Original Article

Elevated remnant cholesterol was associated with the increased metabolically unhealthy obesity risk in Chinese youth

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Background and Objectives: Metabolically unhealthy obesity is characterized by the presence of cardiovascular metabolic risks such as hypertension, dyslipidemia, and hyperglycemia. Research has shown a correlation between remnant cholesterol (RC) concentrations and abdominal obesity in children. However, the effect of RC concentration on metabolically unhealthy obesity remains unclear. **Methods and Study Design:** This study included 3114 Chinese adolescents who received health check-ups. We used logistic regression models and receiver operating characteristic analysis to evaluate the correlation between RC concentration and metabolically unhealthy obesity in a cross-sectional design. **Results:** After controlling for possible confounding variables, we found that individuals in the top and fourth quintiles of RC concentrations had a significantly higher likelihood of developing metabolically unhealthy obesity compared to those in the bottom quintile (ORs, 4.810 and 1.836; 95% CIs, 3.209–7.212 and 1.167–2.890, respectively). The risk of metabolically unhealthy obesity tended to increase with RC concentration (p_{trend}<0.001). In addition, boys showed positive associations between RC concentration and both BMI (r = 0.305, p<0.001) and waist circumference (r = 0.306, p<0.001). According to the analysis, the predictive accuracy of metabolically unhealthy obesity was 0.736 (95% CI, 0.690–0.781) for boys and 0.630 (95% CI, 0.573–0.687) for girls. The ideal prediction threshold was 0.66 for boys and 0.59 for girls. **Conclusions:** Our findings indicate that elevated RC concentration is linked to a higher likelihood of developing metabolically unhealthy obesity in young individuals, regardless of other known risk factors.

Key Words: metabolically unhealthy obesity, association, remnant cholesterol, youth, gender

INTRODUCTION

Obesity has emerged as a significant public health concern, affecting millions of adults and children worldwide. The latest data released by The Lancet shows that the global obese population exceeded one billion in 2022, accounting for approximately one-eighth of the global population. Among these obese individuals, approximately 159 million are children or adolescents 5 to 19 years of age. From 1990 to 2022, the global obesity rate among children and adolescents of this age group increased more than threefold.[1] In addition to weight gain, obesity is characterized by metabolic irregularities such as high blood pressure, type 2 diabetes, and dyslipidemia.[2] Nevertheless, recent studies have highlighted that not all obese individuals face the same cardiovascular hazards and differentiate between metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO).[3] Studies have shown that MUO is associated with higher cardiovascular disease (CVD) incidence and increased all-cause mortality risk compared to MHO.[4,5] Therefore, identifying different obesity phenotypes and implementing targeted intervention strategies is of great significance.

Dyslipidemia, which frequently accompanies metabolic disorders such as obesity, high blood pressure, and diabetes, contributes significantly to the onset of these ailments.[6] Recent evidence has emphasized the significance of TG-rich lipoproteins (TRLs) in CVD separate from the conventional lipid profiles such as low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C).[7] Regardless of LDL-C concentration, remnant cholesterol (RC), which consists of very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and chylomicron remnants, has demonstrated a significant association with elevated risk of major cardiovascular events such as stroke, coronary artery disease, and systol-

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ic blood pressure (SBP).[8-11] Moreover, abdominal obesity, a metabolic component and risk factor for CVD, is associated with elevated RC concentrations in children.[12]

The onset of CVD can begin in adolescence or young adulthood,[13] and lipid concentrations during childhood and various lipid paths throughout life are associated with subclinical atherosclerosis in middle-aged individuals.[14,15] Therefore, it is imperative to examine the correlation between RC levels and MUO from an early age and provide the necessary interventions to hinder or postpone the emergence of CVD in adulthood.

METHODS

Study population

From September to November 2018, 3450 first-year students at a medical school in Anhui Province, China received health examinations. Inclusion criteria were: 1) freshman who participated in physical examinations; 2) understanding of the study and voluntary participation; and 3) complete information. Exclusion criteria were: 1) incomplete height or weight data (n=101); 2) incomplete biochemical indicators (n=0); or 3) missing questionnaires (n=235).[16] Figure 1 shows a flowchart of the participant inclusion.

