



# OPEN Joint association of triglyceride-glucose index and obesity indicators with stroke risk: a nationwide prospective cohort study

Zhihui Li<sup>1</sup>, Yue Ban<sup>1</sup>, Minli Hu<sup>1</sup>, Liping Deng<sup>2</sup> & Xiaohua Xie<sup>1,2</sup>✉

The triglyceride-glucose (TyG) index has been identified as an independent predictor of stroke risk. However, the comprehensive impact of combined indices, integrating TyG with obesity indicators such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), on stroke risk remains insufficiently explored. Furthermore, there is a paucity of research on combined indices involving TyG and other obesity indicators like the weight-adjusted waist index (WWI), body roundness index (BRI), and a body shape index (ABSI). This study aimed to comprehensively evaluate the combined impact of TyG with various obesity indicators on stroke risk and to investigate their potential associations. This observational cohort study included 8,730 participants from the China Health and Retirement Longitudinal Study (CHARLS). Cox proportional hazards models, smooth curve fitting, and threshold effect analysis were employed to explore the potential relationships between the combined indices and stroke risk. The predictive value of TyG alone, obesity indicators, and the combined indices for stroke risk was compared using the area under the receiver operating characteristic (ROC) curve (AUC), and was validated by Delong test. Kaplan-Meier curves were used to illustrate the cumulative incidence of stroke events. Over a median follow-up of 7 years, 456 (5.20%) incident stroke cases were identified. After adjusting for confounding factors, non-linear relationships were observed between TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI and stroke risk, demonstrating significant dose-response relationships (all  $P < 0.05$  for the log-likelihood ratio test); conversely, TyG, TyG-BMI, and TyG-BRI exhibited linear relationships with stroke risk (The  $p$  values respectively:  $p < 0.001$ ,  $p = 0.004$ ,  $p = 0.019$ ). The highest stroke risk incidence (7.55%) was observed in the Q4 group of TyG-WC. Furthermore, the combined indices showed higher AUC values for stroke risk compared to TyG or obesity indicators alone. Combined indices of TyG and obesity indicators are significantly associated with stroke risk. Combined obesity indicators with the TyG index may provide additional predictive utility for stroke risk compared to the TyG index alone. The combined assessment of the TyG index and obesity indicators could be considered in stroke risk assessment and primary prevention.

**Keywords** Stroke risk, Triglyceride-glucose (TyG), Obesity indicators, Combined indices, China health and retirement longitudinal study

Stroke is the second most common cause of death globally, surpassed only by heart disease (accounting for 11.6% of all deaths)<sup>1</sup>, and is characterized by high rates of disability and recurrence<sup>2</sup>, which collectively bring a heavy burden to society, families, and patients. Research indicates that stroke is often caused by modifiable risk factors such as hypertension, smoking, hyperglycemia, unhealthy lifestyle, obesity, and excessive alcohol consumption<sup>3</sup>. The effective identification and intervention of these factors are essential for the primary prevention of stroke.

Substantial evidence indicates that insulin resistance (IR) is closely associated with cardiometabolic disorders, which may accelerate atherogenesis and lead to stroke<sup>4–7</sup>. The normoglycemic-insulin clamp technique is considered the most accurate way to measure insulin resistance (IR), but its widespread clinical application

<sup>1</sup>School of Nursing, Anhui Medical University, Hefei, China. <sup>2</sup>Department of Nursing, Shenzhen Second People's Hospital, Shenzhen, China. ✉email: 13560779836@163.com

is limited due to constraints related to time, technical complexity, and costs<sup>8,9</sup>. The triglyceride-glucose (TyG) index was regarded as a reliable surrogate method for assessing IR due to its simplicity and reproducibility<sup>9–11</sup>. Studies have shown that the TyG index is an independent risk factor for stroke<sup>12,13</sup>. Obesity is a global health issue associated with increased incidence and mortality of cardiovascular disease (CVD)<sup>14,15</sup>. In addition to body mass index (BMI), which traditionally assess obesity, waist circumference (WC) and waist-to-height ratio (WHtR) showed stronger predictive power for cardiovascular metabolic disease<sup>16</sup>. In recent years, the value of emerging obesity indicators such as body shape index (ABSI) and body roundness index (BRI) in cardiovascular risk assessment has received increasing attention<sup>17–19</sup>. A growing number of studies have combined the TyG index with obesity indicators to explore its potential relationship with stroke risk, including BMI, WHtR and WC<sup>20–22</sup>. Evidence suggests that combining the TyG index with obesity indicators predicts stroke occurrence more accurately than the TyG index alone<sup>23</sup>.

Currently, the research on TyG-obesity combined indicators for stroke risk is still relatively limited. Existing research is mostly limited to the exploration of a single combined index, and there is a lack of systematic comparison and optimization of multiple TyG-obesity combined indicators. Based on the successful application of combined biomarkers in cardiovascular risk prediction, this study hypothesizes that systematic evaluation and comparison of various TyG-obesity combined indicators may provide a new tool for accurate identification of stroke risk. Therefore, this study used large-scale longitudinal data from the China Health and Elderly Care Tracking Survey (CHARLS) to comprehensively assess the comprehensive impact of the TyG index and various obesity indicators on stroke risk, and to explore the potential association between the combined index and stroke risk.

## Materials and methods

### Study population and design

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative cohort study covering approximately 28 provinces and 150 counties<sup>24</sup>. CHARLS was designed to investigate the impact of health and socioeconomic factors on the health outcomes of middle-aged and elderly individuals. Data collection in CHARLS initially employed computer-assisted personal interviewing (CAPI), primarily encompassing demographic information, health status, and lifestyle factors. CHARLS recruited 17,708 participants at its initial data collection wave. Subsequently, follow-up surveys were conducted approximately every two years, with only a small number of new participants recruited at each wave. The study received approval from the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided signed informed consent.

In this study, the primary focus was to investigate the combined indices of TyG and obesity indicators to evaluate their comprehensive impact on stroke risk and their potential association with stroke. To enhance the robustness of this study, several exclusion criteria were established: (1) participants with a history of stroke at baseline or incomplete baseline stroke data ( $n=846$ ); (2) participants with less than two years of follow-up ( $n=1295$ ); (3) participants younger than 45 years ( $n=429$ ); (4) participants lacking baseline information on fasting plasma glucose (FPG) and triglycerides (TG) ( $n=4802$ ); (5) participants lacking baseline information on height, weight, waist circumference, or BMI ( $n=1605$ ). Ultimately, 8,730 participants were included in the study (Fig. 1).

### Definitions of TyG and combined indices

The TyG index and combined indices were primarily calculated using the following formulas:

$$(1) \text{WHtR} = \text{WC}(\text{cm}) / \text{height}(\text{cm})$$

$$(2) \text{WWI} = \frac{\text{WC}(\text{cm})}{\sqrt{\text{weight}(\text{kg})}}^{25}$$

$$\text{BRI} = 364.2 - 365.5 \times \sqrt{1 - \left( \frac{\text{WC}(\text{m})/2\pi}{\text{height}(\text{m})/2} \right)^2}^{26}$$

$$\text{ABSI} = \text{WC}(\text{m}) / \left[ \text{BMI}^{2/3} \times \text{height}^{1/2}(\text{m}) \right]^{27}$$

$$(3) \text{TyG} = \ln [\text{TG}(\text{mg/dL}) \times \text{FPG}(\text{mg/dL})/2]$$

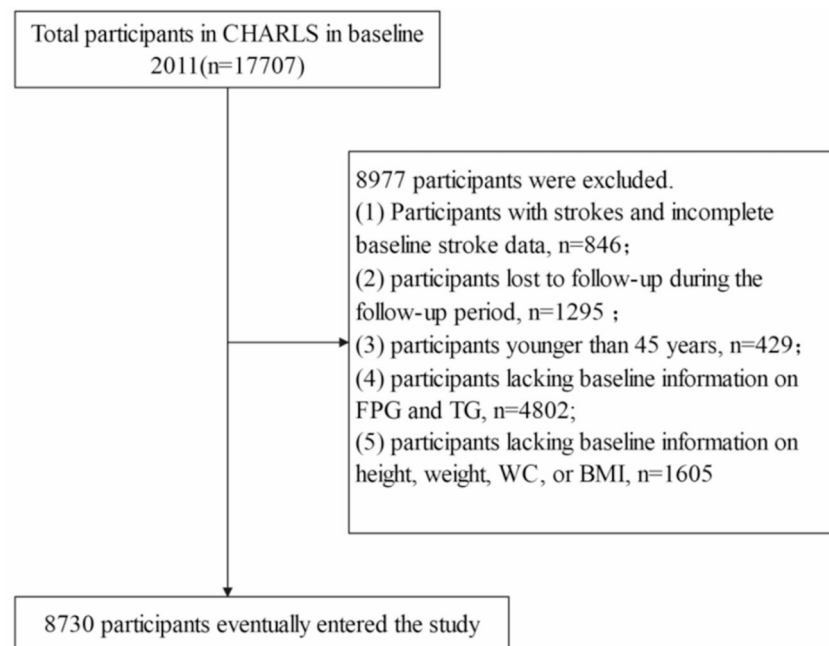
$$(4) \text{TyG} - \text{BMI} = \text{TyG} \times \text{BMI}^{28}, \text{TyG} - \text{WC} = \text{TyG} \times \text{WC}^{29}$$

$$\text{TyG} - \text{WHtR} = \text{TyG} \times \text{WHtR}^{30}, \text{TyG} - \text{WWI} = \text{TyG} \times \text{WWI}^{31}$$

$$\text{TyG} - \text{BRI} = \text{TyG} \times \text{BRI}^{32}, \text{TyG} - \text{ABSI} = \text{TyG} \times \text{ABSI}^{33}$$

### Assessment of stroke

Using face-to-face interview techniques, participants with no history of stroke at baseline who reported experiencing a stroke during the follow-up period were considered to have experienced the outcome event<sup>20,24</sup>. In accordance with previous studies, stroke events were assessed using the following standardized questions: “Have you ever been diagnosed with a stroke by a medical professional? What was the exact date of diagnosis? Are you currently receiving treatment for stroke?”



