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The association between triglyceride-glucose index combined with obesity indicators and stroke risk: A longitudinal study based on CHARLS data

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Abstract

Background and objective The triglyceride-glucose (TyG) index, a surrogate marker for insulin resistance, has been proposed as a predictor of cardiovascular events. However, the combined impact of the TyG index and obesity indicators, such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), on stroke risk was not fully understood. This study aimed to investigate the association between the TyG index combined with these obesity indicators and stroke risk in the Chinese population.

Materials and methods Data on 17,708 participants aged 45 years or older for this study were collected from the China Health and Retirement Longitudinal Study (CHARLS) from baseline (2011) to the Wave 5 follow-up (2020). Cox proportional hazards model, restricted cubic spline (RCS) and receiver operating characteristic (ROC) analysis were employed to examine the association between the TyG index and its combined obesity-related indicators with stroke. Mediation analysis was conducted to explore the mutual potential mediating role of TyG and obesity indicators in the above relationships.

Results A total of 8,207 participants with an average age of 58.2 years were investigated, of which 11.0% were stroke individuals, 44.80% were men and 84.6% were from rural areas. TyG, TyG-BMI, TyG-WHtR, TyG-WC were significantly higher in stroke subjects than in the non-stroke subjects ($P < 0.001$), and were significantly and positively associated with stroke in all 3 models ($P < 0.05$). Restricted cubic spline models revealed nonlinear associations between TyG and TyG-BMI with stroke (P-overall < 0.001, P-nonlinear $= 0.003$ for TyG, and P-overall < 0.001, P-nonlinear $= 0.028$ for TyG-BMI), while TyG-WC and TyG-WHtR (P-overall < 0.001 and P-nonlinear > 0.05) demonstrated linear associations with stroke after adjusting for covariates. TyG-WHtR, TyG-BMI and TyG-WC had more robust predictive power than TyG for risk of stroke. TyG-WHtR or TyG-WC had the highest predictive power for stroke (AUC:0.696, 95% CI 0.677–0.715), slightly higher than the other indicators. Associations between TyG, TyG-WC, TyG-WHtR, and TyG-BMI with stroke were found to be stronger among individuals who were ≥ 55 years of age, male. The relationship between TyG and stroke was significantly mediated by BMI, WHtR and WC (15.79%, 21.72%, and 24.06% respectively), while the relationship between these obesity measures and stroke was significantly mediated by TyG (18.48%, 14.45%, and 14.70% respectively).

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Conclusion The combination of TyG and obesity-related indicators was significantly associated with stroke risk, and could improve predictive power for stroke compared to the single TyG. Obesity indicators and TyG mediated each other in their respective associations with stroke risk.

Keywords Triglyceride glucose (TyG), Triglyceride glucose, Waist circumference (TyG, WC), Triglyceride glucose, Waist height ratio (TyG, WHtR), Triglyceride glucose, Body mass index (TyG, BMI), Stroke; China Health and Retirement Longitudinal Study (CHARLS)

Introduction

Stroke, a principal type of cerebrovascular disease, is a predominant cause of mortality and disability-adjusted life years in the global population, contributing significantly to the global disease burden [1, 2]. Its impact on health deterioration and elevated healthcare expenditures is profound. Therefore, the identification of predictive indicators for stroke risk is crucial for facilitating early disease prevention strategies.

The Triglyceride-glucose (TyG) index is a quantitative representation of insulin resistance (IR), assessing an individual's sensitivity to insulin by integrating two biological markers, namely, triglyceride and fasting blood glucose [3, 4]. IR is a physiological state characterized by reduced sensitivity and response to insulin in the body, leading to the inefficient transportation of glucose into cells and subsequent metabolic disorders such as hyperglycemia [5]. It is identified as a substantial risk factor for numerous metabolic diseases, including type 2 diabetes [6], obesity [7], and cerebrovascular disease [8–10]. Recent studies have illustrated that the TyG index not only anticipates the risk and severity of stroke, but also has implications for its prognosis [11–14].

Obesity, a global health concern, is intrinsically linked to a variety of health hazards, such as glucose intolerance [15], IR [16], and metabolic abnormalities [17], all of which can precipitate the onset, progression, and prognosis of cerebrovascular disease [18]. The TyG index, in conjunction with obesity indices, has been identified to be closely related to IR [19], metabolic syndrome [20], uric acid [21], diabetes mellitus [22], and fatty liver [23]. Body Mass Index (BMI), Waist Circumference (WC), and Waist-to-Height Ratio (WHtR) are key anthropometric measures utilized to assess obesity, where BMI provides a general assessment of body fat, WC specifically targets abdominal obesity, and WHtR is increasingly recognized for its superior accuracy in predicting obesity-related health risks and metabolic disorders [24]. WC and WHtR showed a stronger correlation and more discriminative power for cardiometabolic multimorbidity compared to BMI [25]. One study noted that stable, low levels of body and fat mass across measures like WC, BMI, and WHtR are linked to lower stroke risk [26]. Another study showed that the combination of the TyG index with adiposity indices may outperform the TyG index alone in assessing stroke risk [27].

However, researches on the combined impact of the TyG index and adiposity indices on stroke were still insufficient and lacked systematic exploration. there were more cross-sectional studies than longitudinal ones, and comparisons between indices were inadequate. In a longitudinal study among the Chinese population, the relationship between the TyG index, adiposity indices, and stroke incidence remained unclear. Therefore, our study leverages The China Health and Retirement Longitudinal Study (CHARLS) to analyze the association of the TyG index combined with obesity indices and stroke risk.

