Association Between the Triglyceride-Glucose Index and High Risk of Cardiovascular Disease in Middle-Aged Obese Residents by Gender in Anhui: Postprint

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Abstract

Background The triglyceride-glucose (TyG) index is an indicator for evaluating insulin resistance (IR) and obesity-related metabolic diseases, and is closely associated with high risk of cardiovascular disease (CVD). However, the relationship between the TyG index and high CVD risk may differ among middle-aged obese populations of different genders.

Objective To investigate the relationship between the TyG index and high CVD risk in middle-aged obese populations by gender, and to evaluate its role in CVD prevention and treatment.

Methods The study subjects were derived from 10 early screening and comprehensive intervention projects for high-risk CVD populations conducted in Anhui Province. A total of 30,425 middle-aged obese individuals were selected. The uniformly designed preliminary screening questionnaire and basic information registration form from the National Cardiovascular Center were used, and the survey was conducted by uniformly trained and qualified investigators. The main survey content included gender, age, hypertension, dyslipidemia, diabetes, smoking status, alcohol consumption, etc. Participants were divided into male and female groups. The male group was further divided into quartile groups based on TyG index: T1 (7.417-8.870), T2 (8.871-9.204), T3 (9.205-9.578), and T4 (9.579-11.435). The female group was divided into F1 (7.579-8.876), F2 (8.877-9.183), F3 (9.184-9.526), and F4 (9.527-11.647). Binary logistic regression analysis was used to explore the relationship between the TyG index and high CVD risk, and Z-test was used to compare differences in effect values between subgroups.

Results The proportion of high CVD risk was 28.4% in the male group and 26.0% in the female group. Binary logistic regression analysis showed that TyG index T2 (F2), T3 (F3), and T4 (F4) were associated with high CVD risk in the male (female) group (P<0.05), and the association with high CVD risk gradually increased with increasing TyG index. In the male group, the risk of high CVD risk in the T4 group compared with T1 was OR (95%CI)=1.827 (1.622, 2.058); in the female group, the risk compared with T1 was 1.552 (1.410, 1.708). The comparison of the fourth quartile TyG index with high CVD risk between the male and female groups showed a statistically significant difference (P<0.05). After further adjusting for total cholesterol and other indicators (Model 2), the association between T2 (F2), T3 (F3), T4 (F4) and high CVD risk was attenuated, but T2 (F2), T3 (F3), and T4 (F4) remained associated with high CVD risk in both male and female groups (P<0.05), and the association with high CVD risk gradually increased with increasing TyG index levels. Compared with the T1 group, the risk of high CVD risk in the TyG index T4 group was OR (95%CI)=1.804 (1.584, 2.055) in the male group and OR (95%CI)=1.496 (1.345, 1.665) in the female group; the comparison of the fourth quartile TyG index with high CVD risk between the male and female groups showed a statistically significant difference (P<0.05).

Conclusion Middle-aged obese men with high TyG index levels are more prone to high CVD risk, and attention should be focused on TyG index levels in this population.

Full Text

Preamble

Title: Relationship Between Triglyceride-Glucose Index and High-Risk Cardiovascular Disease in Middle-Aged Obese Residents of Different Genders in Anhui Province

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Abstract

Background: The triglyceride-glucose (TyG) index serves as an indicator for evaluating insulin resistance (IR) and obesity-related metabolic diseases, and is closely associated with high cardiovascular disease (CVD) risk. However, the relationship between TyG index and CVD risk may differ across genders among middle-aged obese populations.

Objective: To investigate the relationship between TyG index and high CVD risk in middle-aged obese individuals of different genders, and to evaluate its role in CVD prevention and treatment.

Methods: A total of 30,425 middle-aged obese residents were selected from 10 early screening and comprehensive intervention projects for high-risk CVD populations in Anhui Province. Using a preliminary screening questionnaire and basic information registration form designed by the National Cardiovascular Center, trained and certified investigators collected data on gender, age, hypertension, dyslipidemia, diabetes, smoking status, and alcohol consumption. Participants were divided into male and female groups. The male group was further divided into quartiles based on TyG index: T1 (7.417–8.870), T2 (8.871–9.204), T3 (9.205–9.578), and T4 (9.579–11.435). The female group was divided into F1 (7.579–8.876), F2 (8.877–9.183), F3 (9.184–9.526), and F4 (9.527–11.647). Binary logistic regression analysis was used to explore the relationship between TyG index and high CVD risk, while Z-tests were employed to compare effect values between subgroups.