**Fig. 1.** Patient selection flowchart.

### Assessment of covariates

Covariates selection was based on the current clinical setting and prior research<sup>29,30</sup>. Study characteristics included age, sex, smoking status (never, former, and current), alcohol consumption status (never, former, and current), education level (primary, secondary, and high school), and residence (urban and rural), as well as marital status (married and other). Trained personnel conducted anthropometric assessments, including height, weight, and waist circumference measurements. Systolic and diastolic blood pressure (SBP and DBP) were measured three times, with at least a 45-second interval between each measurement. Participants were required to provide fasting venous blood samples; these samples were primarily transported via cold chain to the Chinese Center for Disease Control and Prevention in Beijing for detailed analysis<sup>34</sup>. Laboratory examinations included platelet count (PLT), blood urea nitrogen (BUN), FPG, serum creatinine (Scr), C-reactive protein (CRP), TC, TG, hematocrit (HCT), hemoglobin concentration (HGB), serum high-density lipoprotein cholesterol (HDL-c), glycated hemoglobin (HbA1c), serum low-density lipoprotein cholesterol (LDL-c), cystatin C, and uric acid (UA). Diabetes was defined as FPG  $\geq 126$  mg/dL or a self-reported history of diabetes. Hypertension was defined as SBP  $\geq 140$  mmHg and/or DBP  $\geq 90$  mmHg, or a self-reported history of hypertension. Other chronic diseases, including liver disease, heart disease, and kidney disease, were determined by participant self-report.

### Statistical analysis

Continuous variables were expressed as medians (IQR: interquartile range) or means (SD: standard deviation), while categorical variables were presented as percentages and counts. To assess differences among groups based on the combined indices, chi-square tests, analysis of variance (ANOVA), or Kruskal-Wallis tests were used for categorical, normally distributed, and skewed data, respectively. Cox proportional hazards models were used to evaluate the relationship between the combined indices and stroke risk, yielding hazard ratios (HRs) and their 95% confidence intervals (CI). The Schoenfeld residual test was used to verify the Cox proportional risk hypothesis.

Furthermore, three models were established to adjust for baseline confounding factors to further test the relationship between the combined indices and stroke risk. These three models included Model 1 (unadjusted for covariates), Model 2 (adjusted for age, sex, smoking, and alcohol consumption status), and Model 3 (adjusted for age, sex, smoking status, alcohol consumption status, HDL-c, LDL-c, CRP, Scr, UA, Cystatin C, HGB, DM, kidney disease, and hypertension). Since BMI and waist circumference were collinear with the comorbidity indicators and constitute components of the corresponding composite index, they were intentionally excluded from the model. For similar collinearity reasons, height, weight, and WC were also excluded from the model (Table S1, Additional File).

Generalized additive models (GAMs) and curve fitting (penalized spline method) were used to assess the dose-response effects between each combined index and stroke<sup>35</sup>. Each combined index was treated as a continuous variable to explore the dose-response relationship per standard deviation increase with stroke risk. To evaluate the threshold effect of each combined index on stroke risk, a two-piece-wise Cox proportional hazard model was employed. The turning point for each combined index was identified through an “exploratory” analysis, where the turning point was dynamically adjusted along a preset interval, ultimately selecting the turning point that maximized model fit<sup>20,36</sup>. Then, in order to optimize the identification of turning points, the combination of

segmented regression and recursive algorithm is used to determine the best turning point. A log-likelihood ratio test was applied to determine the optimal model for the association between each combined index and stroke risk. The bootstrap resampling method was used to estimate the 95% CI of the turning points. Cox proportional hazards models independently analyzed data stratified by age, sex, smoking, alcohol consumption, diabetes, and hypertension status. In addition to stratification parameters, adjustments were made for age, sex, smoking status, alcohol consumption status, HDL-c, LDL-c, CRP, Scr, UA, cystatin C, hypertension, DM, and kidney disease. Interaction analyses were performed using likelihood ratio tests. To determine the robustness of this study, a series of sensitivity analyses were conducted. Specifically, the results were validated in populations without diabetes, without hypertension, without kidney disease, and with BMI < 24 kg/m<sup>2</sup>.

The predictive ability of each combined index for incident stroke risk during follow-up was assessed by the area under the receiver operating characteristic (ROC) curve (AUC), with a significance level set at  $P < 0.05$ . DeLong's test was used to verify the AUC difference between independent TyG index and various combined indices. And the optimal threshold of AUC value was determined by the Youden's index. The cumulative incidence of stroke events based on TyG and each combined index was represented by Kaplan-Meier curves. And the  $p$  values of log rank tests between the index groups were also compared.

Statistical analyses were performed using R 3.4.3 and Empower (R) 4.0, with the significance level set at  $P < 0.05$  (two-tailed).

## Results

### Participant characteristics

A total of 8,730 participants were included in this study, of whom 4,695 (53.82%) were female. Over a median follow-up of 7 years, 456 incident stroke cases (5.20%) occurred. The mean age at baseline was  $59.52 \pm 9.26$  years. Table 1 outlines the baseline characteristics of the study population categorized by stroke status. The results indicated that participants who developed stroke were older and had higher levels of WC, BMI, PLT, BUN, FPG, TC, TG, HCT, LDL-c, CRP, HGB, UA, Scr, TyG, WHtR, WWI, ABSI, BRI, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI compared to those who did not develop stroke. Furthermore, HDL-c levels were significantly lower in the stroke group. A comparison of baseline characteristics between included and excluded participants is detailed in Table S2 (Additional File). No significant differences were observed between these two groups for weight, waist circumference, BMI, SBP, BUN, FPG, HCT, HGB, HbA1c, Scr, WHtR, WWI, ABSI, drinking status, chronic lung disease, kidney disease, diabetes, or liver disease.

### Baseline variables and unadjusted links to stroke incidence

Table S3 (Additional File) presents the results of the univariable analysis exploring the association between various covariates and stroke risk. Significant correlations ( $P < 0.05$ ) were found for age, education level (secondary school), marital status, smoking history, weight, waist circumference, BMI, SBP, DBP, FPG, TC, TG, HDL-c, CRP, Scr, HbA1c, UA, TyG, WHtR, WWI, ABSI, BRI, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, TyG-BRI, hypertension, chronic lung disease, kidney disease, and heart disease. HDL-c levels were negatively correlated ( $P < 0.05$ ). The risk of stroke was not significantly associated with sex, residence, alcohol consumption status, height, PLT, BUN, HCT, HGB, cystatin C, LDL-c, liver disease, or diabetes ( $P > 0.05$ ).

### Relationship between TyG index, combined indices and stroke risk

Generalized additive models (Fig. 2) were used to visually assess the dose-response relationship between the TyG index, combined indices, and stroke risk. After controlling for potential confounding factors, significant non-linear associations were observed between TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI and stroke risk, with specific inflection points determined using a recursive algorithm: TyG-WC ( $P$  for log-likelihood ratio test = 0.014, inflection point = 554.36); TyG-WHtR ( $P$  for log-likelihood ratio test = 0.029, inflection point = 3.51); TyG-WWI ( $P$  for log-likelihood ratio test = 0.041, inflection point = 80.29); and TyG-ABSI ( $P$  for log-likelihood ratio test = 0.040, inflection point = 0.61).

According to Table 2, above the inflection point for TyG-WC, each SD increase (135.81) was associated with a 34% increased risk of stroke (HR = 1.34, 95% CI = 1.16–1.55,  $P < 0.001$ ). However, below the inflection point, the correlation between TyG-WC score and stroke risk lacked significance (HR = 0.77, 95% CI = 0.55–1.08,  $P = 0.124$ ). Above the inflection point for TyG-WHtR, each SD increase (0.87) was associated with a 29% increased risk of stroke (HR = 1.29, 95% CI = 1.12–1.50,  $P < 0.001$ ). Below the inflection point, the TyG-WHtR score was not significantly correlated with stroke risk (HR = 0.79, 95% CI = 0.56–1.11;  $P = 0.170$ ). Above the inflection point for TyG-WWI, each SD increase (14.58) was associated with a 27% increased risk of stroke (HR = 1.27, 95% CI = 1.08–1.51,  $P = 0.005$ ). However, below the inflection point, the association was not significant (HR = 0.89, 95% CI = 0.70–1.13;  $P = 0.329$ ). For TyG-ABSI, above the inflection point, each SD increase (0.10) was associated with a 25% increased risk of stroke (HR = 1.25, 95% CI = 1.06–1.48,  $P = 0.008$ ). Below the inflection point, the association was not significant (HR = 0.90, 95% CI = 0.73–1.12;  $P = 0.356$ ).

Furthermore, the relationships between TyG, TyG-BMI, TyG-BRI and stroke risk appeared to be linear. Each SD increase in TyG (0.67) was associated with a 23% increased risk of stroke (HR = 1.23, 95% CI = 1.14–1.34;  $P < 0.001$  for linear regression). Each SD increase in TyG-BMI (41.68) was associated with an 18% increased risk of stroke (HR = 1.18, 95% CI = 1.05–1.32;  $P = 0.004$  for linear regression). Each SD increase in TyG-BRI (14.33) was associated with a 15% increased risk of stroke (HR = 1.15, 95% CI = 1.02–1.29;  $P = 0.019$  for linear regression). The Cox proportional hazards assumption was verified using Schoenfeld residuals tests, with all models satisfying the assumption ( $P > 0.05$  for all variables) in Table S4 (Additional File).

