2–3 was statistically significant

patients with diabetes or hyperlipidemia, we found that there was still a significant statistical association between TyG and the SARC-F score in the remaining population ($P < 0.001$).

Relationship between TyG level and probable sarcopenia

Combined with the above results, we revealed a clear correlation between TyG and the SARC-F score. According to the AWGS expert consensus, a SARC-F score of ≥ 4 indicated an elevated risk of sarcopenia [3]. We assessed the predictive efficiency of TyG with a score ≥ 4 (i.e., probable sarcopenia) as the diagnostic variable. The corresponding results showed that the area under the curve (AUC) was 65.7%, with 95% confidence intervals (95% CI): 61.9–69.5%. The cutoff value of TyG, determined by the largest Youden index, was found to be 8.855 (sensitivity = 67.4%, specificity = 62.8%). Furthermore, when considering sarcopenic obesity (SO) as the diagnostic variable, Fig. 2 depicts that the AUC of TyG was 65.2% (95%CI: 59.7–70.6%), with a cutoff value of 8.851 (sensitivity = 72.9%, specificity = 57.6%).

Table 2 Correlation between SARC-F score and clinical indices

clinical indices	*r*						
	Total	**Male**	**Female**	**AHI < 15**	**AHI ≥ 15**	**Age < 75**	**Age ≥ 75**
TyG	0.122***	0.101**	0.157**	0.013	0.154***	0.129***	0.406***
Age	0.566***	0.577***	0.550***	0.589***	0.562***	0.417***	0.496
BMI	-0.045	-0.115**	0.067	-0.028	-0.056	0.001	0.103
TBil	-0.015	-0.009	-0.027	-0.100	0.011	-0.028	-0.070
HDL-C	0.063*	0.023	0.136**	0.134*	0.043	0.046	0.095
LDL-C	0.009	-0.004	0.026	0.000	0.011	0.031	0.002
Creatinine	0.036	0.053	0.027	0.026	0.039	-0.044	0.160*
Ccr	-0.258***	-0.305***	-0.185***	-0.245***	-0.263***	-0.098**	-0.178*
Uric acid	0.012	0.013	0.025	-0.026	0.024	0.003	0.098
γ-GT	0.032	0.029	0.035	0.027	0.033	0.036	-0.085
HB	-0.088**	-0.114**	-0.057	-0.013	-0.111**	-0.038	-0.078
AHI	0.042	0.007	0.101*	0.000	0.062	0.080*	0.064
T90	0.078**	-0.021	0.237***	0.148*	0.048	0.090**	-0.061
Mean time of apnea	0.040	0.084*	-0.025	-0.087	0.075*	0.012	-0.044
Longest time of apnea	0.110***	0.127**	0.095*	0.125*	0.106**	0.070*	0.118
Mean SpO_2	-0.157***	-0.083*	-0.276***	-0.266***	-0.120***	-0.150***	-0.088
Lowest SpO_2	-0.116***	-0.044	-0.234***	-0.225***	-0.088**	-0.119***	0.015

BMI: body mass index; TBil: total bilirubin; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Ccr: creatinine clearance rate; γ-GT: γ-glutamyltranspeptidase; HB: hemoglobin; AHI: apnea-hypopnea index; T90: the proportion of time corresponding to pulse oxygen saturation less than 90% in total sleep time; SpO_2: peripheral oxygen saturation. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$

Binary Logistic regression was utilized to analyze the influencing factors in elderly OSA patients with possible sarcopenia as the dependent variable. The statistically significant factors (Supplementary Table 1) were co-substituted into multivariate Logistic regression analysis. After adjusting for age, AHI, mean SpO_2, T90, CA, hypertension, drinking, and Ccr, it was revealed that the TyG level was significantly associated with an increased risk of sarcopenia (aOR: 7.263, 95% CI: 5.033–10.483, $P < 0.001$) and sarcopenic obesity (aOR: 2.626, 95% CI:1.766–3.907, $P < 0.001$, Table 4). Moreover, sensitivity analyses were performed by dividing subgroups, revealing that only in the subgroup with AHI < 15, TyG and SO did not exhibit a statistically significant correlation. However, a certain influence trend was observed ($P < 0.01$); in the other subgroup analyses, all the results remained consistent, indicating that TyG served as a risk-related predictor of sarcopenia and SO (all aOR > 2.0, $P < 0.05$, Table 4).

