Lipids in Health and Disease

RESEARCH

Open Access

Remnant cholesterol in obesity phenotypes: results from NHANES

Tian Yu[1,2,3], Shaohua Liu[1,2,3], Lu Fang[1], Tingting Du[1,2,3*] and Zhelong Liu[1,2,3,4*]

Abstract

Background The association between remnant cholesterol (RC) with obesity phenotypes remains unclear.

Methods This study designed to evaluate the association between RC and obesity phenotypes using data from the National Health and Nutrition Examination Survey (NHANES). The classification systems for obesity phenotypes encompassed both preclinical/clinical obesity and obesity stages, which were assessed based on two authoritative obesity guidelines: the 2025 clinical obesity guideline, and the 2016 obesity guideline established by the American Association of Clinical Endocrinologists and the American College of Endocrinology (AACE/ACE). Participants were selected according to the diagnostic criteria for obesity proposed in the 2025 clinical obesity guideline and were categorized into tertiles based on their RC levels. Their obesity phenotypes, obesity-related clinical manifestations, obesity-related comorbidities, and characteristics were then described. Logistic regression analyses and restricted cubic spline (RCS) models were used to analyze the relationship between RC and adverse obesity phenotypes. Sensitivity analyses were conducted in patients not receiving lipid-lowering drugs.

Results This study comprised 3,207 adult participants, revealing distinct prevalence patterns: 47.80% exhibited preclinical obesity and 17.81% showed clinical obesity, while obesity stage stratification demonstrated 0%, 12.76%, and 21.63% prevalence for stage 0, 1, and 2, respectively. Multivariable regression analyses demonstrated dose-response relationship between RC levels and adverse obesity phenotypes, with individuals in the highest RC tertile showing significantly elevated risks of clinical obesity (OR 1.95, 95% CI 1.19–3.19) and obesity stage progression (OR 1.96, 95% CI 1.06–3.62) compared to the lowest tertile reference group. RCS analyses further revealed similar "J"-shaped association between RC levels and adverse obesity phenotypes (P for nonlinearity < 0.001), sharing a common inflection point at 0.51 mmol/L. The sensitivity analyses confirmed the consistency of the results among patients who were not receiving lipid-lowering therapy.

Conclusions RC was found to be positively and independently associated with adverse obesity phenotypes, particularly when RC levels exceeded 0.51 mmol/L, demonstrating a similar "J"-shaped association. It is recommended that clinicians monitor RC levels for obese patients as a primary screening indicator for adverse phenotypes of obesity.

Keywords Remnant cholesterol, Preclinical/clinical obesity, Obesity stage, Obesity phenotypes, National health and nutrition examination survey

*Correspondence:
Tingting Du
aduttsxx@163.com
Zhelong Liu
liuzhelong@163.com

Full list of author information is available at the end of the article

Introduction

The escalating global obesity rates is a mounting concern [1]. Obesity is recognized as a chronic complex disease that can affect multiple organ functions [2, 3]. Based on this concept, the American Association of Clinical Endocrinologists and the American College of Endocrinology (AACE/ACE) introduced the adiposity-based chronic disease (ABCD) staging system for obesity in 2014 and 2016 [2, 4], which classified obesity into three stages (stages 0, 1, 2) by comprehensively assessing the severity grading (mild, moderate, severe) of multiple obesity-related comorbidities (ORCs). Despite its clinical relevance, the implementation of the ABCD staging system in practice has been limited, primarily due to the time-consuming and resource-intensive nature of multi-system evaluations. As a result, current clinical assessments of obesity remain largely reliant on body mass index (BMI) or, at best, a rudimentary evaluation of individual or non-systematic ORCs, frequently failing to address the broader systemic implications of obesity. Recently, the definitions and diagnostic criteria for clinical obesity, published on *The Lancet Diabetes & Endocrinology* in January 2025, introduced a novel classification framework based on 18 obesity-induced clinical manifestations [3]. This framework categorized obesity into two distinct states—preclinical and clinical obesity—to facilitate risk stratification in obese patients and to inform subsequent therapeutic interventions. Nevertheless, this assessment system also faces the same challenges in clinical implementation, including operational complexity, time consumption, and substantial financial burdens, raising questions about its feasibility and scalability. In summary, given the current severe epidemiological burden of obesity and the challenges in implementing systematic and standardized evaluation frameworks, there is a clinical imperative to identify a robust yet succinct indicator for initial screening of obesity phenotypes.

