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# The nonlinear relationship between triglyceride glucose-waist circumference and stroke risk in middle-aged and elderly people: a nationwide prospective cohort study of the CHARLS

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## Abstract

**Background and aims** Numerous research have focused on the relationship of metabolic markers and stroke risk, yet limited research has focused on the triglyceride glucose-waist circumference (TyG-WC) index. This study explored the possible association of TyG-WC and stroke among moderately aged and old Chinese adults over 45 years of age.

**Methods** This observational cohort analysis involved 9054 participants from the Chinese Longitudinal Study of Health and Retirement and employed a standardized questionnaire administered via in-person interviews. Cox proportional hazard model, smoothed curve fitting, and threshold effect analysis were conducted for examining the potential nonlinear relationships among TyG-WC and stroke risk.

**Results** Within an average follow-up period of six years, 463 new strokes occurred, representing 5.11% of the total number of patients. After adjusting for possible confounding factors, a nonlinear association between TyG-WC and stroke risk was identified, with a significant dose–response relationship ($P=0.023$ for the log-likelihood ratio test). A turning point was identified at the TyG-WC level of 554.48, beyond that the likelihood of stroke increased markedly (HR = 1.323, 95% CI = 1.098–1.594, $P=0.003$).

**Conclusion** This study revealed a specific curvilinear association with the TyG-WC score and stroke risk, identifying a key threshold value. This study focused on Chinese middle-aged and senior adults over the age of 45, emphasizing that increased stroke risk is linked to higher TyG-WC levels.

**Keywords** Triglyceride glucose-waist circumference, Stroke, Nonlinear relationship, China health and retirement longitudinal study

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## Introduction

Stroke, a prevalent neurological disorder, is caused by localized damage to cerebral blood vessels, resulting in neurological deficit in the central nervous system [1]. The incidence rates and related fatalities of stroke have increased alarmingly [2, 3]. As reported in the latest survey, stroke continues to be a primary driver of

disability-adjusted life-years (DALYs) worldwide, causing 160.4 million (148.0–171.1) DALYs [4]. Stroke-related motor disability, cognitive impairment, and death lead to a considerable decline in the quality of life and a significant burden [4–6]. Stroke poses a global public health problem that warrants considerable attention. Obesity, hypertension, diabetes mellitus (DM), and hyperlipidaemia are among the main stroke risk factors that can be avoided and managed early in life. However, evidence from primary and secondary stroke prevention research has not been adequately translated into practical prevention strategies due to implementation barriers [6–9]. Consequently, identifying specific risk factors associated with stroke and directing efforts towards its reduction is of paramount importance.

A body of evidence indicates that insulin resistance is a factor in the onset of type 2 diabetes and an elevated susceptibility to cardiovascular disease. Insulin resistance impairs brain function through several mechanisms and has been linked to adverse outcomes in ischaemic stroke patients [10–13]. The most commonly employed assessments of insulin resistance include the normoglycemic-insulin clamp technique and the homeostatic model insulin resistance assessment [14, 15]. However, time and cost limitations have constrained the extensive clinical utilization of these two measures. A reliable alternative for assessing insulin resistance is the triglyceride-glucose (TyG) index, which is considered a quick, easy, and reproducible method of assessment [16, 17]. The TyG, a robust predictor of cardiovascular disease and stroke, has gained prominence in clinical research [18–21]. Combining waist circumference (WC) with TyG forms the triglyceride glucose-waist circumference(TyG-WC), which offers insights into metabolic health indicators, such as nonalcoholic fatty liver disease (NAFLD), metabolic fatty liver disease, and prediabetes [22–25]. Increased TyG-WC levels are consistently correlated to a greater likelihood of heart attacks and cardiovascular disease [26, 27]. Due to its association with increased cardiovascular risk, this study hypothesizes that the TyG-WC could be a significant contributor to stroke risk. Current research on TyG-WC and its association with stroke risk has been conducted on small, localized samples [28, 29]. Existing studies have failed to examine any possible nonlinear relationship within the TyG-WC and stroke risk. Thus, further studies and validation of this relationship are necessary. This prospective cohort research utilized datasets collected from the China Health and Retirement Longitudinal Study (CHARLS), which encompasses 450 communities throughout China, and presents an opportunity to comprehensively examine the connection among TyG-WC and stroke risk on a larger scale.

## Methods

### Study population and survey methods

Five waves of the CHARLS were analyzed in this study, conducted in 2011, 2013, 2015, 2018, and 2020. The Chinese National Development Research Institute conducted CHARLS, a statewide questionnaire study that involves 150 counties in approximately 28 provinces in China [30]. The baseline survey collected data from 17,708 randomly selected middle-aged and older people aged 45 years and over. The CHARLS was first conducted in 2011–2012 using computer-assisted personal interviews (CAPIs) to obtain demographic data, household data, biomedical measurements, health status, and functional ability. Subsequently, the survey was conducted biennially, with only a few new participants recruited each time. The Ethics Committee at Peking University Faculty of Medicine certified the CHARLS. The Biomedical Ethics Review Board of Peking University authorized the CHARLS investigation (IRB00001052-11015), and all subjects obtained signed informed consent [30]. The CHARLS project website provides access to downloadable data and information. (http://charls.pku.edu.cn/).

This research consisted of information on five CHARLS surveys conducted during June 2011 till March 2012, in which 17,707 participants underwent a baseline questionnaire and physical examination, 11,847 of whom (67%) underwent blood tests. TyG-WC was investigated in this study to assess their relationship with stroke incidence. Several exclusion criteria were developed to refine the study, including the following: (1) participants who suffered a stroke at baseline ($n=735$); (2) participants with follow-up intervals shorter than 2 years ($n=1,336$); (3) participants without sufficient information on fasting blood glucose (FPG) and triglycerides (TG) ($n=5,014$); and (4) participants with missing waist measurement data ($n=1,568$). Ultimately, this survey included 9054 participants. The study process diagram is depicted in Fig. 1. This investigation corresponds to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) publishing standards of cohort research.

