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Association of cardiometabolic index and new-onset stroke in middle-aged and elderly Chinese: a national prospective cohort study

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Abstract

Background and aims The Cardiometabolic Index (CMI), a novel metabolic marker, has been associated with various metabolic diseases in previous studies. However, its relationship with stroke risk remains underexplored. This study investigates the potential correlation between CMI and stroke risk among Chinese adults aged 45 and older.

Methods In the China Health and Retirement Longitudinal Study (CHARLS), participants were categorized into four groups based on CMI quartiles. The primary outcome was the incidence of new strokes during the follow-up period. A Cox proportional hazards model was used to analyze the relationship between CMI and stroke risk among the elderly. Kaplan–Meier survival analysis compared incidence rates across CMI levels, and restricted cubic splines (RCS) assessed potential non-linear relationships between CMI and stroke. Subgroup analyses verified the robustness of these findings.

Results The study included 6620 patients (45% male), with 417 new stroke cases reported over an average follow-up of seven years. Multivariate analysis indicated a significant association between increased CMI and higher stroke risk [HR, 1.132 (1.021–1.273), $P = 0.003$]. The RCS model revealed a nonlinear increase in stroke risk with rising CMI levels (P for nonlinearity = 0.006). No significant interactions were detected between CMI and the selected subgroups (all P values for interaction > 0.05).

Conclusion CMI significantly correlates with stroke risk in the elderly Chinese population, suggesting its potential utility in early risk stratification.

Keywords Cardiometabolic Index, The China Health and Retirement Longitudinal Study, Stroke, Nonlinear relationship, Obesity

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Introduction

A stroke is defined by an acute neurological deficit caused by ischemia or hemorrhage, with symptoms lasting 24 h or more, or until death [1]. The 2019 Global Burden of Disease Study identifies stroke as the second leading cause of death globally and the third leading cause of both death and disability. From 1990 to 2019, the absolute number of incident strokes increased by 70.0%, while the number of stroke-related deaths rose by 43.0% [2]. Despite progress in stroke treatment and rehabilitation, treatment rates and outcomes are still concerning [3, 4]. Many stroke survivors are left with disabilities that significantly diminish their quality of life and impose substantial burdens on families and society. Thus, improving primary prevention of stroke is essential.

Previous research has identified several stroke risk factors, including hypertension, high body mass index (BMI), low physical activity, and renal dysfunction [5, 6]. Recent evidence suggests that insulin resistance (IR) is linked to both the development and prognosis of cardiovascular disease (CVD) [7–9]. The triglyceride-to-high-density lipoprotein cholesterol ratio (TG/HDL-C) is a reliable surrogate for assessing insulin resistance and may facilitate the early identification of high-risk patients [10]. The waist-to-height ratio (WHtR), a common surrogate for visceral adipose tissue, has been shown to have a stronger association with cardiovascular disease risk than BMI [11]. The Cardiometabolic Index (CMI), which integrates TG/HDL-C and WHtR, was initially proposed for diabetes prediction [12]. Clinical research has since revealed that CMI is associated with the progression of hypertension [13], peripheral artery atherosclerosis [14], and metabolic health indicators such as metabolic associated fatty liver disease (MAFLD) [15], metabolically obese normal weight (MONW) phenotype [16] and declining kidney function [17]. Given its association with increased cardiovascular risk factors, this study hypothesizes that CMI can effectively predict stroke risk. Existing research on CMI and stroke risk has been limited to cross-sectional studies with small, localized samples and has not explored potential non-linear relationships [18, 19]. This study aims to utilize data from the China Health and Retirement Longitudinal Study (CHARLS) to clarify the association between CMI and stroke risk, providing a more comprehensive understanding of this relationship.

Methods

Study design and population

The China Health and Retirement Longitudinal Study (CHARLS) is a large-scale interdisciplinary research project collaboratively undertaken by Wuhan University and Peking University. It aims to collect high-quality, micro-level data from individuals aged 45 and older across China, with a focus on addressing issues related to population aging and promoting interdisciplinary research in this field. The national baseline survey, launched in 2011, sampled over 10,000 households from 150 counties/districts and 450 villages throughout the country. Data collection is carried out through standardized questionnaires administered during individual interviews, covering diverse topics such as demographics, family structure, economic support, health conditions, physical measurements, healthcare utilization and insurance, employment, retirement, pensions, income, consumption, assets, and community characteristics. Follow-up surveys are conducted every two to three years. CHARLS adheres to the principles set out in the Helsinki Declaration and has received approval from the Institutional Review Board (IRB00001052-11015) at Peking University. Written informed consent is obtained from all participants before their involvement in CHARLS [20].

