Association of combined high-sensitivity C-reactive protein and residual cholesterol levels with new-onset metabolic syndrome

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Abstract

Introduction: Metabolic syndrome (MetS) involves dyslipidaemia and inflammation. However, the joint association of high-sensitivity C-reactive protein (hsCRP) and residual cholesterol (RC) with the risk of MetS remains unclear.
Material and methods: This longitudinal study enrolled 7,063 participants from the China Health and Retirement Longitudinal Study (CHARLS). Participants were grouped by median RC (17 mg/dl) and hsCRP threshold (1 mg/l). Multivariate logistic regression and restricted cubic spline (RCS) analyses were used to evaluate the joint association of RC and hsCRP with the risk of MetS.
Results: During the 4-year follow-up period, 920 participants (11.5%) developed new-onset MetS. Compared with the group with low RC and low hsCRP, the fully adjusted odds ratio (OR) was 1.43 (p = 0.005) for the high RC only group and 2.56 (p < 0.001) for the group with both elevated levels, with a significant trend (p < 0.001). The residual cholesterol inflammation index (RCII) was positively associated with incident MetS risk. The fully adjusted OR (with 95% confidence interval [CI]) for quartile (Q) 4 vs. Q1 was 2.52 (1.92–3.30, p < 0.001), with a non-linear trend (p < 0.001). This association was consistent across age, sex, and BMI subgroups (all p for interaction > 0.05) and remained robust after excluding participants taking lipid-lowering drugs and using multiple imputation.
Conclusions: Elevated hsCRP and RC were independently and synergistically associated with a higher MetS risk. Combined evaluation of inflammatory and lipid-related markers may help identify individuals at increased risk of MetS. The findings provide further evidence of the association between these pathways and MetS development.

Key words: metabolic syndrome, high-sensitivity C-reactive protein, residual cholesterol, China Health and Retirement Longitudinal Study.

Introduction

Metabolic syndrome (MetS) is a cluster of interrelated metabolic abnormalities, characterized by elevated fasting glucose, hypertension, abdominal obesity, and dyslipidaemia [1]. With economic development and lifestyle changes, the prevalence of MetS has increased worldwide,

becoming a major public health concern. Statistics show that in the United States, the prevalence of MetS increased from 37.6% in 2011–2012 to 41.8% in 2017–2018 [2], and the prevalence in other countries and regions also shows an upward trend [3]. The series of metabolic disorders included in MetS are closely associated with the risk of chronic diseases such as cardiovascular disease (CVD) and diabetes [4]. Therefore, finding early biomarkers for the early assessment and subsequent intervention of MetS has become a current research focus.

The pathogenesis of MetS is complex and multifactorial. Obesity is the core driving factor for the development of MetS [5]. The interplay between chronic low-grade inflammation and lipid metabolism disorders is a key aspect in the onset and progression of this condition [6]. Adipose tissue, as an endocrine organ that stores excess lipids, becomes imbalanced in obesity, triggering the release of pro-inflammatory factors, activating inflammatory signalling pathways, inhibiting insulin signalling, and exacerbating insulin resistance [7]. Meanwhile, the inflammatory response also affects the activity of lipid metabolism enzymes [8] and promotes the synthesis and secretion of very low-density lipoproteins in the liver, leading to triglyceride (TG) accumulation and decreased high-density lipoprotein cholesterol (HDL-C), thereby causing dyslipidaemia [9]. Lipid metabolism disorders and chronic inflammation may contribute to a reinforcing cycle in which metabolic disturbances are associated with inflammatory activation and further metabolic deterioration [10].

Residual cholesterol (RC), as a cholesterol component rich in TG-containing lipoproteins, including very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and chylomicron remnants, plays a key role in the pathogenesis of atherosclerosis and CVD [11, 12], possibly affecting the development of MetS through inflammatory responses, lipotoxicity and endothelial dysfunction [13, 14]. As RC levels rise, the body often experiences persistent low-grade inflammation. High-sensitivity C-reactive protein (hsCRP), as a sensitive marker of systemic low-grade inflammation, may contribute to the development of MetS through pathways involving endothelial dysfunction, oxidative stress and impaired insulin signalling. The combined effect of RC and hsCRP, as well as the residual cholesterol inflammation index (RCII), has shown predictive value for adverse cardiometabolic outcomes, including stroke, diabetes, and cardiovascular-kidney-metabolic risk [15–17]. However, the association of combined RC and hsCRP levels with incident MetS is not well established, and the association between RCII and MetS remains unclear.