### Study variables

#### *Calculation of TyG-WC*

The TyG is determined through combining triglyceride (TG) and fasting glucose (FPG) data: the TyG index = ln[FPG (mg/dL) × TG] (mg/dL)/2], and the TyG-WC = TyG × WC [20, 31, 32].

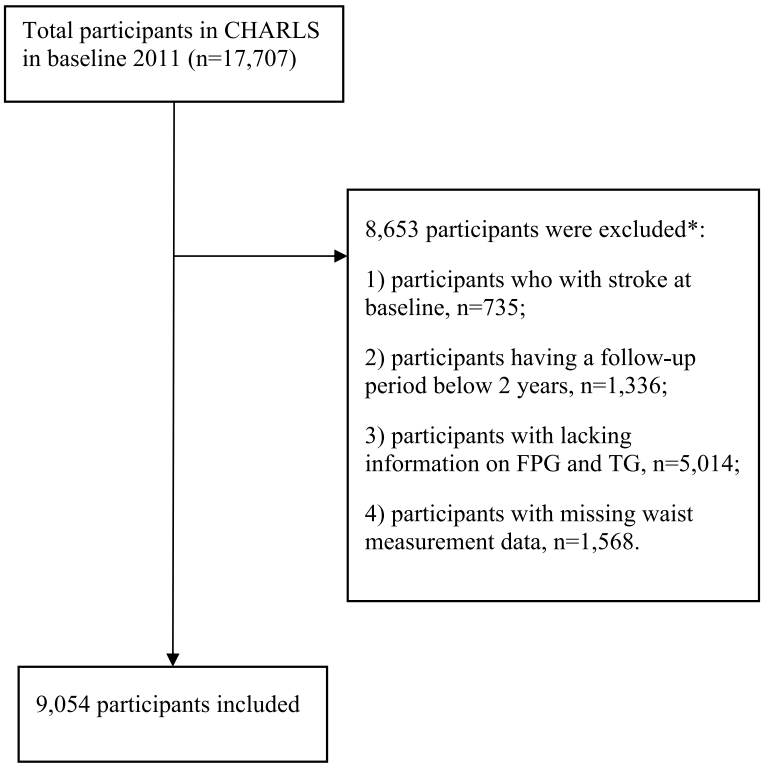


**Fig. 1** Flowchart illustrating the participant selection process. * Subjects selected after each step

#### *Assessment of stroke*

Using a self-assessment methodology, the study outcome was the incidence of a new stroke within the designated follow-up time. To this end, the trained staff posed standardized questions to participants, including the following: (1) Has your doctor ever diagnosed you with a stroke? (2) When was the illness initially detected or diagnosed for you? (3) Are you receiving continuing therapy for your stroke? If the interviewee indicated that they had suffered a stroke, the self-identified time (year or age) was recorded during monitoring. For individuals who hadn't suffered a stroke during observation, the duration of monitoring was defined as the period between the initial evaluation and the final study day [30, 33].

#### *Assessment of covariables*

Covariables were chosen based on the clinical environment and prior studies [30, 33, 34]. The study covered characteristics such as age, sex, smoking status (never, current, and ever), drinking status (never, current, and ever), educational attainment (primary and below, primary school, middle school, and high school and above), area of residence (urban and rural), and marital status (married and other), which were collected from each participant in a face-to-face interview as previously described [30]. Standing height was measured by a standardized stadiometer, and weight was assessed on a validated scale. The formula for calculating body mass index (BMI) was weight (kg) divided by height squared ($m^2$). Using soft tape, the WC was measured to the nearest 0.1 cm. Using a digital sphygmomanometer, the systolic and diastolic blood pressures (SBP and DBP) were measured three times at least 45 s apart. Blood samples were also obtained from the participants, and they were asked to fasted overnight before blood sampling. However, blood samples were still collected if participants were not fasting. Data indicates that over 92% of participants were fasting at the time of blood collection. The blood analyses were performed in two stages. Full blood analysis was carried out at the local county health centre shortly after sampling. These blood samples were then safely transported via the cold chain to Beijing for in-depth analysis at the Chinese Centre for Disease Control and Prevention [35]. Laboratory examinations included platelet (PLT), blood urea nitrogen (BUN), FPG, serum creatinine (Scr), C-reactive protein (CRP), total cholesterol (TC), TG, haematocrit (HCT), haemoglobin concentration (HGB), serum high-density lipoprotein cholesterol (HDL-c), haemoglobin A1c (HBA1c), serum low-density lipoprotein cholesterol (LDL-c), uric acid (UA), and cystatin C levels. Chronic diseases included hypertension, dyslipidaemia,

DM, cancer or malignant tumours, chronic lung diseases, liver disease, heart attack and kidney disease. Hypertension was characterized as an SBP ≥ 140 mmHg and/or a DBP ≥ 90 mmHg or taking antihypertensive medication. The dyslipidaemia criteria included TC ≥ 240 mg/dl (to convert to millimoles/litre, multiply by 0.0259), TG ≥ 150 mg/dl, LDL-c ≥ 160 mg/dl, or HDL-c < 40 mg/dl. Additionally, the present usage of lipid-lowering medicine or a previous diagnosis of dyslipidaemia was considered. The diagnosis of DM is either based on an FPG ≥ 7.0 mmol/L or a physician-diagnosed condition. Other chronic disorders, including chronic lung disease, liver disease, heart attack, kidney disease and cancer, were identified via self-reported medical diagnosis or treatment for linked diseases or sequelae [36].

