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1 **Remnant Cholesterol Inflammatory Index** as a Predictive Biomarker for Stroke
2 **Risk in Middle-Aged and Elderly Individuals: Insights from the China Health and**
3 **Retirement Longitudinal Study**

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Abstract

Objective: The present study investigated the **Remnant Cholesterol Inflammatory Index**¹ (RCII), a novel biomarker integrating remnant cholesterol (RC) and high-sensitivity C-reactive protein (hs-CRP), to elucidate its association with stroke risk and explore its potential as a predictive tool among middle-aged and older adults in China.

Methods: A⁴ total of 7,940 middle-aged and elderly participants from the China Health and Retirement Longitudinal Study (CHARLS) were included. The primary endpoint was stroke event occurrence. The RCII was calculated⁶ as follows: $\text{RC (mg/dL)} \times \text{hs-CRP (mg/L)}/10$. The relationship between RCII⁴⁶ and stroke risk across different blood glucose levels was analyzed²³ using Kaplan-Meier curves, Cox proportional hazards models, and restricted cubic spline methods.

Results:⁵ During the follow-up period, 611 participants (7.7%) experienced a stroke. The baseline RCII and stroke occurrence had a significant positive linear relationship, where each unit¹³ increase in RCII was associated with an 11% higher stroke risk, particularly evident in individuals with impaired glucose regulation. Additionally, the RCII correlated positively with stroke risk¹ in the middle-aged population, whereas the association was not observed in the elderly population.¹ Mediation analysis indicated that diastolic blood pressure partially mediated the association between the RCII and stroke risk, with approximately 3.1% mediation.

Conclusion: Baseline RCII was a potential risk factor independently associated with incident stroke, highlighting its potential to reduce stroke burden and promote healthy aging, particularly in populations with prediabetes and middle-aged individuals. This

finding supported the development of targeted prevention strategies tailored to different glycemic statuses, contributing to health equity in stroke prevention.

Keywords: Remnant Cholesterol; Inflammation; Glycemic Status; Stroke; Prospective Studies

1 Introduction

Stroke remains a leading cause of morbidity and mortality worldwide, profoundly influencing public health systems and socioeconomic structures. The global stroke burden continues to rise despite marked advancements in acute management and secondary prevention, and is partly driven by aging populations and the persistence of modifiable risk factors[1]. Notably, stroke is characterized by high incidence, significant disability rate, and substantial recurrence risk, rendering it an important target for ongoing research and health policy intervention[2]. Stroke consequences extend far beyond the immediate clinical setting, affecting patients' long-term functionality and quality of life and imposing considerable financial strain on families and healthcare providers. This scenario underscores the urgent need for improved risk stratification and primary prevention strategies.

Epidemiological analyses revealed that China has one of the heaviest stroke burdens worldwide, where both stroke prevalence and incidence rates are among the highest globally[2]. Recent data indicated that the annual stroke incidence in high-risk Chinese populations can approach or exceed 5%[2], reflecting not only the vast population size but also the persistence of traditional risk factors such as hypertension, diabetes, and dyslipidemia[3]. Furthermore, there is an emerging trend of stroke onset at younger ages,

with increasing cases reported among middle-aged adults, amplifying the societal and economic effects through loss of productive years and escalating long-term care needs[4]. Despite ongoing public health campaigns and improved management of established risk factors, the overall decline in stroke incidence remains modest, and recurrent strokes constitute a substantial proportion of total events[5]. These epidemiological realities highlight the limitations of current prevention paradigms and the need for novel predictive approaches.

While conventional risk factors are the cornerstone of stroke risk assessment and prevention, a significant proportion of stroke events nevertheless occurs in individuals without overt risk factor elevation, or persist in those with well-controlled traditional markers[6]. This phenomenon, frequently termed “residual risk”, suggests that additional, unrecognized biological mechanisms may be important in stroke pathogenesis[7]. Accumulating evidence has implicated both lipid-related pathways, such as remnant cholesterol (RC), and chronic low-grade inflammation as key contributors to residual cardiovascular and cerebrovascular risk[8, 9]. Landmark studies have demonstrated that residual inflammatory risk, indexed by biomarkers such as hs-CRP, confers an increased risk of major vascular events even with optimal lipid-lowering therapy[10]. However, these pathways have largely been examined in isolation, and the interplay between dysregulated lipid metabolism and inflammation, and their combined effect on stroke risk, remains insufficiently addressed, especially in large, diverse, and longitudinally followed populations.

An important gap persists in the identification and validation of integrated biomarkers that can capture the synergistic effect of dyslipidemia and chronic inflammation on stroke

89 risk. The recently proposed Remnant Cholesterol Inflammatory Index (RCII) represents a
90 promising composite biomarker. ⁴² RC is a component of atherosclerotic lipoprotein [such
91 as ²¹ High-density lipoprotein (HDL) and intermediate-density lipoprotein], directly
92 ⁴⁵ promoting foam cell formation and inflammatory response, while ¹³ hs-CRP is a classic
93 systemic low-grade inflammation marker, and the two represent the key links of lipid
94 deposition and inflammation activation in atherosclerosis initiation and progression.
95 While ¹ initial studies suggested that both RC and hs-CRP are individually associated with
96 adverse cardiovascular outcomes[11], the predictive utility of their combined index
97 (RCII) for incident stroke has not been systematically evaluated, especially in Asian
98 populations or among individuals with varying glycemic states. Moreover, whether RCII
99 provides incremental value over established risk stratification tools or can identify high-
100 risk subgroups, such as those with impaired glucose metabolism or younger age, that may
101 benefit from targeted preventive interventions remains unclear. Therefore, addressing
102 these questions is essential for advancing precision medicine approaches in stroke
103 prevention and refining risk stratification beyond the conventional paradigms.

104 Based on the aforementioned evidence, the ²⁴ RCII, a composite index integrating RC
105 and hs-CRP, was hypothesized to be associated with incident stroke risk, potentially
106 ³¹ providing incremental predictive value beyond traditional risk factors. However, this
107 hypothesis has not been systematically evaluated in large, community-based Asian
108 cohorts, particularly among individuals with varying glycemic statuses.

Therefore, the present study investigated the association between RCII and incident stroke risk in a large, community-based Chinese cohort, and explored whether this association varies by glycemic status and age, to provide evidence for the incorporation of composite lipid-inflammation indices into stroke prediction models.