In total, 9,887 participants were excluded from the study according to specific exclusion criteria: (1) Missing stroke information, which included 1,314 participants lost to follow-up, 133 with incomplete baseline stroke data, and 721 individuals who had a stroke at baseline; (2) Missing CMI data, involving 3,182 participants lacking height or waist circumference measurements and 3,342 with missing triglyceride or high-density lipoprotein cholesterol data; (3) Missing age information or participants under 45 years old (307 individuals); (4) Missing confounding factors for 867 participants; (5) Additionally, 21 participants had CMI values that exceeded three standard deviations from the mean [21]. As a result, 6620 participants were included in the final analysis cohort.

Calculation of CMI

The Cardiometabolic Index (CMI) was computed using the following formula: CMI = triglyceride (TG, mmol/L)/high-density lipoprotein cholesterol (HDL-C, mmol/L) × waist circumference (WC, cm)/height (cm).

Stroke diagnosis

The study investigates new stroke cases occurring during the follow-up period (from Wave 2 to Wave 4) among participants who were stroke-free at baseline. Stroke data is collected through standardized questionnaires that ask participants whether they have ever been diagnosed with a stroke and informed by a healthcare provider, including the date of the first diagnosis. Responses indicating a positive stroke diagnosis during follow-up are recorded as first-time occurrences, and the time between the stroke event and the baseline assessment is calculated. For participants who do not report a stroke during the follow-up, the follow-up period is defined as the interval

between the baseline assessment and the final survey date.

Data collection and definitions

Demographic and clinical information from participants were collected, including age, gender, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), place of residence, marital status, education level, smoking habits, alcohol consumption, hypertension, diabetes, cardiovascular disease, and depressive symptoms. Additionally, the use of antihypertensive and antidiabetic medications was documented. Laboratory tests included total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), C-reactive protein (CRP), hemoglobin concentration (HGB), uric acid (UA), white blood cell count (WBC), and platelet count. Hypertension was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg (average of three measurements), self-reported diagnosis of hypertension, or the use of any antihypertensive medications [22]. Diabetes was defined as fasting blood glucose ≥ 126 mg/dL or HbA1c ≥ 6.5%, self-reported diagnosis of diabetes, or the use of any antidiabetic medications. Depressive symptoms were assessed using the 10-item Center for Epidemiological Studies Depression Scale (CESD-10), with a cutoff value of 12 used to identify individuals with depressive symptoms [23].

Statistical analyses

Before analysis, normality of all continuous variables was assessed using the Kolmogorov–Smirnov test. Categorical variables are presented as frequencies and percentages, while continuous variables are reported as means with standard deviations (SD) or medians with interquartile ranges (25th–75th percentile), depending on their distribution. Group differences were tested using chi-square tests for categorical variables, the Kruskal–Wallis H test for skewed data, and one-way ANOVA or t-tests for normally distributed data. Kaplan–Meier survival analysis was used to evaluate endpoint incidence across different CMI groups, with differences assessed by the log-rank test.

To assess the correlation between CMI and outcomes, both univariate and multivariate Cox proportional hazards models were employed. To avoid multicollinearity and model overfitting, variance inflation factors (VIF) were calculated, and variables with a VIF ≥ 5 were excluded. Clinically relevant and prognostic variables were included in the multivariate models as follows: Model 1 (unadjusted), Model 2 (adjusted for age and gender), Model 3 (adjusted for age, gender, residence, marital status, education level, smoking, drinking status, hypertension, diabetes, depressive symptoms, BMI, LDL-C, CRP, HbA1c, and UA). CMI was modeled both as a continuous and categorical variable, with the lowest CMI quartile as the reference group. A p-value for trend was calculated by treating quartile levels as ordered variables.

Restricted cubic splines (RCS) based on Model 3 were used to explore potential non-linear relationships between CMI and stroke. Stratified analyses by age (< 65 years vs ≥ 65 years), gender, smoking status, drinking status, hypertension, diabetes, and depression were performed to assess the consistency of CMI's predictive value. Interaction effects between CMI and stratification variables were examined using likelihood ratio tests. All statistical analyses were conducted using SPSS (version 27.0.1, IBM Corp.), R (version 4.4.0, The R Project for Statistical Computing), and GraphPad Prism (version 10.1.2, GraphPad Software). A two-sided p-value < 0.05 was considered statistically significant.