This study was approved by the Wannan Medical College, Yijishan Hospital Ethics Committee (ethical approval number: 32 [2018]) and adhered to tenets put forth in the Declaration of Helsinki. All participants in the epidemiological interviews of the study conducted in 2018 gave their consent in writing; if they were younger than 18 years of age, their parent and/or legal guardian provided consent.

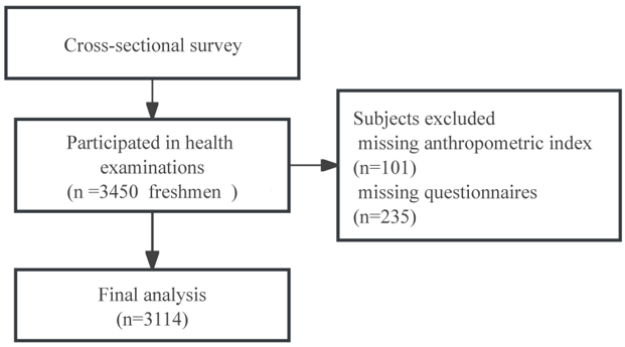

Figure 1. The flowchart for the inclusion of excluded populations in the study

Data collection and measurement

Standard questionnaires were used to collect demographic information from the participants, while physical examinations were conducted to measure anthropometric parameters including height, weight, waist circumference, and blood pressure. Serum biochemical indicators were obtained from the hospital's laboratory center. Participants' height and weight were assessed using an ultrasound device (Henan Shengyuan, Zhengzhou, China) while wearing socks or bare feet and lightweight clothing. A horizontal plane was used to measure the waist circumference above the belly button. After participants sat quietly for 5 min, we took two blood pressure measurements with an electronic monitor (Omron U30; Omron Healthcare, Shanghai, China) at an interval of no less than 2 min.

In the morning, after fasting for 10 h, peripheral venous blood samples were taken from the participants and analyzed using an autoanalyzer to measure concentrations of HDL-C, LDL-C, TC, TG, and fasting blood glucose (FBG). The RC = TC-(HDL-C+LDL-C).

Definitions

Obesity was determined according to Chinese-specific standards by calculating the BMI, derived from dividing the weight (kg) by the square of height (meters). For adolescents aged 16, 17, and ≥18 years, obesity was defined as having a BMI equal to or greater than 27.1, 27.6, and 28.0, respectively, according to Health Industry Standards of the People's Republic of China.[17] Metabolically unhealthy obesity (MUO) was defined as having at least one metabolic abnormality in addition to being obese. These abnormalities included TG concentrations of 100 mg/dL (1.1 mmol/L) or higher, HDL concentrations less than 50 mg/dL (1.3 mmol/L) (except for boys aged 15 to 19 years, for whom the cutoff point was below 45 mg/dL [<1.3 mmol/L]), FBG concentrations of 100 mg/dL (5.6 mmol/L) or higher, and SBP and/or diastolic blood pressure (DBP) equal to or above the 90th percentile for sex, age, and height.[18,19] MUO in adults was defined by the existence of at least one metabolic anomaly alongside obesity. These anomalies included TG concentrations equal to or greater than 150 mg/dL (1.7 mmol/L), HDL-C concentrations less than 40 mg/dL (1.0 mmol/L) in men and less than 50 mg/dL (1.3 mmol/L) in women, FBG concentrations equal to or greater than 100 mg/dL (5.6 mmol/L), and SBP equal to or greater than 130 mmHg and/or DBP equal to or greater than 85 mmHg.[20, 21] A habit of exercise was defined as exercising more than 30 minutes per day accompanied by excessive sweating, breathing, or a significant increase in heart rate.

Statistical analysis

The statistical analyses were conducted using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). Means ± standard deviation was used to report continuous variables, and t-tests or one-way ANOVA were used to compare differences between groups. Percentages were used to report categorical variables, and the chi-square (χ^2) test was used to compare their distributions. We used multivariate logistic regression models to calculate the ORs for the connections between RC concentrations and MUO. Model 2 was adjusted for age and sex, and Model 3 was adjusted for age, sex, exercise habit, SBP, DBP, FBG, smoking status, and drinking status. To evaluate the predictive significance of RC concentrations for MUO, we analyzed the receiver operating characteristic (ROC) curve and calculated the area under the curve (AUC). Statistical significance was determined by a *p*-value less than 0.05 with a two-tailed test.