### Statistical analysis

Continuous data are provided by medians (interquartile ranges) or means (SDs, standard deviations), while categorical factors are displayed by percentages and frequencies. For determining distinctions among the TyG-WC groups, chi-squared tests, one-way ANOVAs, or Kruskal–Wallis tests were applied for categorical variables, normally distributed data, and data with a skewed distribution, respectively.

Cox proportional hazard modelling was utilized for assessing the relationship between TyG-WC score and stroke risk, and the hazard ratio (HR) and 95% confidence interval (CI) were determined. To account for the consequences of other potential confounding variables, three distinct models were developed for testing the connection of the TyG-WC score to stroke risk. The three models included Model 1 (not adjusted for covariables), Model 2 (adjusted for age, sex, BMI, smoking status, and drinking status), and Model 3 (adjusted for age, sex, BUN, HDL-c, LDL-c, CRP, Scr, BMI, smoking status, hypertension, DM, HBA1C, UA, drinking status, cystatin C and kidney disease).

The dose–response effect between the TyG-WC and stroke was evaluated by an additive Cox proportional hazard model and fitting curve (penalized spline method) [37]. A two-piece-wise Cox proportional hazard model was then used to examine the threshold effect of the TyG-WC on stroke. The turning point for the TyG-WC was determined by "exploratory" analyses, which was to move the trial turning point along the pre-defined interval and pick up the one which gave maximum model likelihood. A log-likelihood ratio test was also performed and compared the one-line Cox proportional hazard model with the two-piece-wise Cox proportional hazard model. The 95% CI for the turning point was calculated by the bootstrap resampling method [38, 39]. Cox proportional hazard models were used to independently analyse subgroups based on age, sex, DM status, smoking status, and drinking habits to stratify the data. Besides the stratification parameters, age, hypertension, DM, kidney disease, drinking status, BMI, BUN, HDL-c, HBA1C, UA, LDL-c, CRP, Scr, cystatin C, sex, and smoking status were adjusted. The likelihood ratio test was applied for interaction analysis.

The study's robustness was evaluated through several sensitivity analyses. The TyG-WC was categorized to evaluate stroke risk concurrently within specific population groups. Dummy variables were employed to address missing covariable values exceeding 20%. Finally, to determine the potential impact of unmeasured covariables, the E value was estimated [40].

Statistical analyses were carried out with R (version 4.2) and EmpowerStats (version 4.2). *P* values below 0.05 (two-sided) were regarded as statistical significance.

## Results

### Characteristics of the participants

The study ultimately included 9054 participants for analysis. The average (SD) age at baseline was 59.15 (9.53), the mean (SD) WC was 84.16 (12.48) cm, the mean (SD) TyG was 8.68 (0.67), and the average (SD) TyG-WC was 732.84 (135.59). Table 1 provides the baseline attributes of the entire study stratified by TyG-WC quartiles. The results indicated that the proportions of women, nonsmokers, urban residents, those with a junior high school education or above, and individuals suffering from hypertension, DM, or heart problems increased with the increase in TyG-WC. TyG, FPG, TC, TG, LDL-c, HBA1C, UA, HCT, and HGB were all significantly greater when TyG-WC increased, but BUN and HDL-c decreased.

### Newly onset stroke risk in individuals in the different models

The mean (SD) follow-up duration was 6.46 (1.46) years. Throughout this period, 463 newly onset strokes occurred, resulting in a 5.11% incidence of new strokes. As illustrated in Table 1, the incidence of stroke notably increased as the TyG-WC increased. Across the four TyG-WC subgroups (≤ 649.54, 649.54–724.71, 724.86–815.06, and ≥ 815.07, 76 (3.36%), 100 (4.42%), 124 (5.48%), and 163 (7.20%) strokes occurred, respectively.

### Unadjusted associations between baseline variables and stroke incidence

Table S1(Additional file 1) shows the outcomes of the univariable analysis, revealing associations between stroke risk and various factors. Positive associations were observed with age, marital status, smoking history, weight, WC, Scr, TC, TG, BMI, SBP, DBP, HBA1C, UA, the TyG index, the TyG-WC index, FPG, CRP,