Variables	All participants	No stroke	Stroke	P value
N	8730	8274	456	
Age (year, mean $\pm$ SD)	59.52 $\pm$ 9.26	59.39 $\pm$ 9.26	61.87 $\pm$ 8.89	< 0.001
Height (cm, median $\pm$ SD)	157.95 $\pm$ 8.53	157.93 $\pm$ 8.51	158.23 $\pm$ 8.91	0.474
Weight (kg, median $\pm$ SD)	58.78 $\pm$ 11.55	58.67 $\pm$ 11.48	60.85 $\pm$ 12.62	< 0.001
WC (cm, median $\pm$ SD)	84.20 $\pm$ 12.49	84.05 $\pm$ 12.43	86.98 $\pm$ 13.18	< 0.001
BMI (kg/m <sup>2</sup> , median $\pm$ SD)	23.49 $\pm$ 3.90	23.46 $\pm$ 3.89	24.20 $\pm$ 4.00	< 0.001
SBP (mmHg, median $\pm$ SD)	132.63 $\pm$ 22.56	132.14 $\pm$ 22.32	141.47 $\pm$ 25.08	< 0.001
DBP (mmHg, median $\pm$ SD)	76.65 $\pm$ 12.77	76.47 $\pm$ 12.73	79.90 $\pm$ 13.08	< 0.001
PLT (10 <sup>9</sup> /L, median $\pm$ SD)	211.20 $\pm$ 72.68	211.07 $\pm$ 72.56	213.64 $\pm$ 74.83	0.466
BUN (mmol/L, median $\pm$ SD)	15.75 $\pm$ 4.50	15.74 $\pm$ 4.50	15.86 $\pm$ 4.52	0.589
FPG (mg/dL, median $\pm$ SD)	110.19 $\pm$ 36.68	109.78 $\pm$ 35.94	117.59 $\pm$ 47.64	< 0.001
TC (mg/dL, median $\pm$ SD)	193.97 $\pm$ 38.87	193.76 $\pm$ 38.83	197.65 $\pm$ 39.42	0.038
TG (mg/dL, median, quartile)	105.00 (74.00-154.00)	105.00 (74.00-153.00)	113.00 (83.00-165.00)	0.007
HDL-c (mg/dL, median $\pm$ SD)	51.38 $\pm$ 15.32	51.50 $\pm$ 15.34	49.21 $\pm$ 14.73	0.002
LDL-c (mg/dL, median $\pm$ SD)	116.63 $\pm$ 35.05	116.51 $\pm$ 34.89	118.89 $\pm$ 37.87	0.158
CRP (mg/L, median $\pm$ SD)	2.60 $\pm$ 7.11	2.55 $\pm$ 6.91	3.47 $\pm$ 10.10	0.007
HCT (% , median $\pm$ SD)	41.48 $\pm$ 6.24	41.46 $\pm$ 6.23	41.86 $\pm$ 6.34	0.176
HGB (g/L, median $\pm$ SD)	14.42 $\pm$ 2.22	14.41 $\pm$ 2.22	14.56 $\pm$ 2.29	0.152
Scr (mg/dL, median $\pm$ SD)	0.97 $\pm$ 0.23	0.97 $\pm$ 0.23	0.99 $\pm$ 0.15	0.229
HbA1c (% , median, quartile)	5.00 (5.00–5.00)	5.00 (5.00–5.00)	5.00 (5.00–6.00)	< 0.001
UA (mg/dL, median $\pm$ SD)	4.45 $\pm$ 1.28	4.44 $\pm$ 1.27	4.57 $\pm$ 1.35	0.035
Cystatin C (mg, median $\pm$ SD)	1.04 $\pm$ 0.26	1.04 $\pm$ 0.26	1.04 $\pm$ 0.23	0.966
TyG (median $\pm$ SD)	8.69 $\pm$ 0.67	8.68 $\pm$ 0.67	8.84 $\pm$ 0.73	< 0.001
WHtR (median $\pm$ SD)	0.53 $\pm$ 0.08	0.53 $\pm$ 0.08	0.55 $\pm$ 0.08	< 0.001
WWI (median $\pm$ SD)	11.05 $\pm$ 1.34	11.04 $\pm$ 1.34	11.21 $\pm$ 1.36	0.007
ABSI (median $\pm$ SD)	0.08 $\pm$ 0.01	0.07 $\pm$ 0.01	0.08 $\pm$ 0.01	0.049
BRI (median $\pm$ SD)	4.15 $\pm$ 1.51	4.13 $\pm$ 1.51	4.50 $\pm$ 1.62	< 0.001
TyG-WHtR (median $\pm$ SD)	4.65 $\pm$ 0.87	4.64 $\pm$ 0.87	4.88 $\pm$ 0.93	< 0.001
TyG-WWI (median $\pm$ SD)	96.05 $\pm$ 14.58	95.88 $\pm$ 14.51	99.22 $\pm$ 15.36	< 0.001
TyG-ABSI (median $\pm$ SD)	0.71 $\pm$ 0.10	0.71 $\pm$ 0.10	0.73 $\pm$ 0.11	< 0.001
TyG-BRI (median $\pm$ SD)	36.31 $\pm$ 14.33	36.11 $\pm$ 14.23	40.04 $\pm$ 15.53	< 0.001
TyG-WC (median $\pm$ SD)	733.38 $\pm$ 135.81	731.30 $\pm$ 134.86	771.21 $\pm$ 147.10	< 0.001
TyG-BMI (median $\pm$ SD)	204.78 $\pm$ 41.68	204.23 $\pm$ 41.46	214.72 $\pm$ 44.37	< 0.001
Sex (N, %)				0.507
Male	4029 (46.18%)	3812 (46.10%)	217 (47.69%)	
Female	4695 (53.82%)	4457 (53.90%)	238 (52.31%)	
Area of residence (N, %)				0.124
Rural	7260 (83.16%)	6889 (83.26%)	371 (81.36%)	
Urban	1427 (16.35%)	1347 (16.28%)	80 (17.54%)	
Rural missing	43 (0.49%)	38 (0.46%)	5 (1.10%)	
Educational attainment (N, %)				0.032
Primary and below	6132 (70.26%)	5788 (69.97%)	344 (75.44%)	
Middle school	1728 (19.80%)	1658 (20.04%)	70 (15.35%)	
High school and above	868 (9.95%)	826 (9.99%)	42 (9.21%)	
Marital status (N, %)				< 0.001
Married	7668 (87.84%)	7290 (88.11%)	378 (82.89%)	
Other	1062 (12.16%)	984 (11.89%)	78 (17.11%)	
Smoking status (N, %)				0.025
Never	5321 (60.96%)	5064 (61.22%)	257 (56.36%)	
Current	2662 (30.50%)	2516 (30.42%)	146 (32.02%)	
Former	745 (8.54%)	692 (8.37%)	53 (11.62%)	
Drinking status (N, %)				0.440
Current	2188 (25.07%)	2066 (24.97%)	122 (26.75%)	
Former	691 (7.92%)	661 (7.99%)	30 (6.58%)	
Never	5850 (67.02%)	5546 (67.04%)	304 (66.67%)	
Hypertension (N, %)				< 0.001
Continued				



Variables	All participants	No stroke	Stroke	P value
No	6655 (76.69%)	6389 (77.69%)	266 (58.59%)	
Yes	2023 (23.31%)	1835 (22.31%)	188 (41.41%)	
Dyslipidemia (N, %)				<0.001
No	7806 (91.42%)	7422 (91.72%)	384 (85.91%)	
Yes	733 (8.58%)	670 (8.28%)	63 (14.09%)	
Chronic lung diseases (N, %)				0.354
No	7788 (89.64%)	7386 (89.71%)	402 (88.35%)	
Yes	900 (10.36%)	847 (10.29%)	53 (11.65%)	
Liver disease (N, %)				0.009
No	8309 (95.95%)	7885 (96.08%)	424 (93.60%)	
Yes	351 (4.05%)	322 (3.92%)	29 (6.40%)	
Heart disease (N, %)				<0.001
No	7689 (88.60%)	7328 (89.09%)	361 (79.69%)	
Yes	989 (11.40%)	897 (10.91%)	92 (20.31%)	
Kidney disease (N, %)				0.177
No	8098 (93.37%)	7682 (93.45%)	416 (91.83%)	
Yes	575 (6.63%)	538 (6.55%)	37 (8.17%)	
Dm (N, %)				0.003
No	7523 (86.17%)	7151 (86.43%)	372 (81.58%)	
Yes	1207 (13.83%)	1123 (13.57%)	84 (18.42%)	

**Table 1.** Baseline characteristics the study population based on stroke occurrence. The data are expressed as the means  $\pm$  SD, median (25th–75th percentile), or percentages. Abbreviations: *N* quantity; *WC* waist circumference; *BMI* body mass index; *SBP* systolic blood pressure; *DBP* diastolic blood pressure; *PLT* platelet count, *BUN* blood urea nitrogen, *FPG* fasting plasma glucose, *Scr* serum creatinine, *TC* total cholesterol, *TG* triglyceride, *HDL-c* high-density lipoprotein cholesterol, *LDL-c* low-density lipoprotein cholesterol, *CRP* C-reactive protein, *HbA1C* glycated hemoglobin, *HGB* hemoglobin concentration, *UA* uric acid, *TyG* triglyceride glucose, *TyG-WC* triglyceride glucose waist circumference, *TyG-WHtR*, triglyceride glucose waist circumference Height, *TyG-BMI*, triglyceride glucose body mass index, *TyG-ABSI* TyG-a body shape index; *TyG-BRI* TyG-body roundness index; *TyG-WWI* TyG- weight-adjusted waist index.