Discussion

In this study of elderly patients with OSA, we observed a predicted sarcopenia prevalence of 24.0%. Estimates of prevalence varied with changes and advancements in the definition of sarcopenia. A systematic review of elderly people in community settings revealed that employing the 2010 European Working Group on Sarcopenia in Older People (EWGSOP) definition yielded a lower prevalence estimate (12.9%), while relying solely on muscle mass assessment leads to a higher estimate (40.4%) [28]. Another Asia-wide epidemiological study, utilizing the Asian Working Group for Sarcopenia (AWGS) diagnostic criteria, reported a prevalence ranging from 5.5 to 25.7%, slightly higher in men than in women [29]. The corresponding prevalence of patients in this study was significantly high, with no significant difference observed between the sexes. This trend could be attributed to the specific study population of OSA in the elderly. Moreover, it was observed that with age, the effects of OSA on the body tend to reduce in relation to sex differences [30]. Additionally, this study showed that the SARC-F score, a predictor of sarcopenia, indicates a positive and negative correlation with AHI level and mean SpO_2, respectively. This suggests that in addition to uncontrollable factors such as aging, the onset of OSA may elevate the risk of sarcopenia.

The plausibility of an association between the two diseases is biologically supported, particularly in relation to one of the main features of OSA, namely intermittent hypoxia. Oxygen plays a vital role in adenosine triphosphate (ATP) production, which is crucial for maintaining protein synthesis productivity under normal oxygen conditions. Hypoxia significantly slows down and impairs the rate of classical protein synthesis pathways due to the limited ATP availability and cellular energy supply [31]. Meanwhile, hypoxia impairs the function of the endoplasmic reticulum, leading to reduced protein synthesis [32]. Hypoxia also boosts inflammation and oxidative stress responses, disrupting the efficiency of the mitochondrial electron transport chain. This disruption leads to electron leakage into molecular oxygen, resulting in the production of reactive oxygen species (ROS) [33]. NF-κB signaling pathway—mediated by ROS—is closely