RESULTS

Baseline participant characteristics

The analysis included 3114 first-year students (1264 boys and 1850 girls) who satisfied the inclusion criteria. The average age was 18.52 ± 1.01 years, with a range of 15 to 27 years. The prevalences of obesity and MUO among the participants were 12.2% (n=380) and 9.0% (n=280), respectively. Obesity and MUO were more prevalent among boys than among girls, with obesity rates of 16.1% and 9.5% and MUO rates of 12.5% and 6.6%, respectively. Table 1 shows the participants' baseline characteristics based on gender.

Baseline characteristics in the RC quintiles

The RC data were categorized into quintiles, and the participants were divided into five groups. Table 2 shows the baseline characteristics of the participants in the RC quintile groups categorized by gender. Both boys and girls in the highest RC group (Q5) exhibited elevated BMI, weight, waist circumference, TC, TG, LDL-C, obesity prevalence, and MUO in comparison to the other groups (Q1-Q4). Furthermore, boys in Q5 demonstrated higher SBP and DBP, while girls displayed higher FBG concentrations. Boys in Q5 had lower HDL-C concentrations than those in Q1-Q4.

Association of RC with MUO

In the original model, when compared with participants in the Q1 group, those in the Q4 and Q5 groups exhibited a higher likelihood of MUO, with ORs (95% CIs) of 1.698 (1.082−2.665) and 4.793 (3.205−7.167), respectively. After modifications in Models 2 and 3, the correlation remained noteworthy, displaying ORs (95% CIs) of 1.836 (1.167-2.890) and 4.810 (3.209-7.212) in the Q4 and Q5 groups, respectively, when compared to the Q1 group. The risk of MUO tended to increase with the RC concentration (p_{trend}<0.001). The correlation between RC and the risk of MUO is shown in Table 3.

Subgroup analysis by sex

We also analyzed the association between RC and MUO after stratification by sex. After adjusting for age, exercise habit, smoking status, drinking status, FBG, SBP, and DBP, boys and girls in the Q5 group were found to have an association with MUO, with ORs (95% CIs) of 5.670 (2.975−10.805) and 2.497 (1.405−4.439), respectively, when compared to boys and girls in the Q1 group (Table 3).

Correlation between RC concentration and metabolic index

In both genders, there were positive correlations between RC concentration and BMI and waist circumference (r=0.208 and 0.186, respectively; p<0.05). Stratification by sex revealed positive correlations between RC concentration and BMI and waist circumference in boys (r=0.305 and 0.306, respectively; p<0.05). However, in girls, the correlation between RC concentration and BMI was weak (r=0.112, p<0.05). The data is presented in Table 4.

ROC analysis results

We conducted ROC analysis to determine the AUC of RC in various genders and evaluate the prognostic significance of RC concentration in MUO. Figure 2 shows the AUCs (95% CI) of RC in all individuals, boys, and girls to be 0.690 (0.654-0.726), 0.736 (0.690-0.781), and 0.630 (0.573-0.687), respectively. In boys, the optimal threshold for predicting MUO was 0.66, while in girls it was found to be 0.59. Notably, the predictive value of RC concentration for MUO was significantly higher in boys than in girls.

DISCUSSION

In this observational study with a relatively large sample size, we investigated the relationship between RC concentration and MUO in Chinese adolescents. Our findings revealed a positive association between higher RC concentrations and MUO in a cross-sectional population, independent of other confounding factors.

The cholesterol content of RC includes all cholesterol components except LDL-C and HDL-C. Numerous studies have indicated that RC in plasma represents around one-third of the total cholesterol.[22] Recent findings from observational and genetic research suggest that RC may pose a potential hazard for different aspects of metabolic syndrome and could have a notable impact on remaining risks (apart from LDL-C).[23] The fact that CVD typically begins in early life and is worsened by obesity and metabolic syndrome is widely recognized. Increased concentrations of RC have been linked to the onset of high blood pressure,[24] diabetes mellitus,[25] and their simultaneous occurrence.[26] In Copenhagen, a study of 16,207 people from the general population revealed that, in overweight and obese individuals, RC may be a more effective indicator of atherosclerotic CVD than LDL-C.[27] The possible causes may include 1) the abundant presence of serum RC, which may result in enhanced infiltration of the arterial wall, leading to the quick development of foam cells;[28] 2) RC promoting oxidative stress and causing dysfunction in the endothelium by suppressing the production of nitric oxide;[29] 3) increased RC concentrations leading to insulin resistance,[30] and 4) RC triggering the inflammatory response. According to genetic evidence, increased RC concentrations are linked to mild inflammation.[31]