To address the above research gaps, using the China Health and Retirement Longitudinal Study (CHARLS) data, we examined the joint associations of hsCRP, RC, and RCII with incident MetS to improve risk stratification.

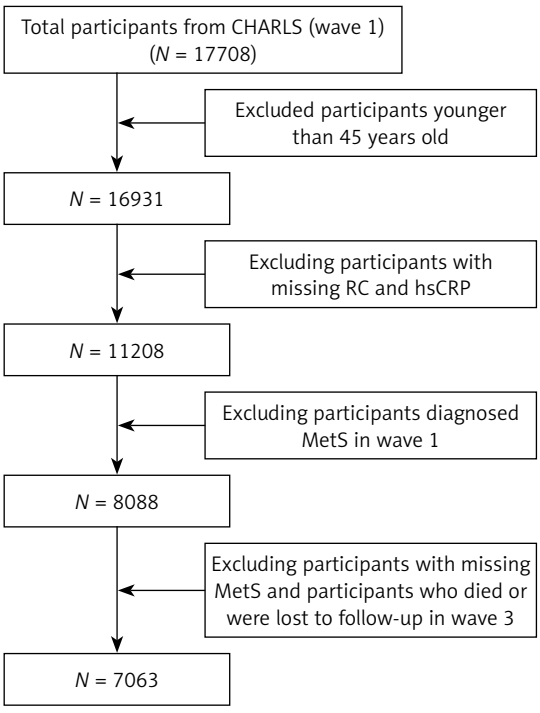

Figure 1. The flowchart of the sample selection

RC – residual cholesterol, hsCRP – high sensitivity C-reactive protein, CHARLS – China Health and Retirement Longitudinal Study.

Material and methods

Study design

The data for this study were sourced from CHARLS, which included a total of 17,708 participants aged 45 and above. The baseline survey was conducted in 2011, with follow-up surveys carried out in 2013, 2015, 2018, and 2020 [18]. Blood biomarkers (blood lipids, fasting blood glucose, hsCRP) were only collected in 2011 and 2015; therefore, 2011 was used as the baseline and 2015 as the follow-up [19]. The research methods and data collection procedures implemented by CHARLS have been published previously [20]. The CHARLS study was approved by the Ethics Committee of Peking University (Approval No: IRB00001052-11015), and all participants provided informed consent.

Study population

The inclusion and exclusion criteria for study participants are shown in Figure 1. Initially, the 2011 baseline dataset included 17,708 participants. Participants aged ≥ 45 years were screened, and 777 participants were excluded; in addition, 5,723 participants were excluded due to missing

RC and hsCRPdata; furthermore, 3,120 participants already diagnosed with MetS at the 2011 baseline were excluded. Finally, 1,025 participants were excluded due to missing 2015 MetS diagnosis data or because they died or were lost to follow-up by 2015, leaving a final cohort of 7,063 participants.

Assessment of exposure

The calculation formula for RC is: total cholesterol (TC) minus low-density lipoprotein cholesterol (LDL-C) and HDL-C [11]. Participants were stratified into four different groups based on the median RC level (17 mg/dl) and hsCRP threshold of 1 mg/l. Group 1 participants had lower levels of both hsCRP and RC, with hsCRP < 1 mg/l and RC < 17 mg/dl. Group 2 participants had low RC levels but elevated hsCRP levels, with hsCRP ≥ 1 mg/l and RC < 17 mg/dl. Group 3 consisted of participants with elevated RC but low hsCRP, defined as hsCRP < 1 mg/l and RC ≥ 17 mg/dl. Finally, Group 4 participants had elevated levels of both RC and hsCRP, with hsCRP ≥ 1 mg/l and RC ≥ 17 mg/dl. The RCII was calculated using the formula: RCII = (RC [mg/dl] × hsCRP [mg/l])/10 [15].