Materials and methods

Data source and study population

The CHARLS study received approval from The Institutional Review Board of Peking University, and written informed consent was obtained from all participants. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guide lines [29].

Data on 17,708 participants aged 45 years or older for this study were collected from CHARLS from baseline (2011) to the Wave 5 follow-up (2020). Exclusion criteria comprised the following: (1) 394 participants with missing data on age or age less than 45 years; (2) 6,443 participants with missing data on triglyceride-glucose index and its combinations with indicators of obesity; (3) 237 participants with stroke in 2011 and 2,664 participants with missing data on stroke in 2020. Finally, a comprehensive, nationally representative cohort, encompassing 8,207 participants across China, was enlisted for our exploration. Figure 1 depicts the flowchart for the screening procedure.

Definitions of TyG, TyG-WC, TyG-WHtR, and TyG-BMI

The TyG index offered a numerical representation of IR by amalgamating fasting glucose and triglyceride levels. Baseline measurements of fasting plasma glucose (FPG) and triglycerides (TG) were procured when participants offered their blood specimens. Body metrics including weight, height, and waist circumference were assessed during physical examinations at a mobile examination

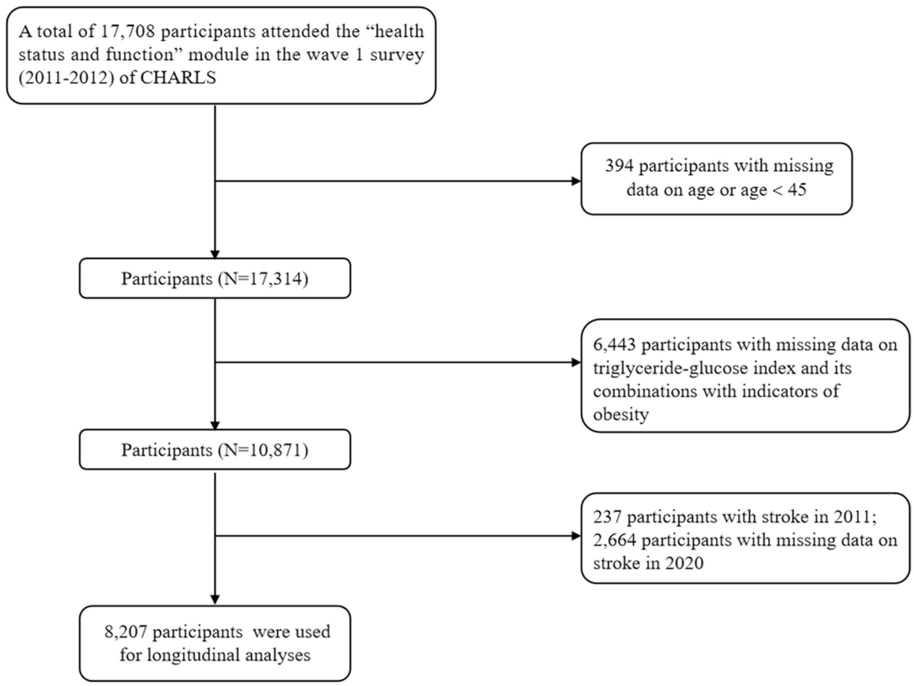

Fig. 1 Flow diagram for the screening procedure

center. Additionally, the body mass index and waist-to-height ratio were computed. Participants were categorized into four distinct quartiles (Q1, Q2, Q3, Q4) based on the quartile values of the TyG index, TyG-WC, TyG-WHtR, and TyG-BMI, respectively, with the Q1 quartile serving as a reference group. The formulas used to derive TyG, TyG-WC, TyG-WHtR, and TyG-BMI are as follows:

(a) BMI = Weight (kg) / height (m).^{2}
(b) WHtR = Weight (kg) / height (m).
(b) TyG index = Ln [1/2 × FPG (mg/dL) × TG (mg/dL)].
(c) TyG − BMI = BMI × TyG index.
(d) TyG − WHtR = WHtR × TyG index.
(e) TyG − WC = WC × TyG index.

Stroke ascertainment

In accordance with established methodologies [30], the identification of stroke events was reliant on self-reporting, in which participants confirmed that they had been officially diagnosed with stroke by a medical professional. The recorded date of stroke diagnosis was designated as falling within the timeline between the date of the most recent interview and the date of the interview wherein the stroke incident was reported.

Assessment of covariates

Professionally trained interviewers employed a systematic questionnaire to collect baseline data involving health-related elements and sociodemographic information. The sociodemographic attributes encompassed age, gender (male, female), place of residence (rural, urban), educational achievement (elementary school or lower, secondary school or higher), and marital status (married, unmarried).

Lifestyle factors incorporated alcohol consumption (never drinking, less than once per month, more than or equal to once per month) and tobacco usage (non-smoker, ex-smoker, current smoker). Health-related parameters included BMI, medical history (yes, no), cardiac events (yes, no), hypertension (yes, no), dyslipidemia (yes, no), and diabetes. Hypertension was established either when the participant's diastolic blood pressure reached or exceeded 90 mmHg and systolic blood pressure was at or above 140 mmHg, or on the basis of participant self-reports. Dyslipidemia was recognized when total cholesterol levels exceeded 200 mg/dL, low-density lipoprotein levels were over 130 mg/dL, high-density lipoprotein levels were less than 35 mg/dL, and triglyceride levels surpassed 150 mg/dL, or according to participant self-reports. Diabetes was confirmed when random blood glucose measurements exceeded 200 mg/dL, or based on self-disclosure by the participants [31].