Results

Baseline characteristics

This study involved 6,620 participants with a median age of 56 years, 55% of whom were female. Over a median follow-up period of 7 years, 417 participants experienced a stroke. The participant selection process is illustrated in Fig. 1. The median Cardiometabolic Index (CMI) for the entire cohort was 0.49 (IQR: 0.31–0.86). Table 1 summarizes the baseline characteristics based on stroke incidence. Participants who experienced a stroke were older, had lower education levels, and exhibited higher rates of hypertension and diabetes, as well as a higher body mass index (BMI) compared to those who did not have a stroke. Laboratory results showed that the stroke group had higher levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), C-reactive protein (CRP), uric acid (UA), hemoglobin (HGB), and white blood cell count (WBC), along with lower levels of high-density lipoprotein cholesterol (HDL-C) (all $P < 0.05$). Table 2 presents the baseline characteristics of participants stratified by CMI quartiles: Q1 (0.03–0.31), Q2 (0.32–0.49), Q3 (0.50–0.86), and Q4 (0.87–10.22). Compared to participants in the lower quartiles, those in the highest CMI quartile were more likely to be female, reside in urban areas, have lower rates of smoking and alcohol consumption, and have higher rates of hypertension and diabetes (all $P < 0.05$).

Relationship between CMI and the risk of stroke

The Kaplan–Meier survival curves for stroke incidence, stratified by CMI quartiles, shown in Fig. 2, indicate that participants in the highest CMI group (Q4) had

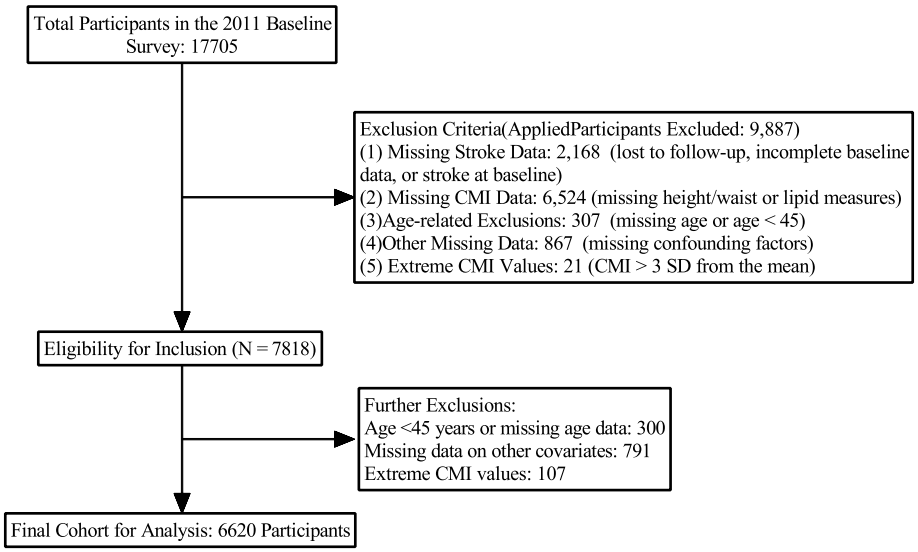

Fig. 1 Patient selection flowchart

Table 1 The baseline characteristics of participants grouped according to new-onset stroke

Characteristic	Total (*N* = 6620)	Non-Stroke (*N* = 6203)	Stroke (*N* = 417)	*P*
Age (years)	56 (50, 65)	56 (50, 64)	62 (56, 67)	< 0.001
Gender, n (%)				0.375
Male	2979 (45%)	2915 (47%)	204 (49%)	
Female	3641 (55%)	3288 (53%)	213 (51%)	
Education level, n (%)				0.034
Primary	4700 (71%)	4383 (68%)	317 (76%)	
Secondary	1390 (21%)	1323 (19%)	67 (16%)	
Third	530 (8%)	497 (12%)	33 (7.8%)	
Current smoker, n (%)	2052 (31%)	1923 (31%)	129 (32%)	0.612
Current drinker, n (%)	2185 (33%)	2047 (33%)	138 (35%)	0.417
Hypertension, n (%)	2648 (40%)	2419 (39%)	229 (62%)	< 0.001
Diabetes, n (%)	1059 (16%)	992 (16%)	67 (23%)	< 0.001
Depressive symptom (%)	1853 (28%)	1737 (28%)	116 (32%)	0.034
BMI (kg/m^2)	24.13 (21.83, 26.73)	24.07 (21.10, 26.67)	25.20 (22.64, 27.73)	< 0.001
SBP (mmHg)	128(116, 143)	128(115, 142)	138 (124, 154)	< 0.001
DBP (mmHg)	76 (68, 84)	75 (68, 84)	80 (72, 89)	< 0.001
TC (mg/dL)	191.69(161.88, 216.44)	191.21 (168.50, 215.96)	197.69 (172.66, 225.62)	< 0.001
TG (mg/dL)	106.33(76.23, 154.20)	104.44 (75.35, 153.33)	117.92 (85.97, 167.48)	< 0.001
HDL-C (mg/dL)	50.49 (41.69, 61.41)	50.77 (41.99, 61.32)	48.27 (40.82, 57.86)	< 0.001
LDL-C (mg/dL)	111.53 (94.95, 138.74)	115.15 (94.67, 137.96)	121.15 (98.51, 143.33)	0.002
FBG (mg/L)	103.32 (95.50, 114.22)	103.24 (95.32, 113.96)	106.31 (97.51, 120.34)	< 0.001
HbAlc (%)	6.20 (5.90,6.40)	6.11 (5.91, 6.50)	6.21 (5.90, 9.51)	0.004
CRP (mg/L)	1.03 (0.56, 3.22)	1.11 (0.66, 2.18)	1.44 (0.67, 2.77)	< 0.001
UA (mg/dL)	4.58 (3.66, 5.49)	4.59 (3.87, 5.51)	4.89 (3.91, 5.92)	0.013
HGB (g/L)	15.21 (14.05, 16.63)	15.31 (14.01, 16.63)	15.72 (14.43, 16.89)	0.005
CMI	0.48 (0.29, 0.85)	0.48 (0.29, 0.84)	0.60 (0.37, 1.05)	< 0.001