Materials and Methods

Study Design

The study data were derived from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal cohort study. CHARLS used a multi-stage stratified probability proportional sampling method, and completed its first national baseline survey in 2011, which covered 450 communities (villages/residential areas) across 28 provinces in China, and included a total of 17,708 middle-aged and elderly residents aged ≥ 45 years. Follow-ups were conducted in 2013, 2015, and 2018. The key blood biomarker data used to calculate the RCII were collected during the first round (2011: 11,847 participants) and the third round (2015: 13,420 participants) of the survey. The detailed CHARLS sampling design, anthropometric measurements, and laboratory testing methods have been published previously[12, 13].

This study was approved by the Peking University Ethics Review Committee (IRB00001052-11015), and all participants provided written informed consent before enrollment. The present report adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[12].

Study Population

Figure 1 details the participant selection process. Specifically, 11,847 individuals from the CHARLS 2011 wave (Wave 1) who had provided blood samples were included. Subsequently, Wave 1 participants were systematically excluded according to the following criteria pre-established during the study design phase:

1. Missing data: Individuals with missing basic demographic information (n = 97), or missing data on hs-CRP, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and HDL cholesterol (HDL-C) from Wave 1 (n = 216), and fasting blood glucose and glycated hemoglobin A1c (HbA1c) from Wave 1 (n = 110);
2. Non-compliance with inclusion criteria: Individuals aged <45 years or missing (n = 338);
3. Loss to follow-up: Individuals who were lost to follow-up (n = 2,652);
4. Outliers: Individuals with extreme RCII values (less or more than 3 standard deviations from the mean) (n = 77);
5. Pre-existing disease: Individuals diagnosed with stroke at baseline (n = 417).

After the above screening, the primary analysis included a total of 7,940 participants. Furthermore, the dynamic changes of RCII in relation to stroke risk were explored through the further selection of participants with available RCII data from both Wave 1 and 3 of the survey, forming a 5,962-individual subset for analysis (Figure S1, flowchart).

Exposure and Outcomes

The definitions and calculation methods for the core variables, and the criteria for determining the primary research outcomes, were as follows:

RC was calculated as follows: $RC\ (mg/dL) = TC - (HDL-C + LDL-C)$.

RCII is a new indicator that integrates lipid and inflammatory status, and was calculated as follows: $RCII = RC\ (mg/dL) \times hs-CRP\ (mg/L)/10$ [15].

Cumulative RCII (cumRCII) was calculated to assess long-term exposure, defined as the average of two RCII measurements multiplied by the time interval (years): $cumRCII = [(RCII_{2012} + RCII_{2015})/2] \times (2015 - 2012)$ [16]. The interval in the present study was 3 years.

Based on RCII levels, the participants were categorized into three RCII trajectory groups through k-means clustering: Cluster 1 (stable low risk), Cluster 2 (high to low risk), and Cluster 3 (low to high risk) (Figure S6).

Prevalent stroke at baseline was defined based on the participants' self-report of a physician-diagnosed stroke during the baseline interview. The question used was: "Have you ever been diagnosed with stroke by a doctor?" (CHARLS 2011 baseline questionnaire, Section D, Item D-12). Participants who answered "yes" were considered to have prevalent stroke and excluded from the analysis. All stroke subtypes (ischemic, hemorrhagic, unspecified) were grouped together, as the primary aim of exclusion was to remove individuals with any prior stroke event.

The primary outcome was the incidence of new stroke events. Stroke events were collected through standardized questionnaires, which included the participants' self-

174 reported and physician-diagnosed history of stroke, diagnosis date, and treatment
175 status[17, 18]. For event determination, participants who reported a physician-diagnosed
176 stroke for the first time during the follow-up period were classified as having experienced
177 an outcome event. The onset date was defined as the date of diagnosis reported by the
178 patient. Regarding person-years calculation, the follow-up time for participants who
179 experienced a stroke¹ was calculated as the interval from the baseline survey date to the
180 onset date. For participants who did not experience a stroke, the follow-up time was
181 calculated from the baseline survey date to the date of their last participation in the
182 survey.

184 **Data Collection**

185 The participants' baseline data¹ were collected by trained interviewers using a
186 standardized questionnaire system. The information covered: (1)¹ sociodemographic and
187 behavioral characteristics [gender, age, residence (urban/rural), education level, marital
188 status, smoking and drinking status]. (2) Clinical and biochemical indicators: physical
189 measurements [height, weight, systolic blood pressure (SBP), diastolic blood pressure
190 (DBP)] and body mass index (BMI). Laboratory tests involved collecting fasting venous
191 blood samples to measure fasting blood glucose (FBG), glycated hemoglobin (HbA1c),
192 TC, triglycerides (TG),³⁷ HDL-C, LDL-C, and hs-CRP levels.⁷ Medical professionals
193 collected the blood specimens, which were maintained at -20°C during storage, and
194 transported via temperature-controlled delivery to the Chinese Center for Disease Control
195 and Prevention in Beijing. FBG and lipid profiles were measured using enzyme-based
196 colorimetric methods.²⁶ HbA1c was determined by boronate affinity high-performance

liquid chromatography, and hs-CRP was quantified through immunoturbidimetric assay on a Hitachi 7180 automated analyzer[19]. (5) Medical history and medication use: self-reported medical history of stroke, hypertension, diabetes, dyslipidemia, liver disease, kidney disease, and the use of antihyperlipidemic, antihypertensive, and antidiabetic medications. These comprehensive baseline data provided extensive covariate information for subsequent analyses.

Definitions

The major disease states in the present study were defined as follows and were all based on baseline survey information: hypertension was defined by meeting any of the following criteria: (1) self-reported physician-diagnosed history of hypertension; (2) currently receiving any antihypertensive medication; and (3) measured SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg[20].

Diabetes was defined by meeting any of the following criteria: (1) self-reported physician-diagnosed history of diabetes; (2) currently receiving any antidiabetic medication; (3) FBG $\geq$ 7.0 mmol/L (126 mg/dL); and (4) HbA1c $\geq$ 6.5%[21].

Prediabetes was defined as having no history of diabetes and meeting any of the following criteria: (1) FBG between 5.6 and 6.9 mmol/L (100–125 mg/dL); and (2) HbA1c between 5.7% and 6.4%.