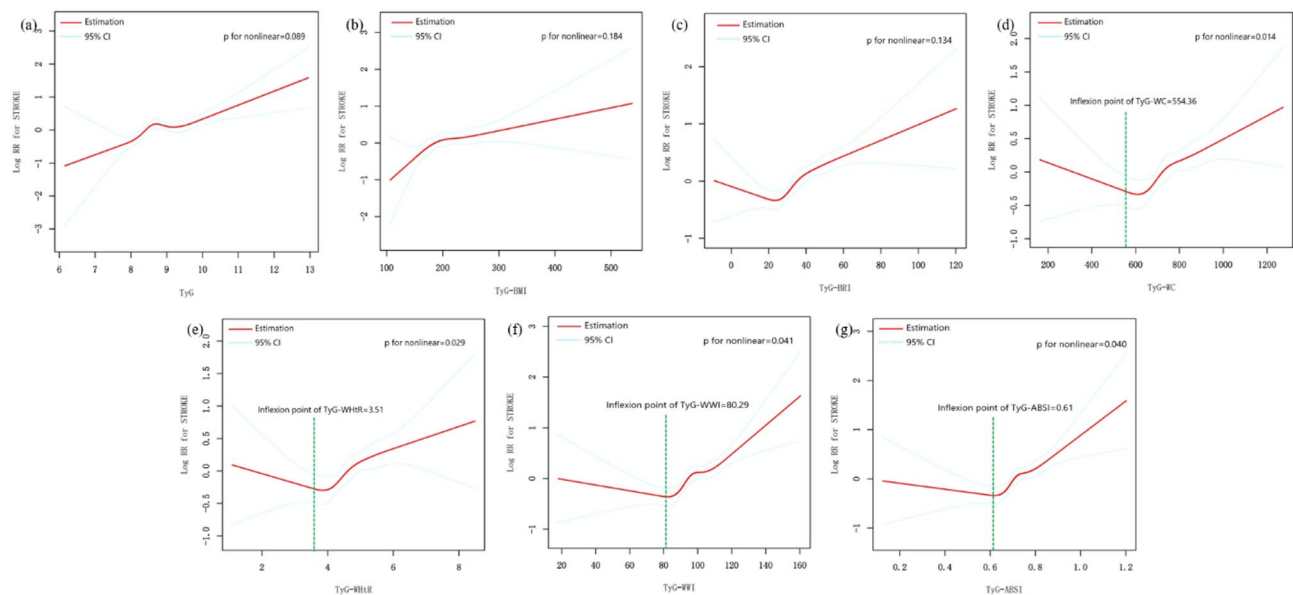
### Joint analyses of TyG and obesity indicators with incidence of stroke

The Kaplan-Meier cumulative incidence curve showed a gradual upward trend in the cumulative incidence of stroke events with TyG and each combined index (Fig. 3). And the Kaplan-Meier survival analysis demonstrated significant differences among groups for TyG, TyG-BMI, and TyG-ABSI (log-rank  $P < 0.05$  per group comparison) in Table S5 (Additional File). No significant differences were observed between Q1 and Q2 groups or Q2 and Q3 groups in TyG-WC (log-rank  $P > 0.05$ ). Similarly, no significant differences were found between Q1 and Q2 groups for TyG-WHtR and TyG-BRI indices (log-rank  $P > 0.05$ ). For TyG-WWI index, no significant differences were observed between Q2 and Q3 groups or Q3 and Q4 groups (log-rank  $P > 0.05$ ). All other subgroups showed statistically significant differences (log-rank  $P < 0.05$  per group comparison). Higher levels of TyG and the combined indices were associated with the greatest stroke risk. Additionally, Table 3 presents the stroke incidence rates categorized by quartiles of the TyG index and each combined index, with the TyG-WC Q4 group exhibiting the highest incidence rate (7.55%). The stroke incidence rates were 6.23% for the high TyG group, 6.96% for the high TyG-BMI group, 7.55% for the high TyG-WC group, 7.28% for the high TyG-WHtR group, 6.83% for the high TyG-WWI group, 6.92% for the high TyG-ABSI group, and 7.38% for the high TyG-BRI group. Notably, there was a corresponding increase in the incidence of stroke with rising quartiles (Q1–Q4) of the composite index.

As shown in Fig. 4, the AUC values of the combined indices were higher than those of the TyG index or obesity index alone. The Delong test results (as shown in Table S6) showed that only TyG-WC combination had a statistically significant increase compared with TyG alone ( $P = 0.029$ ), while other combinations had differences at the numerical level but did not reach statistical significance ( $P > 0.05$ ). In addition, the AUC differences of the four combined indices, TyG-ABSI, TyG-BRI, TyG-BMI and TyG-WWI showed statistically significant improvement compared with the use of obesity index alone ( $P < 0.05$ ). Among those results, the AUC value of the combined index of waist circumference and TyG was the highest (TyG-WC: AUC = 0.619, 95% CI = 0.558–0.634, optimal threshold = 768.079).

### Subgroup analyses and sensitivity analyses

Table S7 (Additional File) presents the risk assessment for TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, TyG-BRI and stroke, stratified by age, sex, smoking status, alcohol consumption status, diabetes, and hypertension. Adjustments were made for age, sex, smoking status, alcohol consumption status, HDL-c, LDL-c, CRP, Scr, UA, cystatin C, hypertension, DM, and kidney disease. No significant interactions were found with the



**Fig. 2.** Generalized additive models reveal how TyG and the combined indices relate to the stroke risk.

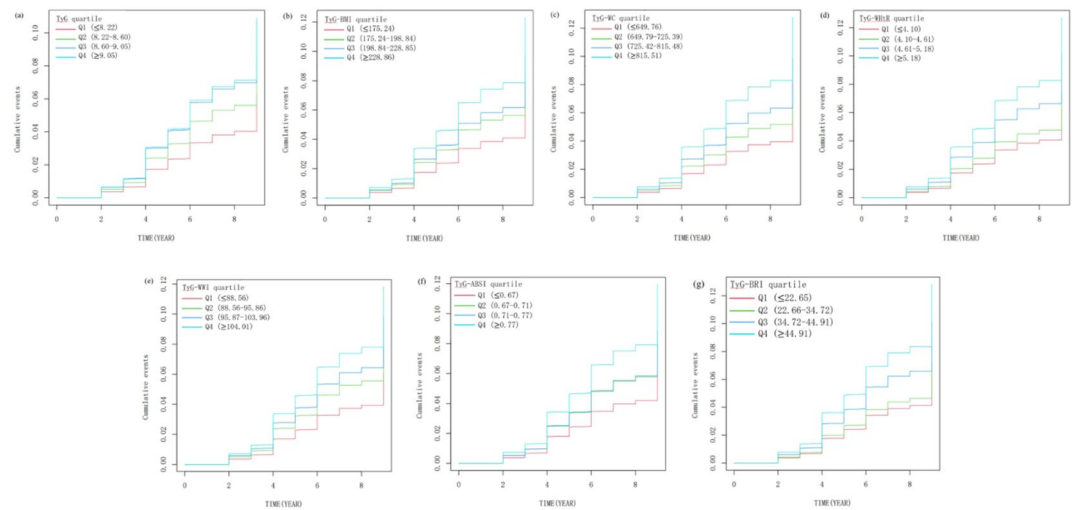
\*Generalized additive models fitting for the associations of TyG-related obesity indices and AIP index with stroke risk. (a) TyG and stroke risk; (b) TyG-BMI and stroke risk; (c) TyG-BRI and stroke risk; (d) TyG-WC and stroke risk; (e) TyG-WHtR and stroke risk; (f) TyG-WWI and stroke risk; (g) TyG-ABSI and stroke risk; Controlled for age, sex, smoking status, alcohol consumption status, HDL-c, LDL-c, CRP, Scr, UA, Cystatin C, HGB, DM, kidney disease, and hypertension. The resulting figures show the predicted log (stroke relative risk) on the y-axis and the TyG and combined indices on the x-axis.

Index		Per-unit increase		Per-SD increase	
		HR (95% CI)	P value	HR (95% CI)	P value
TyG <sup>a</sup>	Linear effect	1.37 (1.21, 1.55)	<0.001	1.23 (1.14, 1.34)	<0.001
TyG-BMI <sup>a</sup>	Linear effect	1.00 (1.00, 1.01)	0.004	1.18 (1.05, 1.32)	0.004
TyG-BRI <sup>a</sup>	Linear effect	1.01 (1.00, 1.02)	0.019	1.15 (1.02, 1.29)	0.019
TyG-WC <sup>b</sup>	Inflexion point	554.36		-1.32	
	< 554.36	1.00 (1.00, 1.00)	0.123	0.77 (0.55, 1.08)	0.124
	> 554.36	1.00 (1.00, 1.00)	<0.001	1.34 (1.16, 1.55)	<0.001
	P for log-likelihood ratio test	0.014		0.014	
TyG-WHtR <sup>b</sup>	Inflexion points	3.51		-1.3	
	< 3.51	0.76 (0.51, 1.13)	0.171	0.79 (0.56, 1.11)	0.170
	> 3.51	1.34 (1.13, 1.59)	<0.001	1.29 (1.12, 1.50)	<0.001
	P for log-likelihood ratio test	0.029		0.029	
TyG-WWI <sup>b</sup>	Inflexion points	80.29		-1.08	
	< 80.29	0.99 (0.98, 1.01)	0.329	0.89 (0.70, 1.13)	0.329
	> 80.29	1.02 (1.01, 1.03)	0.005	1.27 (1.08, 1.51)	0.005
	P for log-likelihood ratio test	0.041		0.041	
TyG-ABSI <sup>b</sup>	Inflexion points	0.61		-1	
	< 0.61	0.37 (0.04, 3.02)	0.352	0.90 (0.73, 1.12)	0.356
	> 0.61	9.02 (1.77, 45.91)	0.008	1.25 (1.06, 1.48)	0.008
	P for log-likelihood ratio test	0.040		0.040	