Abbreviations: *CMI* cardiometabolic index, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *FPG* fasting plasma glucose, *HbA1c* glycosylated hemoglobin, *CRP* C-reactive protein, *HGB* hemoglobin concentration, *UA* Uric acid

Table 2 The baseline characteristics of participants grouped according to CMI

Characteristic	Q1 (*N* = 1765)	Q2 (*N* = 1743)	Q3 (*N* = 1663)	Q4 (*N* = 1449)	*P*
Age (years)	59 (53, 64)	59 (54, 66)	59 (52, 65)	59 (52, 65)	0.064
Gender, n (%)					< 0.001
Male	987 (56%)	854 (49%)	765 (44%)	607 (42%)	
Female	778 (44%)	889 (51%)	978 (56%)	842 (58%)	
Residence, n (%)					< 0.001
Urban	230 (13%)	279 (16%)	314 (18%)	320 (22%)	
Rural	1535 (87%)	1464 (84%)	1429 (82%)	1129 (78%)	
Marital status, n (%)					0.090
Married	1500 (85%)	1506 (86%)	1429 (82%)	1217 (84%)	
Other	265 (15%)	237 (14%)	314 (18%)	232 (16%)	
Education level, n (%)					0.255
Primary	1273 (72%)	1273 (73%)	1169 (67%)	1001 (69%)	
Secondary	335 (19%)	296 (17%)	402 (23%)	304 (21%)	
Third	159 (9.0%)	174 (10%)	174 (10%)	174 (12%)	
Current smoker, n (%)	671 (38%)	574 (33%)	471 (27%)	378 (26%)	< 0.001
Current drinker, n (%)	776 (44%)	610 (35%)	471 (27%)	406 (28%)	< 0.001
Hypertension, n (%)	530 (30%)	574 (33%)	785 (45%)	755 (52%)	< 0.001
Diabetes, n (%)	147 (8.3%)	192 (11%)	296 (17%)	420 (29%)	< 0.001
Depressive symptom (%)	494 (28%)	488 (28%)	523 (30%)	378 (26%)	0.010
BMI (kg/m^2)	22.32 (20.44, 24.22)	23.34 (21.42, 25.63)	24.72 (22.10, 27.36)	26.46 (24.73, 28.67)	< 0.001
SBP (mmHg)	124 (113, 139)	126 (114, 141)	130 (117, 144)	132 (120, 147)	< 0.001
DBP (mmHg)	73 (66, 81)	75 (67, 83)	77 (69, 85)	78 (71, 87)	< 0.001
TC (mg/dL)	186.85(166.95, 209.85)	186.96(164.54, 212.09)	192.15(170.34, 216.73)	199.72 (175.37, 227.56)	< 0.001
TG (mg/dL)	63.84 (53.23, 75.35)	89.51 (78.01, 103.67)	124.91 (107.21, 144.38)	206.33 (166.50, 271.82)	< 0.001
HDL-C (mg/dL)	65.96 (57.84, 75.62)	54.36 (48.18, 61.32)	47.40 (41.99, 53.20)	38.12 (33.10, 43.92)	< 0.001
LDL-C (mg/dL)	109.64 (91.47, 129.75)	116.60 (97.27, 138.64)	122.02 (101.14, 144.46)	114.29 (88.75, 139.01)	< 0.001
FBG (mg/L)	98.19 (92.99, 108.83)	100.81 (93.25, 110.27)	103.25 (95.69, 113.87)	110.09 (99.55, 125.75)	< 0.001
HbAlc (%)	5.21 (4.91, 5.41)	5.21 (4.91, 5.51)	5.31 (4.90, 5.51)	5.31 (4.90, 5.71)	< 0.001
CRP (mg/L)	0.86 (0.55, 1.81)	0.97 (0.61, 1.94)	1.12 (0.62, 2.23)	1.46 (0.84, 2.81)	< 0.001
UA (mg/dL)	4.23 (3.51, 4.97)	4.21 (3.49, 4.99)	4.31 (3.61, 5.21)	4.73 (3.92, 5.51)	< 0.001
HGB (g/L)	14.11 (13.19, 16.29)	14.31 (13.16, 15.67)	14.34 (13.19, 15.64)	14.76 (13.43, 15.92)	< 0.001
WBC (10^9/L)	5.73 (4.81, 6.92)	5.94 (4.91, 7.23)	6.13 (5.15, 7.38)	6.41 (5.49, 7.62)	< 0.001
Platelet (10^9/L)	203 (163, 248)	205 (160, 254)	206(163, 256)	214 (168, 263)	< 0.001
Stroke	58 (3.3%)	89 (5.1%)	101 (6.1%)	104 (7.2%)	< 0.001