Baseline measurements of SBP (systolic blood pressure), DBP (diastolic blood pressure), TC (total cholesterol), HDL (high density lipoprotein), LDL (low density lipoprotein), TG, FPG were recorded when participants provided blood specimens, and these were treated as continuous variables. For further details on the measurement of covariates, refer to the official CHARLS website.

Statistical analysis

For the description of baseline characteristics, mean values and standard deviations (SDs) were used for normally distributed continuous variables, and frequencies and percentages were used for categorical variables.

The Cox proportional hazards model was used to estimate hazard ratios (HRs) and 95% confidence levels (CIs) for the association between TyG index and its combination with obesity indicators and stroke. In addition, linear trends between TyG, TyG-WC, TyG-WHtR, and TyG-BMI quartiles were assessed by the median value within each quartile as a continuous variable. Model 1 was unadjusted, Model 2 adjusted for age, gender, ethnicity, education, marital status, rural, drinking, and medicine history. Model 3 adjusted for the same variables as Model 2 and for cardiac events, hypertension, dyslipidemia and diabetes.

To account for the nonlinear relationship between TyG, TyG-WC, TyG-WHtR, and TyG-BMI and stroke, restricted triple spline analyses adjusted for the same variables as in Model 3 were performed. Non-linearity tests were performed using the likelihood ratio test. Receiver operating characteristic (ROC) curves were used for diagnostic value analysis, and the area under the curve, as measured by the C-statistic, was computed to quantify the predictive power of TyG and their combination with obesity-related indices for stroke. Furthermore, after adjusting for the factors in model 3, we used mediation analysis to investigate the mutual mediation of TyG and the obesity indices with stroke. Stratified analyses were conducted to assess potential moderating effects of age (45–55, 55–65, $\geq$65) and gender (male, female). The above assessments were conducted using R 4.3.1 software, and statistical significance was determined using a two-sided p-value threshold of less than 0.05.

Results

Basic characteristics of participants according to the quartile of stroke

A total of 8,207 participants with an average age of 58.2 years were investigated, of which 11.0% were stroke individuals, 44.80% were men and 84.6% were from rural areas. TyG, TyG-BMI, TyG-WHtR, TyG-WC were significantly higher in stroke subjects than in the non-stroke subjects ($P<0.001$). Participants with stroke were more likely to be male, older, to live in urban, to have lower level of educational level and HDL, and to be higher levels of BMI, WC, WHtR, SBP, DBP, FPG, TC, TG, LDL (Table 1).

Relationship between TyG, WC, BMI and WHtR

The Spearman algorithm was used to evaluate the relationship between TyG, BMI, WHtR and WC (Table 2). We found that some correlation between TyG with BMI, WHtR, and WC, all slightly higher than 0.3. There was a high correlation between BMI, WHtR, and WC pairwise, with a minimum of 0.79 and a maximum of 0.9. WC, BMI, and WHtR were grouped according to the quartile of TyG with significant differences between the groups (Fig. 2).

Relationship between TyG, TyG-WC, TyG-WHtR, TyG-BMI with stroke

We utilized three cox-proportional hazard models to examine the relationship between TyG and its combined obesity indicators with stroke (Table 3). From the results, we noticed a statistically significant positive relationship between TyG, TyG-WC, TyG-WHtR, TyG-BMI with stroke in all models ($P<0.05$). After adjusting for potential confounders in Model 3, by comparing quartile 4 of these four indicators with quartile 1 for stroke events, the adjusted HRs were 1.51 (95% CI 1.22–1.88) for TyG, 1.57 (95% CI 1.26–1.95) for TyG-BMI, 1.62 (95% CI 1.30–2.03) for TyG-WHtR, and 1.68 (95% CI 1.35–2.09) for TyG-WC. The trend test was statistically significant in all models ($P<0.001$).

Restricted cubic splines (RCS) regression models investigating the relationship between TyG, TyG-BMI, TyG-WHtR, and TyG-WC with stroke

In Fig. 3, We employed restricted cubic spline to flexibly model and visualize the associations between TyG, TyG-WC, TyG-WHtR, and TyG-BMI with risk of stroke. After adjusting for all covariates in the master analytical model 3 above, a nonlinear correlation was observed between TyG and TyG-BMI with stroke (P-overall <0.001, P-nonlinear $=0.003$ for TyG, and P-overall <0.001, P-nonlinear $=0.028$ for TyG-BMI). Moreover, TyG-WC and TyG-WHtR exhibited linear associations with stroke (P-overall <0.001 and P-nonlinear >0.05).

Receiver operating characteristic (ROC) curves for stroke

We assessed the enhanced predictive value of combining TyG and obesity indicators compared to their individual performance. The ROC curve in Fig. 4 showed that TyG-WHtR or TyG-WC had the highest predictive power for stroke (AUC:0. 696, 95% CI 0.677–0.715), followed by WC (AUC:0. 695, 95% CI 0.676–0.713), WHtR or TyG-BMI (AUC:0. 694, 95% CI 0.675–0.713), BMI