Assessment of outcome

Diagnosis of MetS: The diagnosis of MetS was carried out according to the Joint Interim Societies' definition of MetS, using their categorizations of waist circumference (WC) for Chinese people [1]. In brief, participants with WC ≥ 80 cm for females and WC ≥ 90 cm for males who also met any two of the following criteria were diagnosed with MetS: (1) TG > 150 mg/dl (1.7 mmol/l); (2) HDL-C < 40 mg/dl (1.03 mmol/l) in men or < 50 mg/dl (1.29 mmol/l) in women; (3) systolic blood pressure (SBP) ≥ 130 mm Hg or diastolic blood pressure (DBP) ≥ 85 mm Hg or use of anti-hypertensive medicine; (4) fasting plasma glucose (FPG) ≥ 100 mg/dl (5.6 mmol/l) or the use of anti-diabetic medicine.

Assessment of covariates

This study adjusted for sociodemographic characteristics, health-related behaviours and anthropometric indicators in the analysis [21, 22]. Demographic variables included age, gender, educational level ("primary school or below", "high school", "university or above"), place of residence ("urban/town" and "rural"), and marital status ("married" and "unmarried/separated/widowed"). Health-related behaviour variables covered smoking status ("non-smoker", "former smoker", "current smoker"), alcohol consumption ("drinking", "never"), medical conditions (heart disease, stroke, arthritis, cancer, kidney disease), and medication usage (lipid-lowering drugs). Anthropometric variables including height (m) and weight (kg) were measured by trained medical staff according to a standard protocol. The body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Baseline data for participants were carefully collected by well-trained interviewers using standardized structured questionnaires.

Statistical analysis

Continuous variables are presented as mean (standard deviation, SD) or median (interquartile range, IQR). Categorical variables are presented as frequencies (percentages). One-way analysis of variance, the Kruskal-Wallis H test, or the χ^2 test was used to compare baseline characteristics according to disease occurrence groups. We used three logistic regression models to evaluate the combined effect of hsCRP and RC on the occurrence of MetS. Model I was unadjusted; Model II adjusted for age, sex, education level, residence, and marital status; Model III further adjusted for smoking status, alcohol consumption, BMI, heart disease, stroke, arthritis, cancer, kidney disease, and use of lipid-lowering medications. Participants were divided into six different groups based on median RC levels and hsCRP clinical thresholds of 1 mg/l and 3 mg/l. The combined association of hsCRP and RC with MetS incidence was further quantified using multinomial logistic regression. In addition, two logistic regression models were used to assess the individual effects of hsCRP and RC on the incidence of MetS. Finally, RCII was analysed in quartiles to examine its association with the risk of MetS, and restricted cubic splines (RCS) were used to visualise whether there was a nonlinear relationship between RCII and MetS incidence.

We employed various sensitivity analyses to verify the robustness of the outcomes. Firstly, subgroup analyses were conducted based on age, sex and BMI. Secondly, considering that RC levels may be influenced by medication, the primary analysis was repeated after excluding individuals using lipid-lowering drugs. Finally, we used the multiple imputation method by chained equations in the R package "mice". The first complete dataset was selected and merged to form the final analysis dataset, after which a preliminary analysis was conducted again.

All statistical analyses were performed using R software (version 4.5.2, R Foundation for Statistical Computing, Vienna, Austria). RCS was conducted using the "rms" package; multiple imputation was performed using the "mice" package, with statistical significance set at $p < 0.05$.

Results

Baseline characteristics

Based on the inclusion and exclusion criteria, this study included a total of 7,063 participants.

Among them, 920 (11.5%) were diagnosed with MetS, with a median age of 57 years, and 66.3% were female. Supplementary Table SI provides a stratified analysis of participant characteristics according to MetS status, showing that, compared with participants without MetS, those with MetS had higher levels of hsCRP, RC, and RCII. Furthermore, within the MetS group, the proportion of individuals with high hsCRP and RC levels was greater than that of individuals with low hsCRP and RC levels ($p < 0.001$).