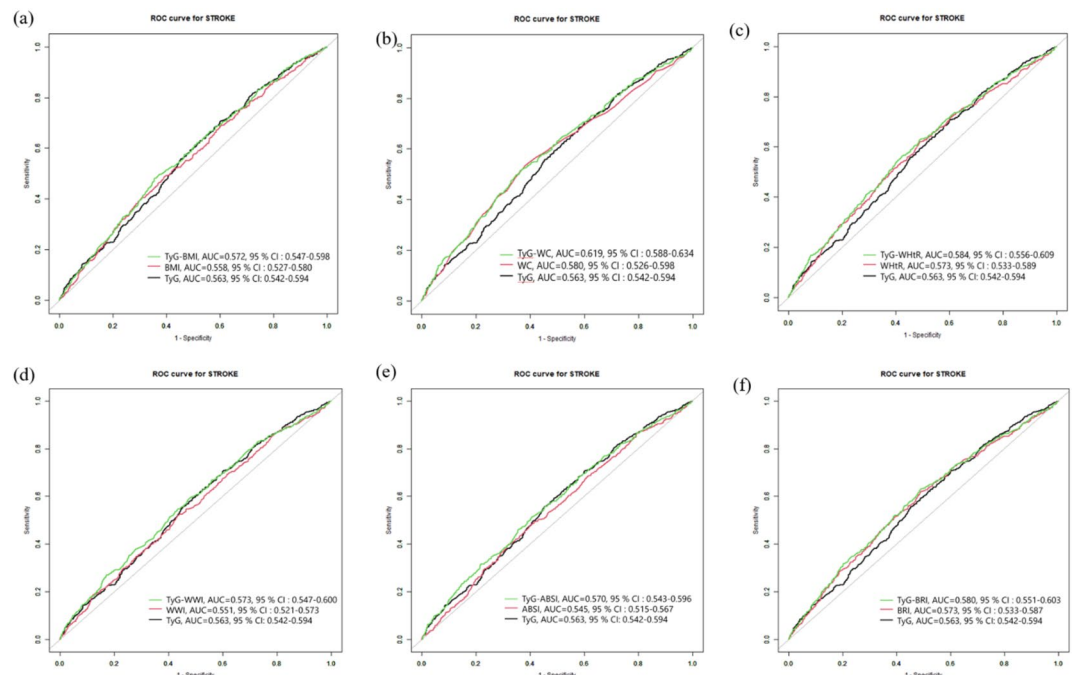
**Table 2.** The results of the relationship between TyG and the combined indices with stroke risk using threshold effect analysis. Adjusted for age, sex, smoking status, drinking status, HDL-c, LDL-c, CRP, Scr, UA, Cystatin C, HGB, DM, Kidney Disease, Hypertension, a linear model, b threshold effect model

quartiles of TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, or TyG-BRI, indicating consistent associations across subgroups.

To further validate these findings, sensitivity analyses were conducted using a series of methods. The trends observed in the sensitivity analyses were consistent with the results of the primary analysis. TyG, TyG-BMI,



**Fig. 3.** The Kaplan–Meier analysis for stroke was based on TyG and combined indices quartiles: (a) TyG quartiles; (b) TyG-BMI quartiles; (c) TyG-WC quartiles; (d) TyG-WHtR quartiles; (e) TyG-WWI quartiles; (f) TyG-ABSI quartiles; (g) TyG-BRI quartiles.



**Fig. 4.** Receiver operating characteristic curves for TyG, obesity indicators and combined indices predicting stroke incidence. (a) TyG, BMI, TyG-BMI; (b) TyG, WC, TyG-WC; (c) TyG, WHtR, TyG-WHtR; (d) TyG, WWI, TyG-WWI; (e) TyG, ABSI, TyG-ABSI; (f) TyG, BRI, TyG-BRI.

TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI were converted into quartiles, and these categorical variables were then re-entered into the regression models for analysis. In Table 3, the range of effect sizes for each group was consistent. Even after controlling for confounding variables (in Model 3), TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI, as categorical variables, showed significant positive associations with stroke risk in Q3, with the following results respectively: HR = 1.67, 95% CI = 1.18–2.37; HR = 1.60, 95% CI = 1.11–2.29; HR = 1.60, 95% CI = 1.12–2.28; HR = 1.46, 95% CI = 1.03–2.09; HR = 1.43, 95% CI = 1.01–2.03; HR = 1.30, 95% CI = 0.92–1.85; HR = 1.50, 95% CI = 1.05–2.13. (all  $p < 0.05$ ). Similar results were obtained for Q4: HR = 1.45, 95% CI = 0.98–2.16; HR = 1.85, 95% CI = 1.26–2.71; HR = 1.85, 95% CI = 1.27–2.70; HR = 1.89, 95% CI = 1.29–2.77; HR = 1.50, 95% CI = 1.02–2.21; HR = 1.45, 95% CI = 1.11–2.21; HR = 1.87, 95% CI = 1.29–2.70. This study also explored the association between TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, TyG-BRI and stroke risk in specific populations (without diabetes, without hypertension,



	Case	Model 1 HR (95% CI) <i>P</i> value	Model 2 HR (95% CI) <i>P</i> value	Model 3 HR (95% CI) <i>P</i> value
TyG				
TyG Per-SD		1.23 (1.14, 1.34) <0.001	1.25 (1.15, 1.36) <0.001	1.25 (1.08, 1.44) 0.003
TyG quartile				
Q1(≤ 8.22)	77(3.54%)	Ref	Ref	Ref
Q2(8.22–8.60)	108(4.94%)	1.40 (1.05, 1.88) 0.024	1.44 (1.07, 1.93) 0.015	1.33 (0.94, 1.90) 0.108
Q3(8.60–9.05)	135(6.18%)	1.75 (1.32, 2.32) <0.001	1.77 (1.34, 2.35) <0.001	1.67 (1.18, 2.37) 0.004
Q4(≥ 9.05)	136(6.23%)	1.79 (1.36, 2.37) <0.001	1.87 (1.41, 2.49) <0.001	1.45 (0.98, 2.16) 0.046
TyG-BMI				
TyG-BMI Per-SD		1.23 (1.14, 1.33) <0.001	1.29 (1.19, 1.39) <0.001	1.18 (1.05, 1.32) 0.005
TyG-BMI quartile				
Q1(≤ 175.24)	78(3.57%)	Ref	Ref	Ref
Q2(175.25–198.84)	107(4.90%)	1.38 (1.03, 1.85) 0.029	1.54 (1.14, 2.06) 0.004	1.59 (1.12, 2.25) 0.009
Q3(198.84–228.85)	119(5.45%)	1.52 (1.14, 2.02) 0.004	1.77 (1.32, 2.36) 0.0001	1.60 (1.11, 2.29) 0.011
Q4(≥ 228.86)	152(6.96%)	1.95 (1.49, 2.57) <0.001	2.37 (1.79, 3.15) <0.001	1.85 (1.26, 2.71) 0.002
TyG-WC				
TyG-WC Per-SD		1.34 (1.22, 1.46) <0.001	1.35 (1.23, 1.48) <0.001	1.22 (1.07, 1.40) 0.003
TyG-WC quartile				
Q1(≤ 649.76)	76(3.48%)	Ref	Ref	Ref
Q2(649.79–725.39)	99(4.54%)	1.31 (0.97, 1.77) 0.075	1.32 (0.98, 1.79) 0.067	1.37 (0.96, 1.97) 0.081
Q3(725.41–815.48)	121(5.35%)	1.62 (1.21, 2.15) 0.001	1.66 (1.24, 2.21) 0.0006	1.60 (1.12, 2.28) 0.009
Q4(≥ 815.51)	160(7.55%)	2.13 (1.62, 2.80) <0.001	2.19 (1.66, 2.88) <0.001	1.85 (1.27, 2.70) 0.001
TyG-WHtR				
TyG-WHtR Per-SD		1.31 (1.20, 1.44) <0.001	1.34 (1.21, 1.47) <0.001	1.19 (1.04, 1.36) 0.009
TyG-WHtR quartile				
Q1(≤ 4.10)	78(3.57%)	Ref	Ref	Ref
Q2(4.10–4.61)	91(4.17%)	1.17 (0.87, 1.59) 0.301	1.21 (0.90, 1.65) 0.211	1.27 (0.89, 1.81) 0.194
Q3(4.61–5.18)	128(5.87%)	1.65 (1.24, 2.18) <0.001	1.74 (1.31, 2.32) <0.001	1.46 (1.03, 2.09) 0.035
Q4(≥ 5.18)	159(7.28%)	2.07 (1.58, 2.71) <0.001	2.22 (1.67, 2.95) <0.001	1.89 (1.29, 2.77) 0.001
TyG-WWI				
TyG-WWI Per-SD		1.28 (1.16, 1.42) <0.001	1.26 (1.13, 1.40) <0.001	1.14 (0.99, 1.31) 0.063
TyG-WWI quartile				
Q1(≤ 88.56)	76(3.48%)	Ref	Ref	Ref
Q2(88.57–95.86)	106(4.86%)	1.42 (1.06, 1.91) 0.019	1.39 (1.03, 1.86) 0.030	1.23 (0.87, 1.75) 0.243
Q3(95.87–103.96)	125(5.73%)	1.65 (1.24, 2.20) <0.001	1.63 (1.22, 2.18) 0.001	1.43 (1.01, 2.03) 0.045
Q4(≥ 104.01)	149(6.83%)	2.01 (1.53, 2.65) <0.001	1.94 (1.45, 2.60) <0.001	1.50 (1.02, 2.21) 0.041
TyG-ABSI				
TyG-ABSI Per-SD		1.27 (1.14, 1.40) <0.001	1.21 (1.09, 1.34) <0.001	1.12 (0.98, 1.27) 0.099
TyG-ABSI quartile				
Q1(≤ 0.67)	81(3.71%)	Ref	Ref	Ref
Q2(0.67–0.71)	111(5.09%)	1.39 (1.04, 1.85) 0.024	1.33 (1.00, 1.77) 0.053	1.33 (0.94, 1.89) 0.105
Q3(0.71–0.77)	113(5.18%)	1.40 (1.06, 1.87) 0.019	1.29 (0.96, 1.72) 0.087	1.30 (0.92, 1.85) 0.047
Q4(≥ 0.77)	151(6.92%)	1.92 (1.47, 2.52) <0.001	1.71 (1.29, 2.26) <0.001	1.45 (1.01, 2.11) 0.034
TyG-BRI				
TyG-BRI Per-SD		1.28 (1.18, 1.40) <0.001	1.30 (1.19, 1.43) <0.001	1.15 (1.02, 1.29) 0.019
TyG-BRI quartile				
Q1(≤ 26.65)	79(3.62%)	Ref	Ref	Ref
Q2(26.66–34.72)	89(4.08%)	1.12 (0.83, 1.52) 0.447	1.16 (0.86, 1.58) 0.334	1.19 (0.83, 1.70) 0.339
Q3(34.72–44.91)	127(5.82%)	1.61 (1.21, 2.13) <0.001	1.72 (1.29, 2.30) <0.001	1.50 (1.05, 2.13) 0.024
Q4(≥ 44.91)	161(7.38%)	2.06 (1.57, 2.69) <0.001	2.24 (1.68, 2.97) <0.001	1.87 (1.29, 2.70) <0.001

