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Triglyceride–Glucose Index Combined with Frailty Index and Incident Stroke in Older Chinese Adults with Arthritis: A Prospective Cohort Study

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Abstract

Introduction: Conventional stroke risk models inadequately capture metabolic and biological vulnerability in aging populations with chronic inflammatory conditions. This study examined whether the triglyceride–glucose–frailty index (TyGFI), integrating insulin resistance and deficit accumulation, predicts incident stroke in Chinese adults with arthritis.

Methods: We analyzed 3,649 participants aged ≥ 45 years with physician-diagnosed arthritis and no prior stroke from the China Health and Retirement Longitudinal Study (2011–2020), followed for a median of 9 years. TyGFI was calculated as the product of the triglyceride–glucose index and a 40-item frailty index. Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs), with sequential adjustment for demographics, lifestyle, and body mass index (BMI). Nonlinearity was assessed using restricted cubic splines.

Results: During follow-up, 398 participants (10.9%) developed incident stroke. Each 1-standard deviation increase in TyGFI was associated with a 33% higher stroke risk (HR 1.33, 95% CI 1.22–1.47). A significant nonlinear relationship was observed (P = 0.001), with a steeper risk increase below TyGFI = 54.62 (HR 2.44, 95% CI 1.64–3.62) than above it (HR 1.18, 95% CI 1.04–1.34). Compared with the lowest tertile, the highest tertile showed a 2.15-fold higher risk (95% CI 1.63–2.82). Associations remained robust in sensitivity analyses.

Conclusion: Higher TyGFI was independently associated with increased incident stroke risk in Chinese adults with arthritis, exhibiting a nonlinear dose–response relationship with a pronounced threshold effect. TyGFI may serve as a practical, low-cost composite biomarker for stroke risk stratification in aging populations with chronic inflammatory conditions.

Introduction

Stroke remains a major public health challenge, ranking among the leading causes of mortality and disability worldwide. Globally, estimates indicated 93.8 million (95% UI 89.0–99.3 million) prevalent cases and 11.9 million (95% UI 10.7–13.2 million) incident strokes in 2021[1]. In China, stroke is the leading cause of death, with approximately 3.4 million new cases annually[2]. Traditional stroke risk factors (e.g. hypertension, smoking, diabetes, dyslipidemia) explain a large proportion of stroke incidence but not all. This gap highlights the need to identify additional contributors to stroke risk, particularly in aging populations with complex comorbidities.

Frailty is an age-related clinical syndrome characterized by diminished strength, endurance, and resilience to stressors[3]. It is prevalent in older adults – roughly 10% of community-dwelling seniors are frail, and between one-quarter to one-half of people over 85 years old are frail[4]. Frailty increases the risk of adverse outcomes including falls, disability, hospitalization, cardiovascular events, and mortality. Two major models describe frailty: the frailty phenotype proposed by Fried et al. (weight loss, weakness, exhaustion, slowness, low activity) which identifies frail individuals by clinical criteria[5], and the

cumulative deficit model by Rockwood and colleagues, which quantifies frailty as a Frailty Index (FI) based on the proportion of age-related health deficits a person has accumulated[3]. The FI approach, initially formulated by Mitnitski et al., treats frailty as a quantitative trait reflecting biological age[6]. In practice, FIs are constructed following standardized protocols (e.g. a 10-step procedure by Theou et al. [7]) to ensure consistent deficit selection and scoring. Frailty has emerged as a significant independent risk factor for incident stroke and is consistently associated with adverse post-stroke outcomes, including prolonged hospitalisation, functional decline and mortality[8]. Notably, a recent nationally representative analysis demonstrated that each 0.1-unit increment in the frailty index was associated with a 2.90-fold (NHANES) and 1.78-fold (CHARLS) increase in the odds of stroke, respectively[9]. Given its impact on health, frailty is increasingly recognized as an important factor in risk stratification for older adults.

Another emerging risk marker is the triglyceride–glucose index (TyG index), calculated from fasting triglyceride and glucose levels. TyG index is a simple, low-cost surrogate for insulin resistance, correlating strongly with the gold-standard euglycemic clamp measure[10]. Elevated TyG index has been linked to metabolic disorders and atherosclerotic diseases including type 2 diabetes, hypertension, coronary disease, and carotid atherosclerosis[11]. Importantly, several studies indicate that a higher TyG index is associated with increased stroke risk[12]. For example, a large 11-year Chinese cohort (n ≈ 95,000) reported a 1.32-fold greater risk of stroke among individuals with higher TyG levels[13]. A nationwide study in Korea (5.59 million adults) similarly found that stroke incidence rose across TyG quartiles, with multivariable-adjusted hazard ratios (HRs) of 1.25 in the highest vs lowest quartile[14]. A 2023 meta-analysis (18 studies, 592,000 participants) confirmed that elevated TyG index is an independent risk factor for ischemic stroke (pooled OR 1.37 for highest vs lowest TyG)[12]. Notably, in a UK Biobank study of diabetics, each 1-SD increase in TyG was associated with 19% higher stroke risk (HR 1.19)[15]. These findings underscore insulin resistance as a contributor to cerebrovascular risk[16, 17].