Association of combined hsCRP and RC with new-onset MetS

Table I shows the association between combined hsCRP and RC levels and incident MetS. After adjusting for all covariates, higher odds of MetS were observed in individuals with elevated RC alone (OR = 1.43), with the highest odds observed in those with concurrent elevation of hsCRP and RC (OR = 2.56), compared with those with lower levels of hsCRP and RC.

To more accurately assess the joint association of RC and hsCRP with the incidence of new-onset MetS, a logistic regression analysis was conducted, stratifying participants based on median RC levels and hsCRP thresholds of 1 mg/l and 3 mg/l (Table II). Participants with lower levels of hsCRP and RC were used as the reference group. After adjusting for all covariates, in the low RC stratum (RC < 17 mg/dl), participants with hsCRP levels of 1–3 mg/l had a 1.40-fold higher risk of MetS compared

Table I. Graded association between combined hsCRP and RC levels and new-onset MetS in CHARLS

Parameter	Events *N* (%)	Model I		Model II		Model III	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
The combination of RC and hsCRP							
Group 1	194 (21.1)	Ref.		Ref.		Ref.	
Group 2	156 (17.0)	1.14 (0.92–1.43)	0.234	1.29 (1.03–1.62)	0.026	1.29 (0.98–1.70)	0.072
Group 3	217 (23.6)	1.33 (1.09–1.64)	0.006	1.41 (1.14–1.73)	0.001	1.43 (1.11–1.85)	0.005
Group 4	353 (38.4)	2.42 (2.01–2.93)	< 0.001	2.74 (2.26–3.33)	< 0.001	2.56 (2.01–3.27)	< 0.001
P for trend			< 0.001		< 0.001		< 0.001

RC – residual cholesterol, hsCRP – high-sensitivity C-reactive protein, OR – odds ratio, 95% CI – 95% confidence interval. Model I was unadjusted; Model II adjusted for age, sex, education level, residence, and marital status; Model III further adjusted for smoking status, alcohol consumption, BMI, heart disease, stroke, arthritis, cancer, kidney disease, and use of lipid-lowering medications.

Table II. Joint association of hsCRP and RC categories with new-onset MetS in CHARLS

Parameter	Events *N* (%)	Model I		Model II		Model III	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
The combination of RC and hsCRP							
hsCRP < 1 mg/l and RC < 17 mg/dl	194 (21.1)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
3 mg/l > hsCRP ≥ 1 mg/l and RC < 17 mg/dl	117 (12.7)	1.31 (1.03–1.67)	0.028	1.45 (1.13–1.86)	0.003	1.40 (1.03–1.89)	0.030
hsCRP ≥ 3 mg/l and RC < 17 mg/dl	39 (4.2)	0.82 (0.57–1.17)	0.292	0.98 (0.67–1.40)	0.911	1.06 (0.675–1.61)	0.795
hsCRP < 1 mg/l and RC ≥ 17 mg/dl	217 (23.6)	1.33 (1.09–1.64)	0.006	1.41 (1.14–1.73)	0.001	1.43 (1.11–1.85)	0.005
3 mg/l > hsCRP ≥ 1 mg/l and RC ≥ 17 mg/dl	238 (25.9)	2.41 (1.97–2.97)	< 0.001	2.69 (2.18–3.32)	< 0.001	2.38 (1.82–3.12)	< 0.001
hsCRP ≥ 3 mg/l and RC ≥ 17 mg/dl	115 (12.5)	2.44 (1.89–3.14)	< 0.001	2.85 (2.19–3.69)	< 0.001	2.96 (2.12–4.11)	< 0.001
P for trend			< 0.001		< 0.001		< 0.001

RC – residual cholesterol, hsCRP – high-sensitivity C-reactive protein, OR – odds ratio, 95% CI – 95% confidence interval. Model I was unadjusted. Model II adjusted for age, sex, education level, residence, and marital status. Model III further adjusted for smoking status, alcohol consumption, BMI, heart disease, stroke, arthritis, cancer, kidney disease, and use of lipid-lowering medications.