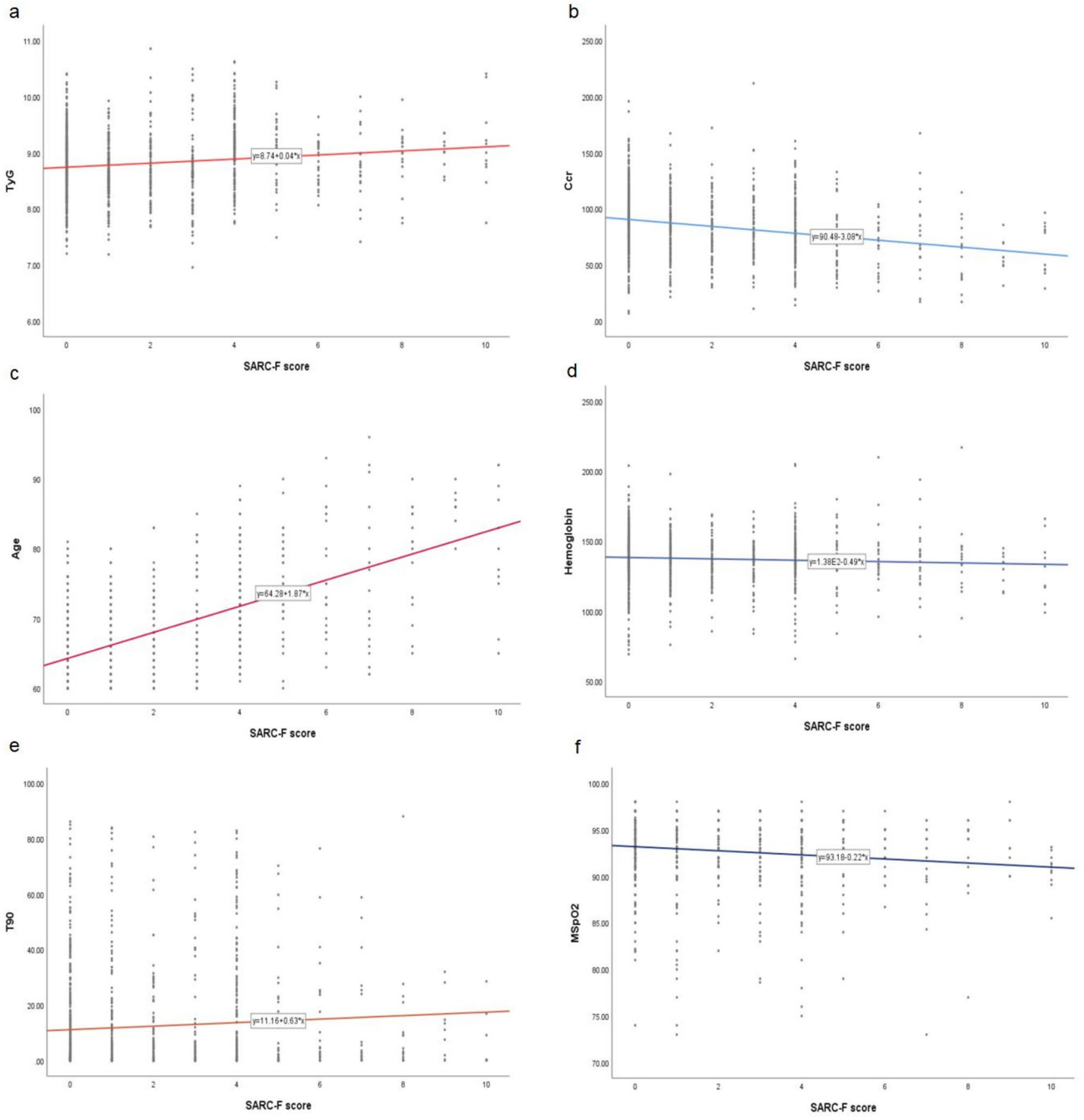

Fig. 1 Scatter plot of the relationships between clinical indicators and SARC-F score

Table 3 Multiple linear regression analysis of SARC-F score with relevant covariates

Indicators	Total			Non-diabetes and non-hyperlipidemia		
	β	*P*-value	R^2%	β	*P*-value	R^2%
Age	0.221	< 0.001	45.9	0.696	< 0.001	46.9
AHI	0.010	< 0.001		0.053	0.073	
Mean SpO_2	-0.039	0.011		-0.096	0.001	
Ccr	0.000	0.768		0.050	0.102	
TyG	0.900	< 0.001		0.177	< 0.001	

Adjusted for Age, apnea-hypopnea index (AHI), peripheral oxygen saturation (SpO_2), creatinine clearance rate (Ccr) and TyG