**Table 3.** Cox-proportional hazard models for the association of TyG and the combined indices with stroke risk. Model 1: unadjusted; Model 2: adjusted for age, sex, smoking status, drinking status; Model 3: adjusted for age, sex, smoking status, drinking status, HDL-c, LDL-c, CRP, Scr, UA, Cystatin C, HGB, DM, Kidney Disease, Hypertension.

without kidney disease,  $BMI < 24 \text{ kg/m}^2$ ). After adjusting for multiple covariates, the results were consistent with those reported above (Table S8, Additional File).

## Discussion

Based on the national longitudinal data of China, this study systematically evaluated the association between TyG combined obesity index and stroke risk, providing a simple and economic stroke risk assessment tool for developing countries. The findings revealed that: (1) Participants who experienced stroke had higher levels of TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI compared to non-stroke participants, and these indices were significantly positively associated with stroke risk across three different models. (2) Generalized additive models visually demonstrated non-linear associations between TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI and stroke risk, with specific inflection points identified; whereas TyG, TyG-BMI, and TyG-BRI showed linear associations with stroke risk. These associations were independent of age, sex, smoking status, alcohol consumption, HDL-c, LDL-c, CRP, Scr, UA, Cystatin C, HGB, diabetes, kidney disease, and hypertension. (3) The cumulative incidence of stroke events for TyG and each combined index showed an increasing trend from Q1 to Q4 groups. Furthermore, the TyG-WC Q4 group had the highest stroke risk rate (7.55%). (4) The combined indices showed higher AUC values for stroke risk compared to TyG or obesity indicators alone. (5) In individuals aged  $\geq 60$  years, females, non-smokers, non-drinkers, and those without diabetes or hypertension, high levels of TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI remained stable risk factors for stroke.

The TyG index was confirmed as a reliable surrogate marker for IR<sup>37–39</sup>. Moreover, body fat content and distribution are also related to insulin resistance. Due to the interplay between IR and obesity, more studies are combining the TyG index with obesity indicators to explore their relationship with stroke<sup>20,22,40</sup>. A Korean study suggests that the TyG-BMI index, which combines TyG and BMI, as an alternative indicator of insulin resistance, may be more accurate than using TyG alone<sup>41</sup>. A longitudinal study reported that TyG-WHtR or TyG-WC had a greater impact on stroke risk than other indicators<sup>42</sup>. Another cohort study indicated that TyG-WC is more accurate in predicting stroke risk compared to TyG-BMI<sup>43</sup>. Data from rural areas in two countries suggested that TyG-BRI might be an accurate predictor of ischemic stroke incidence<sup>32</sup>. Some research has demonstrated that TyG is significantly superior to modified TyG indices in identifying cardiovascular events<sup>44</sup>. Conversely, other studies have shown that TyG-WC and TyG-WHtR are superior to the TyG index for identifying the risk of atherosclerotic cardiovascular disease<sup>45</sup>. Given the inconsistent findings surrounding the impact of combined TyG and obesity indicators on stroke risk, this study comprehensively evaluated the relationship between combinations of TyG with various obesity indicators and stroke risk. This included a series of complex indices such as TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI. This study found that TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI were significantly positively associated with stroke risk, suggesting they may serve as easily measurable and reliable tools for identifying individuals at high risk of stroke.

This study comprehensively explored the relationship between multiple TyG-obesity composite indices and stroke risk in middle-aged and elderly populations in China. Previous studies have found that TyG-BMI and TyG-WC were associated with stroke risk<sup>46</sup>. However, this study expanded the conclusions of these studies by examining more indicators (WWI, ABSI, BRI) and exploring nonlinear relationships. The generalized additive models revealed a non-linear relationship between TyG-WC, TyG-WHtR and stroke risk, and a linear relationship between TyG-BRI and stroke risk, which aligns with previous reports<sup>47,48</sup>. Furthermore, linear relationships were observed between TyG, TyG-BMI and stroke risk, while non-linear relationships were found for TyG-WWI and TyG-ABSI with stroke risk. These findings are inconsistent with some prior studies, potentially due to differences in glucose metabolism status and statistical analysis methods<sup>49–51</sup>. This refined dose-response analysis provides a more accurate scientific basis for risk assessment and avoids the misjudgment that may be caused by traditional linear assumptions.

This study compared the predictive capabilities of the standalone TyG index, obesity indicators, and combined TyG-obesity indices for stroke risk, finding that the AUC value of the combined indices was higher than the individual index<sup>20,32,42</sup>. Among these, compared with other TyG-related indexes, TyG-WC showed better diagnostic effect in stroke risk diagnosis. Additionally, this study found that in individuals aged  $< 60$  years, high levels of TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, and TyG-BRI had a stronger association with stroke risk compared to older populations, which is relatively consistent with research conducted in U.S. populations<sup>52</sup>. With increasing age, risk factors for cardiovascular disease are more susceptible to interference from other factors, which may limit the ability of combined TyG and obesity indices to predict cardiovascular disease risk in older adults. This study also indicated that the association between TyG indices, combined indices and stroke risk was stronger in males than in females. Reports on sex differences in the association between TyG indices, combined indices and stroke risk are currently inconsistent, possibly related to the sample composition of the study populations. A community-based study in northern China suggested that in females, TyG, TyG-BMI, TyG-WC, and TyG-WHtR had stronger associations with atherosclerotic cardiovascular disease than in males<sup>45</sup>. Furthermore, in the present study, the association between TyG indices, combined indices and stroke risk was stronger in non-smokers and non-drinkers compared to smokers and drinkers.

The specific inflection points identified in this study provide quantitative parameters for the development of evidence-based clinical guidelines. TyG-WC showed a significant inflection point at 554.36, beyond which stroke risk increased significantly by 34% ( $HR = 1.34$ , 95%  $CI = 1.16–1.55$ ). Similarly, TyG-WHtR, TyG-WWI and TyG-ABSI also have inflection points at 3.51, 80.29 and 0.61, respectively. These specific values provide clinicians with clear risk assessment criteria that can guide the development of individualized prevention strategies. This finding reminds healthcare professionals to pay attention to these inflection points in subsequent

clinical practice, monitor changes in TyG-WC, TyG-WHtR, TyG-WWI, and TyG-ABSI scores in real time, and consider appropriate risk thresholds when developing personalized prevention protocols. As an index reflecting insulin resistance and obesity, risk management and monitoring of combined index levels in patients with insulin resistance or abdominal obesity should be further strengthened in clinical practice. Furthermore, this study provides a scientific basis for the national chronic disease prevention and control policies. The research indicates that these indicators maintain stable predictive risk capabilities across different subgroups, supporting the inclusion of TyG combined with obesity indicators in the current chronic disease screening system. Specific recommendations include: (1) adding monitoring of simple indicators such as TyG-WC to the existing basic public health services; (2) establishing a stratified management model for high-risk populations; (3) creating synergies with existing diabetes and hypertension management programs to achieve integrated chronic disease prevention and control.

### Strengths and limitations

The core strength of this study lies in its comprehensive assessment of the relationship between combined indices of TyG and obesity indicators and stroke risk. Secondly, the handling of non-linear relationships was significantly improved. Non-linear relationships between TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI scores and stroke risk were identified, and potential risk thresholds were obtained. Additionally, multiple sensitivity analyses were used to ensure the consistency of the study findings. Thirdly, this study examined the associations between TyG, TyG-BMI, TyG-WC, TyG-WHtR, TyG-WWI, TyG-ABSI, TyG-BRI and stroke risk using both categorical and continuous variables. This approach facilitates a comprehensive description of data characteristics, reduces information loss, and accurately quantifies the indicators. Fourthly, all combined indices involved in this study can be easily calculated, requiring only data on fasting plasma glucose, triglycerides, waist circumference, height, and weight, which can be obtained at any time through routine clinical examination or simple measurement. In primary healthcare institutions with limited resources, such simple indicators are more easily applicable, contributing to improved accessibility of stroke risk screening. In addition, this study examined multiple combined indices of TyG and obesity index and conducted several subgroup analyses, so some results may be affected by chance factors. Future research should consider multiple comparative adjustments to ensure robust statistical inference.