Dyslipidemia is a prevalent complications associated with obesity [5, 6]. A hallmark of obesity-related dyslipidemia is the accumulation of cholesterol-loaded remnant particles, consisting of very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), and chylomicron remnants [7]. RC levels are not only positively associated with BMI [5], but emerging evidence also suggested that RC plays a pivotal role in linking simple obesity to morbid obesity, a condition characterized by ectopic fat accumulation and associated metabolic disorders [8]. Furthermore, previous studies have offered preliminary insights into the relationship between RC with obesity and obesity-related disorders [5, 9, 10, 11, 12], highlighting its stronger predictive capacity for cardiovascular risk in obese individuals compared to those with normal weight [12]. However, there remains a paucity of data assessing the role of RC in systematic assessment of obesity phenotypes. Therefore, the objective of the present study is to elucidate the association of RC with obesity phenotypes and whether adherence to RC could serve as an additional screening tool for adverse obesity phenotypes.

Materials and methods

Data and study participants

We utilized data from 4 cycles of the continuous National Health and Nutrition Examination Survey (NHANES) conducted between 2011 and 2018. The NHANES is an ongoing program of study designed to evaluate the nutrition and health status of citizens across the United States. Data were gathered via personal structured interviews, health examinations and specimen analyses. We applied a set of exclusion criteria at outset of the study. These criteria were as follows: participants were excluded if they (1) had incomplete data regarding RC, BMI, waist circumference (WC), dual-energy X-ray absorptiometry (DEXA) measurement, and assessment of preclinical/clinical obesity; (2) miss information on critical covariables, such as age, smoking status, triglyceride (TG) levels, etc.; (3) individuals under the age of 20 or were pregnant; (4) not meet the diagnostic criteria for obesity [3]. Figure 1 depicted the selection process.

Assessment of RC

A morning peripheral blood sample was collected to assess lipid level, with 95% of participants reporting adherence to a fast of at least eight hours. As per the laboratory's standard procedures manual, the concentrations of total cholesterol (TC) and high-density lipoprotein-cholesterol (HDL-C) were measured using enzymatic assays on automated biochemical analyzers. Specifically, the Roche Cobas 6,000 and the Roche Modular P systems were employed for TC quantification. For HDL-C determination, the assay utilized polyethylene glycol-coupled cholesteryl esterase, cholesterol oxidase, and sulfated alpha-cyclodextrin in the presence of magnesiumions.

The Friedewald calculation was employed to estimate low-density lipoprotein-cholesterol (LDL-C) concentration [13] and the measurement of RC concentration was derived by subtracting the combined levels of LDL-C and HDL-C from the TC level [12]. Participants were then stratified into three distinct groups based on their RC levels, arranged into tertiles. The specific ranges for each tertile were defined as follows: Tertile 1 (T1) (0.07–0.41 mmol/L), Tertile 2 (T2) (0.42–0.67 mmol/L), and Tertile 3 (T3) (0.68–2.10 mmol/L).

Definition of preclinical/clinical obesity

According to the 2025 clinical obesity guidelines [3], the diagnostic of clinical obesity primarily involves two steps. The first step was to diagnose obesity according to