Normal glucose regulation (NGR) was defined as having no history of diabetes, with FBG $<$ 5.6 mmol/L (100 mg/dL) and HbA1c $<$ 5.7%[21]. All glycemic indicators (FBG and HbA1c) were measured at the baseline survey. The classification was based solely on baseline data, and changes during follow-up were not considered. Oral glucose tolerance

test (OGTT) results were not available in CHARLS; therefore, the classification relied on FBG, HbA1c, self-report, and medication use, which was consistent with standard epidemiological practice.

Dyslipidemia was¹ defined by meeting any of the following criteria: (1) self-reported physician-diagnosed history of dyslipidemia; (2) currently taking lipid-lowering medications; (3) TG ≥ 1.7 mmol/L (150 mg/dL); (4) TC ≥ 6.2 mmol/L (240 mg/dL); (5) HDL-C < 1.0 mmol/L (40 mg/dL); and (6) LDL-C ≥ 4.1 mmol/L (160 mg/dL). Other disease histories, such as liver disease and kidney disease, were determined based on the participants' self-reported medical history or corresponding medication treatment.

Handling of Missing Variables

Missing data were assessed and addressed by systematically evaluating¹ the missing patterns and proportions for each variable (Table S22, Figure S2). Statistical efficiency was ensured and potential selection bias introduced by deleting cases with missing data was reduced through multiple imputation to address all covariates with missing values.

Statistical Analysis

The statistical analyses used¹ the following methods, with all tests being 2-tailed, and $P < 0.05$ considered statistically significant. Analyses were conducted using R software (version 4.5.0).

1. Description of baseline characteristics and inter-group comparisons: Participants were divided into four groups (Q1–Q4) based on baseline RCII quartiles. Continuous variables were described according to their distribution characteristics: normally distributed

variables were presented as the mean $\pm$ standard deviation, and groups were compared through one-way analysis of variance; non-normally distributed variables were presented as the median (interquartile range), and groups were compared through the Kruskal-Wallis rank-sum test. Categorical variables were presented as the frequency (percentage), and groups were compared through chi-square tests or Fisher's exact tests.

2. Primary analysis methods: For survival analysis and association assessment, result robustness was enhanced by analyzing the RCII both as a categorical variable (quartiles) and a continuous variable. The cumulative stroke incidence among RCII level groups was plotted using Kaplan-Meier curves, and groups were compared using the log-rank test. The association between RCII and stroke risk was assessed using Cox proportional hazards regression models. Confounding factors were controlled by constructing three progressively adjusted models: Crude Model, no adjustment for any variables; Model 1, adjusted for demographic and behavioral factors [gender, age, residence (urban/rural), marital status, education level, smoking, drinking status]; Model 2, further adjusted for clinical factors, including history of hypertension, diabetes, coronary artery disease, kidney disease, liver disease, dyslipidemia, BMI, SBP, and DBP. The dose-response relationship was flexibly modeled between RCII and stroke risk, and restricted cubic spline (RCS) functions with three knots placed at percentile 10, 50, and 90 of the RCII distribution were fitted in multivariate Cox regression models. The reference value was RCII percentile 10. Both the *P*-value for overall association (testing whether any non-flat relationship existed) and the *P*-value for nonlinearity (testing whether the relationship deviated from linearity) were reported. Proportional hazard assumptions for these Cox regression models were confirmed by Schoenfeld residuals (Figure S5). The predictive

266 ability of the RCII and its changes in stroke were⁶ assessed by the area under the receiver
267 operating characteristic curve (AUC), and the RCII AUC was compared with baseline²¹
268 CRP, TC, HDL, and LDL¹⁰ indices using the DeLong test.

269 3. Supplementary and in-depth analyses: The participants were divided into subgroups
270 with distinct characteristics through K-Means clustering using continuous RCII
271 monitoring data from 2012 and 2015.¹ K-Means is an unsupervised learning method that
272 optimizes intra-cluster homogeneity and inter-cluster heterogeneity by minimizing the
273 within-cluster sum of squares (WCSS).³⁰ The optimal number of clusters was determined
274 using the elbow method.¹ The relationship between the WCSS and cluster number was
275 plotted, and the point at which the reduction in the sum of squared distances began to
276 decelerate, commonly designated as the “elbow”, was identified. Three clusters were
277 selected based on this analysis,¹ as this point was identified where the curve flattened,
278 indicating that model simplicity and interpretative accuracy were optimally balanced by
279 three clusters while avoiding overfitting (Figure S6A).¹ The survival analysis, Cox
280 regression, and RCS analyses were repeated¹ stratified by baseline glucose metabolism
281 status (NGR, prediabetes, diabetes). Potential pathways linking RCII to stroke risk were
282 explored through mediation analysis using the Baron and Kenny (1986) approach^[22],
283 combined with 1,000-resample bootstrapping to estimate the indirect effect and its 95%
284 confidence interval (CI). Four potential mediators measured at baseline were examined:
285 FBG, SBP, DBP, and BMI.¹ All mediation models were adjusted for the same covariates
286 as Model 2. The temporal order assumed that RCII (reflecting long-term lipid
287 metabolism) preceded the mediator, and the mediator preceded the outcome (incident
288 stroke). However, as both exposure and mediator were measured at baseline, this

289 assumption could not be fully verified. Therefore, the results should be interpreted as
290 exploratory associations, not causal estimates.¹ Subgroup analyses were performed based
291 on gender, age (45–60 years vs. ≥60 years), smoking, drinking, residence, and disease
292 history. The cut-off of 60 years was chosen based on literature indicating an accelerated
293 increase in stroke incidence and vascular aging after age 60 years, and the clinical
294 relevance of this threshold in cardiovascular risk stratification[23].¹ Whether these factors
295 significantly modulate the association between RCII and stroke risk was further evaluated
296 through¹ interaction tests between RCII and each stratified factor.⁴⁰ Whether the association
297 between RCII and stroke risk varied by age (45–60 years vs. ≥60 years) was evaluated
298 using a formal interaction test¹² by including a product term (RCII × age group) in the fully
299 adjusted Cox model. The results were validated using a series of sensitivity analyses.
300 First, a re-analysis was conducted following the exclusion of all participants with missing¹
301 variables. Second, a re-analysis was performed after participants with non-fasting status
302 at baseline were removed. Third, a re-analysis was conducted following the exclusion of
303 participants who died during the follow-up period.⁶ Fourth, the Cox models were replaced
304 by logistic and Poisson regression models for the analysis. Fifth, a re-analysis was
305 conducted after analyses that included extreme RCII values. Sixth, the potential over-
306 adjustment caused by covariate adjustment was evaluated using the stepwise adjustment
307 method. Model 1 included demographic and behavioral variables (age, gender, smoking¹
308 status, drinking status, residence, education level, marital status), after which metabolic
309 indicators⁴ (SBP, DBP, BMI) and history of comorbidities (hypertension, diabetes
310 mellitus, coronary heart disease, dyslipidemias, liver disease, nephrosis) were stepwise
311 included. Comparing the magnitude of change in the RCII effect estimate (hazard ratio