Recently, the contribution of RC to abdominal obesity has been explored in a study of 5959 Chinese children, with continuous RC concentrations divided into quartiles. Children with higher RC concentrations had a considerably increased likelihood of developing abdominal obesity than those with the lowest RC concentrations.12 Our study further confirms the association between RC and MUO in young individuals. A linear trend in obesity risk according to RC quartiles was also found in our work. Di et al.[32] found that RC concentrations were significantly correlated with age and sex. Differences in RC concentrations and quartile grouping between children and adolescents may explain this inconsistency. The findings indicate that maintenance of a minimal concentration of RC may not be associated with a higher likelihood of MUO, whereas maintenance of higher concentrations of RC may be linked to an elevated risk of MUO. Likewise, Di et

Table 1. Participant characteristics

Characteristic	Total (n=3114)	Boys (n=1264)	Girls (n=1850)	t/χ^2	*p*
Age, years	18.5 ± 1.01	18.6 ± 1.01	18.5 ± 1.01	2.42	0.016
BMI, kg/m^2	22.3 ± 3.53	23.1 ± 3.97	21.8 ± 3.09	9.87	<0.001
SBP, mmHg	114 ± 13.7	122 ± 13.6	108 ± 11.1	27.9	<0.001
DBP, mmHg	70.9 ± 10.6	73.2 ± 11.0	69.4 ± 9.92	9.90	<0.001
FBG, mmol/L	4.57 ± 0.40	4.51 ± 0.38	4.6 ± 0.41	6.27	<0.001
TC, mmol/L	4.05 ± 0.68	4.01 ± 0.74	4.08 ± 0.63	2.95	0.001
TG, mmol/L	0.83 ± 0.40	0.87 ± 0.47	0.81 ± 0.35	3.83	<0.001
HDL-C, mmol/L	1.42 ± 0.28	1.31 ± 0.25	1.49 ± 0.27	18.9	<0.001
LDL-C, mmol/L	2.09 ± 0.56	2.15 ± 0.63	2.05 ± 0.5	4.85	<0.001
RC, mmol/L	0.55 ± 0.18	0.55 ± 0.20	0.55 ± 0.16	0.14	0.888
Habit of exercise, n (%)	873 (28.0)	523 (41.4)	350 (18.9)	188	<0.001
Current smoking status, n (%)	76 (2.4)	68 (5.4)	8 (0.4)	77.2	<0.001
Current drinking status, n (%)	428 (13.7)	329 (26.0)	99 (5.4)	270	<0.001
Obesity, n (%)	380 (12.2)	204 (16.1)	176 (9.5)	30.8	<0.001
MUO, n (%)	280 (9.0)	158 (12.5)	122 (6.6)	32.0	<0.001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol triglycerides; HDL-C, high-density lipoprotein triglycerides; RC, remnant cholesterol; MUO, metabolically unhealthy obesity

