

RESEARCH

Open Access



The interaction between triglyceride-glucose index and visceral adiposity in cardiovascular disease risk: findings from a nationwide Chinese cohort

Yuhao Yang^{1†}, Shengxi Li^{2†}, Qiao Ren^{3†}, Yu Qiu^{1†}, Mengjia Pan^{1†}, Guanglei Liu^{3†}, Rise Zheng^{1†}, Zhenmei An³ and Shuangqing Li^{1*}

Abstract

Background Globally, cardiovascular disease (CVD) constitutes the primary cause of death, with insulin resistance (IR), measured by the triglyceride-glucose (TyG) index, and visceral obesity, reflected by the Chinese Visceral Adiposity Index (CVAI), as key contributors. However, the relationship between the TyG index and CVAI regarding CVD risk remains insufficiently understood. This research investigates the interactive impact of the TyG index and CVAI on the risk of cardiovascular disease.

Methods We analyzed data from 8,358 participants from the China Health and Retirement Longitudinal Study (CHARLS) over a 9-year follow-up period. Participants were classified into four groups based on median TyG index (8.59) and CVAI values (101.26), and baseline characteristics were summarized. Missing data were addressed using multiple imputation by chained equations (MICE). Cox proportional hazards models assessed associations between TyG index, CVAI, CVD, coronary heart disease (CHD), and stroke risks, with Kaplan-Meier analysis used for cumulative hazard. Interaction effects were evaluated using both multiplicative and additive measures. Subgroup analyses by age, gender, and clinical conditions were conducted to explore interaction effects across different populations. Sensitivity analyses re-tested models, excluding the covariates BMI and diabetes, using tertiles for classification, and re-evaluating imputed data.

Results Over the 9-year follow-up, 1,240 participants (14.8%) developed CVD, including 896 cases of CHD and 475 strokes. Kaplan-Meier curves indicated that participants with low TyG index but high CVAI had the highest cumulative hazard of CVD. Cox regression showed that this group had the highest CVD risk (HR = 1.87, 95% CI: 1.57–2.24), followed by those with both high TyG index and high CVAI (HR = 1.75, 95% CI: 1.49–2.06). Interaction analysis revealed a negative interaction effect between high TyG and high CVAI on CVD and CHD risks, with no significant effect

[†]Yuhao Yang, Shengxi Li, Qiao Ren, Yu Qiu, Mengjia Pan, Guanglei Liu, and Rise Zheng have equally contributed to this work and should be considered co-first authors.

*Correspondence:
Shuangqing Li
1259594471@qq.com

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

on stroke. Subgroup and sensitivity analyses further confirmed these findings, showing consistent results across demographic groups and under various analytical conditions.

Conclusion This study suggests that the interaction between IR (TyG index) and visceral fat accumulation (CVAI) plays a complex role in CVD risk, with a potential antagonistic effect observed between high TyG and high CVAI on CVD events. These findings highlight the importance of considering both IR and visceral adiposity in CVD risk assessments to improve the identification of high-risk individuals.

Introduction

With 31% of all fatalities globally occurring each year, CVD is the major cause of death worldwide [1]. Since 1990, the number of global CVD cases has increased from 271 million to 523 million, and the number of deaths has risen from 12.1 million to 18.6 million, reflecting increases of 92% and 54%, respectively [2]. In China, CVD is also the primary cause of death, accounting for 40% of the national mortality rate [3, 4]. In 2016, approximately 94 million Chinese people were living with CVD, with deaths caused by atherosclerotic cardiovascular disease (ASCVD) representing 61% of total CVD deaths [1]. Despite advancements in the prevention and treatment of CVD in China, the incidence of ischemic heart disease (IHD) and ischemic stroke (IS) continues to increase, presenting a significant public health challenge [5].

Insulin resistance, a common metabolic disorder in type 2 diabetes, has been closely linked to CVD. IR contributes to metabolic abnormalities such as dyslipidemia, hypertension, and hyperglycemia, all of which are risk factors for CVD [6, 7]. The TyG index has recently emerged as a widely used surrogate marker for IR due to its simplicity, low cost, and strong correlation with CVD risk [8]. Studies have shown that the TyG index is associated with increased risks of coronary artery calcification, carotid atherosclerosis, and adverse cardiovascular outcomes such as heart failure [9–12]. Beyond serving as a marker of IR, emerging research suggests that the TyG index may be involved in pathways linking IR to increased CVD risk, including lipid metabolism disturbances, chronic inflammation, and endothelial dysfunction. These mechanisms—characterized by pro-inflammatory cytokines, oxidative stress, and alterations in vascular function—indicate that the TyG index reflects significant metabolic processes associated with cardiovascular risk [13–17].

In parallel, obesity, particularly visceral adipose tissue (VAT) accumulation, has been recognized as an independent risk factor for CVD [18]. Recent research has indicated that VAT plays a more prominent role in increasing cardiometabolic risk compared to subcutaneous adipose tissue (SAT) [19]. Although imaging techniques can accurately assess visceral fat, their application is limited due to high costs, time consumption, and radiation risks [20]. Therefore, non-invasive and cost-effective alternatives such as the CVAI have been developed. CVAI, designed

to reflect the unique body fat distribution in Asian populations, has proven effective in assessing visceral obesity and predicting diabetes and CVD risk [21–23]. VAT contributes to CVD risk not only directly but also by promoting inflammation, oxidative stress, and abnormal adipokine secretion [24, 25]. These processes suggest that visceral fat can influence CVD both independently and in conjunction with IR.

Given the complex and potentially synergistic relationship between IR, visceral obesity, and CVD, further investigation is needed to elucidate their combined effects. Using data from the CHARLS, this study aims to analyze the relationship between the TyG index and CVAI with CVD incidence and explore potential interactions between these factors. This research may provide new insights into how IR and visceral fat accumulation jointly influence CVD risk, informing more nuanced approaches to CVD risk assessment and prevention.

Materials and methods

Data source and study population

This study utilized data from the CHARLS, a nationally representative survey that tracks Chinese residents aged 45 and above. The survey began in 2011, with follow-up assessments conducted every two years, and as of 2020, five waves have been completed. Participants were selected through a multi-stage, stratified probability sampling method proportional to population size, covering 150 counties or districts across 28 provinces in China. The baseline survey achieved a high response rate of 80.5%, significantly reducing the potential for selection bias and enhancing the representativeness of the cohort. This sampling approach ensures that the CHARLS dataset reflects the diverse demographic, socioeconomic, and geographic characteristics of China's middle-aged and elderly population. Detailed information on study design and cohort characteristics can be found on the official CHARLS website [26].

In this study, we defined the baseline cohort as participants who completed the first wave (2011–2012), and these participants were subsequently followed in the next four survey waves (2013–2014, 2015–2016, 2017–2018, and 2020). The follow-up time for each participant was calculated as the period from the baseline interview date to the date of their last completed follow-up interview [26].

In the baseline survey conducted in 2011, 17,705 individuals participated. For our analysis, we applied the following exclusion criteria: participants lacking blood measurements necessary for calculating the TyG index (fasting triglyceride and fasting plasma glucose) were excluded ($N=6,069$); Participants missing the necessary data to calculate CVAI, such as WC, age, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and body mass index (BMI), were excluded ($N=1,908$); Additionally excluded were those who at baseline had a diagnosis of CVD ($N=1,370$). After applying these criteria, the final analysis contained 8,358 participants. Figure 1 illustrates the flow chart of participant inclusion and exclusion.