Abbreviations: *CMI* cardiometabolic index, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *FPG* fasting plasma glucose, *HbA1c* glycosylated hemoglobin, *CRP* C-reactive protein, *HGB* hemoglobin concentration, *UA* Uric acid, *WBC* white blood cell count

a significantly higher risk of stroke compared to those in the other three groups (log-rank test, $P < 0.001$). Cox proportional hazards models (Table 3) demonstrated a significant association between CMI as a continuous variable and stroke risk across all models: unadjusted [HR, 1.173 (1.067–1.358), $P < 0.001$], partially adjusted [HR, 1.177 (1.069–1.295), $P < 0.001$], and fully adjusted [HR, 1.132 (1.021–1.273), $P = 0.003$]. When CMI was treated as a categorical variable, the highest CMI group exhibited the highest stroke risk compared to the lowest group in all three models: [model 1: HR, 2.124 (1.549–2.691); model 2: HR, 2.336 (1.479–3.167); model 3: HR, 1.899 (1.231–2.672); all $P < 0.001$]. Additionally, restricted cubic spline regression models revealed a nonlinear increase in stroke risk with rising CMI (P for nonlinearity = 0.006) (Fig. 3).

Results of subgroup analysis

The risk stratification value of the CMI for new-onset stroke was further assessed across various subgroups

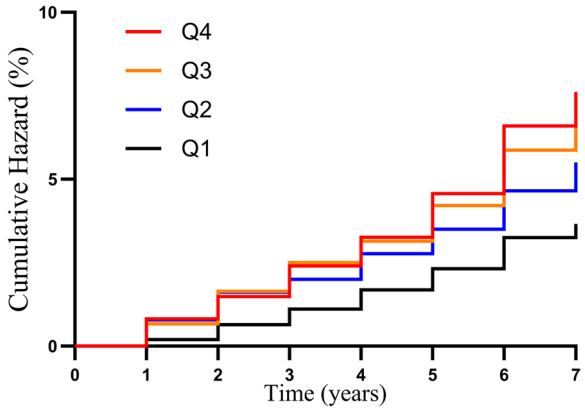

Fig. 2 Kaplan- Meier survival analysis curves for stroke

within the study population. No significant interactions were observed between CMI and these subgroups, indicating that the relationship between CMI and stroke risk is not influenced by factors such as age, gender, smoking status, alcohol consumption, hypertension, diabetes, or depression (all *P*-values for interaction > 0.05). The results of the subgroup analysis can be found in Table 4.

Discussion

In this study, we examined the association between the CMI and the incidence of stroke among middle-aged and older individuals. Our findings indicate that higher CMI levels are significantly associated with an increased risk of stroke, even after adjusting for potential confounding factors. Furthermore, we observed a significant nonlinear relationship between CMI and stroke risk within this population.

Despite considerable advancements in stroke treatment and the ongoing refinement of clinical guidelines, stroke remains a leading cause of death globally. Non-traditional lipid markers, such as the TG/HDL-C ratio, have been identified as effective indicators of insulin resistance and may provide a quicker assessment of metabolic syndrome risk compared to individual lipid measurements. A large prospective study involving 96,542 participants demonstrated a significant independent association between a higher TG/HDL-C ratio and stroke risk [24]. Additionally, previous research, including studies by Zhang et al., has highlighted a nonlinear relationship between the TG/HDL-C ratio and stroke [25]. Unlike traditional lipid markers such as LDL-C and HDL-C, the TG/HDL-C ratio plays a more prominent role in predicting diabetes, hypertension, and cardiovascular events [26–29]. Moreover, lifestyle modifications and pharmacological treatments aimed at reducing triglyceride-rich lipoproteins and increasing HDL-C have been shown to lower the TG/HDL-C ratio, thus preventing atherosclerosis and reducing cardiovascular disease risk [30–32].