Table 1 The characteristics of the study participants at baseline

Characteristic	Total ($n=8207$)	Non-Stroke ($n=7304$)	Stroke ($n=903$)	*P-value*
Age, mean (SD), y	58.20 (8.60)	57.82 (8.52)	61.31 (8.61)	< 0.001
Gender (male, n, %)	3677 (44.8)	3240 (44.4)	437 (48.4)	0.024
Rural (n, %)	6947 (84.6)	6198 (84.9)	749 (82.9)	0.146
Educational level (n, %)				
Elementary and below	5652 (68.9)	4991 (68.4)	661 (73.4)	0.007
Middle	2444 (29.8)	2211 (30.3)	233 (25.9)	
High and above	102 (1.2)	95 (1.3)	7 (0.8)	
Marital status (married, n, %)	7390 (90.0)	6614 (90.6)	776 (85.9)	< 0.001
Smoking status (n, %)				
Non-smoker	5092 (63.1)	4585 (63.8)	507 (56.9)	< 0.001
Ex-smoker	629 (7.8)	525 (7.3)	104 (11.7)	
Current smoker	2353 (29.1)	2073 (28.9)	280 (31.4)	
Drinking status (n, %)				
Never	5485 (67.0)	4875 (66.9)	610 (67.8)	0.082
< 1 time/month	653 (8.0)	598 (8.2)	55 (6.1)	
≥ 1 time/month	2046 (25.0)	1811 (24.9)	235 (26.1)	
Medicine history (yes, n, %)	2040 (24.9)	1643 (22.5)	397 (44.0)	< 0.001
Cardiac events (yes, n, %)	899 (11.0)	729 (10.1)	170 (19.0)	< 0.001
Hypertension (yes, n, %)	3053 (37.3)	2531 (34.7)	522 (57.9)	< 0.001
Dyslipidemia (yes, n, %)	2882 (35.1)	2479 (33.9)	403 (44.6)	< 0.001
Type 2 diabetes (yes, n, %)	1259 (15.3)	1067 (14.6)	192 (21.3)	< 0.001
BMI, mean (SD), kg/m^2	23.60 (3.62)	23.52 (3.60)	24.30 (3.68)	< 0.001
WHtR mean (SD)	0.54 (0.07)	0.54 (0.07)	0.56 (0.07)	< 0.001
WC mean (SD), (cm)	85.63 (10.05)	85.28 (9.94)	88.46 (10.44)	< 0.001
SBP mean (SD), mmHg	129.63 (21.08)	128.57 (20.48)	138.25 (23.71)	< 0.001
DBP mean (SD), mmHg	75.60 (11.98)	75.15 (11.82)	79.22 (12.69)	< 0.001
FPG mean (SD), mg/dl	109.45 (34.26)	108.71 (33.07)	115.47 (42.25)	< 0.001
TC mean (SD), mg/dl	193.69 (38.53)	193.18 (38.44)	197.84 (39.07)	0.001
TG mean (SD), mg/dl	134.54 (111.09)	132.90 (111.59)	147.72 (106.17)	< 0.001
HDL mean (SD), mg/dl	51.12 (15.21)	51.38 (15.21)	49.02 (15.07)	< 0.001
LDL mean (SD), mg/dl	116.58 (34.61)	116.19 (34.41)	119.74 (36.04)	0.004
TyG mean (SD), mg/dl	8.69 (0.67)	8.67 (0.67)	8.84 (0.70)	< 0.001
TyG-BMI mean (SD)	205.77 (39.51)	204.56 (39.16)	215.50 (40.96)	< 0.001
TyG-WHtR mean (SD)	4.73 (0.77)	4.70 (0.76)	4.97 (0.82)	< 0.001
TyG-WC mean (SD)	746.02 (119.64)	741.33 (118.12)	783.98 (125.06)	< 0.001

Data are shown mean ± *SD* for continuous variables and *n* (%) categorical variables

BMI Body mass index, *WHtR* Waist height ratio, *WC* Waist circumference, *DBP* Diastolic blood pressure, *SBP* Systolic blood pressure, *FPG* Fasting plasma glucose, *TG* Triglyceride, *TyG* Triglyceride-glucose index, *TC* Total cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *HDL* High-density lipoprotein cholesterol

[*] *P*-value was obtained t-test Chi-square test

Table 2 The correlation between TyG, WC, BMI and WHtR

	TyG	BMI	WHtR	WC
TyG	1.00	-	-	-
BMI	0.31[**]	1.00	-	-
WHtR	0.32[**]	0.79[**]	1.00	-
WC	0.32[**]	0.82[**]	0.90[**]	1.00

(AUC:0.692, 95% CI 0.673–0.710) and TyG (AUC:0.691, 95% CI 0.672–0.710).

Stratification of TyG, TyG-BMI, TyG-WHtR, and TyG-WC in relation to stroke

The relationships between TyG, TyG-BMI, TyG-WHtR, and TyG-WC with the risk of stroke morbidity stratified by age and gender were shown in Fig. 5. After adjusting for potential confounders, no interaction was found

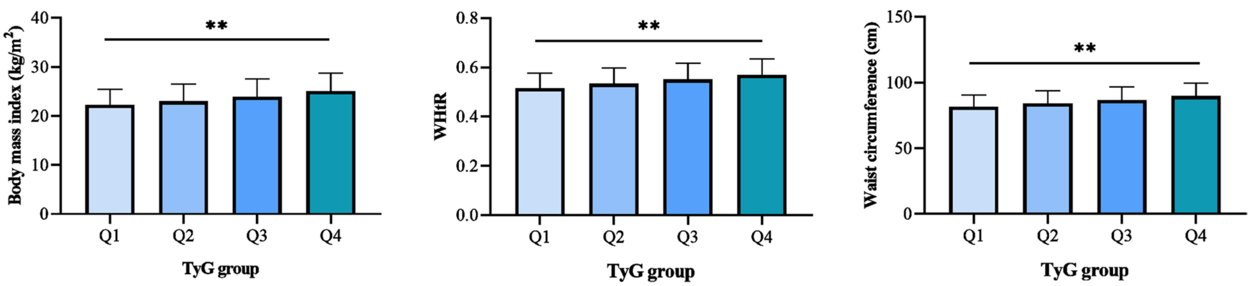

Fig. 2 The distribution of WC,BMI,WHtR according by TyG group

Table 3 Cox-proportional hazard models for the association of TyG, TyG-BMI, TyG-WHtR and TyG-WC with stroke risk