Results: The proportion of participants at high risk for CVD was 28.4% in the male group and 26.0% in the female group. Binary logistic regression analysis revealed that TyG index levels T2 (F2), T3 (F3), and T4 (F4) were significantly associated with high CVD risk in both groups ($P<0.05$), with the strength of association increasing as TyG index rose. In the male group, the risk of high CVD risk in T4 compared to T1 was OR (95% CI) = 1.827 (1.622, 2.058). In the female group, the corresponding risk in F4 compared to F1 was 1.552 (1.410, 1.708). The difference in CVD risk associated with the highest TyG quartile between genders was statistically significant ($P<0.05$). After further adjusting for total cholesterol and other indicators (Model 2), the associations between T2 (F2), T3 (F3), T4 (F4) and high CVD risk were attenuated but remained significant in both groups ($P<0.05$), with risk increasing progressively with TyG index level. Compared to T1, the risk in T4 was OR (95% CI) = 1.804 (1.584, 2.055) for males and 1.496 (1.345, 1.665) for females. The gender difference in the highest quartile remained statistically significant ($P<0.05$).

Conclusion: Middle-aged obese men with high TyG index levels are more susceptible to high CVD risk. Monitoring TyG index levels in this population should be prioritized.

Keywords: Obesity; Triglyceride-glucose index; Different genders; Cardiovascular diseases; Middle age; High risk

Introduction

With accelerating population aging, cardiovascular disease (CVD) has become an increasingly significant public health problem in China, with continuously rising incidence and mortality rates [1]. In 2019, the number of CVD patients across 204 countries and regions increased by 252 million compared to 271 million in 1990, with CVD deaths rising by 6.5 million, making it one of the leading causes of death worldwide [2]. Unhealthy lifestyles have driven upward trends in overweight and obesity prevalence. Obesity increases CVD risk, and middle-aged populations are particularly vulnerable to obesity-related CVD risk, necessitating targeted prevention strategies to control risk factors and delay CVD progression [3].

The triglyceride-glucose (TyG) index, a marker of insulin resistance (IR), offers an inexpensive and readily accessible alternative for detecting IR and pancreatic function while effectively predicting type 2 diabetes risk [4-5]. IR and obesity increase the risk of glucose and lipid metabolism disorders, thereby elevating CVD risk. The relationship between TyG index and CVD risk may differ significantly between genders. Therefore, this study investigated the association between TyG index and high CVD risk in middle-aged obese populations by gender, aiming to provide evidence-based guidance for CVD prevention and screening in this demographic.

Methods

1.1 Study Participants

Participants were selected from 10 early screening and comprehensive intervention projects for high-risk CVD populations conducted in Anhui Province. A total of 30,425 middle-aged obese individuals were included. Inclusion criteria were: (1) residence at the project site for $ $6 months within the past year; (2) voluntary participation with full survey completion; and (3) age 45–65 years with body mass index (BMI) $ $25kg/m^{2}$. Exclusion criteria included: (1) incomplete survey data; (2) inability to perform self-care; and (3) advanced malignancy, severe hepatic or renal impairment, or acute infection. The study was approved by the Ethics Committee of Suzhou Municipal Hospital (Approval No. A2022033), and all participants provided informed consent.

1.2 Methods

1.2.1 Questionnaire Survey Using a preliminary screening questionnaire and basic information registration form designed by the National Cardiovascular Center, trained and certified investigators collected data on gender, age, hypertension, dyslipidemia, diabetes, smoking status, and alcohol consumption.

1.2.2 Physical Examination Trained medical staff measured height (cm) and weight (kg) for all participants.

1.2.3 Laboratory Testing After fasting for at least 8 hours, participants underwent fasting venous blood collection between 6:30–9:00 AM. Fasting plasma glucose (FPG) was measured using a glucometer, and triglycerides (TG) were assessed using a rapid lipid analyzer.

1.2.4 Definitions **High-risk CVD individuals** were defined as meeting any one of four criteria: (1) history of myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, or stroke (ischemic or hemorrhagic); (2) systolic blood pressure $ $160 mmHg or diastolic blood pressure $ $100 mmHg; (3) LDL-C $ $160 mg/dl (4.14 mmol/L) or HDL-C <30 mg/dl (0.78 mmol/L); or (4) 10-year CVD risk $ $20% based on the 2008 WHO/ISH risk assessment charts. The project data collection system automatically determined high-risk CVD status based on screening results [6].

Smoking was defined as current smoking at the time of survey. **Alcohol consumption** was defined as drinking $ $1 time per week.