Metabolic risk and frailty often coexist in older adults and may interact to heighten vascular risk[18]. Chronic inflammation, oxidative stress, and endothelial dysfunction are proposed mechanisms linking metabolic dysfunction and frailty to accelerated atherosclerosis[19]. However, conventional risk prediction models (e.g. Framingham Stroke Risk Profile) do not incorporate aging-related factors like frailty or inflammation[19, 20]. Recent work suggests combining metabolic and frailty indicators could improve risk stratification. In a 2025 analysis of Chinese and U.S. cohorts, Zhao et al. introduced the TyG–Frailty Index (TyGFI), multiplying TyG index by a frailty index, and found that higher TyGFI quartiles were associated with markedly increased odds of cardiovascular disease and stroke. In a pooled analysis of two prospective cohorts, the highest TyG-FI quartile was associated with a 12- to 21-fold increased risk of stroke compared with the lowest quartile across Chinese and US populations [21].

Chronic inflammatory conditions such as arthritis might amplify the combined metabolic and frailty risk. Patients with rheumatoid arthritis (RA) and related arthritic diseases face elevated risks of cardiovascular events and stroke (approximately 1.5-fold higher than the general population)[22–24],

likely mediated by systemic inflammation[25]. Older adults with arthritis often have pain, reduced physical activity, and systemic inflammation, which can contribute to frailty and metabolic disturbances. Therefore, this study focused on an arthritis population to investigate whether the TyG–Frailty Index could predict incident stroke.

We aimed to evaluate the association of TyGFI with the risk of first-ever stroke in a prospective cohort of middle-aged and older Chinese adults with arthritis, after adjusting for conventional risk factors. We also assessed the dose–response relationship (including potential nonlinearity) and the incremental value of TyGFI in risk stratification for stroke.

Methods

Study Population and Design

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative cohort of Chinese adults aged ≥ 45 years. The CHARLS collects extensive health, demographic, and socioeconomic data through biennial interviews[26]. We identified participants from the 2011 baseline survey who reported a physician's diagnosis of arthritis (including osteoarthritis or rheumatoid arthritis) and had no history of stroke[27]. We excluded individuals with self-reported stroke or transient ischemic attack at baseline (to capture first-ever stroke outcomes) and those with missing data on variables required for the TyGFI or covariates. Detailed procedures for data extraction from the cohort is depicted in the flowcharts (Fig. 1). All participants gave written informed consent. The original CHARLS study was approved by the Institutional Review Board of Peking University (IRB approval numbers: IRB00001052-11015 for the main household survey including anthropometrics, and IRB00001052-11014 for biomarker collection). This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guide lines[28].

The cohort was followed from baseline (2011) until the occurrence of stroke, loss to follow-up, death, or the end of available follow-up (August 2020), whichever came first. Incident stroke was ascertained via self-reports during follow-up waves (2013, 2015, 2018, and 2020) that a doctor had diagnosed a stroke since the last interview. Prior work supports the reasonable accuracy of self-reported stroke in similar aging studies[29]. Nonetheless, we performed sensitivity analyses excluding events in the first 2 years of follow-up to mitigate potential reverse causation (undiagnosed baseline strokes).

Triglyceride–Glucose (TyG) Index

Fasting blood samples in CHARLS were analyzed for triglycerides (TG) and plasma glucose at baseline. TyG index was calculated as ln([TG, mg/dL] × [glucose, mg/dL]/2)[30], a formula widely used and validated against insulin resistance measures[31]. We expressed TyG in absolute units (a higher TyG reflects greater insulin resistance).

Frailty Index (FI)

We constructed a frailty index following standard deficit-accumulation methodology[3, 32]. A frailty index is the proportion of a set of age-related health deficits (symptoms, signs, comorbidities, functional impairments) and is associated with stroke and poor outcomes[33, 34]. Using CHARLS baseline data, we included 40 variables covering multi-dimensional health domains (e.g. chronic diseases, functional status, cognition, mood) as deficits, consistent with published guidelines for FI construction[35]. Each variable was coded from 0 (no deficit) to 1 (deficit present), with intermediate values for partial impairment when appropriate; the FI was computed as the sum of deficit scores divided by the total number of deficits considered for each person. This approach has been shown to produce a reliable FI that increases with age and predicts adverse outcomes[9]. We ensured the FI did not include acute stroke or its direct manifestations, to avoid tautology in prediction.

TyG–Frailty Index (TyGFI)

We defined TyGFI as the product of the TyG index and the frailty index for each individual[21]. This composite measure is dimensionless and reflects the combined burden of metabolic and frailty-related risk. In effect, TyGFI gives higher values to individuals who have both high insulin resistance and high deficit accumulation (frailty). We treated TyGFI as a continuous exposure and also categorized it into tertiles (T1 = lowest, T3 = highest) based on the distribution in the cohort.