**Table 1** Baseline characteristics and stroke incidence

| Variables | All participants | TyG-WC quartile | | | | |
|---|---|---|---|---|---|---|
| | | Q1 (≤649.54) | Q2 (649.54–724.71) | Q3 (724.86–815.06) | Q4 (≥815.07) | *P* value |
| N | 9054 | 2264 | 2263 | 2263 | 2264 | |
| Age (year, mean ± SD) | 59.15 ± 9.53 | 59.32 ± 9.95 | 59.19 ± 9.58 | 58.93 ± 9.48 | 59.16 ± 9.10 | 0.564 |
| Height (cm, mean ± SD) | 157.91 ± 8.51 | 156.91 ± 8.42 | 157.73 ± 8.49 | 157.96 ± 8.34 | 159.06 ± 8.63 | < 0.001 |
| Weight (kg, mean ± SD) | 58.75 ± 11.51 | 50.47 ± 8.84 | 55.31 ± 8.16 | 60.35 ± 9.01 | 68.91 ± 10.87 | < 0.001 |
| Waist circumference (cm, mean ± SD) | 84.16 ± 12.48 | 70.57 ± 12.79 | 81.35 ± 4.47 | 87.88 ± 4.82 | 96.85 ± 7.01 | < 0.001 |
| Body mass index (kg/m$^2$, mean ± SD) | 23.50 ± 3.88 | 20.44 ± 2.75 | 22.21 ± 2.59 | 24.18 ± 2.96 | 27.19 ± 3.48 | < 0.001 |
| Systolic blood pressure (mmHg, mean ± SD) | 132.41 ± 22.55 | 126.56 ± 21.54 | 129.82 ± 22.08 | 133.57 ± 21.93 | 139.72 ± 22.52 | < 0.001 |
| Diastolic blood pressure (mmHg, mean ± SD) | 76.60 ± 12.82 | 73.04 ± 12.48 | 75.15 ± 12.63 | 77.08 ± 12.21 | 81.13 ± 12.57 | < 0.001 |
| TyG (mean ± SD) | 8.68 ± 0.67 | 8.19 ± 0.45 | 8.46 ± 0.44 | 8.76 ± 0.47 | 9.33 ± 0.70 | < 0.001 |
| TyG-WC (mean ± SD) | 732.84 ± 135.59 | 575.13 ± 99.66 | 686.71 ± 21.80 | 767.94 ± 25.84 | 901.56 ± 75.81 | < 0.001 |
| PLT (10^9/L, mean ± SD) | 211.31 ± 72.94 | 210.52 ± 73.68 | 209.82 ± 71.37 | 210.03 ± 75.65 | 214.87 ± 70.90 | 0.067 |
| BUN (mmol/L, mean ± SD) | 15.71 ± 4.49 | 16.00 ± 4.60 | 15.87 ± 4.69 | 15.52 ± 4.34 | 15.45 ± 4.30 | < 0.001 |
| FPG (mg/L, mean ± SD) | 109.94 ± 36.34 | 98.93 ± 19.09 | 103.23 ± 22.48 | 108.95 ± 28.31 | 128.65 ± 55.63 | < 0.001 |
| Scr (mg/dL, median, quartile) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 0.512 |
| TC (mg/dL, mean ± SD) | 193.52 ± 38.82 | 183.44 ± 35.53 | 189.76 ± 36.04 | 195.33 ± 36.62 | 205.55 ± 43.19 | < 0.001 |
| TG (mg/dL, median, quartile) | 105.00 (74.00–154.00) | 72.00 (57.00–94.00) | 91.00 (72.00–120.00) | 117.00 (89.00–156.00) | 174.00 (126.75–253.00) | < 0.001 |
| HDL-c (mg/dL, mean ± SD) | 51.30 ± 15.27 | 59.67 ± 15.42 | 54.88 ± 14.49 | 49.04 ± 12.88 | 41.62 ± 11.76 | < 0.001 |
| LDL-c (mg/dL, mean ± SD) | 116.29 ± 35.03 | 109.84 ± 30.83 | 116.22 ± 31.97 | 120.97 ± 33.79 | 118.12 ± 41.61 | < 0.001 |
| CRP (mg/L, median, quartile) | 1.00 (1.00–2.00) | 1.00 (0.00–2.00) | 1.00 (0.00–2.00) | 1.00 (1.00–2.00) | 1.00 (1.00–3.00) | 0.061 |
| HBA1C (%, median, quartile) | 5.00 (5.00–5.00) | 5.00 (5.00–5.00) | 5.00 (5.00–5.00) | 5.00 (5.00–5.00) | 5.00 (5.00–6.00) | < 0.001 |
| UA (mg/dL, mean ± SD) | 4.43 ± 1.28 | 4.215 ± 1.204 | 4.292 ± 1.224 | 4.443 ± 1.280 | 4.785 ± 1.327 | < 0.001 |
| HCT (%, mean ± SD) | 46.45 ± 6.23 | 40.51 ± 6.09 | 41.18 ± 6.37 | 41.47 ± 6.07 | 42.64 ± 6.19 | < 0.001 |
| HGB (g/L, mean ± SD) | 14.40 ± 2.22 | 14.01 ± 2.18 | 14.27 ± 2.14 | 14.48 ± 2.21 | 14.85 ± 2.28 | < 0.001 |
| Cystatin C (mg, median, quartile) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 0.051 |
| Sex (N, %) | | | | | | < 0.001 |
| Male | 4102 (45.34) | 1141 (50.44) | 1078 (47.68) | 943 (41.69) | 940 (41.56) | |
| Female | 4945 (54.66) | 1121 (49.56) | 1183 (52.32) | 1319 (58.31) | 1322 (58.44) | |
| Area of residence (N, %) | | | | | | < 0.001 |
| Rural | 7536 (83.23) | 2010 (88.78) | 1961 (86.66) | 1822 (80.51) | 1743 (76.99) | |
| Urban | 1472 (16.26) | 248 (10.95) | 294 (12.99) | 429 (18.96) | 501 (22.13) | |
| Rural missing | 46 (0.51) | 6 (0.27) | 8 (0.35) | 12 (0.53) | 20 (0.88) | |
| Educational attainment (N, %) | | | | | | < 0.001 |
| Primary and below | 6363 (70.29) | 1659 (73.31) | 1617 (71.49) | 1569 (69.33) | 1518 (67.05) | |
| Middle school | 1801 (19.90) | 406 (17.94) | 435 (19.23) | 462 (20.42) | 498 (21.10) | |
| High school and above | 888 (9.81) | 198 (8.75) | 210 (9.28) | 232 (10.25) | 248 (10.95) | |
| Marital status (N, %) | | | | | | 0.070 |
| Married | 7973 (88.06) | 1964 (86.75) | 1989 (87.89) | 1999 (88.33) | 2021 (89.27) | |
| Other | 1081 (11.94) | 300 (13.25) | 274 (12.11) | 264 (11.67) | 243 (10.73) | |