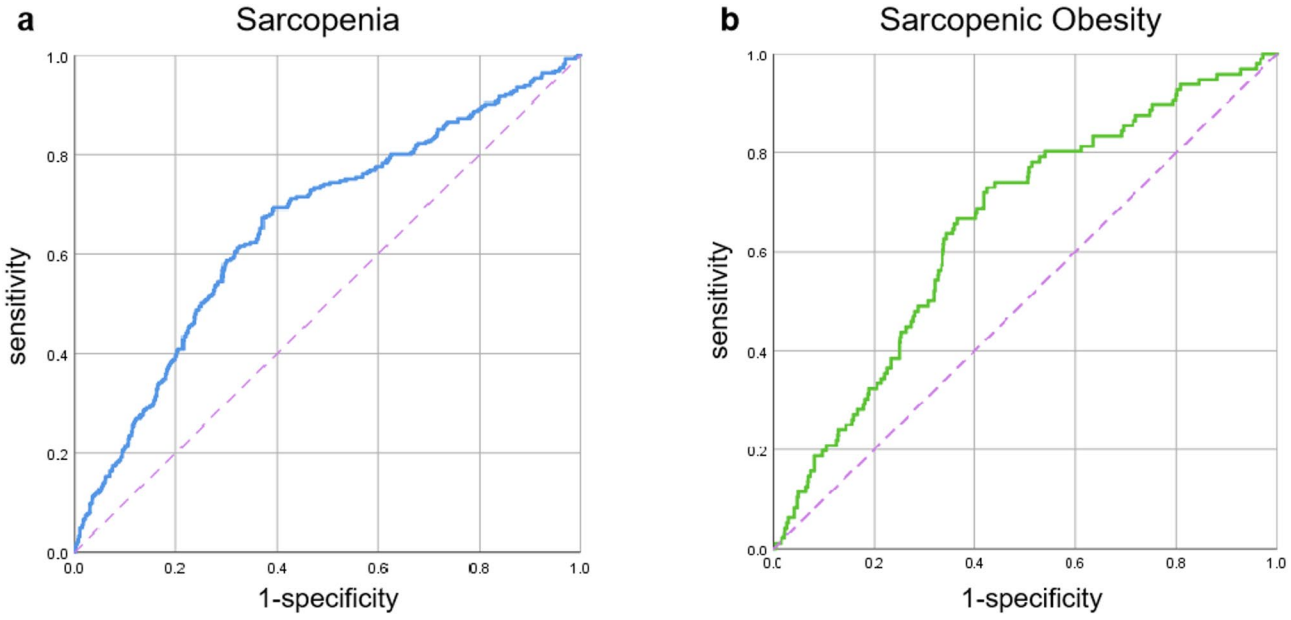

Fig. 2 ROC curves of TyG for sarcopenia and sarcopenic obesity

Table 4 Multivariate logistic regression analysis the influences of TyG on sarcopenia and sarcopenic obesity

	Sarcopenia		SO	
	aOR(95%CI)	*P* value	aOR(95%CI)	*P* value
Total	7.263(5.033–10.483)	< 0.001	2.626(1.766–3.907)	< 0.001
Male	7.183(4.491–11.488)	< 0.001	2.663(1.619–4.382)	< 0.001
Female	7.872(4.290-14.446)	< 0.001	2.308(1.105–4.819)	0.026
AHI < 15	3.036(1.451–6.349)	0.003	2.622(0.895–7.683)[a]	0.079
AHI ≥ 15	9.952(6.379–15.526)	< 0.001	2.804(1.800-4.367)	< 0.001
Age < 75	5.414(3.639–8.055)	< 0.001	2.376(1.442–3.914)	0.001
Age ≥ 75	157.738(25.027-994.162)	< 0.001	3.702(1.678–8.164)	0.001
Non-diabetes and non-hyperlipidemia	8.726(5.012–15.192)	< 0.001	4.726(2.354–9.488)	< 0.001

adjusted for age, AHI, Mean SpO_2, T90, carotid atherosclerosis, hypertension, drinking, and Ccr

[a]: For SO, P value of TyG > 0.05, but OR of $MSpO_2$ = 0.812, *P* = 0.005

linked to inflammatory molecular damage [34]. Subsequently, locally released pro-inflammatory cytokines induce an anabolic response in skeletal muscle cells, ultimately resulting in muscle atrophy or injury [35]. Research also showed that hypoxia inhibits protein synthesis through the mTOR/Akt pathways [36]. Additionally, a sarcopenia phenotype characterized by narrowing of muscle tube diameter and decreased protein synthesis has been observed in a novel in vitro myotube model [37]. In addition, growth hormones play a crucial role in preventing muscle atrophy and promoting the growth of skeletal muscle cells [38]. Moreover, hypoxia and inflammation disrupt the growth hormone axis [39], influencing growth promotion and regulation [40].

These are all intrinsically linked to muscle metabolism, as explained earlier. These findings support the potential involvement of OSA in age-related sarcopenia. Similar clinical studies have suggested consistent results. The HypnoLaus cohort study from Switzerland showed an association between severe OSA and low muscle strength in women aged over 60 years (aOR = 2.64) [8]. Recently, a study utilizing NHANES data indicated that participants with OSA had an elevated risk of early-onset sarcopenia (aOR = 1.50) and early-onset SO (aOR = 1.80) [41].