Table III. Independent associations of RC and hsCRP with new-onset MetS in CHARLS

Parameter	Events *N* (%)	Unadjusted model		Adjusted model	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
hsCRP < 1 mg/l					
RC < 17 mg/dl	194 (47.2)	Ref.	Ref.	Ref.	Ref.
RC ≥ 17 mg/dl	217 (52.8)	1.33 (1.09–1.64)	0.006	1.43 (1.11–1.85)	0.006
hsCRP ≥ 1 mg/l					
RC < 17 mg/dl	156 (30.6)	Ref.	Ref.	Ref.	Ref.
RC ≥ 17 mg/dl	353 (69.4)	2.12 (1.73–2.60)	< 0.001	1.98 (1.51–2.58)	< 0.001
RC < 17 mg/dl					
hsCRP < 1 mg/l	194 (55.4)	Ref.	Ref.	Ref.	Ref.
hsCRP ≥ 1 mg/l	156 (44.6)	1.14 (0.92–1.43)	0.234	1.33 (1.00–1.75)	0.048
RC ≥ 17 mg/dl					
hsCRP < 1 mg/l	217 (38.1)	Ref.	Ref.	Ref.	Ref.
hsCRP ≥ 1 mg/l	353 (61.9)	1.82 (1.51–2.19)	< 0.001	1.80 (1.41–2.29)	< 0.001

RC – residual cholesterol, hsCRP – high-sensitivity C-reactive protein, OR – odds ratio, 95% CI – 95% confidence interval.

with the reference group (OR = 1.40, 95% confidence interval [CI]: 1.03–1.89, $p = 0.030$). Subjects with RC levels at or above the median exhibited an increased risk of MetS across all hsCRP categories: 1.43-fold increase at hsCRP < 1 mg/l, 2.38-fold increase at 1 mg/l ≤ hsCRP < 3 mg/l, and 2.96-fold increase at hsCRP ≥ 3 mg/l.

As shown in Table III, both hsCRP and RC were independently associated with the incidence of MetS. Participants with elevated RC levels have an increased risk of MetS, regardless of hsCRP levels. Conversely, participants with elevated hsCRP levels have a higher risk of MetS, irrespective of RC levels. Receiver operating characteristic (ROC) curve analysis demonstrated that RC was a stronger predictor than hsCRP in predicting incident MetS, with a higher area under the receiver operating characteristic curve (AUC) (0.605 vs. 0.566; 95% CI: 0.585–0.626 vs. 0.547–0.586; $p = 0.003$ by DeLong's test).

Unadjusted model was unadjusted.

Adjusted model adjusted for age, sex, education level, residence, and marital status, smoking status, alcohol consumption, BMI, heart disease, stroke, arthritis, cancer, kidney disease, and use of lipid-lowering medications.

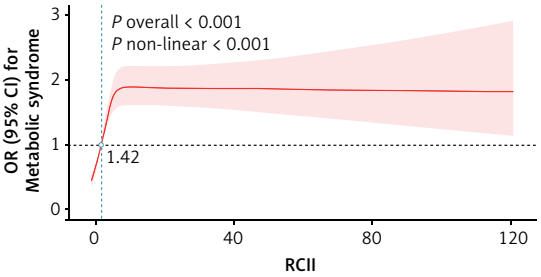

Figure 2. Association between RCII and new-onset MetS modeled using restricted cubic splines

RCII – residual cholesterol inflammation index, MetS – metabolic syndrome, OR – odds ratio, 95% CI – 95% confidence interval.

Relationship of RCII with MetS

This study found a non-linear association between RCII and MetS (Figure 2). Table IV shows that as RCII quartiles (Q) increase, the risk of MetS also rises, with Q2, Q3, and Q4 groups having 48%, 126%, and 152% higher risk of MetS, respectively, compared to Q1.

Table IV. Association between RCII and new-onset MetS in CHARLS

Parameter	Events *N* (%)	Model I		Model II		Model III	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Quartiles of RCII							
Q1	196 (21.3)	Ref.		Ref.		Ref.	
Q2	236 (25.7)	1.40 (1.14–1.71)	0.001	1.49 (1.21–1.82)	< 0.001	1.48 (1.15–1.89)	0.002
Q3	250 (27.2)	1.94 (1.59–2.36)	< 0.001	2.23 (1.82–2.74)	< 0.001	2.26 (1.76–2.91)	< 0.001
Q4	238 (25.9)	2.49 (2.03–3.06)	< 0.001	2.92 (2.37–3.61)	< 0.001	2.52 (1.92–3.30)	< 0.001
P for trend			< 0.001		< 0.001		< 0.001

RCII – residual cholesterol inflammation index, OR – odds ratio, 95% CI – 95% confidence interval. Model I was unadjusted. Model II adjusted for age, sex, education level, residence, and marital status. Model III further adjusted for smoking status, alcohol consumption, BMI, heart disease, stroke, arthritis, cancer, kidney disease, and use of lipid-lowering medications.