**Table 1** (continued)

| Variables | All participants | TyG-WC quartile | | | | |
|---|---|---|---|---|---|---|
| | | Q1 (≤649.54) | Q2 (649.54–724.71) | Q3 (724.86–815.06) | Q4 (≥815.07) | *P* value |
| Smoking status (N, %) | | | | | | < 0.001 |
| Never | 5579 (61.67) | 1273 (56.30) | 1363 (60.28) | 1459 (64.53) | 1484 (65.55) | |
| Current | 2711 (29.97) | 835 (36.93) | 733 (32.42) | 602 (26.63) | 541 (23.90) | |
| Ever | 757 (8.37) | 153 (6.77) | 165 (7.30) | 200 (8.85) | 239 (10.56) | |
| Drinking status (N, %) | | | | | | < 0.001 |
| Current | 2233 (24.68) | 623 (27.54) | 578 (25.56) | 504 (22.29) | 528 (23.32) | |
| Ever | 707 (7.81) | 190 (8.40) | 182 (8.05) | 173 (7.65) | 162 (7.16) | |
| Never | 6108 (67.51) | 1449 (64.06) | 1501 (66.39) | 1584 (70.06) | 1574 (69.52) | |
| Hypertension (N, %) | | | | | | < 0.001 |
| No | 6916 (76.92) | 1974 (87.85) | 1872 (83.42) | 1712 (76.09) | 1358 (60.36) | |
| Yes | 2075 (23.08) | 273 (12.15) | 372 (16.58) | 538 (23.91) | 892 (39.64) | |
| Dyslipidaemia (N, %) | | | | | | < 0.001 |
| No | 8090 (91.41) | 2134 (96.39) | 2105 (95.03) | 2018 (91.19) | 1833 (83.02) | |
| Yes | 760 (8.59) | 80 (3.61) | 110 (4.97) | 195 (8.81) | 375 (16.98) | |
| DM (N, %) | | | | | | < 0.001 |
| No | 8473 (94.67) | 2197 (98.26) | 2178 (97.23) | 2122 (94.82) | 1976 (88.37) | |
| Yes | 477 (5.33) | 39 (1.74) | 62 (2.77) | 116 (5.18) | 260 (11.63) | |
| Cancer or Malignant Tumour (N, %) | | | | | | 0.702 |
| No | 8916 (99.03) | 2228 (98.89) | 2226 (99.15) | 2235 (99.16) | 2227 (98.93) | |
| Yes | 87 (0.97) | 25 (1.11) | 19 (0.85) | 19 (0.84) | 24 (1.07) | |
| Chronic Lung Disease (N, %) | | | | | | 0.007 |
| No | 8078 (89.70) | 1985 (88.14) | 2004 (89.15) | 2046 (90.89) | 2043 (90.60) | |
| Yes | 928 (10.30) | 267 (11.86) | 244 (10.85) | 205 (9.11) | 212 (9.40) | |
| Liver Disease (N, %) | | | | | | 0.260 |
| No | 8617 (96.01) | 2161 (96.09) | 2146 (95.89) | 2166 (96.61) | 2144 (95.46) | |
| Yes | 358 (3.99) | 88 (3.91) | 92 (4.11) | 76 (3.39) | 102 (4.54) | |
| Heart Problems (N, %) | | | | | | < 0.001 |
| No | 7980 (88.72) | 2058 (91.30) | 2022 (90.15) | 2012 (89.50) | 1888 (83.91) | |
| Yes | 1015 (11.28) | 196 (8.70) | 221 (9.85) | 236 (10.50) | 362 (16.09) | |
| Kidney Disease (N, %) | | | | | | 0.073 |
| No | 8398 (93.43) | 2075 (92.35) | 2091 (93.31) | 2116 (93.96) | 2116 (94.09) | |
| Yes | 591 (6.58) | 172 (7.66) | 150 (6.69) | 136 (6.04) | 133 (5.91) | |
| Stroke (N, %) | | | | | | < 0.001 |
| No | 8591 (94.89) | 2188(96.64) | 2163(95.58) | 2139(94.52) | 2101(92.80) | |
| Yes | 463 (5.11) | 76(3.36) | 100(4.42) | 124(5.48) | 163(7.20) | |

The data are expressed as the mean ± SD, median (25th-75th percentile), or percentage.

Among the 9054 participants, the numbers of missing values for the covariables were 7 (0.08%) for sex, 2 (0.02%) for educational attainment, 7 (0.08%) for smoking status, 6 (0.07%) for drinking status, 4 (0.04%) for Scr, 66 (0.73%) for HBA1C, 2203 (24.33%) for cystatin C, 63 (0.7%) for hypertension, 204 (2.25%) for dyslipidaemia, 104 (1.15%) for DM, 51 (0.56%) for cancer or malignant tumours, 48 (0.53%) for chronic lung disease, 79 (0.87%) for liver disease, 59 (0.65%) for heart problems, and 65 (0.72%) for kidney disease.

*Abbreviations*: *SD* standard deviation, *N* number, *TyG* triglyceride glucose, *TyG-WC* triglyceride glucose waist circumference, *PLT* platelet, *BUN* blood urea nitrogen, *FPG* fasting plasma glucose, *Scr* serum creatinine, *TC* total cholesterol, *TG* triglycerides, *HDL-c* high-density lipoprotein cholesterol, *HBA1C* haemoglobin A1c, *UA* uric acid, *HCT* haematocrit, *HGB* haemoglobin concentration, *LDL-c* low-density lipoprotein cholesterol, *DM* diabetes mellitus, *CRP* C-reactive protein.

hypertension, dyslipidaemia, DM, liver disease, and heart problems ($P < 0.05$). Conversely, a negative association existed with HDL-c ($P < 0.05$). No significant connections among stroke risk and sex, area of residence, drinking status, PLT, BUN, LDL-c, HCT, HGB, cystatin C, cancer