Examining the pathophysiological mechanisms, both sarcopenia and OSA are closely linked to oxidative stress and inflammatory responses, and it is logical to assume that the metabolic capacity of the body interacts with both conditions. TyG index, derived from fasting blood glucose and triglyceride levels, serves as a simple indicator of metabolic conditions and is extensively employed in clinical practice. The results of this study showed a positive correlation between the TyG index and SARC-F score, regardless of pairwise correlation or multiple linear regression analysis. OSA tends to induce metabolic abnormalities characterized by heightened sympathetic nerve activation, elevated hepatic glucose output, adipose tissue inflammation-induced insulin resistance, and reduced clearance of triglyceride-rich lipoproteins. These contribute to a fasting lipid profile of hyperlipidemia [42].

Abnormal lipid metabolism is closely linked to sarcopenia. Skeletal muscle plays a central role in dietary fat metabolism. Increased TG deposition and decreased

muscle mass hinder the ability of the skeletal muscle to oxidize fatty acids, leading to the accumulation of fatty acids in the body [43]. Moreover, elderly individuals and those with sarcopenia typically consume fewer calories due to reduced physical function associated with declining physical function. Additionally, the loss of skeletal muscle mass coupled with aging results in a decrease in metabolic rate [44, 45]. Together, the body generally takes in more energy than it expends, leading to lipid deposition. Increased fatty acid uptake and intracellular lipid accumulation in muscle tissue inactivate the PI3K/Akt pathway. This induces persistent inflammation and contributes to muscle loss [46]. Biochemical analysis of the induction of lipid droplet accumulation in the myoblast (C2C12) cell line revealed that inhibition of lipolysis and mitochondrial dysfunction are critical factors contributing to intracellular toxicity [47]. Simultaneously, elevated blood lipids can directly increase lipid deposition in muscles while reducing the synthesis and storage of muscle glycogen [48]. This often coincides with blood sugar abnormalities.

On the one hand, skeletal muscle serves as the largest insulin-sensitive tissue in the human body, the primary site where insulin stimulates glucose utilization, and plays a crucial role in blood glucose homeostasis. However, with the onset and progression of sarcopenia, skeletal muscle insulin sensitivity decreases, leading to the development of insulin resistance [49]. A study utilizing the most comprehensive set of gene expression data from the human skeletal muscle transcriptome to date indicates that inositol and certain glycosaminoglycans may mediate insulin signaling, thus influencing glucose uptake. These compounds also demonstrate insulin sensitization and antidiabetic effects [50]. Therefore, muscle loss and damage can disrupt blood sugar metabolism. On the other hand, chronic hyperglycemia induces oxidative stress and triggers the release of inflammatory cytokines, potentially exacerbating sarcopenia by amplifying apoptosis signal and protein degradation. Conversely, antioxidants can directly neutralize free radicals, thereby preventing oxidative damage to various tissues, such as skeletal muscle [51]. Inhibiting NF-κB, a pivotal molecule in the inflammatory response, has been demonstrated to enhance muscle function and restore muscle mass [52]. Furthermore, under normal circumstances, nerves supply nutrients to the muscles they innervate through the secretion of hormones and substances that support and sustain muscle activity [53]. However, hyperglycemia may induce characteristic peripheral neuropathy [54], as well as decreased muscle glycogen storage and accumulation of intramuscular polyol pathway intermediates [55].