[HR]) across steps determined whether newly included variables excessively influenced the main effect. The risk of over-adjustment was considered low if the HR change between consecutive adjustment steps was <20%. Finally, E-values were computed to quantify the minimum association strength required of unmeasured confounders to account for the observed link between RCII and stroke risk, where the E-value was derived as follows: $E = RR + \sqrt{RR \times (RR - 1)}$ [24].

Results

Population Baseline Characteristics

The present study included a total of 7,940 participants from the CHARLS. The average participant age was 58.23 ± 8.71 years, and there were 3,616 men (45.5%). Baseline characteristic comparisons indicated that participants in the highest RCII quartile (Q4) had significantly different characteristics compared to those in the lowest quartile (Q1): Regarding demographic and behavioral characteristics, Q4 participants were more likely to be urban residents and to have a higher proportion of smoking history.

Regarding disease and medication history, Q4 participants had a higher prevalence of dyslipidemia, hypertension, diabetes, and stroke, and a higher proportion of those receiving antihyperlipidemic, antihypertensive, and antidiabetic medication. Regarding physical and metabolic indicators, Q4 participants had higher BMI, SBP, and DBP. Furthermore, laboratory indicators demonstrated that Q4 participants had significantly elevated HbA1c, FBG, TC, TG, LDL-C, and hs-CRP levels, and lower HDL-C levels.

Table 1 presents the participants' detailed baseline characteristics.

Appendix S1 presents the baseline characteristic comparisons²⁸ of the population following the exclusion of individuals with missing values for all variables. Appendices S2, S3, S4, and S27 contain the³ baseline characteristics comparisons based on cumRCII, cumulative average RCII, stroke occurrence group, and cluster, respectively. Appendix S23 contains² the baseline characteristics between the baseline analysis sample and the subset with repeated measurements (used to calculate cumRCII). Lastly, Appendix S28 contains the⁴³ baseline characteristics between the included population and the lost-to-follow-up population.

¹ Relationship Between RCII and Stroke Risk

First, the relationship between RCII and stroke risk in the overall population was assessed. The core result indicated that higher RCII levels were an independent risk factor for stroke events, but the association primarily manifested in a single measurement (baseline RCII) rather than long-term cumulative exposure (cumRCII).

¹ A total of 611 participants (7.7%) experienced their first stroke during the follow-up period.¹ The stroke incidence significantly increased with ascending RCII quartiles (Q1–Q4: 5.4%, 6.6%, 8.3%, 10.4%, respectively; Table 1, Figure 2). Similarly, the Kaplan-Meier analysis demonstrated significantly different¹ cumulative stroke incidences among the RCII level groups (P for log-rank < 0.001; Figure 3A). The multivariable Cox proportional hazards regression model (Model 2) confirmed that³ the stroke risk increased by 11%¹⁴ per unit increase in RCII (HR = 1.113, 95% CI: 1.048–1.182), and higher quartiles had higher risk trends than¹ the lowest quartile (Q1) (P for trend < 0.001; Table

2). RCS analysis further suggested a significant positive linear dose-response relationship between RCII and stroke risk (P for overall = 0.006, P for nonlinear = 0.485; Figure 4A).

Contrastingly, adjusting for the same confounders identified no significant association between cumRCII and stroke risk (P for trend = 0.117 and 0.104; Appendix S5 and S26). Furthermore, the RCS analysis did not reveal a significant dose-response relationship between the two (P for overall = 0.461, P for nonlinear = 0.923; Figure S3).

The association between the RCII trajectory and stroke risk was explored (Appendix S25). After adjusting for the same confounders, the high-to-low risk group (Cluster 2) had a 98.8% higher risk compared to the stable low-risk group (Cluster 1) (HR = 1.988, 95% CI: 1.253–3.152, $P < 0.003$), while the low-to-high risk group demonstrated no statistically significant difference (Cluster 3).

ROC curve analysis was conducted to distinguish RCII from various single indicators. The RCII (AUC = 0.581) outperformed baseline RC (AUC = 0.560, $P = 0.028$), TC (AUC = 0.528, $P < 0.001$), HDL (AUC = 0.555, $P = 0.047$), LDL (AUC = 0.517, $P < 0.001$), and hs-CRP (AUC = 0.562, $P = 0.014$) in predicting stroke risk (Figure S4).

In summary, baseline RCII levels were significantly associated with increased stroke risk, while cumRCII exposure did not demonstrate a similar association.

Relationship Between RCII and Stroke Risk According to Glucose Status

Stratified analysis based on glucose status (NGR, prediabetes, diabetes) revealed the heterogeneity in the RCII and stroke risk association. The results indicated that the effects of elevated RCII on stroke risk concentrated primarily in the prediabetic population, with

no significant association observed in individuals with normal glucose or those diagnosed with diabetes.

The specific results are as follows: Kaplan-Meier analysis revealed significant differences in cumulative stroke incidence among RCII level groups in both NGR and prediabetic populations ($P < 0.001$). However, diabetes patients did not demonstrate a statistically significant difference ($P = 0.13$) (Figure 3B–D). Multivariable Cox regression analysis revealed a significant positive association between RCII and stroke risk only in the prediabetic individuals. After adjusting for confounders, the stroke risk increased by 17.8% per unit increase in RCII (HR = 1.178, 95% CI: 1.081–1.284). Higher RCII quartiles demonstrated a significant increasing trend in risk as compared to the lowest quartile (Q1) (P for trend < 0.001). Both NGR and diabetic individuals did not demonstrate significant associations ($P > 0.05$) (Table 3). The RCS analysis results were consistent with these results, demonstrating a significant linear positive relationship between RCII and stroke risk only in the prediabetic population (P for overall = 0.002, P for nonlinear = 0.896); no significant dose-response correlation was observed in NGR and diabetic patients (P for overall = 0.107 and 0.652, P for nonlinear = 0.106 and 0.857, respectively) (Figure 4B–D).