The CHARLS study received ethical approval from the Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided informed written consent prior to their involvement. The

study was conducted in accordance with the Declaration of Helsinki principles and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

TyG index assessment

Expert medical staff obtained venous blood samples from fasting patients by following established protocols, and the analyses were conducted in a central laboratory. Serum triglyceride and fasting plasma glucose (FPG) were measured using an enzymatic colorimetric method. The coefficients of variation for TG and FPG were both below 5%, ensuring high reliability. The TyG index was calculated using the formula: $\text{TyG index} = \ln(\text{TG (mg/dL)} \times \text{FPG (mg/dL)} / 2)$ [27], where TG was measured using a Roche Modular P and Cobas 6000 system, and FPG was determined by the hexokinase method using a Roche/

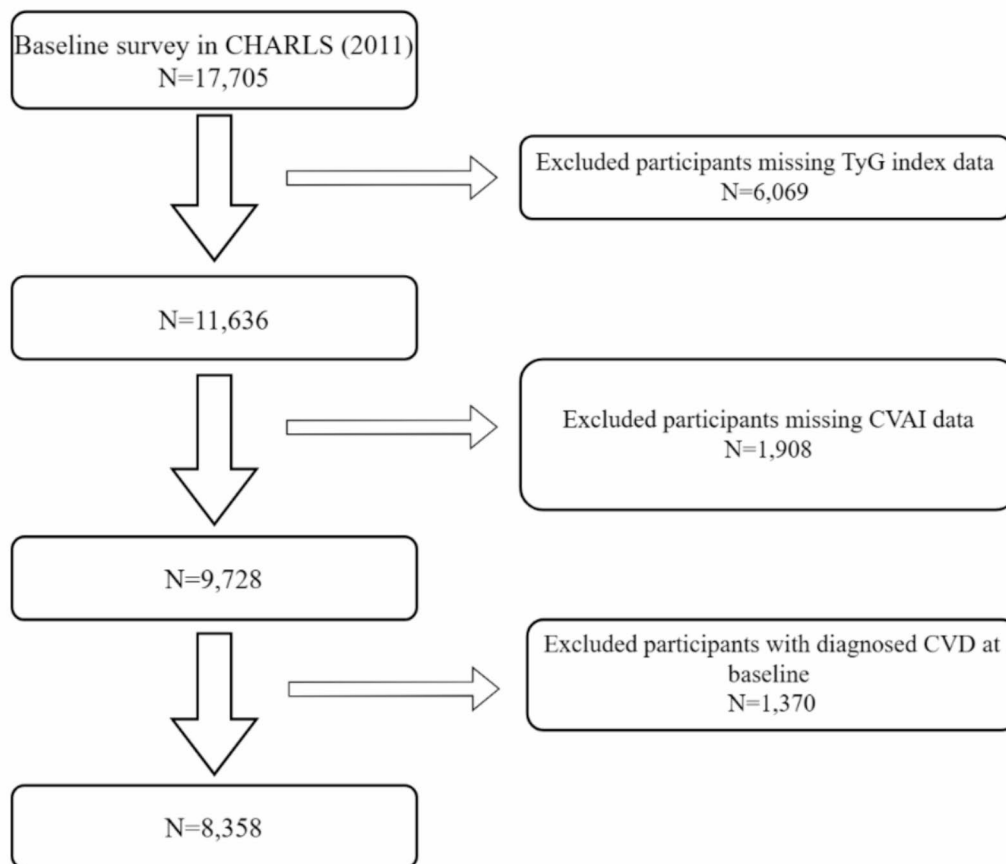


Fig. 1 Flow diagram of clinical research from CHARLS 2011 to 2020

Hitachi Cobas C 501 analyzer. The TyG index was used in this study as an indicator of insulin resistance.

CVAI assessment

Fasting blood samples were taken to assess TG and HDL-C levels, and height, weight, and waist circumference (WC) were measured in accordance with standard protocols. CVAI was used to evaluate visceral fat distribution and function, calculated separately for males and females using specific formulas [21]. For males: $CVAI = -267.93 + 0.68 \times \text{age} + 0.03 \times \text{BMI} + 4.00 \times \text{WC} + 22.00 \times \log_{10}(\text{TG}) - 16.32 \times \text{HDL-C}$; for females: $CVAI = -187.32 + 1.71 \times \text{age} + 4.23 \times \text{BMI} + 1.12 \times \text{WC} + 39.76 \times \log_{10}(\text{TG}) - 11.66 \times \text{HDL-C}$.

CVD events assessment

The primary outcome of this study was the occurrence of CVD events, CHD, and stroke. CVD diagnoses were assessed through standardized questions based on previous research [28]: “Has a doctor ever told you that you had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?” or “Has a doctor ever told you that you had a stroke?” During follow-up, the occurrence of new CVD events was defined if participants reported experiencing heart disease or stroke, with the time of the event recorded as the period between the previous interview and the interview reporting the new CVD event. For secondary outcomes, CHD and stroke were analyzed separately. CHD was defined as any self-reported physician diagnosis of heart-related conditions, including heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems. Stroke was defined as any self-reported physician diagnosis of stroke. The occurrence of new CHD or stroke events was documented in the same manner as for CVD, with the event time defined as the interval between the previous interview and the interview when the new CHD or stroke diagnosis was reported.

Covariates

The covariates in this study included age, gender, education level, BMI, marital status, smoking status, alcohol consumption, obesity, hypertension, diabetes, and dyslipidemia. Education was categorized into four levels: college and above, middle/high school, primary school, and illiterate. Marital status was classified into four categories: married, divorced, widowed, and never married. Smoking status was determined based on participants' responses to whether they had ever used tobacco products and if they currently smoke or have quit. Participants were classified as current smokers, former smokers, or never smokers. Drinking status was based on whether participants had consumed alcohol in the past year, classifying them as drinkers or non-drinkers. Obesity was

defined as $\text{BMI} \geq 28$. Hypertension was defined by a self-reported history of hypertension, systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or current use of antihypertensive medications [29]. Diabetes was determined by fasting glucose levels ≥ 7.0 mmol/L, hemoglobin A1c (HbA1c) $\geq 6.5\%$, current use of antidiabetic medications, or a self-reported history of diabetes [30]. Dyslipidemia was diagnosed based on a self-reported history, use of lipid-lowering medications, or lipid measurements such as $\text{TG} \geq 150$ mg/dL, total cholesterol (TC) ≥ 240 mg/dL, $\text{HDL-C} < 40$ mg/dL, or low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL [31].

Statistical analysis

We used descriptive statistics to summarize the baseline characteristics of the study participants. For continuous variables with a normal distribution, results were presented as mean and standard deviation (SD), while categorical variables were described using frequencies and percentages. Based on previous studies, we used the median values of the TyG index (8.59) and CVAI (101.26) as cut-off points, classifying each into “low” and “high” groups. Using this classification, participants were further grouped into four categories to analyze baseline characteristics. Differences in baseline characteristics between these groups were assessed using the chi-square test for categorical variables and analysis of variance (ANOVA) for continuous variables.

Approximately 21.2% of the data were missing (detailed missing data information is provided in Additional file 1: Table S1 and Fig. S1). To explore the pattern of missing data, we created a missingness matrix and assessed correlations between missing values (Additional file 1: Table S2). High correlations in missingness among certain variables suggested systematic patterns, indicating that these data were likely missing at random (MAR). Therefore, we addressed these missing values using the MICE method. In contrast, missing data for gender and age showed low correlations with other variables, suggesting that these data were likely missing completely at random (MCAR). Given their low proportion and independence, we chose to directly exclude observations with missing values for these two variables. Five imputed datasets were generated, and Rubin's rules were applied to combine the final analysis results (Additional file 1: Fig. S2-S6).

To assess the incidence of CVD, CHD, and stroke, we calculated incidence rates per 1,000 person-years for each outcome. Kaplan-Meier survival analysis was employed to estimate the cumulative incidence of CVD, CHD, and stroke across the four TyG and CVAI combination groups. Cumulative hazard curves were generated using the Kaplan-Meier method, with group differences assessed using the Log-rank test.

To evaluate the association between the TyG index, CVAI, and the risks of CVD, CHD, and stroke, we first classified participants into “low” and “high” groups based on the median values of the TyG index and CVAI. Cox proportional hazards regression models were then used to independently analyze the association of TyG index and CVAI with each of these outcomes. The proportional hazards assumption was assessed using Schoenfeld residuals, with the `cox.zph()` function applied to test each variable and the overall model. No significant violations of the proportional hazards assumption were observed ($P > 0.05$), indicating that the model assumptions were met.