These results suggested that TyG has a strong ability to differentiate sarcopenia and SO (AUC = 65.7% and 65.2%, respectively). The optimum cutoff value, determined by the maximum Youden index, the TyG is > 8.85, indicating a higher risk of developing sarcopenia or SO. Further, the results of multivariate regression analysis with adjustments showed a significant association between TyG level and an increased risk of sarcopenia (aOR: 7.263), and SO (aOR: 2.626). Moreover, the subgroup analyses consistently revealed TyG as a predictor of sarcopenia risk (all aOR > 2.0). These results align with those of similar studies in different populations. A clinical study of patients without diabetes undergoing hemodialysis revealed that the prevalence of sarcopenia increased with a higher TyG index. Furthermore, TyG was also identified as an independent risk factor for sarcopenia (OR = 4.21) [56]. Another study conducted on an elderly population in South Korea found that participants with TyG > 8.66 had a significantly elevated risk of developing SO [57]. Overall, limited studies have identified an appropriate and precise threshold for the TyG index to detect sarcopenia and SO. Therefore, the calculated values across various study populations align, providing a rough validation of the validity and reliability of the respective results. However, a recent nationally representative cohort study in China presented contrasting findings, showing higher hazard ratios of sarcopenia in higher quartiles of the TyG index. Further careful analysis revealed that the difference in results stemmed from BMI, explaining 88.7% of the association between TyG index and sarcopenia in the cohort sample. However, after adjusting for BMI, no significant association was observed [58]. For the participants in this study, there was no significant difference in BMI levels between groups with or without sarcopenia. Reduced muscle mass constitutes a significant aspect of sarcopenia, and muscle mass shows a significantly positive correlation with body weight and BMI [59]. Therefore, employing the BMI-adjusted skeletal muscle mass index (SMI) for comparison is a logical approach. For example, Zhu et al. examined the National Health and Nutrition Examination Survey (NHANES) and detected a linear negative correlation between the TyG index and BMI-SMI [60]. Moreover, a systematic review and meta-analysis encompassing nearly 50,000 individuals revealed that the TyG index serves as a sensitive and specific indicator of metabolic syndrome [61]. As an illustration, relevant studies conducted in Asia showed that when the TyG index > 8.52–8.81, there could be an increased risk probability of metabolic syndrome and insulin resistance [62, 63]. Metabolic and endocrine disorders may lead to significant alterations in the humoral environment containing levels of adipokines and inflammatory cytokines [64]. This can lead to reduced AMPK-dependent fatty acid uptake in myocytes and impaired mitochondrial oxidative phosphorylation [65]. The current consensus suggests that systemic, chronic, low-grade inflammation (SCLGI) is an inherent aspect of sarcopenia

development, and SCLGI regression may serve as a crucial mechanism for mitigating sarcopenia [66]. In support of this, resolving agents targeting SCLGI have shown potential beneficial effects for skeletal muscle mass, strength, and function [67]. Given the recognized adverse effects of metabolic factors, it is credible to consider a TyG index > 8.85 as a potential indicator of sarcopenia and sarcopenic obesity.

Despite the efforts and contributions of this study, it is essential to acknowledge some limitations: (1) This study was observational in nature, preventing the establishment of a causal relationship between sarcopenia and TyG levels. Future prospective cohort studies are warranted to further explore causality. (2) Factors such as lifestyle, exercise, diet, medication (e.g. lipid-control drugs), and history of related diseases were not assessed, potentially introducing unidentified confounding factors. For example, a high-fat diet and less physical activity were associated with higher triglycerides and blood glucose levels, but meanwhile objective blood test index (e.g. TyG) could also partially reflect the effects of diet, drugs and physical activity, reflecting the current physical condition. (3) The majority of participants in this study were urban residents from central and northern China with good health awareness, suggesting the possibility of selection bias. Further external validation in larger populations and diverse subgroups or races would enhance the representativeness of our findings. (4) No device was used to measure objective muscle mass. However, the SARC-F scale employed is a crucial tool for sarcopenia screening and is recommended by majority consensus. Of course, measuring muscle mass parameters would enhance the sensitivity and specificity of screening.

Conclusion

This study validates the association between a high TyG index and increased risk of sarcopenia and SO among the elderly population with OSA. Additionally, it establishes that a TyG index > 8.85 serves as the optimum cutoff value for identifying sarcopenia. The index was also considered a potential indicator of SO. These findings offer practical insights for the prevention and management of sarcopenia in the direction of glycolipid control, and propose evidence-based strategies for addressing the rise in morbidity, mortality, and healthcare costs associated with elderly OSA.

Supplementary Information

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Supplementary Material 1

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Author contributions
LF, JIL, and LL contributed to the research design and critically revised the manuscript. WmC, DR, and ZZ contributed to the data acquisition and collected the samples. LbZ, XqS, and YhG contributed to data interpretation, visualized the data and wrote the manuscript. XX, LL, and QxS contributed to design and coordinate work between multiple centers. All authors gave final approval and agreed to be accountable for all aspects of this work.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by the Ethics Committee of Chinese PLA General Hospital (S2022-366-01). The patients provided their informed consent to participate in this study.

Competing interests
The authors declare no competing interests.

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