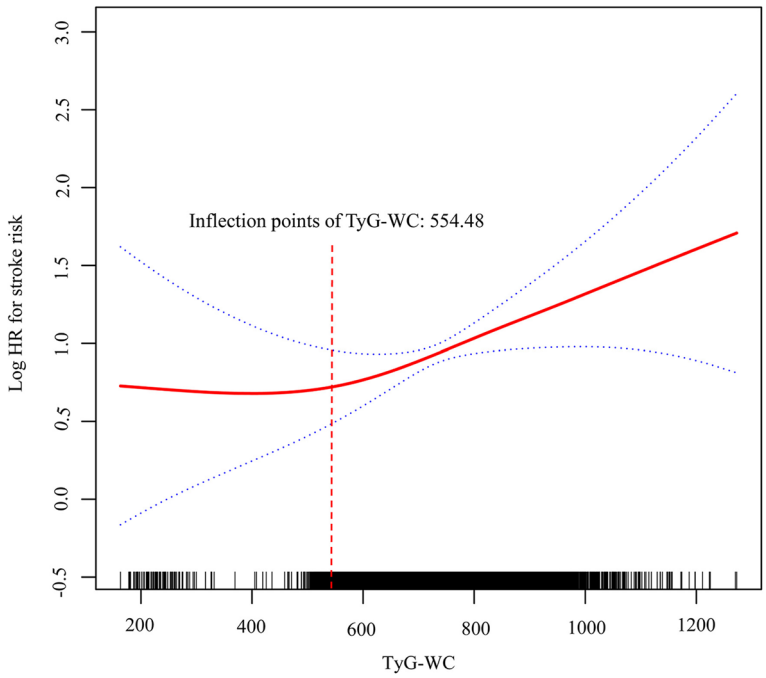


**Fig. 2** Generalized additive models demonstrate the relationship between TyG-WC and stroke risk, controlled for age, sex, HBA1C, UA, cystatin C, smoking status, drinking status, BMI, BUN, kidney disease, LDL-c, CRP, Scr, hypertension, DM, and HDL-c. The resulting figures show the predicted log (relative risk) on the y-axis and the TyG-WC on the x-axis

**Table 2** The results of the nonlinear relationship between TyG-WC and stroke risk using threshold effect analysis

| TyG-WC | Per-unit increase | | Per-SD increase | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Inflexion points | 554.48 | | -1.32 | |
| < 554.48 | 0.998 (0.995, 1.001) | 0.118 | 0.759 (0.538, 1.073) | 0.119 |
| > 554.48 | 1.002 (1.001, 1.003) | 0.003 | 1.323 (1.098, 1.594) | 0.003 |

Adjusted for age, sex, UA, cystatin C, smoking status, drinking status, hypertension, BMI, BUN, LDL-c, CRP, Scr, HBA1C, DM, HDL-c, and kidney disease

or malignant tumours, chronic lung diseases, or kidney disease ($P > 0.05$).

### Identifying the nonlinear relationship of the TyG-WC and stroke status

Generalized additive models (Fig. 2) were used to visually assess functional relationships between the TyG-WC and the risk of stroke. After correcting for latent variables, a nonlinear connection among the TyG-WC score and stroke risk was revealed ($P = 0.023$ for the log-likelihood ratio test). The inflection point of TyG-WC was identified by applying a recursive algorithm, which yielded a value of 554.48. As demonstrated in Table 2, an increase in the SD of the TyG-WC (135.586) above the turning point was related to a 32.3% elevation of stroke risk (HR = 1.323, 95% CI = 1.098- 1.594; $P = 0.003$). Nevertheless, below the inflection point, the association between TyG-WC score with stroke risk lacked significance (HR = 0.759, 95% CI = 0.538–1.073, $P = 0.119$).

### Subgroup analysis

Table S2(Additional file 1) shows the analysis of TyG-WC and stroke risk stratified by age, sex, smoking status, drinking status, and DM. Adjustments for age, sex, BMI, BUN, HDL-c, Scr, LDL-c, CRP, HBA1C, UA, smoking status, cystatin C, hypertension, DM, drinking status, and kidney disease were made. No significant interaction was observed with the TyG-WC quartiles, indicating a consistent association across subgroups.

### Sensitivity analysis

To confirm the findings, several sensitive assessments were performed by utilizing a range of methodologies. The tendency in the sensitivity analysis matches the pattern in the main analysis. First, the TyG-WC was split into quartiles, and the transformed categorical variables were reintroduced into the regression model. As demonstrated in Table 3, the effect size intervals were consistent across groups. Even after controlling for confounding variables, TyG-WC as a categorical variable

**Table 3** Relationships between TyG-WC and stroke risk according to various models

| Exposure | Model 1<br>HR (95% CI) *P* value | Model 2<br>HR (95% CI) *P* value | Model 3<br>HR (95% CI) *P* value |
|---|---|---|---|
| TyG-WC (per 20 units) | 1.044 (1.030, 1.058) < 0.001 | 1.037 (1.019, 1.056) < 0.001 | 1.022 (0.999, 1.046) 0.058 |
| TyG-WC quartile | | | |
| Q1(≤ 649.54) | Ref | Ref | Ref |
| Q2(649.54–724.71) | 1.327 (0.985, 1.788) 0.063 | 1.272 (0.939 1.723) 0.123 | 1.381 (0.921, 1.886) 0.131 |
| Q3(724.86–815.06) | 1.654 (1.243, 2.201) < 0.001 | 1.535 (1.130, 2.085) 0.006 | 1.534 (1.059, 2.221) 0.024 |
| Q4(≥ 815.07) | 2.169 (1.652, 2.848) < 0.001 | 1.900 (1.361, 2.652) < 0.001 | 1.711 (1.111, 2.635) 0.015 |

Model 1: unadjusted;

Model 2: adjusted for age, sex, smoking status, drinking status, and BMI;

Model 3: adjusted for age, sex, smoking status, drinking status, BMI, BUN, HDL-c, LDL-c, CRP, Scr, HBA1C, UA, cystatin C, hypertension, DM, and kidney disease

was substantially and positively linked with stroke risk in the Q3 quartile ($P=0.024$, HR = 1.534, 95% CI = 1.059–2.221), and the same result was obtained in the Q4 quartile ($P=0.015$, HR = 1.711, 95% CI = 1.111–2.635). Moreover, the present research validated the association of TyG-WC and stroke risk focusing on particular populations and correcting for various covariables (Additional file 1: Table S3), and results similar to those described above were observed. In this study, the analysis of threshold effects was repeated after treating indicators with more than 20% missing covariables by adding dummy variables. The results demonstrated the stability of the findings, indicating that they were not affected by the missing data (Additional file 1: Table S4). Finally, the E-value was estimated to gauge the impact from undetected variables, verifying the robustness of the core findings unless an unmeasured confounder of the HR above 1.17 existed.