However, as an observational study, several notable limitations exist. First, despite adjusting for known confounding factors, the observational study design may still be susceptible to unmeasured or unadjusted variables (Such as physical activity levels, dietary patterns, medication use and other variables). In addition, because of the independent cohort study design, it is difficult to confirm the identified turning points and predictive models for external validation, so confirmatory studies in independent populations are needed before clinical application. Second, the study was primarily conducted in a Chinese population aged 45 years and older; therefore, its applicability to other countries and younger populations cannot be guaranteed. More comprehensive research is needed in different age groups and other national and ethnic populations in the future. Third, this study focused on the effects of baseline TyG and obesity marker levels, but did not examine longitudinal changes over time or factors that changed over time (such as weight loss or medication use), so it was not possible to establish a clear cause-effect relationship with stroke risk. Furthermore, this study did not account for competing risks from non-stroke deaths during follow-up, which may have led to biased risk assessments in the elderly population. Future research should adopt the Fine-Gray competing risk model to more accurately predict the interaction risks among different causes of death. Fourth, due to the lack of data on stroke subtypes in CHARLS, this study could not separately assess the impact of the combined indices on ischemic or hemorrhagic stroke. Differentiate between ischemic and hemorrhagic stroke in future studies to tailor prevention strategies. Fifth, stroke data were collected in a self-reported format, introducing potential recall bias and misclassification bias; however, for cardiovascular diseases like stroke, self-reported diagnoses have shown high concordance with corresponding medical records<sup>53–55</sup>. Sixth, there may be selection bias in the excluded population. However, baseline characteristic comparisons revealed that the excluded group exhibited higher metabolic risk and cardiovascular comorbidity prevalence. While this selection bias limits generalizability, its directionality holds significance: The observation of a significant association in relatively low-risk populations suggests that the true association strength might be underestimated. Therefore, this results likely represent a conservative estimate of the predictive efficacy of the TyG combined indices.

### Conclusion

In conclusion, this study elucidates the association between metabolic-obesity combined indices and stroke risk, as well as the potential predictive utility of combined indicators in stroke risk assessment. Combined indices of TyG and obesity indicators are significantly associated with stroke risk. A non-linear association exists between stroke risk and TyG-WC, TyG-WHtR, TyG-WWI, and TyG-ABSI, whereas TyG, TyG-BMI, and TyG-BRI exhibit a linear relationship with stroke risk. These indices have the economic benefits of convenience and low cost, holding promise as surrogate indicators for IR and offering valuable references for future stroke risk assessment, screening, and intervention strategies. More importantly, it provides a viable solution for primary stroke prevention in resource-limited areas and for screening large populations.

### Data availability

The data examined in this study can be obtained from the Institute of Social Science Survey at Peking University in Beijing, China (<http://charls.pku.edu.cn>).

Received: 28 June 2025; Accepted: 19 September 2025

## References

- Ferrari, A. J. et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the global burden of disease study 2021. *Lancet* **403**, 2133–2161. [https://doi.org/10.1016/S0140-6736\(24\)00757-8](https://doi.org/10.1016/S0140-6736(24)00757-8) (2024).
- Feigin, V. L. et al. The global burden of neurological disorders: translating evidence into policy. *Lancet Neurol.* **19**, 255–265. [https://doi.org/10.1016/S1474-4422\(19\)30411-9](https://doi.org/10.1016/S1474-4422(19)30411-9) (2020).
- Feigin, V. L. et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the global burden of disease study 2013. *Lancet Neurol.* **15**, 913–924. [https://doi.org/10.1016/S1474-4422\(16\)30073-4](https://doi.org/10.1016/S1474-4422(16)30073-4) (2016).
- Ding, P.-F. et al. Insulin resistance in ischemic stroke: Mechanisms and therapeutic approaches. *Front. Endocrinol.* **13**–2022. [https://doi.org/10.1016/S1474-4422\(16\)30073-4](https://doi.org/10.1016/S1474-4422(16)30073-4) (2022).
- Chang, Y., Kim, C. K., Kim, M.-K., Seo, W. K. & Oh, K. Insulin resistance is associated with poor functional outcome after acute ischemic stroke in non-diabetic patients. *Sci. Rep.* **11**, 1229. <https://doi.org/10.1038/s41598-020-80315-z> (2021).
- Xiao, D. et al. Assessment of six surrogate insulin resistance indexes for predicting cardiometabolic Multimorbidity incidence in Chinese middle-aged and older populations: insights from the China health and retirement longitudinal study. *Diabetes Metab. Res. Rev.* **40**, e3764. <https://doi.org/10.1002/dmrr.3764> (2024).
- Wieberdink, R. G. et al. Insulin resistance and the risk of stroke and stroke subtypes in the nondiabetic elderly. *Am. J. Epidemiol.* **176**, 699–707. <https://doi.org/10.1093/aje/kws149> (2012).
- Ford, E. S., Giles, W. H. & Dietz, W. H. Prevalence of the metabolic syndrome among US adults: findings from the third National health and nutrition examination survey. *Jama* **287**, 356–359. <https://doi.org/10.1001/jama.287.3.356> (2002).
- Guerrero-Romero, F. et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J. Clin. Endocrinol. Metab.* **95**, 3347–3351. <https://doi.org/10.1210/jc.2010-0288> (2010).
- Tahapary, D. L. et al. Challenges in the diagnosis of insulin resistance: focusing on the role of HOMA-IR and Triglyceride/glucose index. *Diabetes Metabolic Syndrome* **16**, 102581. <https://doi.org/10.1016/j.dsx.2022.102581> (2022).
- Khan, S. H. et al. Metabolic clustering of risk factors: evaluation of Triglyceride-glucose index (TyG index) for evaluation of insulin resistance. *Diabetol. Metab. Syndr.* **10**, 74. <https://doi.org/10.1186/s13098-018-0376-8> (2018).
- Shi, W. et al. Value of triglyceride-glucose index for the Estimation of ischemic stroke risk: insights from a general population. Nutrition, metabolism, and cardiovascular diseases. *NMCD* **30**, 245–253. <https://doi.org/10.1016/j.numecd.2019.09.015> (2020).
- Feng, X. et al. Triglyceride-Glucose index and the risk of stroke: A systematic review and Dose-Response Meta-Analysis. *Hormone and metabolic research = Hormon- und Stoffwechsselforschung = Hormones et métabolisme*. **54**:175–186 (2022). <https://doi.org/10.1055/a-1766-0202>
- Kromhout, D. & Geleijnse, J. M. Body mass index and waist circumference predict both 10-year nonfatal and fatal cardiovascular disease risk: study conducted in 20,000 Dutch men and women aged 20–65 years. *Eur. J. Cardiovasc. Prev. Rehabilitation: Official J. Eur. Soc. Cardiol. Working Groups Epidemiol. Prev. Cardiac Rehabilitation Exerc. Physiol.* **16**, 729–734. <https://doi.org/10.1097/HJR.0b013e328331dfc0> (2009).
- Khan, S. S. et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol.* **3**, 280–287. <https://doi.org/10.1001/jamacardio.2018.0022> (2018).
- Qin, X. et al. Association of adiposity indices with cardiometabolic Multimorbidity among 101,973 Chinese adults: a cross-sectional study. *BMC Cardiovasc. Disord.* **23**, 514. <https://doi.org/10.1186/s12872-023-03543-x> (2023).
- Wang, G. L. et al. Combined effects of A body shape index and serum C-reactive protein on ischemic stroke incidence among Mongolians in China. *Biomed. Environ. Sci.: BES* **32**, 169–176. <https://doi.org/10.3967/bes2019.024> (2019).
- Gan, J. et al. Association between body roundness index and stroke results from the 1999–2018 NHANES. *J. Stroke Cerebrovasc. Diseases: Official J. Natl. Stroke Association* **34**, 108243. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2025.108243> (2025).
- Ye, J. et al. Association between the weight-adjusted waist index and stroke: a cross-sectional study. *BMC public. Health.* **23**, 1689. <https://doi.org/10.1186/s12889-023-16621-8> (2023).
- Shao, Y. et al. Link between triglyceride-glucose-body mass index and future stroke risk in middle-aged and elderly chinese: a nationwide prospective cohort study. *Cardiovasc. Diabetol.* **23**, 81. <https://doi.org/10.1186/s12933-024-02165-7> (2024).
- Fu, L. et al. Exploring the association between the TyG-WhR index and the incidence of stroke in the obese population: based on NHANES data from 1998 to 2018. *J. Stroke Cerebrovasc. Diseases: Official J. Natl. Stroke Association* **34**, 108209. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2024.108209> (2025).
- Huang, Q. et al. Association of novel lipid indicators with the risk of stroke among participants in central china: a population-based prospective study. *Front. Endocrinol. (Lausanne)* **14**, 1266552. <https://doi.org/10.3389/fendo.2023.1266552> (2023).
- Huo, R. R., Liao, Q., Zhai, L., You, X. M. & Zuo, Y. L. Interacting and joint effects of triglyceride-glucose index (TyG) and body mass index on stroke risk and the mediating role of TyG in middle-aged and older Chinese adults: a nationwide prospective cohort study. *Cardiovasc. Diabetol.* **23**, 30. <https://doi.org/10.1186/s12933-024-02122-4> (2024).
- Zhao, Y., Hu, Y., Smith, J. P., Strauss, J. & Yang, G. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int. J. Epidemiol.* **43**, 61–68. <https://doi.org/10.1093/ije/dys203> (2014).
- Park, Y., Kim, N. H., Kwon, T. Y. & Kim, S. G. A novel adiposity index as an integrated predictor of cardiometabolic disease morbidity and mortality. *Sci. Rep.* **8**, 16753. <https://doi.org/10.1038/s41598-018-35073-4> (2018).
- Yang, M. et al. Body roundness index trajectories and the incidence of cardiovascular disease: evidence from the China health and retirement longitudinal study. *J. Am. Heart Association* **13**, e034768. <https://doi.org/10.1161/jaha.124.034768> (2024).
- Krakauer, N. Y. & Krakauer, J. C. A new body shape index predicts mortality hazard independently of body mass index. *PloS One* **7**, e39504. <https://doi.org/10.1371/journal.pone.0039504> (2012).
- Er, L. K. et al. Triglyceride Glucose-Body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. *PloS One* **11**, e0149731. <https://doi.org/10.1371/journal.pone.0149731> (2016).
- Ke, P. et al. Comparison of obesity indices and triglyceride glucose-related parameters to predict type 2 diabetes mellitus among normal-weight elderly in China. *Eat. Weight Disorders: EWD* **27**, 1181–1191. <https://doi.org/10.1007/s40519-021-01238-w> (2022).
- Dang, K. et al. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003–2018. *Cardiovasc. Diabetol.* **23**, 8. <https://doi.org/10.1186/s12933-023-02115-9> (2024).
- Yang, L., Fang, S., Zhang, R. & Xia, R. Associations between different triglyceride glucose index-related obesity indices and periodontitis: results from NHANES 2009–2014. *Lipids Health Dis.* **23**, 213. <https://doi.org/10.1186/s12944-024-02192-z> (2024).
- Yao, F. et al. Evaluating a new obesity indicator for stroke risk prediction: comparative cohort analysis in rural settings of two nations. *BMC public. Health* **24**, 3301. <https://doi.org/10.1186/s12889-024-20631-5> (2024).
- He, H. M. et al. The synergistic effect of the triglyceride-glucose index and a body shape index on cardiovascular mortality: the construction of a novel cardiovascular risk marker. *Cardiovasc. Diabetol.* **24**, 69. <https://doi.org/10.1186/s12933-025-02604-z> (2025).
- Li, X. et al. Predictive effect of triglyceride Glucose-Related Parameters, obesity Indices, and lipid ratios for diabetes in a Chinese population: A prospective cohort study. *Front. Endocrinol. (Lausanne)*. **13**, 862919. <https://doi.org/10.3389/fendo.2022.862919> (2022).