In conclusion, the results suggested that RCII is a significant stroke risk factor in the prediabetic population, but the strength of its association varies across different glucose metabolism states, emphasizing the need to focus on the prediabetic stage in stroke prevention.

399

400 *Subgroup Analysis*

401 The association between RCII and stroke susceptibility was elucidated through a¹
402 subgroup analysis. The results demonstrated that the positive correlation between RCII
403 and stroke risk remained consistent across most pre-specified subgroups, including
404 gender, age strata (45–60 years vs. ≥60 years), residence, smoking status (never/current
405 smoker), drinking status (never/current drinker), and the presence of hypertension,
406 diabetes, dyslipidemia, liver disease, or kidney disease. However, interaction analysis
407 revealed an important effect modifier.³ RCII and age strata demonstrated a significant¹
408 interaction (P for interaction = 0.020), where the strength of the effect of RCII on stroke
409 risk differed significantly between the 45–60- and ≥60-year-old populations (Table 4).

410³ Figure 5 and Appendix S6 present the detailed data.

411 Several analyses consistently indicated that RCII was an independent stroke risk factor¹
412 in the middle-aged individuals (45–60 years): Kaplan-Meier analysis revealed¹
413 significantly increased cumulative stroke incidence with ascending RCII quartiles (P for¹
414 log-rank < 0.001; Figure 6A). Multivariable Cox regression analysis demonstrated that³
415 after adjusting for confounders, the stroke risk significantly increased by 20.1% per unit¹⁴
416 increase in RCII (HR = 1.201, 95% CI: 1.109–1.301; Table 4). Moreover, this
417 relationship persisted even after patients with heart disease and arthritis had been
418 excluded (Table S24).¹ Additionally, higher RCII level groups as compared to the lowest
419 quartile (Q1) presented a significant increasing trend in risk (P for trend < 0.001; Table
420 4). RCS analysis confirmed a significant positive linear dose-response relationship
421 between RCII and stroke risk (P for overall < 0.001, P for nonlinear = 0.122; Figure 7A).³

However, the aforementioned associations did not reach statistical significance in older individuals (≥ 60 years): Kaplan-Meier curves revealed no significant differences ($P = 0.075$; Figure 6B), and Cox regression analysis revealed no significant association between RCII and stroke risk ($P > 0.05$; Table 4). Furthermore, RCS analysis did not indicate a significant dose-response relationship (P for overall = 0.528, P for nonlinear = 0.411; Figure 7B). In conclusion, the positive association between RCII and stroke risk was significantly present only in the middle-aged population, while it was not evident in the older population, strongly suggesting that age is an important effect modifier of the RCII and stroke relationship.

Mediation Analysis

Mediation analysis indicated that DBP partially mediated the association between RCII and stroke risk (approximately 3.1% mediation). This result suggested that in the total effect where elevated RCII leads to increased stroke risk, approximately 3.1% of the effect is achieved through the elevated DBP pathway. Therefore, controlling DBP in interventions may provide some benefits, but the measured mediators could not explain most of the association, suggesting the involvement of other pathways or residual confounding.

The potential mediating roles of FBG, SBP, and BMI were assessed, and demonstrated that they were not significant mediators of the effect of RCII on stroke risk. This result indicated that traditional cardiovascular risk factors did not substantially mediate the RCII and stroke risk association.

1 The intricate interplay between RC and hs-CRP in stroke risk was explored. Mediation analysis did not reveal a stable and significant mediating relationship to explain the joint association of these two factors with stroke risk. Therefore, the effects of RC and hs-CRP on stroke risk are likely to be independent or driven by other unmeasured common upstream factors (confounders) (Figure 8).

Although several potential mediating pathways were explored, the proportion of mediation mediated by diastolic blood pressure was found to be small (3.1%), and other candidate mediators were deemed not significant. This suggests that, within the framework of the current analysis and the range of measured mediating variables, most of 1 the association between RCII and stroke risk could not be explained by these traditional cardiovascular risk factors, indicating the possible existence of residual direct effects or effects through other unmeasured pathways.

457 *Sensitivity Analysis*

4 The robustness of the primary results was validated through a series of sensitivity analyses, which indicated that the positive association between RCII and stroke risk remained consistent across different analytical contexts.

First, a re-analysis was conducted after all individuals with missing data, all non-fasting participants, those who died during follow-up, and those with extreme RCII values had been included. Substantial alterations were not observed in the direction, magnitude, or statistical significance of the HR (Tables S7–S15, S29–S31).

Second, separate statistical models were used for verification; the original Cox proportional hazards model was replaced by logistic and Poisson regression analyses, which confirmed that the primary conclusions were robust (Tables S16–S21).

Third, the RCII remained an independent risk factor for incident stroke after the lost-to-follow-up population was included in the primary analysis (Table S35).

Fourth, the HR of RCII for stroke risk gradually changed from the crude model to the fully adjusted model during the stepwise adjustment process, where the maximum change in HR between steps was <20%, indicating that adjusting for different covariates had a limited influence on the effect estimate and a low likelihood of over-adjustment. Supplementary Tables S32–S34 present the specific changes.

Unmeasured confounding factors in the association of RCII were quantitatively assessed within the multivariable adjusted model (Model 2), which yielded an E-value of 1.46 that suggested that relatively substantial unmeasured confounding effects accounted for the observed HRs.

In summary, sensitivity analyses confirmed the robustness of the main conclusions of the present study regarding RCII and stroke risk association. The E-value suggested that the HRs were explained by relatively large unmeasured confounding effects.

Discussion

The present study demonstrated that baseline RCII is a robust and independent predictor of incident stroke, particularly among individuals with prediabetes and middle-aged individuals. Notably, the high-low trajectory of RCII, but not the low-high trajectory, was associated with a 98.8% increased risk, supporting a “legacy effect” of early

inflammatory exposure. These results surpassed previous work by integrating temporal dynamics, glycemic status, and age to identify high-risk subgroups, providing a novel framework for targeted stroke prevention.