## Discussion

This research sought to explore the connection of the TyG-WC score and stroke risk through a longitudinal analysis that utilized the CHARLS database. A relationship was identified between increased TyG-WC and a greater likelihood of experiencing stroke. Furthermore, an inflection point was found, along with a significant link between TyG-WC and stroke on one side. Notably, the study pinpointed an inflection point at which this association becomes particularly significant, marking a novel discovery in the realm of stroke research.

The TyG index is considered a cheap and reliable alternative biochemical marker to the classic methods for assessing insulin resistance [16, 17, 41], because it is strongly correlated with cardiovascular disease [42–44]. Furthermore, the TyG index exhibits a consistent connection with stroke incidence and adverse consequences [31, 45, 46]. A Chinese cohort study indicated that the TyG index was an independent risk factor for stroke [19]. According to a study conducted by the UK Biobank, every additional unit in the TyG increases the ischaemic stroke risk by 22% (OR = 1.22, 95% CI = 1.16–1.29) [47]. In the present study, Cox proportional hazard model revealed a positive relationship with the TyG index and stroke risk. Obesity remains an alarming risk contributing to stroke [6], and BMI is a frequently used metric for general obesity [48]. Nevertheless, the BMI cannot assess adipose tissue distribution throughout the body [49]. The measurement of WC is gaining attention as an indicator of abdominal obesity. Studies have revealed a significant connection between WC and stroke risk [50, 51]. The TyG-WC index is a composite measure consisting of the TyG index and WC. This combined assessment is a more accurate method of assessing insulin resistance than a single assessment [52]. The association between TyG and obesity with heightened stroke risk underscores a critical hypothesis: TyG-WC can predict stroke risk. Nevertheless, studies evaluating the relationship between TyG-WC and stroke risk are scarce, and only two studies have focused on this association. A longitudinal investigation with a two-year monitoring period [29] conducted in Hunan Province, China, demonstrated that the probability of stroke increased with each standard deviation of the TyG-WC, with an adjusted hazard ratio of 1.23 (95% CI = 1.04–1.46). Another study from Korea [27] reported a substantial association between cardiovascular disease and the TyG-WC, with a notable HR for stroke of 1.75 (95% CI = 1.13–2.70). In contrast with previous studies, the population of this study covers 28 provinces in China and constitutes a more representative sample. This study's findings also supported that the TyG-WC is beneficially linked to stroke risk. In sensitivity analyses, this study examined individuals without diabetes, hypertension, renal disease, or with a BMI ≤ 24 kg/m$^2$. The findings demonstrated the previously observed relationship. Furthermore, subgroup analyses categorized by age, sex, smoking status, alcohol consumption status, and diabetes

status demonstrated the robustness of the findings. No significant interactions between these factors were identified. In Huang's study [29], however, the TyG-WC was found to interact with age and smoking in terms of stroke risk. Population variations contributed to the observed discrepancy. Variations in covariable adjustment exist; however, this study adjusted for a broader spectrum of covariables.

In addition, it was an initial study to identify a nonlinear association between the TyG-WC and stroke risk, pinpointing an inflection point for TyG-WC at 554.48; when the TyG-WC > 554.48, the adjusted HR value was 1.323 (95% CI = 1.098–1.594, $P = 0.003$). That indicates when the TyG-WC > 554.48, each increase in the standard deviation of TyG-WC is associated with a significant increase in stroke risk of 32.3%. Below the inflection point, stroke risk did not change significantly, even with increased TyG-WC levels. Further analyses (Additional file 1: Table S5) revealed that patients with a TyG-WC > 554.48 had increased TC, TG, LDL-c, and UA values, but lower HDL-c levels. Participants whose TyG-WC was > 554.48 had elevated risks of hypertension, diabetes, and chronic lung disease. However, similar age, PLT, BUN, CRP, and cystatin C levels were observed in participants with a TyG-WC ≤ 554.48 compared to those with a TyG-WC > 554.48, with no significant differences among the groups. These indicators are strongly linked to stroke risk [53–58]. Given these variables, TyG-WC had a comparatively small effect on stroke risk when the TyG-WC was ≤ 554.48, but a considerably greater effect when the TyG-WC was > 554.48. The nonlinear association of the TyG-WC and stroke risk could be explained via that. Despite revealing a dose–response connection between cardiovascular disease and TyG-WC in a Korean cohort study [27], stroke incidence was not analysed in detail, and no threshold effect analysis was performed. In a cross-sectional study across the United States [20], a putative nonlinear relationship between the TyG-WC and overall cardiovascular disease was explored, which reported a linear relationship. Furthermore, this previous study did not assess or evaluate any connection among stroke and the TyG-WC independently, limiting its applicability to stroke risk assessment. The current study offers a comprehensive analysis of the TyG-WC-stroke link, with benefits for stroke prevention. This study found that when the level of TyG-WC increased, especially after increasing to a certain level, the risk of stroke also increased significantly. A curvilinear relationship existed between TyG-WC and stroke and inflection points were found. This inflection point may help healthcare professionals better assess a patient's stroke risk and identify those at high risk. It may be possible to reduce the incidence of stroke by identifying a patient's TyG-WC level and taking preventive measures or early intervention if it remains elevated. In patients with known risk factors for insulin resistance or abdominal obesity, TyG-WC levels should be monitored more frequently and accurately. Those at high risk should be encouraged to change poor lifestyle habits, such as modifying their diet, quitting smoking, limiting alcohol consumption, and increasing physical activity to help lower their TyG-WC levels. For patients who cannot effectively reduce TyG-WC through lifestyle modifications, pharmacological interventions, such as lipid-lowering drugs and insulin sensitizers, may be considered as adjunctive therapy. The management of other risk factors, including DM and hypertension, can also be achieved through an integrated approach in high-risk groups. It is recommended that nursing staff reinforce the importance of regular follow-up for high-risk groups to monitor changes in TyG-WC and adjust preventive and control measures in real time. By informing patients of the elevated risk of stroke associated with TyG-WC levels exceeding a certain threshold, it is possible to enhance their engagement and compliance with self-management strategies for health promotion. Additionally, patients should be provided with psychological support and guidance on behavioural change to help them maintain an active lifestyle, reduce the incidence of stroke and improve their health prognosis. Public awareness of medical knowledge, such as stroke recognition and emergency procedures, should also be increased, urging people to seek prompt medical attention if they experience stroke-related symptoms.