	Model 1		**Model 2**		**Model 3**	
	HR (95%CI)	***P***	**HR (95%CI)**	***P***	**HR (95%CI)**	***P***
TyG						
Q1	Ref		Ref		Ref	
Q2	1.34(1.09,1.66)	< 0.001	1.41(1.14,1.74)	0.001	1.35(1.09,1.67)	0.005
Q3	1.70(1.39,2.07)	< 0.001	1.64(1.34,2.02)	< 0.001	1.52(1.24,1.87)	< 0.001
Q4	1.91(1.57,2.32)	< 0.001	1.72(1.40,2.11)	< 0.001	1.51(1.22,1.88)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
TyG-BMI						
Q1	Ref		Ref		Ref	
Q2	1.26(1.03,1.55)	0.026	1.32(1.07,1.63)	0.009	1.30(1.05,1.60)	0.016
Q3	1.45(1.18,1.77)	< 0.001	1.51(1.23,1.86)	< 0.001	1.37(1.11,1.70)	0.003
Q4	1.88(1.56,2.28)	< 0.001	1.83(1.38,2.25)	< 0.001	1.57(1.26,1.95)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
TyG-WHtR						
Q1	Ref		Ref		Ref	
Q2	1.31(1.06,1.62)	0.013	1.34(1.08,1.67)	0.008	1.31(1.05,1.62)	0.017
Q3	1.71(1.39,2.09)	< 0.001	1.66(1.35,2.06)	< 0.001	1.51(1.22,1.87)	< 0.001
Q4	2.15(1.77,2.62)	< 0.001	1.88(1.52,2.33)	< 0.001	1.62(1.30,2.03)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
TyG-WC						
Q1	Ref		Ref		Ref	
Q2	1.51(1.22,1.88)	< 0.001	1.47(1.18,1.83)	< 0.001	1.43(1.15,1.79)	0.001
Q3	1.80(1.46,2.21)	< 0.001	1.67(1.35,2.07)	< 0.001	1.52(1.22,1.89)	< 0.001
Q4	2.37(1.94,2.89)	< 0.001	1.95(1.58,2.41)	< 0.001	1.68(1.35,2.09)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	

Model 1: Unadjusted

Model 2: Adjusted for age, gender, education, marital status, rural, drinking, smoking and medicine history

Model 3: Model 2 + cardiac events, hypertension, dyslipidemia and type 2 diabetes

between these four indicators and subgroup variables (All *P* for interaction > 0.05). Gender may not influence our results, because the higher risk of stroke morbidity in the upper TyG, TyG-BMI, TyG-WHtR, and TyG-WC quartiles was sustained consistently across all subgroups of gender. The association between these four indicators and stroke risk was stronger in males than females. We observed similar tendency in the age groups of 55–65 years and above. However, we did not find these associations among the younger population (45–55 years).

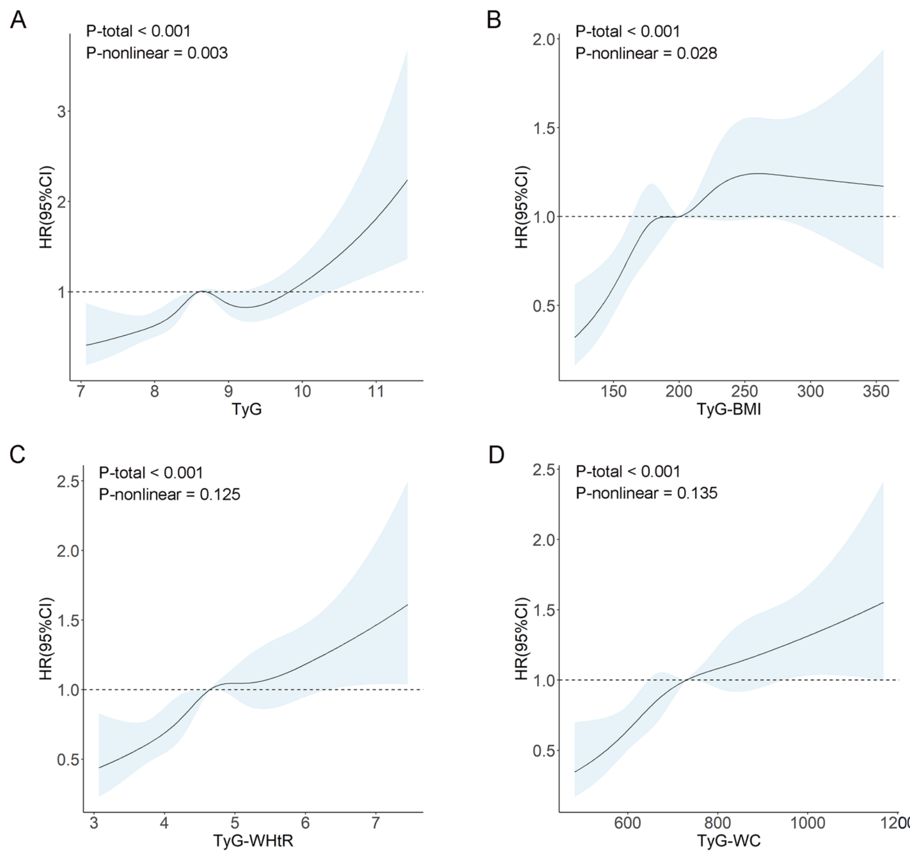

Fig. 3 RCS model of the association between TyG, TyG-BMI, TyG-WHtR and TyG-WC with stroke