After confirming the independent associations of the TyG index and CVAI with CVD, CHD, and stroke risks, we further investigated the potential interaction effect between the TyG index and CVAI. To assess multiplicative interaction, we introduced an interaction term (TyG $\times$ CVAI) into the Cox model and evaluated the significance of this interaction term for each outcome. Additionally, we explored additive interaction to examine the combined effect of TyG index and CVAI on CVD, CHD, and stroke risks. For additive interaction analysis, we calculated the relative excess risk due to interaction (RERI), synergy index (SI), and attributable proportion due to interaction (AP). Specifically, RERI reflects whether the combined effect of both exposures exceeds the sum of their independent effects; SI measures synergy, where $SI > 1$ indicates synergistic interaction, and $SI < 1$ suggests antagonism; AP estimates the proportion of excess risk attributable to the combined exposure.

To further validate the robustness of the interaction effect between the TyG index and CVAI on CVD risk, we conducted subgroup analyses across different age groups, genders, and among individuals with conditions such as diabetes, hypertension, dyslipidemia, as well as obesity status.

In sensitivity analyses, we performed three types of assessments. First, to address potential multicollinearity concerns, given the close association between BMI and visceral adiposity, as well as the derivation of the TyG index from fasting glucose and triglycerides, we re-ran the models excluding the covariates BMI and diabetes. Second, to examine the effect of different cut-off points, we reclassified CVAI and the TyG index into tertiles and repeated the analyses. Third, we used multiple imputation to handle missing data and ensure that the results were not biased by incomplete information.

All statistical analyses were performed using R software (version 4.4.1), with the following packages: “finalfit” for descriptive statistics and baseline characteristic analysis, “survival” for Cox proportional hazards regression, Kaplan-Meier survival analysis, Schoenfeld residuals testing, and multiplicative interaction analysis, “mice”

for multiple imputation by chained equations, “interactionR” for additive interaction calculations (RERI, SI, and AP), “naniar” for missing data analysis, and “dplyr” and “ggplot2” for data manipulation and visualization.

Results

Descriptive statistics

This study included 8,358 participants from the CHARLS dataset, collected between 2011 and 2020, with an average age of 58.8 years (standard deviation: 9.6 years), and 3,896 (46.6%) were male. Among the participants, 891 (10.7%) were obese, 3,166 (38.1%) had hypertension, 594 (7.2%) had diabetes, and 2,017 (24.1%) had dyslipidemia. Based on the median values of the TyG index (8.59) and CVAI (101.26), participants were divided into four groups: 2,874 (34.4%) with low TyG index and low CVAI, 1,349 (16.1%) with low TyG index but high CVAI, 1,305 (15.6%) with high TyG index but low CVAI, and 2,830 (33.9%) with both high TyG index and high CVAI (Table 1). The characteristics of participants based on the presence or absence of CVD are shown in Additional file 1: Table S3.

We observed that, in contrast to participants with low TyG index and low CVAI, individuals with elevated levels of both were generally older, had a higher likelihood of obesity, a greater proportion of females, and were more frequently affected by diabetes, hypertension, and dyslipidemia. Over a maximum follow-up period of 9.0 years, a total of 1,240 participants (14.8%) experienced CVD events, with 896 cases (10.7%) of CHD and 475 cases (5.7%) of stroke. The incidence of CVD was 10.80 per 1,000 person-years among participants with low TyG index and low CVAI, 23.70 per 1,000 person-years in those with low TyG index but high CVAI, 15.10 per 1,000 person-years in participants with high TyG index but low CVAI, and 23.10 per 1,000 person-years in those with both high TyG index and high CVAI (Table 2). Figure 2 shows the Kaplan-Meier curves for cumulative CVD hazard, indicating that participants with low TyG index but high CVAI exhibited the highest hazard of CVD.

Regression results

Table 2 shows the associations between the TyG index, CVAI, and the risk of CVD events after adjusting for multiple potential confounders. In the Cox proportional hazards regression models, both the TyG index and CVAI were independently associated with an increased risk of CVD, CHD, and stroke. Participants in the high TyG group had significantly higher risks of CVD (HR=1.22, 95% CI: 1.08–1.38), CHD (HR=1.15, 95% CI: 1.0–1.33), and stroke (HR=1.37, 95% CI: 1.11–1.67) compared to those in the low TyG group. Similarly, individuals with high CVAI showed elevated risks of CVD (HR=1.61, 95% CI: 1.42–1.83), CHD (HR=1.53, 95% CI: 1.31–1.77), and

Table 1 Characteristics of 8,358 participants according to TyG index and CVAI levels

Characteristics	Overall N=8358	Group 1 N=2874	Group 2 N=1349	Group 3 N=1305	Group 4 N=2830	P value ^a
Age, mean ± SD, years	58.8 (9.6)	57.2 (9.4)	61.9 (10.2)	56.6 (8.8)	60.0 (9.4)	<0.001
Age (%)						<0.001
< 59	4745 (56.8)	1823 (63.4)	594 (44.0)	883 (67.7)	1445 (51.1)	
60–69	2360 (28.2)	706 (24.6)	431 (31.9)	294 (22.5)	929 (32.8)	
> = 70	1253 (15.0)	345 (12.0)	324 (24.0)	128 (9.8)	456 (16.1)	
BMI, mean ± SD	23.7 (12.4)	21.2 (2.6)	25.7 (11.6)	21.8 (15.5)	26.2 (16.0)	<0.001
BMI (%)						<0.001
< 24	5062 (60.6)	2529 (88.0)	487 (36.1)	1145 (87.7)	901 (31.8)	
24–28	2405 (28.8)	329 (11.4)	618 (45.8)	138 (10.6)	1320 (46.6)	
>=28	891 (10.7)	16 (0.6)	244 (18.1)	22 (1.7)	609 (21.5)	
Gender (%)						<0.001
Female	4462 (53.4)	1427 (49.7)	664 (49.2)	709 (54.3)	1662 (58.7)	
Male	3896 (46.6)	1447 (50.3)	685 (50.8)	596 (45.7)	1168 (41.3)	
Education level (%)						<0.001
College/uni+	103 (1.2)	27 (0.9)	29 (2.2)	16 (1.2)	31 (1.1)	
Second/high school	2374 (28.4)	811 (28.2)	364 (27.0)	373 (28.6)	826 (29.2)	
Primary	3441 (41.2)	1238 (43.1)	545 (40.4)	564 (43.3)	1094 (38.7)	
Illiterate	2437 (29.2)	797 (27.7)	410 (30.4)	351 (26.9)	879 (31.1)	
Marital status (%)						<0.001
Married	7384 (88.3)	2585 (89.9)	1144 (84.8)	1170 (89.7)	2485 (87.8)	
Divorced	91 (1.1)	40 (1.4)	15 (1.1)	12 (0.9)	24 (0.8)	
Widowed	824 (9.9)	216 (7.5)	185 (13.7)	110 (8.4)	313 (11.1)	
Unmarried	59 (0.7)	33 (1.1)	5 (0.4)	13 (1.0)	8 (0.3)	
Drinking status (%)						<0.001
Yes	2814 (33.7)	1051 (36.6)	484 (35.9)	443 (33.9)	836 (29.5)	
No	5544 (66.3)	1823 (63.4)	865 (64.1)	862 (66.1)	1994 (70.5)	
Smoking status (%)						<0.001
Non-smoker	5095 (61.1)	1649 (57.6)	822 (61.1)	766 (58.9)	1858 (65.8)	
Ex-smoker	671 (8.1)	181 (6.3)	141 (10.5)	81 (6.2)	268 (9.5)	
Smoker	2567 (30.8)	1035 (36.1)	382 (28.4)	453 (34.8)	697 (24.7)	
Obesity (%)						<0.001
Yes	891 (10.7)	16 (0.6)	244 (18.1)	22 (1.7)	609 (21.5)	
No	7467 (89.3)	2858 (99.4)	1105 (81.9)	1283 (98.3)	2221 (78.5)	
Hypertension (%)						<0.001
Yes	3166 (38.1)	684 (24.0)	623 (46.5)	378 (29.1)	1481 (52.7)	
No	5135 (61.9)	2168 (76.0)	717 (53.5)	920 (70.9)	1330 (47.3)	
Dyslipidemia (%)						<0.001
Yes	2017 (24.1)	235 (8.2)	153 (11.4)	348 (26.7)	1281 (45.3)	
No	6340 (75.9)	2639 (91.8)	1195 (88.6)	957 (73.3)	1549 (54.7)	
Diabetes (%)						<0.001
Yes	594 (7.2)	68 (2.4)	61 (4.6)	93 (7.2)	372 (13.2)	
No	7701 (92.8)	2780 (97.6)	1279 (95.4)	1206 (92.8)	2436 (86.8)	
CVD (%)						<0.001
Yes	1240 (14.8)	270 (9.4)	255 (18.9)	169 (13.0)	546 (19.3)	
No	7118 (85.2)	2604 (90.6)	1094 (81.1)	1136 (87.0)	2284 (80.7)	
CHD (%)						<0.001
Yes	896 (10.7)	197 (6.9)	197 (14.6)	135 (10.3)	367 (13.0)	
No	7462 (89.3)	2677 (93.1)	1152 (85.4)	1170 (89.7)	2463 (87.0)	
Stroke (%)						<0.001