Although BMI is a widely used metric for assessing obesity and has been positively correlated with stroke risk [33–35], it does not always reflect fat distribution accurately. As a result, some studies have failed to find a robust relationship between BMI and stroke [36–38]. To overcome this limitation, markers of abdominal obesity, such as the Waist-to-Height Ratio (WHtR), have gained recognition. WHtR has been shown to more reliably reflect stroke risk than BMI [39, 40]. A meta-analysis revealed that increased WHtR levels are associated with central obesity, with each unit increase in WHtR corresponding to a 16% and 19% rise in all-cause and cardiovascular mortality, respectively [41].

The CMI, an innovative anthropometric measure combining obesity and lipid parameters, was first introduced by Wakabayashi et al. in 2015 and has since proven valuable in identifying diabetes [12]. Building upon this,

Table 3 Relationship between CMI and the risk of stroke in different models

Exposure	Model 1		Model 2		Model 3	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
CMI	1.173 (1.067–1.358)	< 0.001	1.177 (1.069–1.295)	< 0.001	1.132 (1.021–1.273)	0.003
Quartile[a]						
Q1	Reference		Reference		Reference	
Q2	1.541 (1.111–2.112)	0.007	1.552 (1.131–2.153)	0.004	1.501 (1.071–2.049)	0.013
Q3	1.851 (1.383–2.453)	< 0.001	1.921 (1.401–2.594)	< 0.001	1.653 (1.202–2.253)	0.001
Q4	2.124 (1.549–2.691)	< 0.001	2.336 (1.479–3.167)	< 0.001	1.899 (1.231–2.672)	< 0.001
P for trend		< 0.001		< 0.001		0.001

HR hazard ratio, *CI* confidence interval, *Q* quartile, *CMI* cardiometabolic index

Model 1: unadjusted

Model 2: adjusted for age, gender

Model 3: adjusted for age, gender, smoking status, drinking status, hypertension, diabetes, depressive symptom, BMI, LDL-C, CRP, HbA1C, UA

a CMI: Q1 (0.03–0.31), Q2 (0.32–0.49), Q3 (0.50–0.86), Q4 (0.87–10.22)