Covariates

We included covariates known to be associated with stroke risk or that could confound the TyGFI–stroke relationship. Demographic factors were age (years) and sex. Residential area was classified as urban or rural. Socioeconomic status was represented by annual household income level (tertiles). Lifestyle factors included smoking (never,current and ever) and alcohol drinking stutas(never,current and ever). We also adjusted for body mass index (BMI), categorized as < 18.5, 18.5–24.0, or ≥ 24.0 kg/m² (using Chinese criteria for underweight, normal weight and overweight). Hypertension, diabetes, and dyslipidemia were not directly adjusted for in primary models because TyG and frailty components partly capture these conditions. All covariate information was obtained at baseline through structured questionnaires, physical measurements, and lab tests in CHARLS[36].

Statistical Analysis

Continuous variables were presented as means±standard deviations (SD), and categorical variables as counts and percentages. Diferences between groups for continuous data were tested by one-way ANOVA. Differences between groups for propor-tions were tested using Chi-square.

Cox proportional hazards regression was used to estimate hazard ratios for incident stroke associated with TyGFI. For continuous TyGFI, we reported HRs per 1–SD increase to facilitate comparison with other studies[21]. We built three models: Model 1 was unadjusted; Model 2 added age, sex, residence area and

income level; Model 3 additionally adjusted for BMI category, smoking and drinking status. Proportional hazards assumptions were checked using Schoenfeld residuals; no significant violations were observed.

We investigated the dose–response relationship using restricted cubic spline functions of TyGFI in the Cox model (with three knots at the 5th, 50th, and 95th percentiles of TyGFI). We tested for nonlinearity with a likelihood ratio test comparing the spline model to a linear model. Based on spline results suggesting a threshold, we performed a piecewise Cox analysis, estimating separate HRs per 1–SD TyGFI below vs. above the inflection point (TyGFI ≈ 54.62). We also examined stroke risk across TyGFI tertile categories, using the lowest tertile as reference.

Several sensitivity and subgroup analyses were conducted. First, we repeated analyses after excluding stroke events that occurred within 2 years of baseline, to reduce bias from subclinical strokes influencing frailty (reverse causation). Second, we further adjusted for baseline C-reactive protein (a marker of systemic inflammation) in the multivariable model to determine if inflammation mediated the relationship between TyGFI and stroke risk. Finally, we tested for effect modification by age (< 60 vs ≥ 60 years), sex, area(urban vs rural), drinking and smoking(never, current vs ever), annual income groups(< 15000, 15000–20000 vs ≥ 20000 CNY), BMI (under weight, normal weight vs overweight/obese) by including interaction terms. The two-sided alpha level was set at 0.05. All the statistical analyses were performed using the EmpowerStats (www.empowerstats.com, X&Y solutions, Inc. Boston MA) and R software version 4.2.0 (http://www.r-project.org).

Results

Baseline Characteristics

A total of 3,649 participants met inclusion criteria (Table 1). Participants were categorized according to tertiles of the TyG-FI: low (≤ 34.7), middle (34.8–70.2) and high (≥ 70.3). At baseline, the mean age was 59.9 years (SD 9.06). Participants in the highest TyG-FI tertile were older (mean age 62.8 ± 9.3 vs 57.4 ± 8.4 years in the lowest; P < 0.001) and more frequently female (67.9 % vs 50.8 %; *P* < 0.001). Rural residence, illiteracy and annual household income < CNY 15 000 increased monotonically across tertiles (all *P* < 0.001). Lifestyle, anthropometry and cardiometabolic profiles deteriorated across TyG-FI tertiles: current drinking decreased (33.9 to 25.0%), whereas ever-drinking and overweight/obesity increased (5.9 to 12.7% and 32.9 to 38.7%; *P*<0.001); hypertension, diabetes, heart disease and dyslipidaemia increased 2.9-, 9.5-, 4.8- and 2.2-fold, respectively (all *P*<0.001). Systolic BP rose from 125.7±19.0 to 132.8±23.6 mmHg (P<0.001); triglycerides and fasting glucose climbed and HDL-C declined (*P*≤0.013).

Association of TyGFI with Incident Stroke

During a median follow-up of 9 years, 398 incident stroke events were documented, yielding a crude incidence of 10.9%. TyG-FI exhibited a strong, dose-dependent association with new-onset stroke. Per 1-SD increment in TyG-FI Z-score, the hazard of stroke increased by 40% (HR 1.40; 95% CI 1.29–1.53) in unadjusted analyses and remained significant after progressive adjustment (Model 3: HR 1.33; 95% CI

1.22–1.47; *P* < 0.0001 for all models). Compared with participants in the lowest TyG-FI tertile (incidence 6.8%), those in the middle and highest tertiles showed monotonically elevated risk: Middle tertile – HR 1.55 (95% CI 1.18–2.04) unadjusted, attenuating to 1.47 (1.11–1.95) in fully adjusted Model 3 (*P* = 0.0065). Highest tertile – HR 2.44 (95% CI 1.88–3.16) unadjusted, remaining nearly twofold higher after full adjustment (HR 2.15; 95% CI 1.63–2.82; *P* < 0.0001). Tests for trend were highly significant across all models (*P* < 0.0001), confirming a linear rise in stroke hazard with increasing TyG-FI (Table 2). These findings indicate that the TyGFI is independently and robustly associated with future stroke risk in this middle-aged and older Chinese population with arthritis.