¹ The examination of the distinct metabolic and inflammatory profiles of individuals with elevated RCII revealed a pronounced clustering of cardiovascular risk factors (hypertension, diabetes, dyslipidemia) and increased markers of systemic inflammation, particularly among urban residents and those with adverse lifestyle behaviors. Mechanistically, this aggregation may reflect the underlying interplay between chronic low-grade inflammation and metabolic dysregulation, wherein RC exacerbates endothelial dysfunction, while ¹hs-CRP marks persistent vascular inflammation. Research supports the idea that RCII integrates these two axes and more accurately encapsulates the burden of metabolic syndrome and its vascular sequelae than either marker alone[25, 26].

Notably, both US and Chinese population studies have reported a nonlinear, inverse J-shaped association between RCII and metabolic syndrome risk, where risk was amplified at lower thresholds and plateaued at higher levels, possibly due to regulatory feedback mechanisms or survivor bias in the very high-risk strata[25]. Compared to previous epidemiological investigations that frequently isolated either dyslipidemia or inflammation as independent predictors, the nuanced approach of the present study highlighted ²the synergistic and multiplicative risk conferred by their co-elevation, which was supported by recent machine learning analyses of diabetic kidney disease and coronary artery disease cohorts where RCII emerged as a top predictive feature[27, 28]. The distinctive methodological strength of using a large, nationally representative

Chinese cohort enabled robust extrapolation to a broad at-risk demographic, addressing the limitations of smaller or region-specific studies that may have lacked sufficient heterogeneity for generalization[29]. In summary, the clustering of metabolic and inflammatory derangements among individuals with high RCII underscored a complex, multifactorial pathophysiological substrate.

The robust association between baseline RCII and stroke risk in the present cohort provided compelling evidence for RCII as a superior predictive biomarker compared to traditional inflammatory or lipid measures. Mechanistically, RC is implicated in promoting atherogenesis through retention and oxidation within the arterial intima, while hs-CRP is a sensitive marker of vascular inflammation and plaque instability. Therefore, their product may reflect both chronic substrate accumulation and active inflammatory processes in the vasculature[16, 30]. Previous investigations demonstrated that RCII consistently outperformed its constituent components in predicting adverse vascular outcomes³ in both Chinese and Western populations,³ with receiver operating characteristic analyses demonstrating that the RCII AUC surpassed that of RC or hs-CRP alone[16, 30].

¹Notably, the dose-response relationship in the present study aligned with the results of large cohort analyses, which indicated a continuous and graded increase in event rates across RCII quartiles[29, 31]. Conversely, the lack of association between cumRCII and stroke risk may reflect the importance of acute or baseline inflammatory-lipid burden in triggering cerebrovascular events, as opposed to long-term average exposure, a pattern observed in cardiovascular disease progression studies¹ where baseline, but not cumRCII, was most predictive[31]. This divergence supported the hypothesis that dynamic or

534 episodic vascular inflammation and lipid toxicity surges may be more important stroke
535 precipitants than chronic low-level exposure. Essentially, baseline RCII integrates acute¹
536 metabolic and inflammatory status and provides an enhanced lens for vascular risk
537 stratification.

538 Baseline RCII likely captures an individual's inherent, relatively stable state of
539 inflammation and immune responses. This state may be shaped by genetic background,
540 early life environment, and epigenetic programming, and can cause progressive,
541 cumulative, and even irreversible damage to the vascular endothelium early in life (for
542 example, by promoting oxidative stress, endothelial cell senescence, and intercellular
543 adhesion molecule expression). The subsequent vascular disease progression may enter a
544 relatively autonomous stage upon the formation of this "damage imprint". Therefore, the
545 inflammatory burden reflected by the baseline has important "initiation" or "setting"
546 value, while RCII fluctuations during follow-up have a relatively diminished marginal
547 effect on long-term risk.

548 RCII is a composite indicator whose components may exhibit significant physiological
549 fluctuations and measurement errors. These random errors are partially offset in long-
550 term follow-up when calculating the mean of multiple measurements, but may also dilute
551 (regression dilution bias) the true association strength with outcomes. Additionally,
552 inflammation-induced vascular damage may have a critical exposure window period
553 (e.g., during middle age) or nonlinear dose-response relationship. Simple arithmetic
554 means (cumRCII) may not capture such complex temporal patterns, thereby
555 underestimating the exposure effects during specific high-risk periods. Moreover, long
556 intervals between repeated measurements complicate the fine tracking of the dynamic

changes in RCII, particularly potentially missing inflammation fluctuations related to the acute phase or subclinical phase before stroke onset, leading to a weakened association between cumulative indicators and endpoint events. Therefore, baseline RCII may represent an inflammatory phenotype that reveals an individual's long-term cardiovascular susceptibility, integrating cumulative exposure during early life stages and exerting lasting biological effects on the vascular system.

Contrastingly, measurement errors, nonlinear chronobiological effects, and coarse temporal resolution may obscure the associations of the epidemiological calculation metric cumRCII. This difference suggested that a single baseline measurement may be sufficient to capture an individual's inflammation-related long-term risk in risk prediction models, whereas more intensive measurement frequencies and more complex time-varying analytical models are required for accurate assessment of the effects of time-varying exposures.

The differential effects of RCII ¹ across glycemic strata, most pronounced in prediabetes, suggested a stage-specific vulnerability. Heightened endothelial dysfunction and preserved vascular reactivity create a unique susceptibility window in this state, where RCII most effectively captures risk[32, 33], and highlights the need for targeted screening in this population. ¹ Comparative analyses demonstrated that while RCII predicts all-cause and cardiovascular outcomes in both normoglycemic and diabetic cohorts, its strongest associations emerged in those with intermediate dysglycemia, plausibly due to both preserved vascular reactivity and emerging metabolic derangement[11, 32]. This increased risk may be attributable to a setting in which compensatory mechanisms are overwhelmed but irreversible organ damage has not yet occurred, rendering this group

580 most susceptible to acute vascular events in the context of inflammatory-lipid
581 perturbations. Furthermore, subgroup analyses from longitudinal studies confirmed that
582 the predictive value of RCII was more pronounced in individuals without established
583 diabetes, supporting the concept of a critical intervention window before overt
584 disease[33]. Collectively, these results underscored ¹the importance of targeted screening
585 and intervention in the prediabetic population based on integrated inflammatory and lipid
586 risk profiling.