Table 1 (continued)

Characteristics	Overall N=8358	Group 1 N=2874	Group 2 N=1349	Group 3 N=1305	Group 4 N=2830	P value ^a
Yes	475 (5.7)	89 (3.1)	91 (6.7)	58 (4.4)	237 (8.4)	
No	7883 (94.3)	2785 (96.9)	1258 (93.3)	1247 (95.6)	2593 (91.6)	

Group 1 refers to low TyG & low CVAI; Group 2 refers to low TyG & high CVAI; Group 3 refers to high TyG & low CVAI; Group 4 refers to high TyG & high CVAI
Abbreviations: TyG index, triglyceride-glucose index; CVAI, Chinese visceral adiposity index; BMI, body mass index; SD, standard deviation; Uni+, university; CVD, cardiovascular disease; CHD, coronary heart disease
^aP value was based on χ^2 or analysis of variance test where appropriate

stroke (HR=1.75, 95% CI: 1.41–2.16) relative to those with low CVAI. These findings indicate that both a higher TyG index and a higher CVAI are independently associated with increased risks of cardiovascular outcomes.

Interaction analysis

We then examined the interaction between the TyG index and CVAI on the risk of CVD events (Table 2). Results from the multiplicative interaction analysis showed that the interaction term (TyG × CVAI) was significant for both CVD (*P* for interaction<0.05) and CHD (*P* for interaction<0.05) in the Cox model, but not for stroke (*P* for interaction>0.05). Further analysis revealed that, compared to participants with low TyG and low CVAI, those with low TyG but high CVAI had the highest risk of CVD (HR=1.87, 95% CI: 1.57–2.24), followed by those with both high TyG and high CVAI (HR=1.75, 95% CI: 1.49–2.06), and those with high TyG but low CVAI (HR=1.33, 95% CI: 1.10–1.62). A similar pattern was observed for CHD, where participants with low TyG and high CVAI had the highest risk (HR=2.03, 95% CI: 1.65–2.49), followed by those with both high TyG and high CVAI (HR=1.63, 95% CI: 1.34–1.99), and those with high TyG but low CVAI (HR=1.47, 95% CI: 1.18–1.84).

In the additive interaction analysis, we looked at how the TyG index and CVAI together influenced the risks of CVD, CHD, and stroke by calculating RERI, AP, and SI. For CVD, our findings pointed to a negative interaction effect, with a RERI of -0.47 (95% CI: -0.89, -0.14), an AP of -0.28 (95% CI: -0.52, -0.08), and an SI of 0.59 (95% CI: 0.42, 0.83). CHD showed a similar pattern, with a RERI of -0.87 (95% CI: -1.36, -0.37), an AP of -0.53 (95% CI: -0.83, -0.23), and an SI of 0.42 (95% CI: 0.28, 0.63), suggesting an antagonistic interaction between high TyG and high CVAI on CHD risk. For stroke, however, the interaction measures didn't reveal a significant effect, with a RERI of -0.11 (95% CI: -0.74, 0.52), an AP of -0.05 (95% CI: -0.36, 0.25), and an SI of 0.90 (95% CI: 0.52, 1.56). Overall, these results suggest that high TyG and high CVAI together show a negative interaction effect on CVD and CHD risks, though this effect was not seen for stroke.

Subgroup analysis

Table 3 presents the results of subgroup analyses stratified by age, gender, hypertension, diabetes, dyslipidemia, and obesity. No significant interactions were observed between these variables and the combined effect of the TyG index and CVAI on CVD risk (all *P* for interaction>0.05). This suggests that the impact of TyG index and CVAI on CVD risk is consistent across different demographic and clinical subgroups.

Sensitivity analysis

To validate the robustness of our findings, we conducted three sensitivity analyses. First, to address potential multicollinearity arising from the close relationship between BMI and visceral adiposity, as well as the derivation of the TyG index from fasting glucose and triglycerides, we reanalyzed the data, excluding the covariates BMI and diabetes (Additional file 1: Table S4). The results were consistent with the primary analysis, showing significant multiplicative and additive interactions between the TyG index and CVAI for CVD and CHD (*P* for interaction<0.05), but no significant interaction for stroke (*P* for interaction>0.05). Second, when the TyG index and CVAI were categorized into tertiles, significant multiplicative interactions were observed for CVD, CHD, and stroke (*P* for interaction<0.05), whereas additive interactions for CVD and stroke were not statistically significant (95% CI for RERI included zero). Further analysis indicated that participants in the medium TyG × high CVAI group had the highest CVD risk (Additional file 1: Table S5 and Fig. S7). Finally, using multiple imputation to handle missing data yielded results consistent with those before imputation (Additional file 1: Table S6).

Discussion

In this large, nationwide, longitudinal cohort study involving 8,358 middle-aged and older adults in China, followed for up to 9.0 years, we found a significant association between elevated TyG index, CVAI, and the risk of new-onset CVD. Both the TyG index and CVAI were independently associated with increased risks of CVD, CHD, and stroke. When stratified by the TyG index and CVAI, participants with low TyG index but high CVAI exhibited the highest cumulative hazard of CVD,

Table 2 Independent and combined effects of TyG index and CVAI on CVD events risk

Variables	Incidence rate (1,000 PY)	HR (95% CI) ^a	P for interaction ^b	Interaction measures ^c
CVD incidence				
Low TyG	14.50	Reference		
High TyG	20.50	1.22(1.08, 1.38)		
Low CVAI	12.20	Reference		
High CVAI	23.00	1.61(1.42, 1.83)		
Low TyG & low CVAI	10.80	Reference	0.005	RERI: -0.47 (-0.89, -0.14)
Low TyG & high CVAI	23.70	1.87 (1.57, 2.24)		AP: -0.28 (-0.52, -0.08)
High TyG & low CVAI	15.10	1.33 (1.10, 1.62)		SI: 0.59 (0.42, 0.83)
High TyG & high CVAI	23.10	1.75 (1.49, 2.06)		
CHD incidence				
Low TyG	10.90	Reference		
High TyG	14.40	1.15(1.00, 1.33)		
Low CVAI	9.21	Reference		
High CVAI	16.20	1.53(1.31, 1.77)		
Low TyG & low CVAI	7.90	Reference	< 0.001	RERI: -0.87 (-1.36, -0.37)
Low TyG & high CVAI	17.60	2.03 (1.65, 2.49)		AP: -0.53 (-0.83, -0.23)
High TyG & low CVAI	12.10	1.47 (1.18, 1.84)		SI: 0.42 (0.28, 0.63)
High TyG & high CVAI	15.50	1.63 (1.34, 1.99)		
Stroke incidence				
Low TyG	4.99	Reference		
High TyG	8.47	1.37(1.11, 1.67)		
Low CVAI	4.08	Reference		
High CVAI	9.41	1.75(1.41, 2.16)		
Low TyG & low CVAI	3.58	Reference	0.417	RERI: -0.11 (-0.74, 0.52)
Low TyG & high CVAI	8.11	1.82 (1.34, 2.46)		AP: -0.05 (-0.36, 0.25)
High TyG & low CVAI	5.19	1.33 (0.95, 1.86)		SI: 0.90 (0.52, 1.56)
High TyG & high CVAI	10.00	2.03 (1.55, 2.67)		