Nonlinear Relationship and Threshold Effects

On visualizing the TyGFI–stroke relationship with restricted cubic splines (Figure 2), we found evidence of nonlinearity (*P* for nonlinearity = 0.001). The stroke hazard increased steeply with TyGFI in the lower range, then the slope became shallower at higher TyGFI values, suggestive of a threshold or diminishing returns effect. Specifically, the spline curve indicated a sharper risk increase up to approximately TyGFI = 55, beyond which the risk continued to rise but at a reduced slope. We therefore performed a piece-wise Cox analysis. For TyGFI values <54.62 (the estimated knot from spline), each 1–SD increase in TyGFI was associated with an adjusted HR of 2.44 (95% CI 1.64–3.62, *P*<0.0001) for stroke. In contrast, for TyGFI >54.62, the HR per 1–SD was 1.18 (1.04–1.34, *P*=0.0086). (Table 3)

Sensitivity and Subgroup Analyses

Sensitivity analyses corroborated the primary findings (Table 4). After excluding 12 stroke events occurring within the first two years (Model 4, n = 3522; 386 events), each 1-SD increase in TyG-FI Z-score remained significantly associated with incident stroke (HR 1.34; 95 % CI 1.22–1.48; *P* < 0.0001). Compared with the lowest tertile, the middle and highest tertiles showed graded elevations in risk (HR 1.48; 95 % CI 1.11–1.96 and HR 2.12; 95 % CI 1.60–2.80, respectively; *P*-trend < 0.0001).

Further adjustment for C-reactive protein (Model 5) yielded virtually identical effect estimates (per-SD HR 1.33; 95 % CI 1.21–1.46; highest vs lowest tertile HR 2.10; 95 % CI 1.59–2.77; *P*-trend < 0.0001). The consistency of these results indicates that the association between TyG-FI and new-onset stroke is robust to both reverse causation and additional inflammatory confounding.

Figure 3 presents the subgroup analyses of the association between TyG-FI (per 1-SD increment) and incident stroke. The positive association was consistently observed across all pre-specified strata, with HRs ranging from 1.18 to 1.74 and no evidence of meaningful heterogeneity for most subgroups. Statistical interactions were detected for age, residence, smoking and income (*P*-interaction ≤ 0.037), but the direction of effect was uniform: higher TyG-FI conferred elevated stroke risk in every stratum. Thus, the TyG-FI–stroke relationship is robust and generalisable across the study population.

Discussion

In this prospective study of middle-aged and older Chinese adults with arthritis, we found that a higher TyG–Frailty Index was associated with a substantially elevated risk of developing stroke. To our knowledge, this is the first longitudinal study to examine the combined effect of insulin resistance (TyG index) and frailty on stroke risk in Chinese adults with arthritis. The results suggest that the dual burden of metabolic and frailty-related deficits synergistically increases stroke risk beyond the contribution of either factor alone. Participants in the highest TyGFI tertile had more than double the stroke risk of those in the lowest tertile, independent of age, sex, lifestyle, adiposity, and other covariates. Furthermore, the association was non-linear: stroke risk rose most steeply from low to moderate TyGFI levels, then continued to increase at a slower rate thereafter.

Our findings extend prior research on TyG index and frailty as separate predictors of cardiovascular outcomes[8, 9, 37]. Consistent with earlier studies, TyG index by itself was positively associated with stroke risk in a large cohort (HR 1.26 in the highest TyG index quartile[11]). Likewise, frailty alone (as measured by FI) predicted stroke in the data (HR 1.71, (95% CI 1.34, 2.17) in frailty patients)[38], aligning with evidence that frailty is an independent risk factor for cardiovascular events and mortality[18, 19]. By combining these two dimensions into TyGFI, we captured a more pronounced risk gradient. TyGFI per SD had a larger hazard ratio (1.33) for stroke than either TyG or FI alone, suggesting an additive or multiplicative effect. This supports the concept that metabolic dysfunction and frailty together create a “risk accelerator” for vascular events[39]. Biologically, insulin resistance and frailty may jointly exacerbate proinflammatory and prothrombotic states, endothelial dysfunction, and arrhythmogenic potential, thereby heightening stroke susceptibility[39].