#### Strengths and limitations of the study

This research has various merits. First, it offers significant improvements in the treatment of nonlinear relationships compared to previous studies. This study initially identified a nonlinear relationship among the TyG-WC score and stroke risk, including a threshold value that significantly predicts risk. In addition, employing multiple sensitivity analyses ensured the stability of the findings. Second, this study tested the relationship of TyG-WC and stroke risk using both categorical and continuous variables, an approach that helps to reduce information loss and accurately quantify the indicators. Third, the integration of dummy variables for missing covariables not only improves the statistical analysis but also minimizes the effects of bias due to missing covariable data. Finally, the findings were strengthened by applying E-values to measure the impact of putative unmeasured covariables.

However, this investigation also had several notable limitations. First, this study was carried out among middle-aged and senior Chinese individuals; hence, its applicability to other ethnic populations cannot be guaranteed. Future international collaborative studies should

investigate whether such associations exist in other populations. Second, due to the observational nature of the study's methodology, certain other factors associated with stroke, such as medication use, were absent in the original database. Consequently, the potential role of unmeasured or unadjusted variables remained despite adjustment for potential confounding variables. Nevertheless, the E-value was generated for determining the possible effect of unmeasured confounders, indicating minimal impact on outcomes. Third, less than approximately 8% of participants in the complete raw data did not fast at the time of blood collection. Fourth, a self-report format was used to collect data on stroke. Fifth, despite the cohort design of this study, there was loss to follow-up. By analysing the characteristics of participants in the lost-to-follow-up group and the included group (Additional file 1: Table S8), the results showed that participants in the lost-to-follow-up group were younger and had lower levels of TyG-WC than those in the included group. This potential error may bias the null value [59], leading to an underestimation of the association between TyG-WC and stroke. However, the results of this study showed a non-linear association between TyG-WC and stroke. It is considered that loss to follow-up may not affect the main findings of this study. In summary, the available data are insufficient to draw firm causal conclusions, and more evidence on the link between the TyG-WC and stroke risk is needed.

## Conclusion

The present investigation revealed that the TyG-WC and stroke risk existed with a nonlinear relationship among middle-aged and senior Chinese. A further increase in TyG-WC was significantly related to higher stroke risk among individuals who had a TyG-WC greater than 554.48. The findings from this research broaden the theoretical foundation for stroke prevention screening and health education.

### Abbreviations

| | |
|---|---|
| TyG | Triglyceride glucose |
| WC | Waist circumference |
| TyG-WC | Triglyceride glucose waist circumference |
| PLT | Platelet |
| BUN | Blood urea nitrogen |
| FPG | Fasting plasma glucose |
| Scr | Serum creatinine |
| TC | Total cholesterol |
| TG | Triglycerides |
| HDL-c | High-density lipoprotein cholesterol |
| LDL-c | Low-density lipoprotein cholesterol |
| CRP | C-reactive protein |
| HBA1C | Haemoglobin A1c |
| UA | Uric acid |
| HCT | Haematocrit |
| HGB | Haemoglobin concentration |
| DM | Diabetes mellitus |
| SD | Standard deviation |
| N | Number |
| Ref | Reference |
| CI | Confidence interval |
| HR | Hazard ratio |
| OR | Odds ratio |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02259-x.

Additional file 1. Table S1. Unadjusted associations between baseline variables and stroke risk. Table S2. Stratified associations between the TyG-WC and stroke incidence. Table S3. Relationships between the TyG-WC and stroke risk across multiple sensitivity analyses. Table S4. Threshold effect analysis of TyG-WC and stroke risk after dealing with missing covariable values. Table S5. The baseline characteristics of participants on both sides of the inflection point. Table S6. Collinearity screening. Table S7 Baseline characteristics between participants included and excluded. Table S8. Baseline characteristics of the lost and included groups followed for less than 9 years.

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### Authors' contributions

Conceptualization: HY and XXH; Methodology: HY and XXH; Statistical analysis: HY and GMF; Writing—original draft preparation: HY, GMF, HML, and BY; Writing—review and editing: HY, LZH, HSD, CSM, DLP, and XSY; Funding acquisition: XXH and HY; Resources: XXH; Supervision: XXH. All authors participated in the revisions and approved the final version of the manuscript.

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### Availability of data and materials

The data analysed in this study are available from the Institute of Social Science Survey at Peking University, Beijing, China. (http://charls.pku.edu.cn).

## Declarations

### Ethics approval and consent to participate

The CHARLS study protocol received approval from the Peking University Ethics Review Committee (IRB00001052-11015), Beijing, China. Written informed consent was obtained from all participants.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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