Abbreviations: CVD, cardiovascular disease; TyG index, triglyceride-glucose index; CVAI, Chinese visceral adiposity index; HR, hazard ratio; CI, confidence interval; 1,000 PY, per 1,000 person-years; RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; SI, synergy index

^aAge, gender, education level, BMI, marital status, hypertension, diabetes, dyslipidemia, smoking, and alcohol consumption status were adjusted

^bThe significance of the interaction term was evaluated through likelihood tests, which involved comparing the model that included the interaction term with a model that did not

^cAdditive interactions were calculated based on the reference group with low TyG & low CVAI

followed by those with both high TyG index and high CVAI. Additive interaction analysis revealed a negative interaction effect for CVD and CHD, suggesting an antagonistic relationship between high TyG index and high CVAI in these outcomes. Subgroup analyses across different demographic and clinical characteristics, as well as multiple sensitivity analyses, further supported the robustness of our findings. Collectively, these results highlight the importance of considering both insulin resistance (reflected by the TyG index) and visceral adiposity (measured by CVAI) in assessing cardiovascular risk.

A substantial body of research has established a positive correlation between the TyG index, as a marker of IR and metabolic syndrome, and CVD. IR increases CVD risk by inducing hyperglycemia, inflammatory responses, lipid metabolism disorders, and vascular damage [32, 33]. As a measure reflecting triglyceride and glucose levels, the TyG index has been shown to be a reliable predictor of CVD in several cohort studies. For instance, Da Silva et al. analyzed data from 2,330 patients in Brazil and found that a higher TyG index was significantly associated with an increased risk of symptomatic coronary artery disease (CAD) [34]. Similarly, Barzegar et al., in their analysis of the Tehran Lipid and Glucose Study (TLGS) involving 7,521 participants, further validated the positive correlation between the TyG index and increased risks of both CVD and CHD, especially in older populations [35]. Additionally, research conducted by Zhang and Liang revealed that an elevated TyG index was significantly linked to higher rates of CVD and related mortality among individuals with diabetes or prediabetes (1,072 participants) as well as older adults aged 60 and above (6,502 participants) [12, 36].

Visceral fat accumulation is considered a major risk factor for CVD, as it impairs vascular endothelial function through multiple pathways, including the release of pro-inflammatory cytokines and oxidative stress, thereby significantly increasing CVD risk [37, 38]. CVAI, a composite visceral obesity index based on age, BMI, WC, and metabolic parameters, has been validated in several studies as an effective predictor of CVD. For example, in a 10-year study of 1,252 postmenopausal women, Liu et al. found that among several abdominal obesity indices, including WC, WHR, visceral adiposity index (VAI), lipid accumulation product (LAP), and CVAI, the latter had the strongest predictive value for CVD risk in postmenopausal women [21]. Similarly, Qiao et al., in a 59-month follow-up study of 2,328 patients with type 2 diabetes, found that WC, VAI, LAP, and CVAI were all significantly associated with the risk of cardiovascular events, with CVAI showing the best predictive performance [39]. Liu et al. also demonstrated that among seven surrogate markers of IR, CVAI outperformed others in predicting

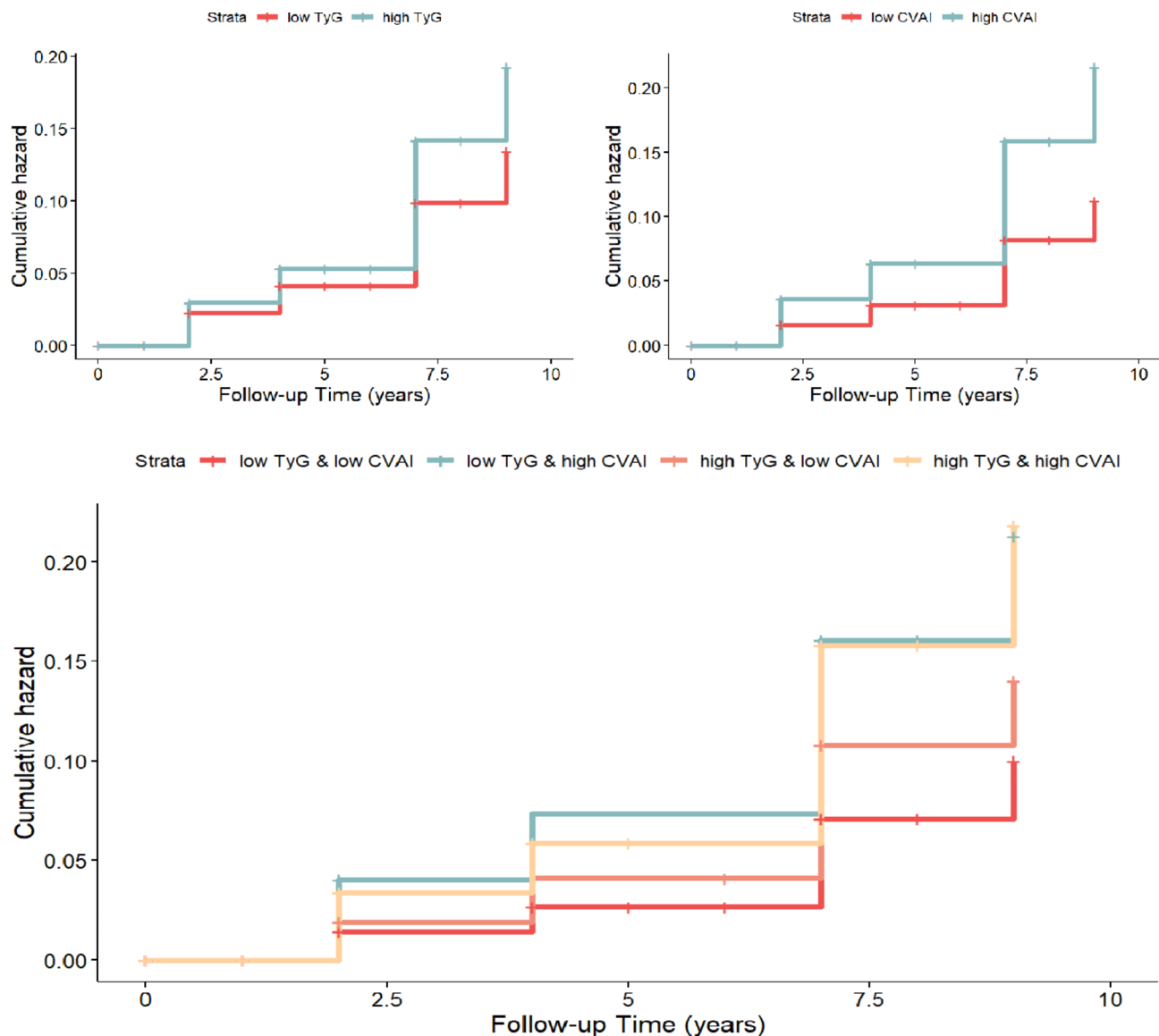


Fig. 2 K-M plot of CVD risk by TyG index and CVAI. Abbreviations: TyG index, triglyceride-glucose index; CVAI, Chinese visceral adiposity index

CHD risk, further supporting its importance as a CVD predictor [40].

In this study, our findings suggest that IR and visceral fat accumulation together increase CVD risk through multiple pathological mechanisms. As an independent risk factor for CVD, IR triggers several metabolic disturbances that heighten cardiovascular risk. Firstly, IR leads to hyperglycemia, which promotes the formation of advanced glycation end products (AGEs) that directly damage vascular endothelium and accelerate atherosclerosis [41]. Additionally, IR-associated hyperinsulinemia stimulates vascular smooth muscle cell proliferation and vasoconstriction, exacerbating vascular hardening and inflammation [42].