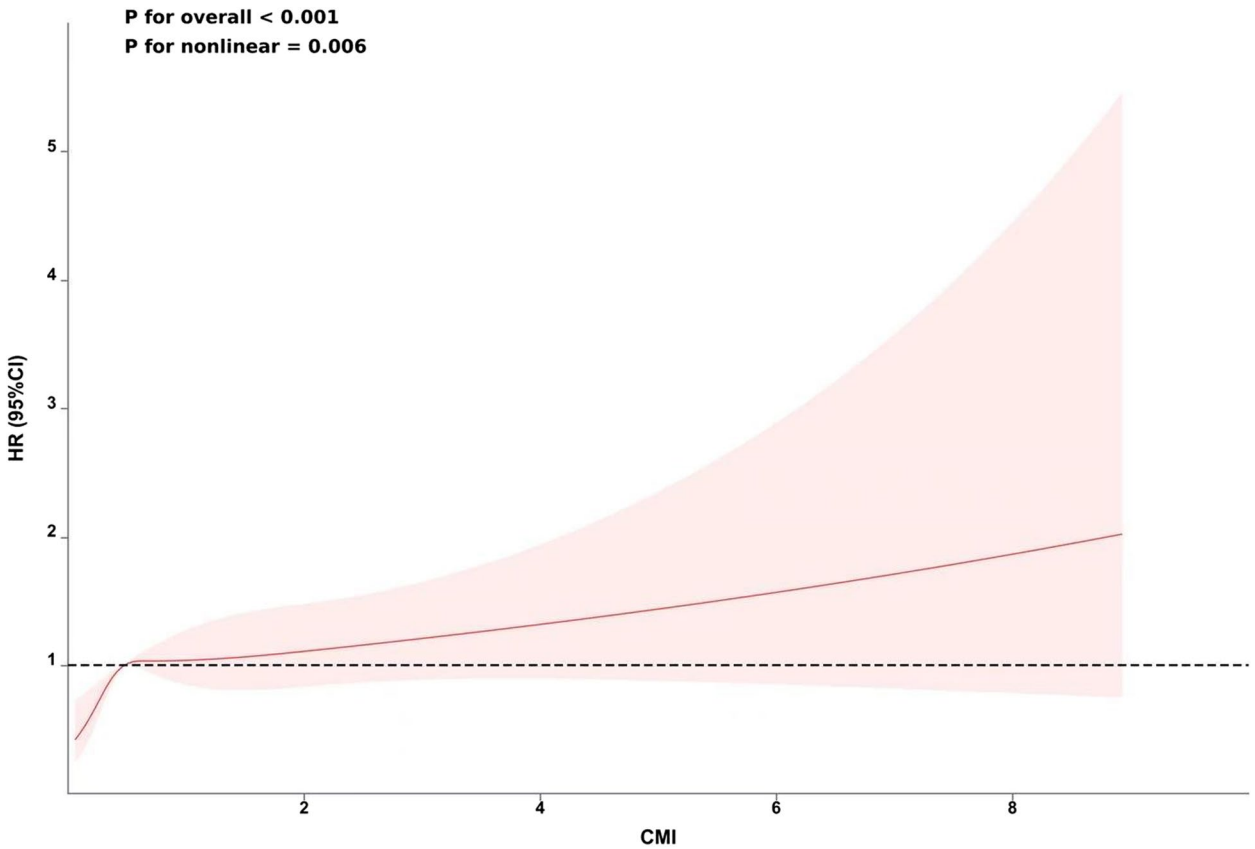

Fig. 3 Restricted cubic spline curves of the association between CMI and stroke

subsequent research has increasingly emphasized its significant role in CVD risk stratification. For instance, a study involving 5,557 participants with atherosclerosis revealed that each standard deviation change in the CMI was associated with a 31% relative increase in cardiovascular events among patients with the highest baseline cardiac metabolic risk (OR = 1.31, 95% CI = 1.14–1.50) [42]. This reinforces the utility of the CMI as a robust predictor for cardiovascular morbidity and highlights its potential as a clinical tool for risk assessment.

Moreover, the CMI has been consistently shown to correlate significantly with insulin resistance and arteriosclerosis, particularly in individuals with type 2 diabetes [43, 44]. These findings suggest that the CMI not only reflects metabolic dysfunction but also serves as an indicator of vascular health, making it valuable for early identification of patients at risk for both metabolic and cardiovascular diseases.

Prospective studies from Japan, with follow-up periods extending over 15 years, have provided further insights into the predictive value of the CMI. These studies suggest that the CMI may offer superior predictive power for ischemic cardiovascular disease when compared to other commonly used metabolic indices, such as the TyG index and the TG/HDL-C ratio [45]. This highlights the CMI's unique ability to integrate key metabolic parameters to provide a comprehensive risk assessment, surpassing the predictive capacity of traditional markers.

In addition to its cardiovascular implications, CMI has been shown to serve as a valid indicator for identifying left ventricular diastolic dysfunction, particularly in asymptomatic women, as reported by Ye et al. [46]. This suggests that CMI can be a valuable tool not only in cardiovascular risk assessment but also in detecting subclinical conditions that could predispose individuals to future cardiovascular events.

Furthermore, research by Miao et al. demonstrated that CMI is independently associated with microproteinuria, especially in diabetic patients [17]. This connection indicates a potential link between CMI and renal dysfunction, underscoring the index's broader clinical relevance. The association of CMI with renal dysfunction points to its potential role in detecting and monitoring multiple organ systems affected by metabolic disorders.

Moreover, studies by Zhou and Cheng identified an interesting association between elevated CMI levels and

Table 4 CMI Predicts Stroke Risk Uniformly Across Diverse Subgroups

Variable	Count	HR (95% CI)	*P* value	P for interaction
Age				0.587
< 65	5243	1.23 (1.01–1.33)	0.014	
≥ 65	1377	1.06 (0.87–1.31)	0.725	
Gender				0.475
Male	3069	1.11 (0.81–1.31)	0.614	
Female	3551	1.23 (1.12–1.41)	0.003	
Smoking				0.510
No	4801	1.11 (1.02–1.43)	0.003	
Yes	1819	0.77 (0.61–1.42)	0.814	
Drinking				0.039
No	4612	1.31 (1.02–1.53)	< 0.001	
Yes	2008	0.39 (0.49–1.32)	0.397	
Hypertension				0.674
No	4095	1.22 (1.01–1.61)	0.032	
Yes	2525	1.31 (0.87–1.43)	0.131	
DM				0.837
No	4950	1.23 (1.04–1.63)	0.042	
Yes	670	1.02 (0.81–1.43)	0.616	
Depression				0.427
No	5047	1.02 (0.72–1.34)	0.173	
Yes	1573	1.42 (1.12–1.73)	0.038	

a higher likelihood of depression in U.S. adults [47, 48]. Given that depression is a known risk factor for cardiovascular disease [49], these findings suggest that CMI may also be a useful tool in identifying patients at risk for comorbid mental health conditions, thereby adding another dimension to its utility in clinical practice.