Sensitivity analyses

To assess the robustness of our findings, we performed several sensitivity analyses. Sensitivity analyses stratified by age, sex, and BMI, excluding lipid-lowering drug users, and using multiple imputation yielded results consistent with the primary analysis (Supplementary Tables SII–SIX).

Discussion

This study showed that elevated hsCRP and RC, individually and jointly, were associated with a higher risk of incident MetS, while higher RCII was nonlinearly associated with greater MetS risk. In addition, sensitivity analyses also confirmed the robustness of these results. Notably, RC was a stronger predictor than hsCRP in predicting incident MetS. Exploratory component-specific analyses showed that RC was mainly associated with hypertriglyceridemia, whereas hsCRP and RCII showed limited discriminatory performance for individual MetS components (Supplementary Table SX).

MetS is considered a high-risk condition resulting from the clustering of central obesity, insulin resistance, dyslipidaemia and elevated blood pressure [23, 24]. HsCRP, as a marker of systemic inflammation, is closely associated with insulin resistance, abdominal obesity, endothelial dysfunction and increased atherosclerosis risk; several epidemiological studies suggest that elevated hsCRP levels can predict the occurrence of MetS and the deterioration of its components [25–27]. RC has been regarded as an important supplementary indicator of "non-LDL cholesterol" risk and is associated with various metabolic and inflammatory diseases, such as atherosclerotic events and diabetes [28–30]. The combined effect of RC and hsCRP has a stronger predictive ability for diseases. For example, a previous study based on CHARLS data indicated that combined RC and hsCRP levels were associated with the onset of diabetes, and a potential mutual mediation effect between the two was suggested [16]; research in the field of CVD also reported that simultaneous elevation of RC and hsCRP was associated with increased risk of myocardial infarction and stroke [31]. This study extends this research direction to MetS, showing that simultaneous elevation of RC and hsCRP was more strongly associated with the incidence of new-onset MetS (OR = 2.56), exceeding that observed for elevated single markers. This synergistic effect may reflect the interplay between lipid metabolism and low-grade inflammation. Given that MetS and diabetes share common pathological pathways including insulin resistance and chronic inflammation, the combined predictive value of RC and hsCRP for MetS aligns with and extends previous findings in diabetes, underscoring the broad relevance of this lipid-inflammatory interplay across metabolic disorders. On one hand, elevated RC may contribute to endothelial dysfunction and macrophage activation, promoting the secretion of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α), and upregulating hsCRP expression by activating related signalling pathways [28, 32]. On the other hand, under chronic inflammatory conditions, cytokines such as TNF-α and IL-1β may inhibit the activity of lipoprotein lipase (LPL), while IL-6 may activate sterol regulatory element-binding protein 1c (SREBP-1c) and carbohydrate-responsive element-binding protein (ChREBP), leading to TG accumulation; simultaneously, IL-6 may activate SREBP-1c and ChREBP in hepatocytes, further affecting hepatic TG synthesis and related pathways, resulting in TG accumulation, lipid homeostasis imbalance, and further elevation of RC levels [33, 34]. These two mechanisms may be interconnected and suggest a potential bidirectional relationship between lipid dysregulation and inflammation, which could contribute to insulin resistance and increased susceptibility to MetS and related CVD [35].

The results of this study are consistent with a large body of literature in the field of metabolic diseases. The combination of RC and hsCRP levels, as well as RCII, was associated with increased risk of developing MetS. Furthermore, subsequent subgroup analyses are also consistent with the main study findings. This study highlights the potential relevance of considering both RC and hsCRP in the context of MetS risk.