587 The accentuated predictive utility ¹in middle-aged adults, but attenuation in the elderly,
588 indicated age-related differences in vascular biology. In middle-aged individuals, RCII
589 reflects active proatherogenic processes, whereas competing risks (e.g., atrial fibrillation)
590 may dilute its contribution in older adults[34]. This result suggested that RCII-based risk
591 stratification is most valuable for middle-aged populations. ¹Large-scale population
592 studies demonstrated that the association between RCII and mortality or major vascular
593 outcomes is strongest in middle-aged individuals, with effect sizes tapering in older
594 cohorts likely due to competing risks, survivor bias, or the dominance of non-modifiable
595 factors in advanced age. Additionally, the predictive power of composite biomarkers such
596 as RCII may be diluted in elderly populations with multiple comorbidities and
597 polypharmacy, which introduce heterogeneity and potentially confound direct
598 mechanistic associations[29].

599 Although related studies have typically adjusted ¹⁹for traditional cardiovascular risk
600 factors such as age, blood lipids, and blood pressure, the possibility of residual
601 confounding remains a significant limitation. This is mainly reflected in two aspects:
602 first, the stroke subtype heterogeneity. Ischemic stroke etiology is complex, and includes

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large artery atherosclerosis, cardioembolism, and small vessel disease[35]. Even patients diagnosed with atherosclerotic stroke may have unrecognized subclinical embolic sources, such as asymptomatic atrial fibrillation or complex aortic arch plaques. The second aspect is individual immune status complexity. Circulating interleukin (IL)-6 or hs-CRP are only a few representative indicators of systemic inflammation. An individual's overall immune status, including innate and adaptive immunity activation levels, the immune cell metabolic state, and the broader cytokine network, exhibits substantial heterogeneity and is difficult to measure comprehensively[36]. These unmeasured immunological variables may be key residual confounding factors, affecting interpretation of inflammatory pathway specificity. Therefore, this result should be validated with more refined stroke subtype classification and more comprehensive immune marker detection.

10

Compared with the stable low-risk trajectory (Cluster 1), the high-low risk trajectory (Cluster 2) was associated with a 98.8% increased risk of stroke, whereas the low-high trajectory (Cluster 3) demonstrated no significant increase. This result suggested a legacy effect of early inflammatory exposure: sustained high RCII may cause persistent vascular damage (e.g., endothelial dysfunction, plaque instability) that translates into long-term risk even after later decline[37-39]. Conversely, the null risk in the low-high group implied a critical time window or cumulative threshold, where the inflammatory exposure may have been too brief to trigger clinically relevant events[40], or its effect may be subtype-specific (e.g., cardioembolism vs. large artery atherosclerosis) and require a longer follow-up[40]. Overall, these results highlighted the importance of considering the history of inflammation instead of only its current level, and support integrating dynamic

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RCII changes into risk prediction models for targeted prevention in individuals with prior high inflammatory burden.

The mediation analysis demonstrated that DBP mediated only 3.1% of the RCII–stroke association, suggesting that RCII’s primary effects are likely through other pathways (e.g., plaque instability). Hence, this exploratory finding should be investigated further. Additionally, ¹the absence of significant mediation by glycemic indices or body mass suggested that RCII captures vascular risk not fully explained by the canonical metabolic syndrome framework, implicating alternative mechanisms such as lipid-induced oxidative stress and immune activation[41].

As an inflammation/immune imbalance marker, the RCII may affect DBP more directly by promoting vascular endothelial dysfunction and increasing peripheral vascular resistance, instead of through traditional metabolic pathways. Vascular wall elastic fibers decrease with age, and collagen increases, leading to arteriosclerosis. Inflammation may accelerate this process, but may first manifest as functional dystonia in the early stages, with elevated DBP becoming a sensitive indicator of sustained increased peripheral vascular resistance. Chronic inflammation has a continuous and progressive role, potentially first causing functional vascular changes (e.g., dystonia) before leading to structural changes (e.g., atherosclerosis). Therefore, elevated DBP may reflect the early and continuous effects of inflammation on the vascular wall, providing an early warning for stroke risk. Traditional risk factors such as LDL-C primarily promote stroke through structural changes (atherosclerosis), a slower process. Contrastingly, RCII-driven inflammation may alter hemodynamics more rapidly through functional dysregulation,

rendering DBP elevation a sensitive and early indicator of this process and suggesting a potential pathway through this functional dysregulation.

In summary, as an inflammatory marker, RCII may preferentially affect DBP by promoting vascular endothelial dysfunction and increasing peripheral vascular resistance, providing a dynamic and functional explanation for stroke risk. This mechanism may be more prominent in populations with reduced vascular elasticity. However, given the small proportion of the mediating effect of DBP and the influence of various confounding factors, its absolute clinical significance must be considered in the context of overall risk assessment. Future research should quantify the direct effects of inflammation on vascular function, validate the mediating role of DBP in longitudinal cohorts, and explore whether interventions targeting inflammation can specifically improve DBP and reduce stroke risk.

Study Strengths and Limitations

The first strength of the present study was the use of a large, nationally representative cohort from CHARLS, which enhanced the generalizability of the results to the Chinese middle-aged and older population. Second, to our knowledge, few studies have evaluated the association between the RCII and incident stroke; therefore, the present study provided novel evidence for integrating lipid inflammation biomarkers into risk prediction. Third, the dose-response analysis and subgroup analyses across glycemic status and age strata enabled a nuanced understanding of effect heterogeneity. Fourth, the mediation analysis presented preliminary mechanistic insights into the pathways linking RCII to stroke.

The limitations of the present study were as follows: first, stroke was ascertained by self-reported physician diagnosis¹ without systematic neuroimaging or medical record verification, which may have introduced misclassification bias, especially in underserved areas. Second, the inability to differentiate ischemic from hemorrhagic stroke subtypes precluded etiology-specific analyses. Third, RCII was measured at only two time points over 4 years, limiting the assessment of dynamic changes and potentially attenuating associations.³⁹ Fourth, despite adjustment for known confounders, residual confounding from unmeasured factors (e.g., medication adherence, lifestyle changes) could not be ruled out. Fifth, participants with RCII values beyond mean $\pm$ 3 SD (<1%) were excluded, which may have omitted clinically high-risk individuals, although this criterion was pre-specified to minimize data errors. Sixth, glycemic status was classified without OGTT data, which may have misclassified individuals with isolated postprandial hyperglycemia. Seventh, predictive performance metrics [e.g., C-statistic, net²⁰ reclassification improvement(NRI), integrated discrimination improvement(IDI), decision curve analysis(DCA)] were not evaluated, as the present study was designed to test association, and not to develop a clinical prediction model. Furthermore, the modest effect size and limited events in the subgroups restricted such analyses.¹⁶ Future studies should address these limitations with more rigorous outcome verification, refined biomarker measurements, and larger validation cohorts.