1.2.5 Index Calculation and Grouping BMI was calculated as weight (kg)/height^2 (m^2). The TyG index was calculated as Ln[serum triglycerides (mmol/L) × fasting plasma glucose (mmol/L)/2]. Participants were stratified by gender and further divided into quartiles based on TyG index: males into T1 (7.417–8.870), T2 (8.871–9.204), T3 (9.205–9.578), and T4 (9.579–11.435); females into F1 (7.579–8.876), F2 (8.877–9.183), F3 (9.184–9.526), and F4 (9.527–11.647).

1.3 Statistical Analysis

SPSS 25.0 software was used for statistical analysis. Non-normally distributed continuous variables were described as M(P25, P75) and compared between groups using non-parametric rank-sum tests. Categorical variables were expressed as percentages and compared using ^{2} tests. Logistic regression analysis examined the relationship between TyG index and high CVD risk in middle-aged obese populations by gender. Z-tests in R software (version 4.1.1) compared OR values between male and female groups. The significance level was set at α=0.05.

Results

2.1 Basic Participant Information

Among 30,425 middle-aged obese residents, 11,566 were male and 18,859 were female. The prevalence of high CVD risk was 28.4% (3,280/11,566) in males and

26.0% (4,909/18,859) in females. In the male group, individuals at high CVD risk showed significantly higher TyG index, total cholesterol, HDL-C, LDL-C, BMI, triglycerides, and fasting glucose compared to non-high-risk individuals (P<0.05). Similar significant differences were observed in the female group for smoking, TyG index, total cholesterol, HDL-C, LDL-C, BMI, triglycerides, and fasting glucose (P<0.05) .

2.2 Characteristics by Gender and TyG Index Quartiles

Median TyG index values were 9.204 for males and 9.183 for females. In the male group, significant differences across TyG quartiles were observed for smoking, alcohol consumption, hypertension, diabetes, dyslipidemia, high CVD risk status, total cholesterol, HDL-C, LDL-C, BMI, triglycerides, and fasting glucose (P<0.05). In the female group, significant differences were found across quartiles for hypertension, diabetes, dyslipidemia, high CVD risk status, LDL-C, total cholesterol, HDL-C, BMI, triglycerides, and fasting glucose (P<0.05) [TABLE:2, TABLE:3].

2.3 Univariate Logistic Regression Analysis

Using TyG index quartiles as the independent variable (coded as T1/F1=1, T2/F2=2, T3/F3=3, T4/F4=4) and CVD high-risk status, hypertension, diabetes, and dyslipidemia as dependent variables, univariate logistic regression analysis showed TyG index was a significant factor for all outcomes in both genders (P<0.05). In males, T4 was associated with 1.956-, 5.389-, 4.633-, and 1.785-fold increases in hypertension, diabetes, dyslipidemia, and high CVD risk, respectively, compared to T1. In females, F4 was associated with 2.287-, 11.479-, 4.237-, and 1.515-fold increases, respectively, compared to F1. The risk of hypertension, diabetes, dyslipidemia, and high CVD risk increased progressively with TyG index level in both groups [TABLE:4, TABLE:5].

2.4 Binary Logistic Regression Analysis of TyG Index and High CVD Risk

Multivariate binary logistic regression models were constructed with TyG quartiles as the independent variable and high CVD risk status as the dependent variable.

Model 1 adjusted for smoking, alcohol consumption, hypertension, diabetes, and dyslipidemia. Results showed significant associations between TyG index T2 (F2), T3 (F3), and T4 (F4) and high CVD risk in both genders (P<0.05), with strengthening associations at higher TyG levels. Compared to T1, the risk in T4 was OR (95% CI) = 1.827 (1.622, 2.058) for males and 1.552 (1.410, 1.708) for females. The gender difference in the highest quartile was statistically significant (P<0.05).

Model 2 further adjusted for total cholesterol, HDL-C, and LDL-C. While associations were attenuated, T2 (F2), T3 (F3), and T4 (F4) remained significantly

associated with high CVD risk in both groups (P<0.05), with progressively increasing risk at higher TyG levels. Compared to T1, the risk in T4 was OR (95% CI) = 1.804 (1.584, 2.055) for males and 1.496 (1.345, 1.665) for females. The gender difference in the highest quartile remained significant (P<0.05) [TABLE:6, TABLE:7].