Data examining the relationship between the CMI and stroke are still limited, with only a few studies providing insights into this association. Wang et al.'s study focused specifically on ischemic stroke in rural populations and found a potential relationship between CMI and stroke, although this research did not explore the linearity of the association [18]. Similarly, Li et al. studied CMI as a categorical variable in relation to stroke but did not consider it as a continuous measure [19]. Both studies were cross-sectional and conducted in northeastern China, limiting their ability to evaluate the dynamics of CMI's effect on stroke incidence over time. In contrast, Cai et al.'s study focused only on hypertensive patients with obstructive sleep apnea, providing a narrower scope that did not encompass the broader population at risk for stroke [50].

Our study expands on these earlier findings by evaluating CMI both as a categorical and continuous variable, thus minimizing potential information loss and offering a more robust and comprehensive view of the relationship between CMI and stroke. By employing restricted cubic splines, we also assessed the potential nonlinear relationship between CMI and stroke risk. In addition, we performed subgroup analyses to evaluate the consistency of our results across various demographic and clinical groups. Our results confirm earlier studies, while also adding new insights by demonstrating a nonlinear association between CMI and stroke risk. Specifically, we show that higher CMI levels are linked to a greater likelihood of incident stroke, independent of factors such as age, gender, smoking status, alcohol consumption, diabetes, or hypertension.

While the exact biological mechanisms underlying the CMI-stroke association remain incompletely understood, it is clear that CMI integrates key metabolic factors such as abdominal obesity and dyslipidemia, which are well-established contributors to stroke risk. Previous research has shown a strong correlation between CMI and insulin resistance (IR), which is characterized by impaired insulin sensitivity and response. This condition predisposes individuals to various metabolic disorders, including dyslipidemia, hypertension, and hyperglycemia, all of which are strongly associated with cardiovascular diseases (CVD) [51].

Hypertriglyceridemia, a hallmark of insulin resistance, has long been identified as a significant risk factor for atherosclerotic cardiovascular disease, as it promotes the accumulation of lipid-rich plaques in the arterial walls [30]. Furthermore, insulin resistance is commonly associated with a chronic, low-grade inflammatory state, which accelerates atherosclerosis by triggering the release of pro-inflammatory markers. These markers not only contribute to plaque formation but also facilitate the progression of cardiovascular disease through increased endothelial dysfunction and arterial stiffness [52].

Obesity, another key component of CMI, is an established risk factor for CVD, particularly in the context of insulin resistance. Obesity-induced dyslipidemia is often characterized by elevated levels of small, dense LDL, which are more prone to penetration into the subendothelial space of blood vessels, further contributing to plaque formation and atherosclerotic processes [53]. Additionally, chronic inflammation, commonly associated with both obesity and insulin resistance, plays a critical role in the development and progression of CVD. The interaction between inflammatory cells and the arterial endothelium has been extensively documented, and recent clinical trials have highlighted the importance of anti-inflammatory treatments in reducing cardiovascular events [54].

Limitations

It must be acknowledged that this study has several limitations.First, it focused only on individuals aged 45

and older, limiting the generalizability to younger populations or other ethnic groups. Future research should include broader age ranges and diverse populations. Second, while we adjusted for known confounders, the observational design cannot account for unmeasured or unknown confounders, such as genetic or environmental factors. This underscores the need for randomized controlled trials to confirm causal relationships. Third, loss to follow-up, particularly in fatal stroke cases, may have led to an underestimation of stroke incidence. Additionally, the lack of stratification between ischemic and hemorrhagic strokes limits our understanding of how CMI relates to different stroke types. Finally, stroke diagnoses were based on self-reports, which could introduce information bias and affect the accuracy of stroke incidence estimates.

Conclusion

In conclusion, there is a significant association between elevated levels of CMI and an increased risk of stroke among middle-aged and older individuals in China. Notably, this relationship is nonlinear. These findings contribute to the growing body of evidence supporting the clinical utility of CMI in predicting stroke risk. They provide valuable insights for developing early risk stratification and intervention strategies for the elderly and aid in the efficient allocation of medical resources.

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Authors' contributions
YY.B and ZK.X: data analysis, software, writing original draft, writing—reviewing and editing. J.T: acquisition and interpretation of data, writing original draft, writing—reviewing and editing. HL.Z, M.Z and YH.D: software, writing—reviewing and editing. B.W and AH.L: conceptualization, funding acquisition, and writing—reviewing and editing. All authors contributed to the article and approved the submitted version.

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Data availability
The data for this study can be accessed online at https://charls.pku.edu.cn/. To obtain the data, you will need to register as a user on the website. After your registration is reviewed and approved, you can follow the provided instructions to download the data set.

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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