Conclusion

⁵ The present large, prospective cohort study demonstrated that baseline RCII is a potential⁴⁴ risk factor independently associated with incident stroke, particularly among individuals

with prediabetes and middle-aged individuals. The present study was¹ among the first to integrate a combined lipid inflammatory index in a large Chinese cohort, highlighting the unique vulnerability of prediabetic individuals and the modifying effect of age on stroke risk.

Clinical Relevance

Our results provided feasible insights for patient care. Specifically, identifying an³ elevated RCII in the prediabetic stage can be a practical tool for:

Enhanced Risk Stratification: Clinicians can use the RCII to identify high-risk individuals beyond traditional risk factors. For example, a middle-aged patient with prediabetes and an elevated RCII may necessitate more intensive lifestyle counseling and closer monitoring than a patient with prediabetes alone.

Targeted Screening: The RCII can be used to prioritize subclinical vascular disease screening³² in high-risk subgroups, such as middle-aged individuals with prediabetes, potentially enabling earlier detection of those who would benefit most from aggressive risk factor management.

Informing Clinical Trial Design: The identification of this specific vulnerable population provides a clear basis for future hypothesis-driven³³ randomized controlled trials to test whether RCII-guided interventions (e.g., with specific lipid-lowering or anti-inflammatory agents) can reduce stroke incidence.

Future Perspectives

Future research can further refine risk prediction by incorporating repeated, high-frequency biomarker assessments and validating stroke outcomes with clinical adjudication. Ultimately, by paving the way for translational research into glycemic status-specific interventions, the present study strengthens primary stroke prevention in aging populations, alleviating disease burden, fostering healthy aging, and advancing health equity.

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Author contributions

YZ conceived and designed the study and wrote the main manuscript text. FF analyzed the data. YZ and BY conducted the literature search and prepared the figures. FF performed the manuscript review. All authors reviewed and approved the final manuscript.

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Availability of Data and Materials

The data supporting the results are available on the CHARLS website (http://charls.pku.edu.cn/).

Ethics Approval and Consent to Participate

The Peking University Ethics Review Committee (institutional review board) approved the present study. All participants granted formal written consent for their involvement.

Consent for Publication

Not applicable.

Competing Interests

The authors declare no competing interests.

Figure Legends

Figure 1. Flowchart of the study population.

Abbreviations: RCII, Remnant Cholesterol Inflammatory Index; hs-CRP, high-sensitivity C-reactive protein; HbA1c, glycated hemoglobin A1c; FBG, fasting blood glucose.

Figure 2. Stroke incidence rates categorized by RCII quartiles.

Abbreviations: Q1, Quartile 1; Q2, Quartile 2; Q3, Quartile 3; Q4, Quartile 4; RCII: Remnant Cholesterol Inflammatory Index.

Figure 3. Kaplan–Meier curves depict the cumulative incidence of stroke by RCII quartiles.

(A) Total participants. (B) Participants with NGR. (C) Participants with Pre-DM. (D) Participants with DM.

Abbreviations: Q1, Quartile 1; Q2, Quartile 2; Q3, Quartile 3; Q4, Quartile 4; RCII: Remnant Cholesterol Inflammatory Index; NGR, normal glucose regulation; Pre-DM, pre-diabetes mellitus; DM, diabetes mellitus.

Figure 4. Association between RCII and stroke risk. Knots were placed at RCII percentiles 10, 50, and 90. The reference value was RCII percentile 10. The solid line represents the hazard ratio (HR), and the shaded area indicates the 95% confidence interval. *P* for overall association and *P* for nonlinearity are reported.

(A) Total participants. (B) Participants with NGR. (C) Participants with Pre-DM. (D) Participants with DM.

Adjusted for age, gender, smoking status, drinking status, residence, education level, marital status, SBP, DBP, BMI, hypertension, dyslipidemia, diabetes, liver disease and kidney disease.

Abbreviations: RCII: Remnant Cholesterol Inflammatory Index; NGR, normal glucose regulation; Pre-DM, pre-diabetes mellitus; DM, diabetes mellitus; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Figure 5. Subgroup and interaction analyses of the association between RCII and stroke risk.

Abbreviations: RCII: Remnant Cholesterol Inflammatory Index; DM, diabetes mellitus; HR, hazard ratio; CI, confidence interval.

Figure 6. Kaplan–Meier curves depict the cumulative stroke incidence by RCII quartile.

(A) Age 45–60 years. (B) Age $\geq$ 60 years.

Abbreviations: Q1, Quartile 1; Q2, Quartile 2; Q3, Quartile 3; Q4, Quartile 4; RCII: Remnant Cholesterol Inflammatory Index.

Figure 7. Association between RCII and stroke risk by age group. Knots were placed at RCII percentile 10, 50, and 90. The reference value was RCII percentile 10. The solid line represents the hazard ratio (HR), and the shaded area indicates the 95% confidence interval. *P* for overall association and *P* for nonlinearity are reported.

(A) Age 45–60 years. (B) Age ≥ 60 years. Adjusted for age, gender, smoking status, drinking status, residence, education level, marital status, SBP, DBP, BMI, hypertension, dyslipidemia, diabetes, liver disease, and kidney disease.

Abbreviations: RCII: Remnant Cholesterol Inflammatory Index; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Figure 8. Mediation analyses of stroke risk factors.

(A) BMI, SBP, FBG, and DBP as mediators of the relationship between RCII and new-onset stroke. (B) Reciprocal mediation of new-onset stroke risk by RC and hs-CRP.

Adjusted for age, gender, smoking status, drinking status, residence, education level, marital status, SBP (with the exception of the SBP models), DBP (with the exception of the DBP models), BMI (with the exception of the BMI models), hypertension, dyslipidemia, diabetes, liver disease, and kidney disease.

Abbreviations: RCII, Remnant Cholesterol Inflammatory Index; RC, remnant cholesterol; hs-CRP, high-sensitivity C-reactive protein; BMI, body mass index; FBG, fasting blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.

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