Table 2. Baseline characteristics by quintile

Variable	RC quintile					
Boys	Q1 (<0.43)	Q2 (0.43-0.50)	Q3 (0.51-0.57)	Q4 (0.58-0.67)	Q5 (≥0.68)	*p*
No. of participants	235	269	247	247	266	
Age, years	18.6 ± 1.11	18.5 ± 0.97	18.6 ± 1.11	18.6 ± 0.95	18.5 ± 0.90	0.460
BMI, kg/m^2	22.2 ± 3.27	21.9 ± 3.08	22.4 ± 3.29	23.3 ± 4.21	25.6 ± 4.56	<0.001
Height, cm	172 ± 5.84	172 ± 5.50	173 ± 5.54	173 ± 6.06	173 ± 6.87	0.873
Weight, kg	66.2 ± 10.2	65.6 ± 9.99	67.0 ± 10.3	69.8 ± 13.3	77.0 ± 14.9	<0.001
WC, cm	74.7 ± 7.81	74.5 ± 7.35	75.4 ± 7.98	78.0± 10.1	83.3 ± 11.2	<0.001
TG, mmol/L	0.69 ± 0.31	0.64 ± 0.22	0.75 ± 0.25	0.89 ± 0.34	1.36 ± 0.64	<0.001
TC, mmol/L	3.44 ± 0.56	3.57 ± 0.41	3.87 ± 0.39	4.24 ± 0.46	4.86 ± 0.75	<0.001
HDL-C, mmol/L	1.35 ± 0.29	1.32 ± 0.22	1.33 ± 0.24	1.32 ± 0.23	1.24 ± 0.24	<0.001
LDL-C, mmol/L	1.84 ± 0.57	1.78 ± 0.36	2.00 ± 0.37	2.30 ± 0.45	2.81 ± 0.69	<0.001
FBG, mmol/L	4.53 ± 0.39	4.48 ± 0.35	4.49 ± 0.37	4.52 ± 0.37	4.54 ± 0.42	0.313
SBP, mmol/L	119 ± 11.8	120 ± 14.5	120 ± 12.4	121 ± 13.6	126 ± 14.2	<0.001
DBP, mmol/L	71.5 ± 10.3	72.1 ± 10.7	72.6± 10.1	72.9 ± 10.4	76.5 ± 12.5	<0.001
RC, mmol/L	0.29 ± 0.12	0.47 ± 0.02	0.54 ± 0.02	0.62 ± 0.03	0.82 ± 0.16	<0.001
Habit of exercise, n (%)	107 (45.7)	102 (37.9)	102 (41.5)	112 (45.5)	100 (37.6)	0.304
Current smoking status, n (%)	10 (4.3)	16 (5.9)	15 (6.1)	10 (4.0)	17 (6.4)	0.666
Current drinking status, n (%)	66 (28.1)	64 (23.8)	59 (23.9)	69 (27.9)	71 (26.7)	0.167
Obesity, n (%)	17 (7.2)	18 (6.7)	29 (11.7)	45 (18.2)	95 (35.7)	<0.001
MUO, n (%)	13 (5.5)	12 (4.5)	18 (7.3)	31 (12.6)	84 (31.6)	<0.001
Girls	Q1 (<0.44)	Q2 (0.44-0.51)	Q3 (0.52-0.57)	Q4 (0.58-0.65)	Q5 (≥0.66)	*p*
No. of participants	343	377	343	393	394	
Age, years	18.4 ± 1.03	18.6 ± 1.02	18.4 ± 0.94	18.5 ± 1.03	18.4 ± 1.01	0.097
BMI, kg/m^2	21.5 ± 3.19	21.7 ± 3.13	21.5 ± 2.55	21.8 ± 3.00	22.4 ± 3.37	<0.001
Height, cm	160 ± 5.44	160 ± 5.49	160 ± 5.60	160 ± 5.45	160 ± 5.39	0.636
Weight, kg	55.0 ± 8.91	55.5 ± 8.47	55.1 ± 7.60	56.1 ± 8.45	57.3 ± 9.17	0.001
WC, cm	69.1 ± 7.19	69.1 ± 6.82	69.1 ± 5.95	69.5 ± 7.12	71.0 ± 7.59	<0.001
TG, mmol/L	0.67 ± 0.24	0.71 ± 0.33	0.73 ± 0.23	0.83 ± 0.27	1.08 ± 0.43	<0.001
TC, mmol/L	3.63 ± 0.54	3.81 ± 0.49	3.96 ± 0.40	4.23 ± 0.44	4.70 ± 0.62	<0.001
HDL-C, mmol/L	1.50 ± 0.29	1.48 ± 0.26	1.51 ± 0.25	1.50 ± 0.27	1.46 ± 0.28	0.052
LDL-C, mmol/L	1.83 ± 0.47	1.86 ± 0.40	1.91 ± 0.36	2.11 ± 0.37	2.48 ± 0.53	<0.001
FBG, mmol/L	4.58 ± 0.41	4.55 ± 0.37	4.62 ± 0.39	4.59 ± 0.45	4.68 ± 0.43	<0.001
SBP, mmol/L	109 ± 11.8	107 ± 10.9	108 ± 11.1	108 ± 10.8	109 ± 11.1	0.185
DBP, mmol/L	69.8 ± 9.84	68.5 ± 9.90	69.2 ± 9.89	69.5 ± 9.58	69.9 ± 10.4	0.327
RC, mmol/L	0.33 ± 0.09	0.48 ± 0.02	0.54 ± 0.02	0.61 ± 0.02	0.77 ± 0.13	<0.001
Habit of exercise, n (%)	62 (18.1)	79 (21.0)	63 (18.4)	70 (17.8)	96 (19.3)	0.811
Current smoking status, n (%)	0 (0)	1 (0.3)	1 (0.8)	3 (0.8)	3 (0.8)	0.422
Current drinking status, n (%)	26 (7.6)	21 (5.6)	13 (3.8)	22 (5.6)	17 (4.3)	0.204
Obesity, n (%)	27 (7.9)	31 (8.2)	20 (5.8)	39 (9.9)	59 (15.0)	<0.001
MUO, n (%)	19 (5.5)	16 (4.2)	9 (2.6)	29 (7.4)	49 (12.4)	<0.001