Several limitations should be acknowledged. First, the study population was limited to Chinese adults aged ≥ 45 years from CHARLS, which may limit generalizability to younger or non-Chinese populations. Future studies in multi-ethnic and younger cohorts are warranted. Second, RC was estimated using a calculated formula rather than directly measured, potentially introducing measurement bias. Direct quantification via advanced lipidomic techniques is recommended in future research. Third, the observational design precludes causal inference. Interventional studies targeting RC and hsCRP are needed to establish causality. Fourth, longitudinal changes in RC and hsCRP were not assessed. Future studies with repeated measurements are encouraged to examine the dynamic trajectories of these biomarkers in relation to MetS onset. Finally, although physical activity is known to influence inflammation and metabolic syndrome, it was not adjusted for in our models due to a high missing rate of 63.08% at the 2011 baseline. This may introduce residual confounding, and future studies with more complete data are warranted to validate our findings.

In conclusion, this study indicates that in Chinese adults, elevated RC and hsCRP were in-

dependently and jointly associated with an increased risk of incident MetS, and the risk was substantially higher when both metabolic stress factors were present. Incorporating RC and hsCRP into routine metabolic risk assessment may aid in identifying individuals at increased risk for MetS and support more individualized risk assessment. These findings also highlight the potential complementary roles of lipid- and inflammation-related biomarkers in MetS risk evaluation.

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Ethical approval

Approval number: IRB00001052-11015.

Conflict of interest

The authors declare no conflict of interest.