We observed a threshold around TyGFI 55, below which stroke risk increased sharply with higher TyGFI. Interestingly, in a cohort of patients with coronary artery disease, a U-shaped relationship between TyG index and stroke was reported with a threshold TyG 8.1 (log scale)[40]. Those authors postulated that extremely low TyG (perhaps reflecting malnutrition or severe illness) could also confer risk in that specific patient group[41]. In our generally healthier community sample, we did not see a U-shape but rather a plateau at high TyGFI. This plateau might indicate that once individuals accumulate a high load of metabolic and frailty deficits, they are already very high-risk and additional increments in TyGFI yield smaller relative increases in risk. It is also possible that beyond a certain frailty level, competing risks (e.g. death from other causes) limit further observed increase in stroke incidence[42]. Nonetheless, even at high TyGFI, the stroke risk remained elevated compared to low TyGFI, reinforcing that any reduction in metabolic or frailty burden could be beneficial.

Our study specifically focused on an arthritis subset of the population. This is notable because chronic inflammatory conditions like rheumatoid arthritis are known to heighten cardiovascular risk, including stroke[22, 25, 43]. Metabolic dysfunction and physiological vulnerability frequently coexist in older adults with arthritis. Inflammation from arthritis may both promote insulin resistance and contribute to frailty (through reduced physical activity, muscle loss, etc.), thereby elevating TyGFI. Indeed, the results of our study were similar to those from two prospective cohorts of general participants in the US and China without a specific focus on arthritis.[21]. We found that TyGFI predicted stroke similarly in those with RA

and those with other arthritis, suggesting the utility of TyGFI is not limited to a specific subtype of arthritis but rather applies to the broader context of chronic joint disease. It also implies that beyond traditional inflammatory markers, the integrated TyGFI measure captures relevant risk in patients with chronic inflammation. This could have clinical implications: patients with arthritis often receive risk factor counseling for CVD prevention, and our results indicate that evaluating frailty and metabolic indices together might improve identification of those at highest stroke risk.

In comparison to the cross-sectional study by Zhao et al. who first introduced TyGFI[21], our prospective design establishes a temporal relationship between elevated TyGFI and future stroke events. Zhao et al. reported extremely high odds ratios for stroke with high TyGFI in CHARLS (OR > 20 in the highest quartile), which are larger than the HRs in our study. This discrepancy is likely due to different outcome definitions (their analysis included any history of stroke by study end, combining prevalence and incidence, and possibly survivorship bias) and the use of logistic ORs which can overestimate risk ratios for more common outcomes. Our HR of 2.15 for the top vs bottom tertile is more modest, yet it is still clinically meaningful. Notably, both studies consistently show a dose-dependent relationship and support TyGFI as a strong risk indicator. Our work adds nuance by demonstrating nonlinearity and by focusing on an arthritis subgroup which Zhao et al. did not specifically analyze.

From a preventive perspective, our findings highlight the importance of managing both metabolic health and frailty to reduce stroke risk in older adults. While intensive lifestyle and pharmacologic interventions exist for metabolic syndrome and diabetes (which correlate with TyG)[44], addressing frailty requires a multidomain approach[42]. Exercise programs (especially those incorporating resistance training and balance exercises) have been shown to improve frailty status and could potentially mitigate some stroke risk by improving vascular health and reducing falls that can trigger vascular events indirectly. Nutritional support (adequate protein, vitamin D, etc.) and managing polypharmacy are also key in frailty interventions. Our results suggest that a person with a given level of traditional risk factors may have a very different stroke risk depending on their TyGFI. For instance, two 65-year-old women with hypertension and similar BMI might diverge in risk if one has high insulin resistance and is frail while the other does not-the former would be at much higher stroke risk according to TyGFI. Clinicians might consider simple proxies for TyG (routine blood tests) and frailty (questionnaires or FI calculations) to identify such high-risk patients. In particular, an older arthritis patient who is slowing down (becoming frail) and has signs of metabolic syndrome might warrant closer monitoring and more aggressive modification of risk factors (e.g. tighter blood pressure and glucose control, physical therapy to improve function).

This study has several strengths. It leveraged a well-characterized, population-based cohort with longitudinal follow-up and rich data to construct a frailty index. We adjusted for an array of confounders and performed extensive sensitivity checks, all of which support the robustness of the TyGFI–stroke association. The focus on an arthritis population is a novel aspect that addresses a group with unmet prevention needs; our findings may be especially relevant for managing older adults with chronic

inflammatory conditions. Additionally, we explored nonlinearity in detail, which provided insight into risk dynamics across different TyGFI levels.