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, cholesterol; LDL-C, low-density lipoprotein cholesterol triglycerides; HDL-C, high-density lipoprotein triglycerides; RC, remnant cholesterol; MUO, metabolically unhealthy obesity

Table 3. Association of RC and metabolically unhealthy obesity

Characteristic	*OR (95%CI)*		
	Model 1	Model 2	Model 3
Total			
Q1 (<0.44)	Ref	Ref	Ref
Q2 (0.44-0.50)	0.790 (0.459-1.358)	0.806 (0.468-1.387)	0.808 (0.469-1.391)
Q3 (0.51-0.57)	0.938 (0.565-1.557)	0.969 (0.583-1.611)	0.973 (0.585-1.619)
Q4 (0.58-0.66)	1.698 (1.082-2.665)*	1.835 (1.166-2.887)*	1.836 (1.167-2.890)*
Q5 (≥0.67)	4.793 (3.205-7.167)**	4.848 (3.235-7.264)**	4.810 (3.209-7.212)**
p_{trend}	< 0.001	< 0.001	< 0.001
Boys			
Q1 (< 0.43)	Ref	Ref	Ref
Q2 (0.44-0.50)	0.797 (0.357-1.783)	0.795 (0.355-1.778)	0.622 (0.267-1.449)
Q3 (0.51-0.57)	1.342 (0.642-2.805)	1.341 (0.642-2.802)	1.235 (0.578-2.641)
Q4 (0.58-0.67)	2.451 (1.249-4.810)*	2.460 (1.253-4.829)*	2.021 (1.002-4.076)*
Q5 (≥0.68)	7.882 (4.256-14.595)**	7.842 (4.234-14.525)**	5.670 (2.975-10.805)**
p_{trend}	< 0.001	< 0.001	< 0.001
Girls			
Q1 (< 0.44)	Ref	Ref	Ref
Q2 (0.44-0.51)	0.756 (0.382-1.494)	0.757 (0.382-1.498)	0.903 (0.448-1.818)
Q3 (0.52-0.57)	0.460 (0.205-1.031)	0.46 (0.205-1.031)	0.482 (0.212-1.099)
Q4 (0.58-0.65)	1.359 (0.747-2.469)	1.359 (0.748-2.470)	1.477 (0.795-2.741)
Q5 (≥0.66)	2.422 (1.396-4.202)*	2.422 (1.396-4.202)*	2.497 (1.405-4.439)*
p_{trend}	< 0.001	< 0.001	< 0.001

RC remnant cholesterol, OR Odds ratio, CI confidence interval.
Model 1: Crude
Model 2: Adjusted for age and gender
Model 3: Adjusted for model 1 plus, habit of exercise, smoking status, drinking status, FBG, SBP and DBP
*Compared with Q1, $p<0.05$
**Compared with Q1, $p\leq0.001$

Table 4. Correlation between RC concentration and metabolic index

Characteristic	Total		Boys		Girls	
	r	*p*	*r*	*p*	*r*	*p*
Age	-0.010	0.579	-0.010	0.716	-0.010	0.680
BMI	0.208	<0.0001	0.305	<0.0001	0.112	<0.0001
WC	0.186	<0.0001	0.306	<0.0001	0.092	<0.0001
SBP	0.078	<0.0001	0.147	<0.0001	0.032	0.174
DBP	0.083	<0.0001	0.137	<0.0001	0.037	0.113
FBG	0.040	0.026	0.030	0.285	0.048	0.039