References

1. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome--a new worldwide definition. Lancet 2005; 366: 1059-62.
2. Liang X, Or B, Tsoi MF, et al. Prevalence of metabolic syndrome in the United States National Health and Nutrition Examination Survey 2011-18. Postgrad Med J 2023; 99: 985-92.
3. Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, et al. Geographic distribution of metabolic syndrome and its components in the general adult population: a meta-analysis of global data from 28 million individuals. Diabetes Res Clin Pract 2022; 188: 109924.
4. Valdez Vega RI, Noboa-Velástegui JA, Fletes-Rayas AL ,et al. Predicting metabolic syndrome using supervised machine learning: a multivariate parameter approach. Int J Mol Sci 2025; 26: 9897.
5. Bhupathiraju SN, Hu FB. Epidemiology of obesity and diabetes and their cardiovascular complications. Circ Res 2016; 118: 1723-35.
6. Dobrowolski P, Prejbisz A, Kuryłowicz A, et al. Metabolic syndrome – a new definition and management guidelines. Arch Med Sci 2022; 18: 1133-56.
7. Zheng L, Zeng A, Liu L, et al. Metabolic syndrome: molecular mechanisms and therapeutic interventions. Mol Biomed 2025; 6: 59.
8. Andersson DP, Arner P. Decreased adipose lipid turnover associates with cardiometabolic risk and the metabolic syndrome. Arterioscler Thromb Vasc Biol 2025; 45: 277-84.
9. Suren Garg S, Kushwaha K, Dubey R, et al. Association between obesity, inflammation and insulin resistance: insights into signaling pathways and therapeutic interventions. Diabetes Res Clin Pract 2023; 200: 110691.
10. Lumeng CN, Saltiel AR. Inflammatory links between obesity and metabolic disease. J Clin Invest 2011; 121: 2111-7.
11. Stürzebecher PE, Katzmann JL, Laufs U. What is "remnant cholesterol"? Eur Heart J 2023; 44: 1446-8.
12. Quispe R, Martin SS, Michos ED, et al. Remnant cholesterol predicts cardiovascular disease beyond LDL and ApoB: a primary prevention study. Eur Heart J 2021; 42: 4324-32.
13. Wu Y, Wei Q, Li H, et al. Association of remnant cholesterol with hypertension, type 2 diabetes, and their coexistence: the mediating role of inflammation-related indicators. Lipids Health Dis 2023; 22: 158.
14. Jin J, Hu X, Francois M, et al. Association between remnant cholesterol, metabolic syndrome, and cardiovascular disease: post hoc analysis of a prospective national cohort study. Eur J Med Res 2023; 28: 420.
15. Chen J, Wu Q, Liu H, et al. Predictive value of remnant cholesterol inflammatory index for stroke risk: evidence from the China health and Retirement Longitudinal study. J Adv Res 2025; 76: 543-52.
16. Wang L, Li H, Wang L, et al. Remnant cholesterol inflammatory index and mortality in cardiovascular-kidney-metabolic syndrome: a national study. Arch Med Sci 2026; 22; 672-83.
17. Shao Y, Li Z, Wu Q, et al. Effects of combined high-sensitivity C-reactive protein and residual cholesterol levels on new-onset diabetes: evidence from two prospective cohort studies. J Transl Med 2025; 24: 57.
18. Chen X, Crimmins E, Hu P, et al. Venous blood-based biomarkers in the china health and retirement longitudinal study: rationale, design, and results of the 2015 wave. Am J Epidemiol 2019; 188: 1871-7.
19. Zhao Y, Strauss J. China Health and Retirement Longitudinal Study: 2011-2012 National Baseline User's Guide, National School of Development, Peking University.
20. Zhao Y, Hu Y, Smith JP, et al. Cohort profile: the China health and retirement longitudinal study (CHARLS). Int J Epidemiol 2014; 43: 61-8.
21. Chung G, Jung HS, Kim HJ. Sociodemographic and health characteristics associated with metabolic syndrome in men and women aged ≥ 50 years. Metab Syndr Relat Disord 2021; 19: 159-66.
22. Maw SS. Prevalence of metabolic syndrome, its risk factors and associated lifestyles in Myanmar adult people: a community based cross-sectional study. Metabol Open 2021; 12: 100135.
23. Cooke AA, Connaughton RM, Lyons CL, et al. Fatty acids and chronic low grade inflammation associated with obesity and the metabolic syndrome. Eur J Pharmacol 2016; 785: 207-14.
24. Fahed G, Aoun L, Bou Zerdan M, et al. Metabolic syndrome: updates on pathophysiology and management in 2021. Int J Mol Sci 2022; 23: 786.
25. Ridker PM, Buring JE, Cook NR, et al. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events. Circulation 2003; 107: 391-7.
26. Festa A, D'Agostino R Jr, Howard G, et al. Chronic subclinical inflammation as part of the insulin resistance syndrome. Circulation 2000; 102: 42-7.
27. Wang L, Liu C, Zheng X, et al. Association of C-reactive protein to albumin ratio with prevalence and mortality in metabolic syndrome: NHANES 1999-2010. Eur J Med Res 2025; 31: 20.
28. Varbo A, Benn M, Tybjærg-Hansen A, et al. Remnant cholesterol as a causal risk factor for ischemic heart disease. J Am Coll Cardiol 2013; 61: 427-36.
29. Drexel H, Mader A, Larcher B, et al. Remnant cholesterol and long-term incidence of death in coronary artery disease patients. Atherosclerosis 2025; 401: 119048.
30. Castañer O, Pintó X, Subirana I, et al. Remnant cholesterol, not LDL cholesterol, is associated with incident cardiovascular disease. J Am Coll Cardiol 2020; 76: 2712-24.

31. Yu Y, Zhang Y, Zhu C, et al. Remnant cholesterol inflammatory index, calculated from residual cholesterol to C-reactive protein ratio, and stroke outcomes: a retrospective study using the National institutes of health stroke scale and modified Rankin scale. Lipids Health Dis 2025; 24: 228.
32. Bernelot Moens SJ, Verweij SL, Schnitzler JG, et al. Remnant cholesterol elicits arterial wall inflammation and a multilevel cellular immune response in humans. Arterioscler Thromb Vasc Biol 2017; 37: 969-75.
33. Khovidhunkit W, Kim MS, Memon RA, et al. Effects of infection and inflammation on lipid and lipoprotein metabolism: mechanisms and consequences to the host. J Lipid Res 2004; 45: 1169-96.
34. Björnson E, Packard CJ, Adiels M, et al. Apolipoprotein B48 metabolism in chylomicrons and very low-density lipoproteins and its role in triglyceride transport in normo- and hypertriglyceridemic human subjects. J Intern Med 2020; 288: 422-38.
35. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. Nature 2017; 542: 177-85.