35. Lin, X. & Zhang, D. Inference in generalized additive mixed models by using smoothing splines. *J. Royal Stat. Soc. Ser. B: Stat. Methodol.* **61**, 381–400. <https://doi.org/10.1111/1467-9868.00183> (2002).
36. Lin, L., Chen, C. Z. & Yu, X. D. The analysis of threshold effect using empower stats software. *Zhonghua Liu Xing Bing Xue Za zhi = Zhonghua Liuxingbingxue Zazhi* **34**, 1139–1141. <https://doi.org/10.3760/cma.j.issn.0254-6450.2013.011.021> (2013).
37. Sánchez-García, A. et al. Diagnostic accuracy of the triglyceride and glucose index for insulin resistance: A systematic review. *Int. J. Endocrinol.* **2020**, 4678526. <https://doi.org/10.1155/2020/4678526> (2020).
38. Simental-Mendía, L. E., 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.* **6**, 299–304. <https://doi.org/10.1089/met.2008.0034> (2008).
39. Hong, S., Han, K. & Park, C. Y. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: a population-based study. *BMC Med.* **18**, 361. <https://doi.org/10.1186/s12916-020-01824-2> (2020).
40. Ren, Q. et al. Association between triglyceride glucose-waist height ratio index and cardiovascular disease in middle-aged and older Chinese individuals: a nationwide cohort study. *Cardiovasc. Diabetol.* **23**, 247. <https://doi.org/10.1186/s12933-024-02336-6> (2024).
41. Lim, J., Kim, J., Koo, S. H. & Kwon, G. C. Comparison of triglyceride glucose index, and related parameters to predict insulin resistance in Korean adults: an analysis of the 2007–2010 Korean National health and nutrition examination survey. *PloS One* **14**, e0212963. <https://doi.org/10.1371/journal.pone.0212963> (2019).
42. Liang, W. & Ouyang, H. The association between triglyceride-glucose index combined with obesity indicators and stroke risk: A longitudinal study based on CHARLS data. *BMC Endocr. Disorders.* **24**, 234. <https://doi.org/10.1186/s12902-024-01729-8> (2024).
43. Zhao, Y. et al. Comparison of six surrogate insulin resistance indexes for predicting the risk of incident stroke: the rural Chinese cohort study. *Diabetes Metab. Res. Rev.* **38**, e3567. <https://doi.org/10.1002/dmrr.3567> (2022).
44. Cui, C. et al. Comparison of triglyceride glucose index and modified triglyceride glucose indices in prediction of cardiovascular diseases in middle aged and older Chinese adults. *Cardiovasc. Diabetol.* **23**, 185. <https://doi.org/10.1186/s12933-024-02278-z> (2024).
45. Xia, X. et al. Association of triglyceride-glucose index and its related parameters with atherosclerotic cardiovascular disease: evidence from a 15-year follow-up of Kailuan cohort. *Cardiovasc. Diabetol.* **23**, 208. <https://doi.org/10.1186/s12933-024-02290-3> (2024).
46. Li, X. et al. Triglyceride-glucose index prediction of stroke incidence risk in low-income Chinese population: a 10-year prospective cohort study. *Front. Endocrinol. (Lausanne)*. **15**, 1444030. <https://doi.org/10.3389/fendo.2024.1444030> (2024).
47. 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.* **22**, 279. <https://doi.org/10.1186/s12933-023-02030-z> (2023).
48. Bai, W. et al. Association between the triglyceride glucose-body roundness index and the incidence of cardiovascular disease among Chinese middle and old-aged adults: a nationwide prospective cohort study. *Acta Diabetol.* <https://doi.org/10.1007/s00592-025-02499-y> (2025).
49. Jiang, L. et al. Assessment of six insulin resistance surrogate indexes for predicting stroke incidence in Chinese middle-aged and elderly populations with abnormal glucose metabolism: a nationwide prospective cohort study. *Cardiovasc. Diabetol.* **24**, 56. <https://doi.org/10.1186/s12933-025-02618-7> (2025).
50. Zhang, R. et al. Joint association of triglyceride glucose index (TyG) and a body shape index (ABSI) with stroke incidence: a nationwide prospective cohort study. *Cardiovasc. Diabetol.* **24**, 7. <https://doi.org/10.1186/s12933-024-02569-5> (2025).
51. Huo, G. et al. Association between triglyceride glucose weight adjusted waist index and stroke risk in different glucose metabolism status. *Sci. Rep.* **15**, 15813. <https://doi.org/10.1038/s41598-025-99618-0> (2025).
52. Hou, X. Z. et al. Association between different insulin resistance surrogates and all-cause mortality in patients with coronary heart disease and hypertension: NHANES longitudinal cohort study. *Cardiovasc. Diabetol.* **23**, 86. <https://doi.org/10.1186/s12933-024-02173-7> (2024).
53. Valtorta, N. K., Kanaan, M., Gilbody, S. & Hanratty, B. Loneliness, social isolation and risk of cardiovascular disease in the english longitudinal study of ageing. *Eur. J. Prev. Cardiol.* **25**, 1387–1396. <https://doi.org/10.1177/2047487318792696> (2018).
54. Glymour, M. M. & Avendano, M. Can self-reported strokes be used to study stroke incidence and risk factors? Evidence from the health and retirement study. *Stroke* **40**, 873–879. <https://doi.org/10.1161/strokeaha.108.529479> (2009).
55. He, D. et al. Changes in frailty and incident cardiovascular disease in three prospective cohorts. *Eur. Heart J.* **45**, 1058–1068. <https://doi.org/10.1093/eurheartj/ehad885> (2024).

# Acknowledgements

We would like to express our sincere gratitude to the researchers and staff of the China Health and Retirement Longitudinal Study (CHARLS) for their essential contributions. We also wish to extend our special appreciation to the study participants for their vital role in this research. Their involvement was key to the data collection and analysis. Furthermore, we extend our thanks to Xinglin Chen for providing statistical support and for the collaborative research efforts.

# Author contributions

Conceptualization: LZH and XXH; method: LZH and XXH; Statistical analysis: LZH and BY; writing-draft preparation: LZH, BY and HML; writing-comment and editing: LZH, DLP; fund acquisition: XXH and LZH; Resources: XXH; supervision: XXH. All authors contributed to the revision, and all have read and approved the final manuscript.

# Funding

This study was supported by the Shenzhen Science and Technology Program (Grant number: JCYJ20230807115119040), the Sanming Project of Medicine in Shenzhen (Grant number: SZSM202111014) and the School of Nursing, Anhui Medical University (Grant number: Hlqm12025106). The funding organization was not involved in the study's design, data handling, analysis, interpretation, manuscript preparation, or publication decision. The authors declare no conflicts of interest.

# Declarations

# Competing interests

The authors declare no competing interests.



### Ethics approval and consent to participate

The CHARLS study protocol was approved by the Peking University Ethics Review Committee (IRB00001052-11015) in Beijing, China. All participants provided written informed consent.

### Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-21331-9>.

**Correspondence** and requests for materials should be addressed to X.X.

**Reprints and permissions information** is available at [www.nature.com/reprints](http://www.nature.com/reprints).

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**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/>.

© The Author(s) 2025