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; RC, remnant cholesterol

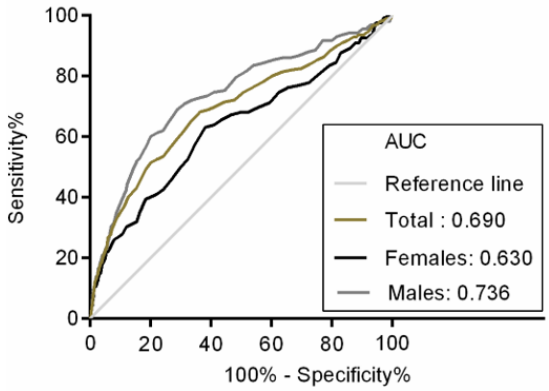

Figure 2. ROC curve analysis of RC concentrations in boys and girls. ROC, receiver operating characteristic; MUO, metabolically unhealthy obesity; RC, remnant cholesterol

al.[32] found that the percentage of individuals classified as overweight or obese (85.7%) in the top RC tertile was considerably greater than those in the middle (66.7%) and lowest (68.4%) tertiles. Additionally, RC concentration exhibited significant correlations with BMI, waist circumference, blood pressure, and lipid concentrations among 767 young participants. Moreover, a study involving 135 children and adolescents indicated that fasting RC con-

centrations were significantly higher in obese individuals.[33] As stated in the study conducted by Tian et al.,[34] individuals who are obese have a greater likelihood of experiencing elevated concentrations of RC during non-fasting periods; this indicates that an increase in RC may result in overweight-related diseases even in the non-fasting state. Our research uncovered that the prognostic significance of RC concentration for MUO was notably greater in boys than in girls (higher AUC in boys). The discrepancy between sexes implies that RC concentration might have a greater influence on the formation of MUO in boys than in girls.

Additional research is necessary to fully comprehend the mechanisms that connect RC and MUO, as the underlying pathways are not fully understood. Research indicates that RC has the ability to increase the production of proinflammatory cytokines and is causally linked to low-grade inflammation. C-reactive protein increases by approximately threefold with each 1 mmol/L rise in RC.[35] Hence, our hypothesis is that the inflammatory response triggered by an elevated RC concentration may significantly impact the progression of MUO. In contrast, obesity is mainly attributed to an imbalance between lipid storage and consumption.[36] Regarding the total cholesterol content of TRLs, whether RC is similar to traditional lipid metabolism in the development of obesity requires more basic research because of the complexity of lipid metabolism. RC may contribute to MUO by affecting lipid metabolism, oxidative stress, inflammation, and insulin resistance. Additionally, other factors such as genetics, lifestyle, and environment may interact with RC to influence MUO risk.

Strengths of our study include the considerable sample size, standardized measurements of physical and chemical parameters, and accounting for potential factors that could influence the results. Even so, there were some limitations. To establish a temporal relationship between RC and MUO, longitudinal studies are necessary due to the limitations of the cross-sectional design of this study, which does not allow for causal inference. Furthermore, the research sample was exclusively composed of Chinese adolescents; thus, the outcomes may not be applicable to different ages or ethnically diverse cohorts. We also only measured RC concentrations in fasting blood samples. Further studies should consider assessing postprandial RC concentrations to better understand their role in MUO. Finally, as with any observational study, residual confounding could not be completely ruled out despite our efforts to adjust for potential confounding factors.

Conclusion

Our findings indicate that increased RC concentration is positively correlated with MUO among Chinese adolescents and has a more significant predictive capacity in boys than in girls. The results emphasize the possible contribution of RC to the advancement of MUO, and additional investigation is required to gain a deeper comprehension of the fundamental mechanisms at work and examine their clinical significance. Additional longitudinal studies involving varied populations are necessary to validate our discoveries and substantiate the association between RC concentration and MUO.

CONFLICT OF INTEREST AND FUNDING DISCLOSURES

All authors declare that there are no conflicts of interest.

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