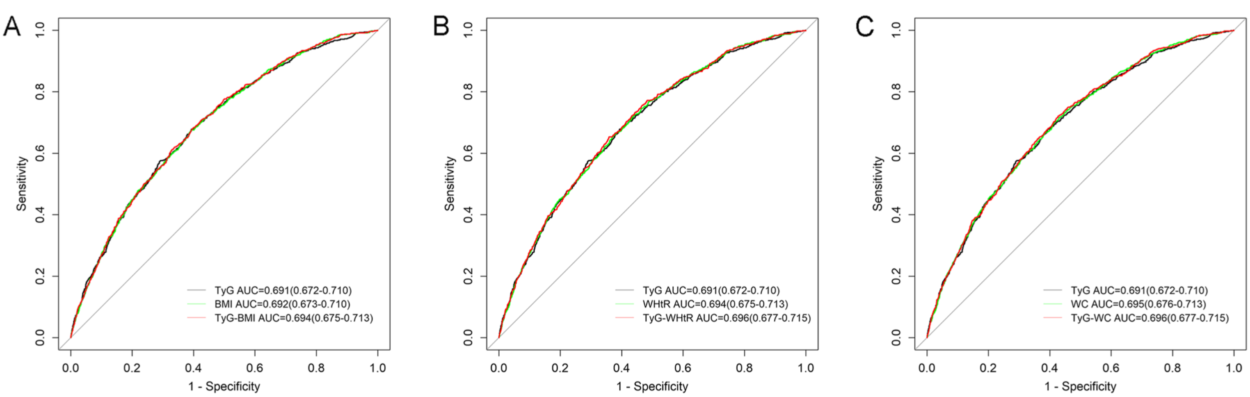

Fig. 4 Receiver operating characteristic (ROC) curves of TyG, TyG-WC, TyG-WHtR, TyG-BMI for stroke

Mediation analysis of TyG, TyG-BMI, TyG-WHtR, and TyG-WC with stroke

Mediation analysis, adjusted for age, gender, education, smoking, drinking, exercise, presented the direct and indirect effects of TyG on stroke with obesity measures as mediators (Fig. 6). All three obesity measures mediated the relationship between TyG and stroke. The direct and indirect effects were both significant ($P < 0.05$). For TyG, the proportion of indirect effects of BMI, WHtR and WC mediated stroke were 15.79%, 21.72%, and 24.06% respectively.

Similarly, Fig. 7 presented the direct and indirect effects of three obesity measures on stroke with TyG as mediators. TyG mediated the relationship between these three