Visceral fat accumulation is also an independent risk factor for CVD and promotes risk through several

pathways. Firstly, visceral fat releases pro-inflammatory factors that drive chronic low-grade inflammation, impair vascular endothelial function, and exacerbate oxidative stress, thereby accelerating the progression of atherosclerosis [43–45]. Visceral fat can also accumulate in ectopic sites such as the heart and liver, disrupting lipid metabolism and resulting in elevated triglyceride levels, reduced HDL-C, and an increase in small, dense LDL particles—all of which significantly increase CVD risk, even in individuals with mild IR [46–49]. Moreover, visceral fat affects adipokine secretion, decreasing anti-inflammatory adiponectin and increasing pro-inflammatory leptin. Reduced adiponectin levels weaken vascular protection, while elevated leptin promotes inflammation and lipid deposition, further aggravating vascular damage and substantially raising CVD incidence [50–53].

Table 3 Subgroup analysis for the combined effect of the TyG index and CVAI on CVD risk

Subgroup (cases/total)	Incidence rate (1,000 PY)	Variables	HR (95% CI) ^a	P for interaction ^b
Overall (N = 8358)	10.80	Low TyG & low CVAI	Reference	0.93
	23.70	Low TyG & high CVAI	1.87 (1.57, 2.24)	
	15.10	High TyG & low CVAI	1.33 (1.10, 1.62)	
	23.10	High TyG & high CVAI	1.75 (1.49, 2.06)	
Age, years				0.93
< 59 (4745/8358)	9.96	Low TyG & low CVAI	Reference	
	22.04	Low TyG & high CVAI	1.96 (1.52, 2.52)	
	13.34	High TyG & low CVAI	1.26 (0.98, 1.63)	
	20.92	High TyG & high CVAI	1.70 (1.36, 2.12)	
60–69 (2360/8358)	12.96	Low TyG & low CVAI	Reference	
	23.95	Low TyG & high CVAI	1.72 (1.25, 2.35)	
	19.73	High TyG & low CVAI	1.45 (1.01, 2.08)	
	27.29	High TyG & high CVAI	1.71 (1.28, 2.29)	
≥ 70 (1253/8358)	11.31	Low TyG & low CVAI	Reference	
	22.41	Low TyG & high CVAI	1.92 (1.22, 3.03)	
	17.24	High TyG & low CVAI	1.34 (0.73, 2.47)	
	21.39	High TyG & high CVAI	1.70 (1.07, 2.70)	
Gender				0.14
Female (4462/8358)	11.80	Low TyG & low CVAI	Reference	
	25.68	Low TyG & high CVAI	1.94 (1.51, 2.48)	
	17.39	High TyG & low CVAI	1.43 (1.11, 1.84)	
	24.05	High TyG & high CVAI	1.69 (1.35, 2.10)	
Male (3896/8358)	9.91	Low TyG & low CVAI	Reference	
	19.91	Low TyG & high CVAI	1.79 (1.37, 2.33)	
	12.47	High TyG & low CVAI	1.17 (0.86, 1.60)	
	21.69	High TyG & high CVAI	1.86 (1.45, 2.39)	
Obesity				0.96
Yes (891/8358)	6.94	Low TyG & low CVAI	Reference	
	31.33	Low TyG & high CVAI	3.77 (0.52, 27.38)	
	10.47	High TyG & low CVAI	1.42 (0.13, 15.85)	
	29.93	High TyG & high CVAI	3.28 (0.45, 23.71)	
No (7467/8358)	10.87	Low TyG & low CVAI	Reference	
	20.89	Low TyG & high CVAI	1.40 (1.13, 1.75)	
	15.21	High TyG & low CVAI	1.35 (1.11, 1.64)	
	21.24	High TyG & high CVAI	1.32 (1.08, 1.62)	
Hypertension				0.79
Yes (3166/8358)	14.52	Low TyG & low CVAI	Reference	
	27.44	Low TyG & high CVAI	1.94 (1.47, 2.57)	
	20.21	High TyG & low CVAI	1.38 (0.99, 1.92)	
	28.22	High TyG & high CVAI	1.91 (1.47, 2.46)	
No (5135/8358)	9.73	Low TyG & low CVAI	Reference	
	18.94	Low TyG & high CVAI	1.83 (1.44, 2.33)	
	13.21	High TyG & low CVAI	1.31 (1.03, 1.68)	
	17.68	High TyG & high CVAI	1.61 (1.29, 2.02)	
Diabetes				0.79
Yes (594/8358)	24.52	Low TyG & low CVAI	Reference	
	29.23	Low TyG & high CVAI	1.18 (0.53, 2.62)	
	27.85	High TyG & low CVAI	1.19 (0.59, 2.41)	
	29.55	High TyG & high CVAI	1.04 (0.55, 1.97)	

Table 3 (continued)

Subgroup (cases/total)	Incidence rate (1,000 PY)	Variables	HR (95% CI) ^a	P for interaction ^b
No (7701/8358)	10.54	Low TyG & low CVAI	Reference	0.98
	22.52	Low TyG & high CVAI	1.91 (1.59, 2.30)	
	14.28	High TyG & low CVAI	1.33 (1.08, 1.63)	
	22.33	High TyG & high CVAI	1.84 (1.55, 2.18)	
Dyslipidemia				
Yes (2017/8358)	10.76	Low TyG & low CVAI	Reference	
	21.99	Low TyG & high CVAI	1.63 (0.91, 2.93)	
	15.46	High TyG & low CVAI	1.54 (0.91, 2.58)	
	24.09	High TyG & high CVAI	1.66 (1.04, 2.64)	
No (6340/8358)	10.86	Low TyG & low CVAI	Reference	
	22.74	Low TyG & high CVAI	1.91 (1.58, 2.31)	
	15.01	High TyG & low CVAI	1.33 (1.07, 1.66)	
	22.24	High TyG & high CVAI	1.75 (1.46, 2.10)	

Abbreviations: CVD, cardiovascular disease; TyG index, triglyceride-glucose index; CVAI, Chinese visceral adiposity index; HR, hazard ratio; CI, confidence interval; 1,000 PY, per 1,000 person-years

^aAge, gender, education level, BMI, marital status, hypertension, diabetes, dyslipidemia, smoking, and alcohol consumption status were adjusted

^bP for interaction was derived from Cox proportional hazards models by including multiplicative interaction terms to test for heterogeneity across subgroups

Notably, the combined analysis of IR and visceral fat accumulation reveals a more complex mechanism. We observed that when the TyG index and CVAI were divided into two or three groups, individuals with high CVAI had a lower incidence of CVD at high TyG index levels compared to those with low or medium TyG levels. This finding differs from the typical positive correlation observed when the TyG index or CVAI are analyzed separately [54–57]. These results suggest that in the presence of significant visceral fat accumulation, a high TyG index may not act as a risk factor for CVD and could even have a protective effect.

This phenomenon may be due to prolonged insulin resistance leading to the gradual exhaustion of pancreatic β-cells, resulting in a decrease in insulin secretion levels in the body [58, 59]. With lower insulin levels, insulin’s regulatory effect on lipid metabolism is weakened, and the extent of lipid metabolism disorders may be somewhat alleviated [60, 61]. Furthermore, in individuals with high CVAI, visceral fat accumulation triggers the release of pro-inflammatory cytokines (such as TNF-α and IL-6) and free fatty acids (FFA), which continuously impair insulin signaling pathways and further aggravate insulin resistance [62, 63]. This excessive inflammatory load gradually reduces the effectiveness of insulin, leading to further declines in insulin levels.

In contrast, individuals with low or medium TyG index levels may maintain higher insulin levels, and hyperinsulinemia itself is a risk factor for CVD. Hyperinsulinemia can directly harm vascular health by promoting the proliferation of vascular smooth muscle cells, increasing vasoconstriction, and enhancing inflammatory responses [7, 64, 65]. Therefore, in individuals with mild to moderate insulin resistance but significant visceral fat

accumulation, the combined harmful effects of hyperinsulinemia and visceral fat may lead to an elevated risk of CVD.