We acknowledge some limitations. Stroke events were ascertained by self-report, which could lead to misclassification; however, prior validation in similar cohorts suggests reasonably good specificity[21]. Any misclassification would likely be non-differential, biasing results towards the null. Residual confounding is possible – for instance, unmeasured variables like physical activity, diet quality, or inflammatory biomarkers might influence stroke risk and be related to TyGFI. We adjusted for lifestyle factors and indirectly accounted for inflammation via frailty deficits and sensitivity CRP adjustment, but cannot exclude residual confounding by inflammation or socioeconomic factors. The CHARLS frailty index, while comprehensive, included some self-reported health deficits that might be subject to reporting bias. We tried to minimize overlap between TyGFI components and covariates (e.g. not adjusting for diabetes in primary models, since glucose is part of TyG), but some over-adjustment or under-adjustment could occur. Our analysis of nonlinearity was data-driven; the exact threshold value (TyGFI 54.62) should be interpreted with caution and may not generalize to other populations. Nonetheless, the broader concept of a nonlinear association is likely valid. Finally, our cohort was exclusively Chinese, and all had arthritis at baseline; thus, results may not directly generalize to ethnically different populations or to adults without arthritis. However, we suspect the underlying biological interactions between insulin resistance, frailty, and stroke are not unique to arthritis, and similar patterns might be observed in other older cohorts.

In this cohort of Chinese adults with arthritis, a higher TyGFI was associated with increased risk of incident stroke. The association was strongest at lower TyGFI levels and persisted, albeit attenuated, at higher levels, indicating a nonlinear dose–response. This composite index may capture synergistic effects of metabolic dysfunction and biological vulnerability, underscoring the importance of managing both insulin resistance and frailty in stroke prevention.

Conclusion

Our findings suggest that the TyGFI, a composite measure integrating metabolic and geriatric vulnerability, is independently associated with increased incident stroke risk in older Chinese adults with arthritis. By capturing the dual impact of insulin resistance and deficit accumulation, TyGFI outperforms single-domain risk markers and may serve as a practical, low-cost tool for stroke risk stratification in aging populations with chronic inflammatory conditions. These results support the growing recognition that metabolic dysfunction and frailty are intertwined determinants of cardiovascular outcomes, underscoring the need for integrated management of glycemic control, lipid profiles, and physical resilience in primary stroke prevention.

Declarations

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Human Ethics and Consent to Participate declarations

The China Health and Retirement Longitudinal Study was approved by the Ethics Review Committee of Peking University. All respondents provided written informed consent. The CHARLS data used in this study are publicly available, de-identified datasets that do not require ethical or administrative approval.

Confficts of Interest: The authors declare no confficts of interest.

Data Availability Statement

All data are publicly available, on research approval access, from CHARLS on the website (http:// charls. pku. edu. cn/ en).

Auther contribution

Chunyan Zhang contributed to the study design and participated in writing the manuscript. Canran Liu contributed to data analysis. Pengfei Meng and Jiajia Zhao prepared the tables and figures. All authors approved the final manuscript.

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Tables

Tables 1 to 4 are available in the supplementary files section.