Discussion

CVD remains the leading cause of health burden among Chinese residents. Individuals at high risk for CVD are highly susceptible to cardiovascular events, making risk factor control and risk assessment essential for prevention [7]. In China, over half of middle-aged individuals are obese, and this population is particularly prone to hypertension and diabetes, significantly increasing CVD risk [8]. This study analyzed CVD risk status and related risk factors in middle-aged obese residents by gender, finding a higher prevalence of high CVD risk in males (28.4%) than females (26.0%), consistent with previous research [9,10].

Among high-risk individuals, hypertension prevalence (34.5%) exceeded that of diabetes (13.6%) and dyslipidemia (6.4%) in both genders, highlighting hypertension prevention and control as paramount for CVD prevention [11]. Smoking emerged as an important risk factor for high CVD risk in females, likely reflecting changing social norms as more women enter the workforce and adopt smoking behaviors. Smoking increases risks of hypertension and stroke [12] and represents a major CVD risk factor [13], warranting lifestyle interventions. While some studies suggest even moderate alcohol consumption increases risks of diabetes, hypertension, and dyslipidemia in high-risk populations [14], this study found no association between alcohol consumption and CVD risk, possibly due to our limited definition that did not capture drinking type or quantity [15].

Type 2 diabetes mellitus (T2DM) is a global epidemic and CVD risk factor, with midlife obesity increasing T2DM risk in older age [16]. The TyG index, incorporating both metabolic (hypertriglyceridemia) and glycemic (fasting glucose) components, effectively reflects IR-induced metabolic abnormalities and serves as an efficient, simple tool for diabetes prediction [17]. Our results showed that the highest TyG quartile was associated with 5.389-fold and 11.479-fold increases in diabetes risk in males and females, respectively, with risk escalating progressively across quartiles. IR is closely linked to atherosclerosis, thrombosis, oxidative stress, and inflammation, and elevated TyG index may accelerate atherosclerotic progression while increasing hypertension and dyslipidemia incidence [19]. The 2022 ADA standards recommend enhanced lifestyle interventions for patients with elevated TG and glucose to slow atherosclerotic CVD progression [18].

A prospective cohort study found high TyG index levels are an independent risk factor for hypertension [20]. Our results demonstrated progressively increasing

hypertension risk with higher TyG index in both genders. Hypertension and dyslipidemia are mutually influential [21], and combined antihypertensive and lipid-lowering therapy better controls CVD risk and reduces adverse events. The highest TyG quartile was associated with 4.633-fold and 4.237-fold increases in dyslipidemia risk in males and females, respectively. Dyslipidemia-induced metabolic disorders underlie cardiovascular and cerebrovascular pathology and are strongly associated with CVD mortality [22]. Thus, reducing TyG index may help control hypertension and dyslipidemia development, delaying progression to high CVD risk.

After controlling for confounders, TyG index remained a significant risk factor for high CVD risk, with risk increasing progressively across quartiles. In males, T4 carried 1.827-fold higher risk than T1, while in females, F4 carried 1.552-fold higher risk than F1. After further adjustment for lipid parameters, these associations were attenuated but remained significant (OR = 1.804 for males, 1.496 for females). Z-tests revealed significant gender differences in the highest quartile, indicating males with high TyG index are more susceptible to CVD risk than females. This may reflect higher smoking (48.6% vs 1.2%), alcohol consumption (34.5% vs 3.0%), hypertension (34.5% vs 29.8%), and diabetes (13.6% vs 11.3%) prevalence among males. Additionally, obese middle-aged men have higher aldosterone levels and hypertension incidence than women, amplifying CVD risk at high TyG levels [23-24]. However, one study found no gender difference in the TyG-CVD risk relationship among individuals without traditional risk factors [25], contrasting with our findings. Our study demonstrates a dose-response relationship between TyG index and CVD risk in middle-aged obese individuals, with significant gender differences at high TyG levels, though underlying mechanisms require further investigation. A 25-year cohort study of 4,754 young adults found that high TyG index levels and trajectories were positively associated with future CVD events [26], suggesting TyG index is also predictive in younger populations.

This study's strengths include its gender-specific analysis of a large, representative sample from Anhui's CVD screening program with high-quality measurements. Limitations include the cross-sectional design, which precludes assessment of temporal changes in triglyceride and glucose levels, and the restriction to middle-aged obese residents in Anhui, limiting generalizability to other regions, age groups, and non-obese populations.

Conclusion

The TyG index is closely associated with high CVD risk in middle-aged obese residents of Anhui Province across both genders. The association is more pronounced in men at high TyG levels, providing a basis for early, targeted interventions in this population. Future efforts should focus on implementing effective measures to reduce TyG index levels among middle-aged obese individuals to

decrease CVD risk in Anhui.

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