In summary, this study reveals the complex interactive roles of IR and visceral fat accumulation in influencing CVD risk among middle-aged and older adults in China. We found that both the TyG index and CVAI independently contributed to increased risks of CVD, CHD, and stroke. Notably, the combined analysis showed that in cases of significant visceral fat accumulation, high IR levels may not increase CVD risk as traditionally expected; instead, it may exhibit a protective effect, suggesting a potential antagonistic interaction between IR and visceral fat accumulation. This finding highlights the importance of assessing the combined effects of IR and visceral fat, as their interaction may produce distinct CVD risk profiles. Moving forward, a comprehensive assessment incorporating both IR and visceral fat indicators will help to more accurately identify high-risk individuals and develop more targeted prevention strategies to reflect the nuanced relationship between these risk factors and cardiovascular health.

Limitations

This study has several limitations. First, as an observational study, while we revealed associations between the TyG index, CVAI, and CVD risk, causality cannot be established. Second, although we adjusted for various known confounders (e.g., age, gender, smoking status), unmeasured confounders (e.g., diet, physical activity, socioeconomic status) may still affect the results. Third, we lacked direct measurements of insulin levels and could not assess the direct impact of insulin secretion and hyperinsulinemia on CVD risk. Fourth, while CVAI and TyG index serve as indirect markers, they may not

fully capture true visceral fat content and insulin sensitivity; more precise measurement methods (e.g., MRI, CT, or HOMA-IR) might provide more accurate assessments. Finally, as the study population comprised middle-aged and older Chinese individuals, the results may not be generalizable to other ethnic groups, age ranges, or lifestyles, and validation in other populations is necessary.

Conclusion

Our study suggests that the interaction between IR and visceral fat may influence CVD risk differently than traditionally expected, with high IR possibly acting as a protective factor in individuals with significant visceral fat. Considering both IR and visceral adiposity may improve CVD risk assessment and help identify high-risk individuals more accurately.

Abbreviations

CVD	Cardiovascular disease
IR	Insulin resistance
TyG	Triglyceride-glucose
CVAI	Chinese visceral adiposity index
CHARLS	China health and retirement longitudinal study
ASCVD	Atherosclerotic cardiovascular disease
IHD	Ischemic heart disease
IS	Ischemic stroke
VAT	Visceral adipose tissue
SAT	Subcutaneous adipose tissue
WC	Waist circumference
WHR	Waist-to-hip ratio
TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
BMI	Body mass index
FPG	Fasting plasma glucose

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12933-024-02518-2>.

Additional file 1

Author contributions

YY, QR, and SheL designed the study. YY, YQ, and MP analyzed the data. GL and RZ assisted with data collection and interpretation. ZA and ShuL supervised the study. YY wrote the manuscript with input from all authors. All authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The data that support the findings of this study are available from the China Health and Retirement Longitudinal Study (CHARLS) repository. Access to these data can be obtained by registering and submitting a request through the official CHARLS website at <http://charls.pku.edu.cn>.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Review Committee of Peking University (IRB00001052-11015), and written informed consent was obtained from all participants.

Competing interests

The authors declare no competing interests.

Author details

¹General Practice Ward/International Medical Center Ward, General Practice Medical Center, West China Hospital, Sichuan University, Chengdu, China

²Clinical Medical College, Southwest Medical University, Luzhou, China

³Department of Endocrinology and Metabolism, West China Hospital, Sichuan University, Chengdu, China

Received: 6 October 2024 / Accepted: 18 November 2024

Published online: 27 November 2024

References

1. Zhao D, Liu J, Wang M, Zhang X, Zhou M. Epidemiology of cardiovascular disease in China: current features and implications. *Nat Rev Cardiol*. 2019;16(4):203–12.
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: Update from the GBD 2019 study. *J Am Coll Cardiol*. 2020;76(25):2982–3021.
3. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, Zhou M, et al. Rapid health transition in China, 1990–2010: findings from the global burden of disease study 2010. *Lancet*. 2013;381(9882):1987–2015.
4. Zhou M, Wang H, Zhu J, Chen W, Wang L, Liu S, et al. Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the global burden of disease study 2013. *Lancet*. 2016;387(10015):251–72.
5. Li H, Ge J. Cardiovascular diseases in China: current status and future perspectives. *Int J Cardiol Heart Vasc*. 2015;6:25–31.
6. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol*. 2018;17(1):122.
7. Hill MA, Yang Y, Zhang L, Sun Z, Jia G, Parrish AR, et al. Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism*. 2021;119:154766.
8. Tao LC, Xu JN, Wang TT, Hua F, Li JJ. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. *Cardiovasc Diabetol*. 2022;21(1):68.
9. Park K, Ahn CW, Lee SB, Kang S, Nam JS, Lee BK, et al. Elevated TyG index predicts progression of coronary artery calcification. *Diabetes Care*. 2019;42(8):1569–73.
10. Xiao S, Zhang Q, Yang HY, Tong JY, Yang RQ. The association between triglyceride glucose-body mass index and all-cause and cardiovascular mortality in diabetes patients: a retrospective study from NHANES database. *Sci Rep*. 2024;14(1):13884.
11. Yang Z, Gong H, Kan F, Ji N. Association between the triglyceride glucose (TyG) index and the risk of acute kidney injury in critically ill patients with heart failure: analysis of the MIMIC-IV database. *Cardiovasc Diabetol*. 2023;22(1):232.
12. Zhang Q, Xiao S, Jiao X, Shen Y. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or pre-diabetes: evidence from NHANES 2001–2018. *Cardiovasc Diabetol*. 2023;22(1):279.
13. Zhao J, Fan H, Wang T, Yu B, Mao S, Wang X, et al. TyG index is positively associated with risk of CHD and coronary atherosclerosis severity among NAFLD patients. *Cardiovasc Diabetol*. 2022;21(1):123.
14. Li Y, Yi M, Wang X, Zhang Y, Xiao K, Si J, et al. Association between triglyceride-glucose index and endothelial dysfunction. *Endocrine*. 2024;85(2):717–23.
15. Cai XL, Xiang YF, Chen XF, Lin XQ, Lin BT, Zhou GY, et al. Prognostic value of triglyceride glucose index in population at high cardiovascular disease risk. *Cardiovasc Diabetol*. 2023;22(1):198.
16. Yang M, Shangquan Q, Xie G, Sheng G, Yang J. Oxidative stress mediates the association between triglyceride-glucose index and risk of cardiovascular and all-cause mortality in metabolic syndrome: evidence from a prospective cohort study. *Front Endocrinol (Lausanne)*. 2024;15:1452896.
17. Liu H, Wang L, Wang H, Hao X, Du Z, Li C, et al. The association of triglyceride-glucose index with major adverse cardiovascular and cerebrovascular events after acute myocardial infarction: a meta-analysis of cohort studies. *Nutr Diabetes*. 2024;14(1):39.

18. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism*. 2019;92:98–107.
19. Aparecida Silveira E, Vaseghi G, de Carvalho Santos AS, Kliemann N, Masoudkabar F, Noll M et al. Visceral obesity and its shared role in cancer and cardiovascular disease: a scoping review of the pathophysiology and pharmacological treatments. *Int J Mol Sci*. 2020;21(23).
20. Powell-Wiley TM, Poirier P, Burke LE, Després JP, Gordon-Larsen P, Lavie CJ, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143(21):e984–1010.
21. Liu L, Peng J, Zang D, Zhang Y, Wu Z, Song C, et al. The Chinese visceral adiposity index: a novel indicator more closely related to cardiovascular disease than other abdominal obesity indices among postmenopausal women. *J Transl Med*. 2024;22(1):855.
22. Wang Y, Zhao X, Chen Y, Yao Y, Zhang Y, Wang N, et al. Visceral adiposity measures are strongly associated with cardiovascular disease among female participants in Southwest China: a population-based prospective study. *Front Endocrinol (Lausanne)*. 2022;13:969753.
23. Zhang Z, Zhao L, Lu Y, Meng X, Zhou X. Association between Chinese visceral adiposity index and risk of stroke incidence in middle-aged and elderly Chinese population: evidence from a large national cohort study. *J Transl Med*. 2023;21(1):518.
24. Kolb H. Obese visceral fat tissue inflammation: from protective to detrimental? *BMC Med*. 2022;20(1):494.
25. Jia G, Jia Y, Sowers JR. Contribution of maladaptive adipose tissue expansion to development of cardiovascular disease. *Compr Physiol*. 2016;7(1):253–62.
26. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int J Epidemiol*. 2014;43(1):61–8.
27. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord*. 2008;6(4):299–304.
28. Li H, Zheng D, Li Z, Wu Z, Feng W, Cao X, et al. Association of depressive symptoms with incident cardiovascular diseases in middle-aged and older Chinese adults. *JAMA Netw Open*. 2019;2(12):e1916591.
29. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39(33):3021–104.
30. Yu J, Yi Q, Chen G, Hou L, Liu Q, Xu Y, et al. The visceral adiposity index and risk of type 2 diabetes mellitus in China: a national cohort analysis. *Diabetes Metab Res Rev*. 2022;38(3):e3507.
31. Zheng X, Han L, Shen S. Hypertension, remnant cholesterol and cardiovascular disease: evidence from the China health and retirement longitudinal study. *J Hypertens*. 2022;40(11):2292–8.
32. Khan SH, Sobia F, Niazi NK, Manzoor SM, Fazal N, Ahmad F. Metabolic clustering of risk factors: evaluation of triglyceride-glucose index (TyG index) for evaluation of insulin resistance. *Diabetol Metab Syndr*. 2018;10:74.
33. Muzurović E, Mikhailidis DP, Mantzoros C. Non-alcoholic fatty liver disease, insulin resistance, metabolic syndrome and their association with vascular risk. *Metabolism*. 2021;119:154770.
34. da Silva A, Caldas APS, Hermsdorff HHM, Bersch-Ferreira AC, Torreglosa CR, Weber B, et al. Triglyceride-glucose index is associated with symptomatic coronary artery disease in patients in secondary care. *Cardiovasc Diabetol*. 2019;18(1):89.
35. Barzegar N, Tohidi M, Hashemina M, Azizi F, Hadaegh F. The impact of triglyceride-glucose index on incident cardiovascular events during 16 years of follow-up: Tehran lipid and glucose study. *Cardiovasc Diabetol*. 2020;19(1):155.
36. Liang D, Liu C, Wang Y. The association between triglyceride-glucose index and the likelihood of cardiovascular disease in the U.S. population of older adults aged ≥ 60 years: a population-based study. *Cardiovasc Diabetol*. 2024;23(1):151.
37. Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature*. 2006;444(7121):881–7.
38. Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. *Physiol Rev*. 2013;93(1):359–404.
39. Qiao T, Luo T, Pei H, Yimingniyazi B, Aili D, Aimudula A, et al. Association between abdominal obesity indices and risk of cardiovascular events in Chinese populations with type 2 diabetes: a prospective cohort study. *Cardiovasc Diabetol*. 2022;21(1):225.
40. Liu L, Peng J, Wang N, Wu Z, Zhang Y, Cui H, et al. Comparison of seven surrogate insulin resistance indexes for prediction of incident coronary heart disease risk: a 10-year prospective cohort study. *Front Endocrinol (Lausanne)*. 2024;15:1290226.
41. Goldin A, Beckman JA, Schmidt AM, Creager MA. Advanced glycation end products: sparking the development of diabetic vascular injury. *Circulation*. 2006;114(6):597–605.
42. Jia G, Bai H, Mather B, Hill MA, Jia G, Sowers JR. Diabetic vasculopathy: molecular mechanisms and clinical insights. *Int J Mol Sci*. 2024;25(2).
43. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. *Nature*. 2006;444(7121):875–80.
44. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. *JAMA*. 1999;282(22):2131–5.
45. Lumeng CN, Bodzin JL, Saltiel AR. Obesity induces a phenotypic switch in adipose tissue macrophage polarization. *J Clin Invest*. 2007;117(1):175–84.
46. Howard BV, Ruotolo G, Robbins DC. Obesity and dyslipidemia. *Endocrinol Metab Clin North Am*. 2003;32(4):855–67.
47. Jensen MD. Is visceral fat involved in the pathogenesis of the metabolic syndrome? Human model. *Obes (Silver Spring)*. 2006;14(Suppl 1):s20–4.
48. Navab M, Reddy ST, Van Lenten BJ, Fogelman AM. HDL and cardiovascular disease: atherogenic and atheroprotective mechanisms. *Nat Rev Cardiol*. 2011;8(4):222–32.
49. Bastien M, Poirier P, Lemieux I, Després JP. Overview of epidemiology and contribution of obesity to cardiovascular disease. *Prog Cardiovasc Dis*. 2014;56(4):369–81.
50. Vaiopoulos AG, Marinou K, Christodoulides C, Koutsilieris M. The role of adiponectin in human vascular physiology. *Int J Cardiol*. 2012;155(2):188–93.
51. Rojas E, Rodríguez-Molina D, Bolli P, Israili ZH, Faria J, Fidilio E, et al. The role of adiponectin in endothelial dysfunction and hypertension. *Curr Hypertens Rep*. 2014;16(8):463.
52. Libérale L, Bonaventura A, Vecchiè A, Casula M, Dallegrì F, Montecucco F, et al. The role of adipocytokines in coronary atherosclerosis. *Curr Atheroscler Rep*. 2017;19(2):10.
53. Poetsch MS, Strano A, Guan K. Role of leptin in cardiovascular diseases. *Front Endocrinol (Lausanne)*. 2020;11:354.
54. Sánchez-Iñigo L, Navarro-González D, Fernández-Montero A, Pastrana-Delgado J, Martínez JA. The TyG index may predict the development of cardiovascular events. *Eur J Clin Invest*. 2016;46(2):189–97.
55. Gao A, Liu J, Hu C, Liu Y, Zhu Y, Han H, et al. Association between the triglyceride glucose index and coronary collateralization in coronary artery disease patients with chronic total occlusion lesions. *Lipids Health Dis*. 2021;20(1):140.
56. Wu Y, Xu W, Guo L, Li W, Zhang L, Gao L, et al. Association of the time course of Chinese visceral adiposity index accumulation with cardiovascular events in patients with hypertension. *Lipids Health Dis*. 2023;22(1):90.
57. Wu X, Wang C, Lv D, Chen B, Wu Y, Wu X, et al. Associations between Chinese visceral adiposity index and risks of all-cause and cause-specific mortality: a population-based cohort study. *Diabetes Obes Metab*. 2024;26(4):1264–72.
58. Halban PA, Polonsky KS, Bowden DW, Hawkins MA, Ling C, Mather KJ, et al. β -cell failure in type 2 diabetes: postulated mechanisms and prospects for prevention and treatment. *Diabetes Care*. 2014;37(6):1751–8.
59. Hudish LI, Reusch JE, Sussel L. β cell dysfunction during progression of metabolic syndrome to type 2 diabetes. *J Clin Invest*. 2019;129(10):4001–8.
60. Dimitriadis G, Mitrou P, Lambadiari V, Maratou E, Raptis SA. Insulin effects in muscle and adipose tissue. *Diabetes Res Clin Pract*. 2011;93(Suppl 1):S52–9.
61. Norton L, Shannon C, Gastaldelli A, DeFronzo RA. Insulin: the master regulator of glucose metabolism. *Metabolism*. 2022;129:155142.
62. Hotamisligil GS. Inflammation and metabolic disorders. *Nature*. 2006;444(7121):860–7.
63. Bays HE. Adiposopathy is sick fat a cardiovascular disease? *J Am Coll Cardiol*. 2011;57(25):2461–73.
64. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. *Circulation*. 2016;133(11):1104–14.
65. Geraldine P, King GL. Activation of protein kinase C isoforms and its impact on diabetic complications. *Circ Res*. 2010;106(8):1319–31.

Publisher's note

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