Figures

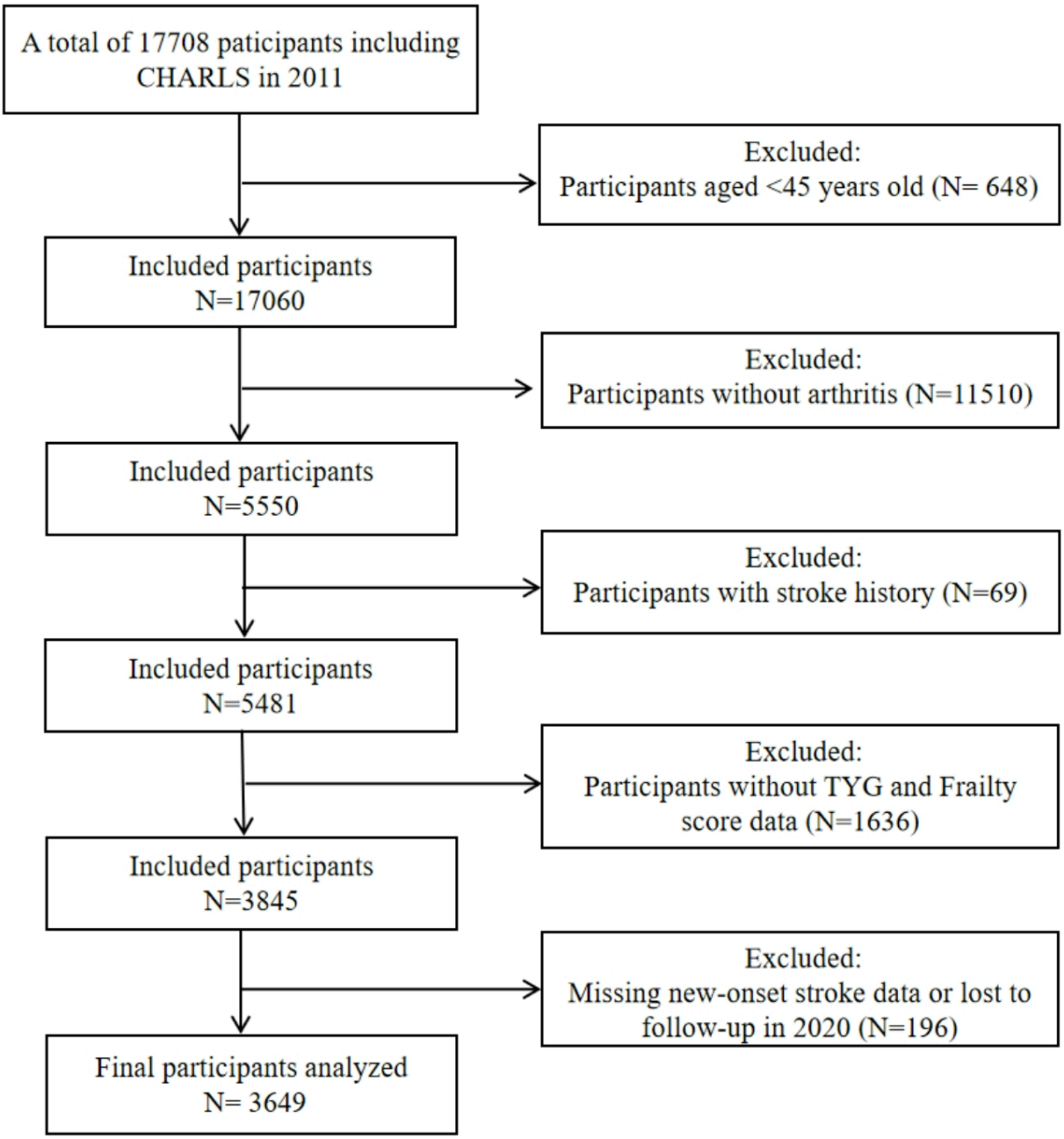


Figure 1

Flowchart of participant selection from the CHARLS.