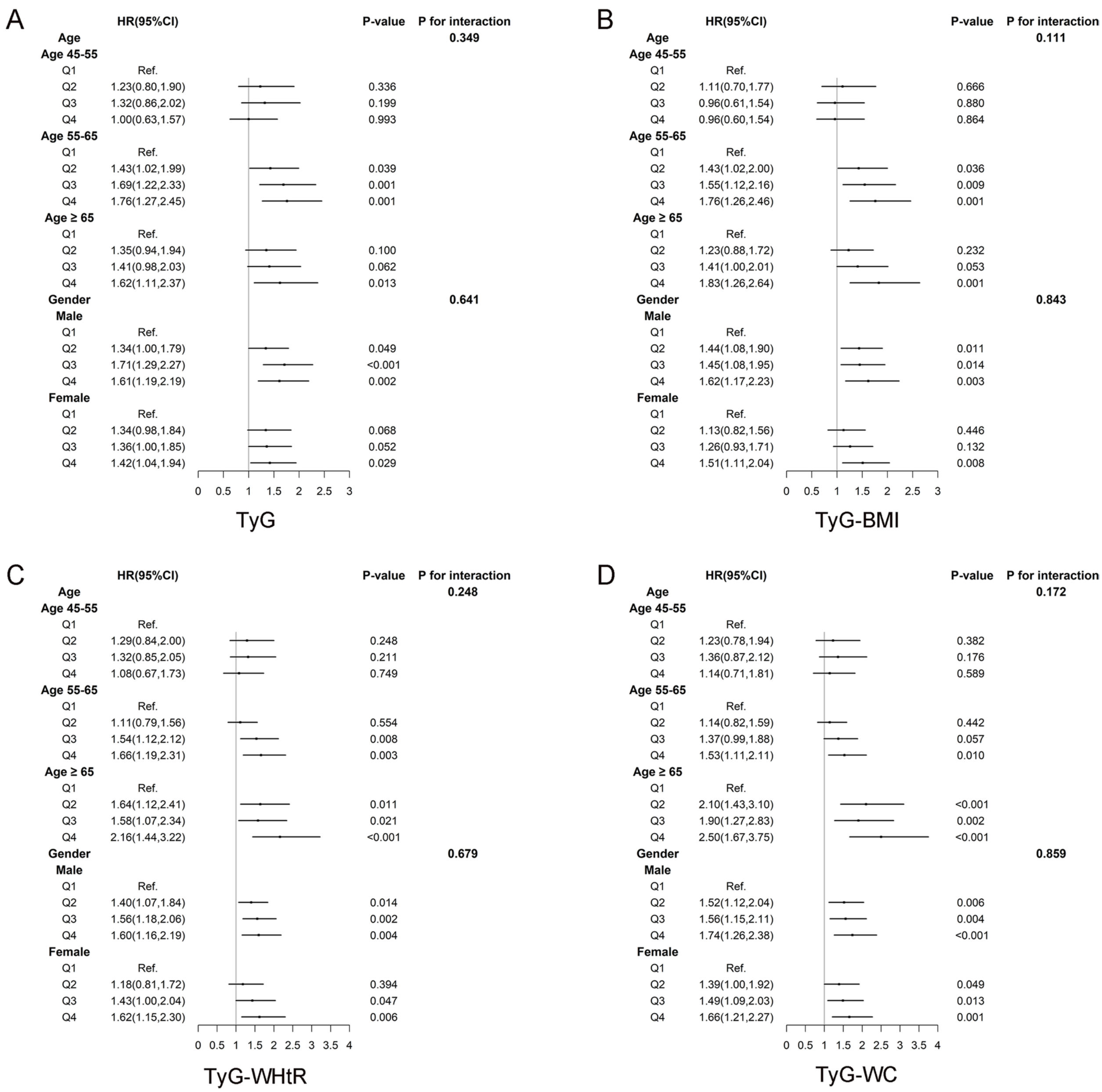

Fig. 5 Subgroup analysis stratified by age and gender

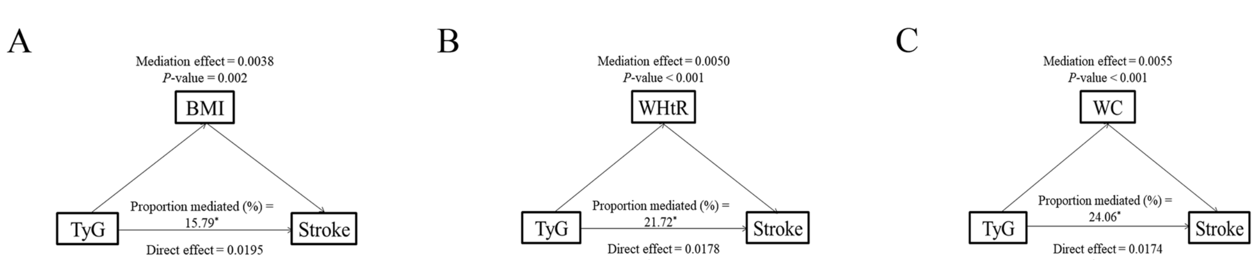

Fig. 6 Mediation analyses of obesity indexes in the association of TyG with stroke

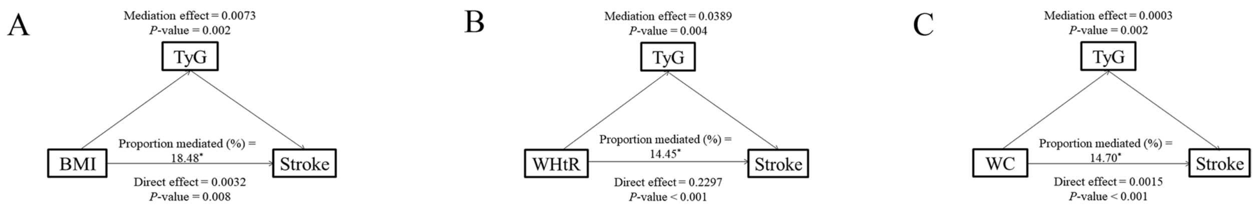

Fig. 7 Mediation analyses of TyG in the association of obesity indexes with stroke

obesity measures and stroke. The direct and indirect effects were both significant ($P < 0.05$). For BMI, WHtR and WC, the proportion of indirect effects of TyG mediated stroke were 18.48%, 14.45%, and 14.70% respectively.

Discussion

The longitudinal study based on CHARLS data aimed to evaluate the association between TyG combined with obesity indicators and stroke risk. The results showed that: (1) TyG, TyG-BMI, TyG-WHtR, TyG-WC were significantly higher in stroke subjects than in the non-stroke subjects, and were significantly and positively associated with stroke in all 3 models; (2) Restricted cubic spline models revealed nonlinear associations between TyG and TyG-BMI with stroke, while TyG-WC and TyG-WHtR demonstrated linear associations with stroke after adjusting for covariates; (3) TyG-WHtR, TyG-BMI and TyG-WC had more robust predictive power than TyG for risk of stroke. TyG-WHtR or TyG-WC had the highest predictive power for stroke, slightly higher than the other indicators; (4) Associations between TyG, TyG-WC, TyG-WHtR, and TyG-BMI with stroke were found to be stronger among individuals who were ≥ 55 years of age, male; (5) The relationship between TyG and stroke was significantly mediated by BMI, WHtR and WC, while the relationship between these obesity measures and stroke was significantly mediated by TyG.

TyG, a biomarker derived from fasting glucose and triglyceride concentrations, has recently been recognized as a potential surrogate marker for IR due to its easy-to-calculate nature and its high sensitivity and specificity [32–34]. Our study elucidated a significant and positive association between TyG and stroke prevalence in the Chinese population, corroborating the findings of previous investigations [35–37]. Crucially, after accounting for potential covariates such as hypertension, dyslipidemia and diabetes, our analysis further substantiated that TyG combined with obesity indices maintained a substantial and positive association with stroke risk. TyG and obesity indicators such as BMI, WHtR, and WC have a reciprocal effect on stroke risk, with each partially mediating the relationship between the other and stroke incidence.