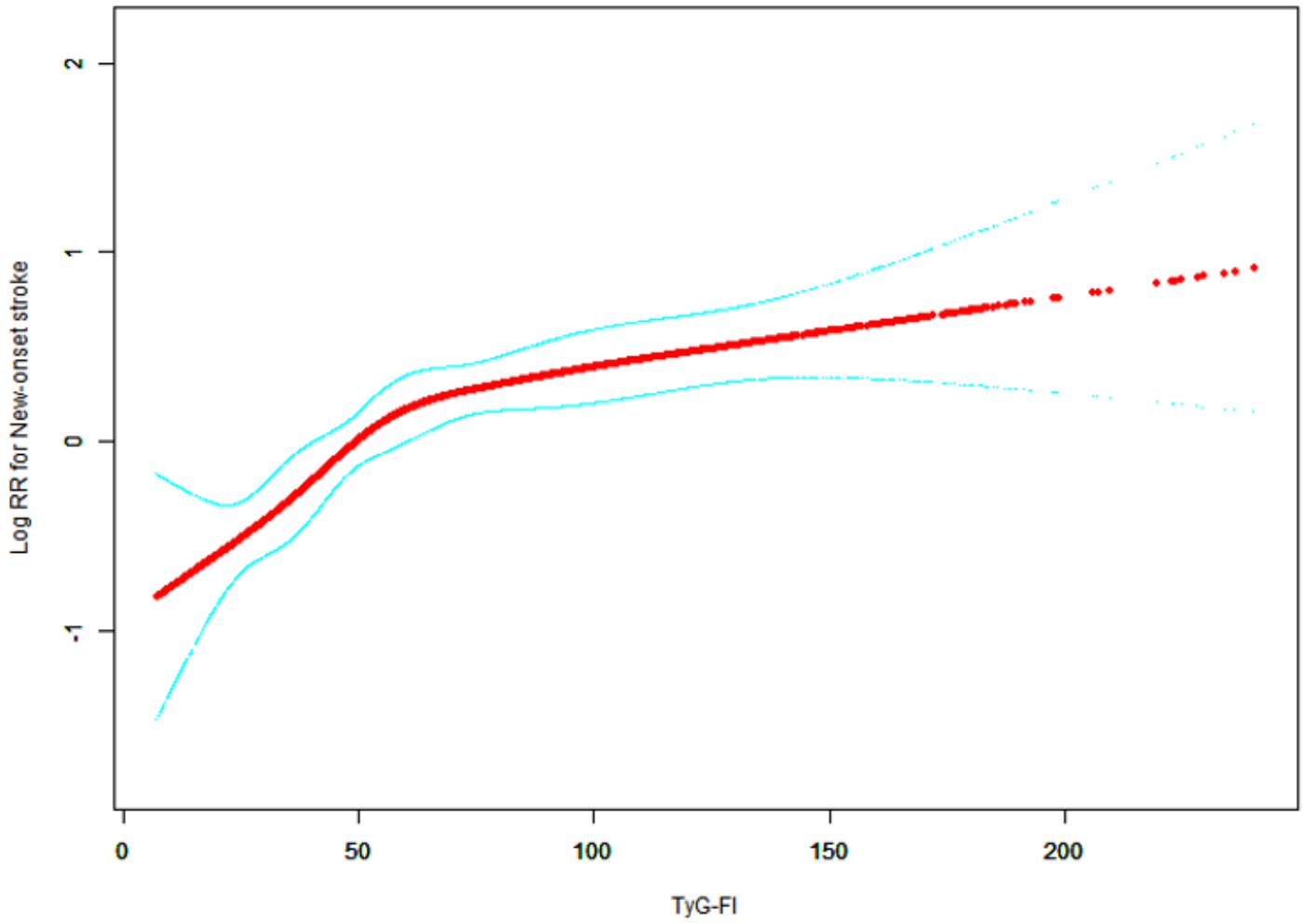


Figure 2

Non-linear relationship between TyG-FI and incidence of stroke. Adjust for age, sex, area of residence, annual household income level, smoking and drinking status, BMI groups.

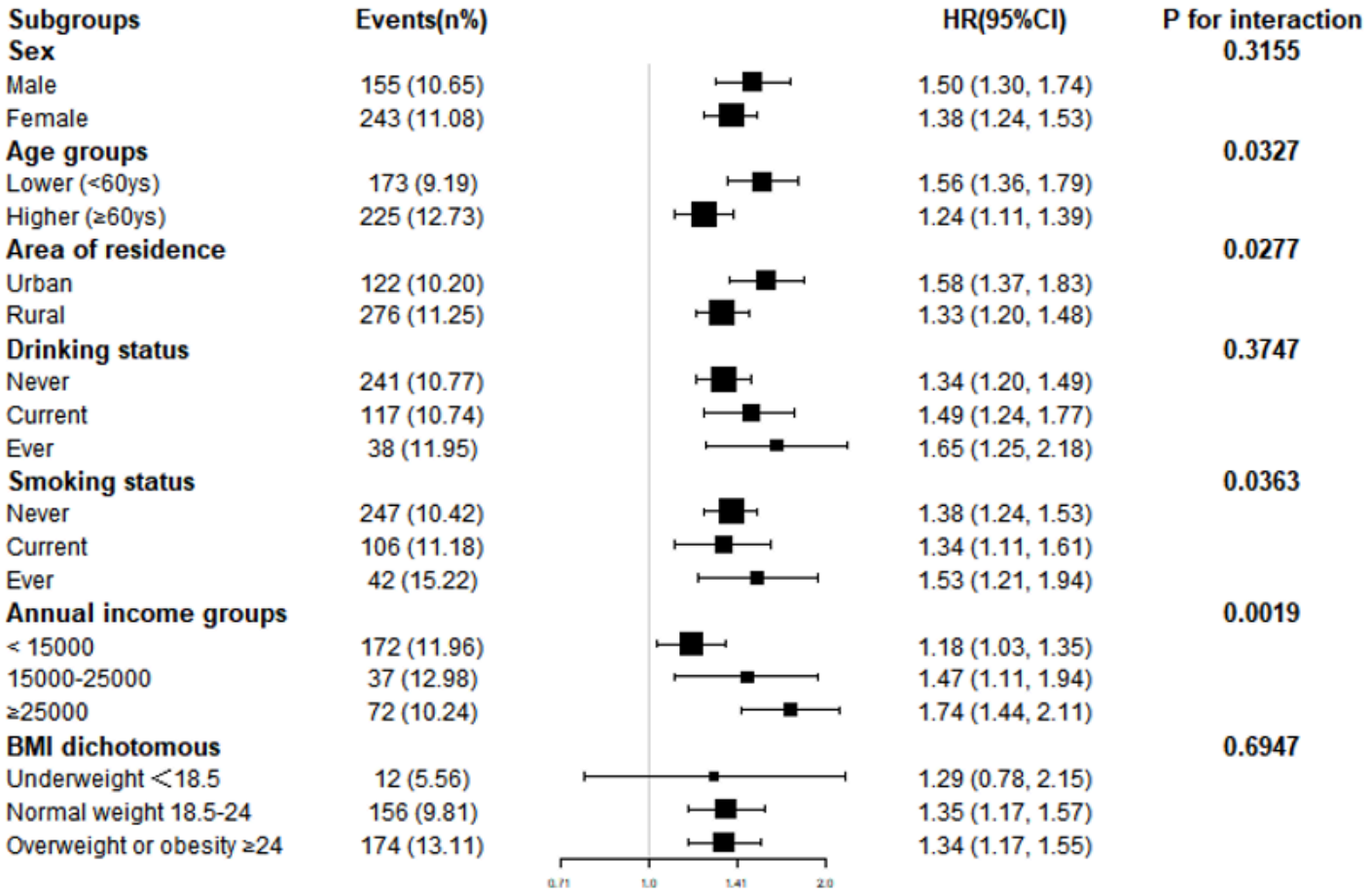


Figure 3

Multivariable adjusted HRs for the associations between TyG-FI and incidence of stroke within subgroups. Adjust for age, sex, area of residence, drinking, smoking, annual income groups, BMI groups.

Supplementary Files

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- Tables.docx