Our study is the inaugural investigation into the correlation between TyG combined with obesity indicators and stroke based on a longitudinal survey in the Chinese population. The findings of our study reveal that TyG, TyG-WC, TyG-WHtR, and TyG-BMI were significantly and positively associated with stroke. RCS analyses showed that relationships between TyG-WC and TyG-WHtR with stroke were linear, but TyG and TyG-BMI were non-linearly associated with stroke. This is consistent with a previous report [28], which indicated that the association between cumulative TyG-BMI and stroke risk was nonlinear, with TG emerging as the primary contributor when assigning weights to the constituent elements of TyG-BMI from a prospective cohort study of CHARLS. Long-term elevation of the TyG index in hypertensive patients was associated with an increased risk of stroke, particularly ischemic stroke [14]. It has been suggested that extreme values of TyG, TyG-WC, and TyG-BMI indices, either excessively high or low, may be associated with an increased risk of stroke death. This association may be attributed to aberrant IR, inflammatory response, oxidative stress, and impaired vascular endothelial function, which collectively contribute to an elevated risk of stroke death.

Our research found that the combination of TyG and obesity indexes had similar diagnostic predictive probability of stroke, in which TyG-WHtR or TyG-WC was slightly higher, and the combination of TyG and obesity indexes were slightly better than that of TyG alone. The result suggested that the combination of TyG and obesity indexes slightly outperforms TyG alone in terms of predictive probability for stroke. A study involving 8231 participants from CHARLS [27], the results also showed that combining BMI and TyG enhanced predictive performance for stroke when compared to their individual. One study showed that the TyG-BMI index was associated with increased odds of developing hypertension and could be used as a new clinical index for the early diagnosis of hypertension [38]. Among the possible reasons, obesity can contribute directly to the development of stroke risk factors, including IR, abnormal glucose/lipid metabolism, hypertension, a pro-inflammatory and prothrombotic state, endothelial dysfunction [38, 39]. Furthermore, integrating TyG with obesity indices presents a more accurate IR evaluation than the Homeostatic Model Assessment of IR or TyG index alone [40]. Compared to

HOMA-IR, TyG is an efficient and cost-effective test for the diagnosis of insulin resistance [41]. Our results provide significant proof for the literature on TyG, TyG-BMI, TyG-WC, and TyG-WHtR as predictors of stroke risk.

Our research made the first findings that the associations between TyG, TyG-WC, TyG-WHtR, and TyG-BMI with stroke were found to be stronger among older male individuals. One study partially consistently concluded that significant alterations in TyG-BMI in middle-aged and older adults were independently associated with an elevated risk of stroke and that regular monitoring of long-term changes in TyG-BMI would facilitate early detection of individuals at higher risk of stroke [42]. However, in a larger cardiovascular disease category, the findings of existing studies were significantly different [43, 44]. A study from the American population conducted that TyG index was significantly linked to a higher probability of heart failure in a younger age group [43], and another study from Iran also had a similar conclusion [44]. It may differ because of sample differences by regions and ethnicity, and for age-related factors for stroke. An essential finding of the study is that TyG and the three obesity indicators partially mediated each other in the association with stroke. A study from the same database also had consistent conclusions on the association analysis of TyG-mediated BMI with stroke [27]. Our findings suggested that public health efforts aiming at the reduction of body weight might decrease the stroke risk due to IR and the burden of stroke.

The mechanism behind TyG, TyG-WC, TyG-WHtR, and TyG-BMI and increased risk of stroke may be due to elevated levels of TyG, TyG-WC, TyG-WHtR, and TyG-BMI, which are associated with IR [28, 45]. IR promotes ischemic stroke through embolization and atherosclerosis [8]. IR could lead to impaired endothelial cell function, increasing platelet adhesion, activation, and aggregation, thereby contributing to thrombosis formation [46]. Endothelial cells perform various functions, including both pro-coagulation and anti-coagulation roles, which are typically balanced under normal physiological conditions. However, when endothelial cell function is compromised, the risk of thrombosis is elevated [47]. Additionally, hyperinsulinemia resulting from IR can worsen atherosclerosis by promoting vascular inflammation, the proliferation of vascular smooth muscle cells, an unfavorable cholesterol profile, hypertension, and the recruitment of immune cells to the endothelium [48].

Limitations

The limitations of this study include the omission of undiagnosed stroke cases due to reliance on self-report data and the inability to assess the longitudinal impact of TyG combined with obesity indexes on stroke for blood samples at a certain time. Moreover, our study is based on data from the Chinese population, and it remains to be seen whether these findings are consistent in different regions within China and whether they can be widely used in other national regions.

Conclusion

The combination of TyG and obesity-related indicators was significantly associated with stroke risk, and could improve predictive power for stroke compared to the single TyG. Obesity indicators and TyG mediated each other in their respective associations with stroke risk. This finding could help refine new clinical indicators for early diagnosis of stroke.

Abbreviations

TyG	Triglyceride-glucose
CHARLS	China Health and Retirement Longitudinal Study
TyG-BMI	Glucose triglyceride-body mass index
TyG-WHtR	Glucose triglyceride-waist height ratio
TyG-WC	Glucose triglyceride-waist circumference
RCS	Restricted cubic spline
ROC	Receiver operating characteristic
FSG	Fasting blood glucose

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Authors'contributions

W.C.L. was involved in all parts of the study: design, acquisition of data, analysis, interpretation, drafting of paper, and final approval. H.C.O supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final version as submitted, and agree to be accountable for all aspects of the work.

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Availability of data and materials

Data supporting the results of this study are available upon reasonable request from the first author.

Declarations

Ethics approval and consent to participate

ALL CHARLS data of this study involving human participants, human materials, or human data were ethically approved by the BGU Institutional Review Board. During the field survey, each respondent who agreed to participate was required to sign two informed consent forms, one of which was kept in the CHARLS file and saved in PDF format.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing financial interests. They have no relationships or activities that might bias or be perceived to bias the publication of this research.

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