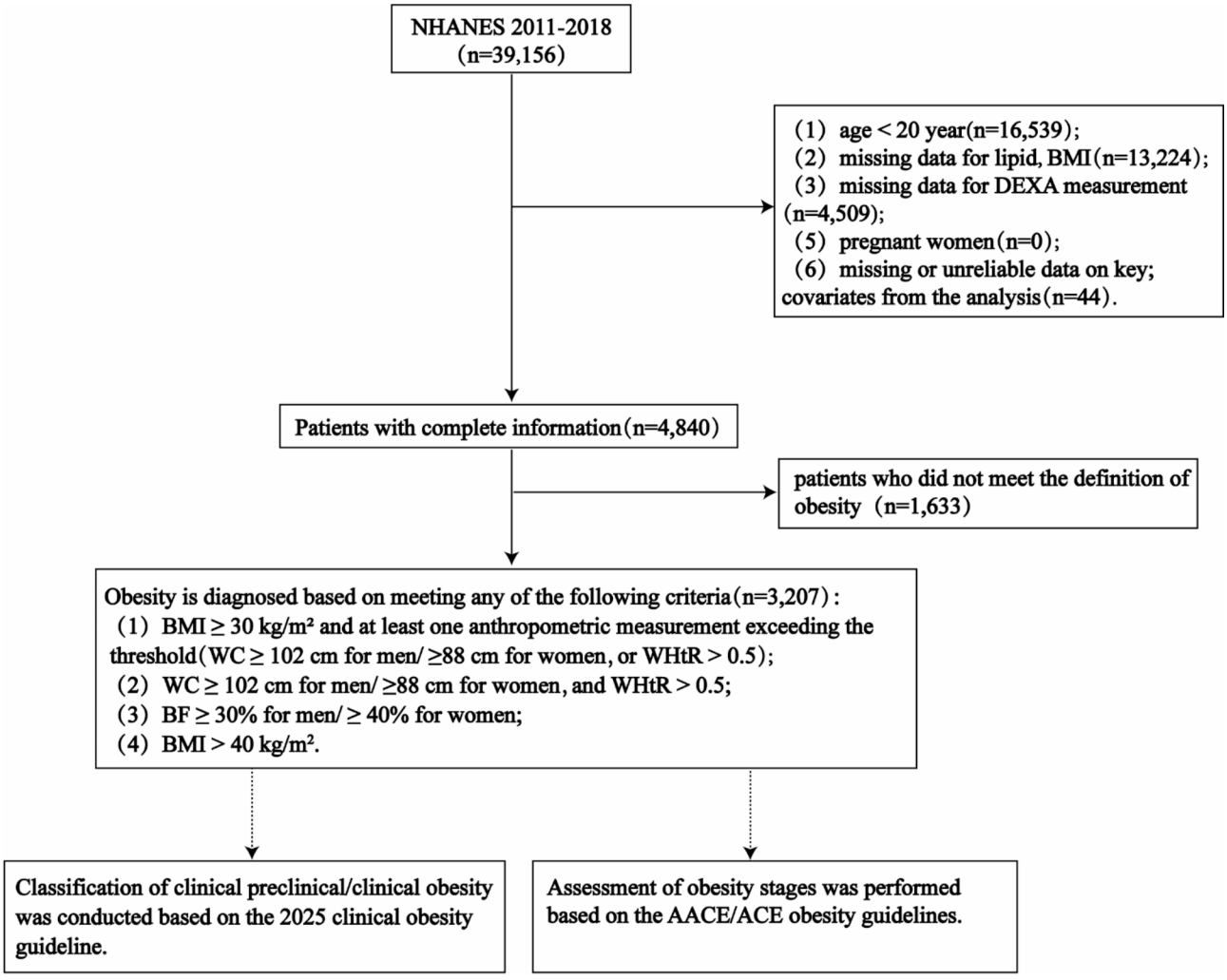

Fig. 1 The flow chart of participant selection. **Abbreviations**: WC, waist circumference; WHtR, waist-to-height ratio; BMI, body mass index; BF, body fat percentage

the new criteria, which requiring meeting any one of the following conditions [3]: (1) BMI > 30 kg/m² combined with at least one additional anthropometric measurement exceeding the threshold (WC ≥ 102 cm for men / ≥ 88 cm for women, or waist-to-height ratio (WHtR) > 0.5); (2) WC > 102 cm for men / > 88 cm for women, and WHtR > 0.5; (3) body fat percentage (BF) ≥ 30% for men / ≥ 40% for women; (4) BMI > 40 kg/m² [14, 15].The second step was to differentiate clinical obesity from preclinical obesity by evaluating the function of multi-organ systems, including 18 specific items for adults. The complete diagnostic criteria and detailed items are comprehensively listed in Table S1 of additional file [Additional file 1]. The NHANES includes relevant data for assessing signs and symptoms across the following 9 systems: cardiovascular (ventricular), cardiovascular (arterial), metabolism, liver, renal, urinary, male and female reproductive systems, and limitations of day-to-day activities. The specific criteria used in this study for the assessment of clinical obesity are described below and are also presented in tabular form in Table S1 [Additional file 1].

Cardiovascular (ventricular) disorder was defined based on a patient-reported history of heart failure. Increased arterial pressure in cardiovascular (arterial) was defined as systolic blood pressure (SBP) ≥ 130 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg [14], or the use of antihypertensive medication, or a self-reported history of hypertension. The assessment of metabolic health encompassed abnormalities in glucose and lipid metabolism. Diabetes was defined as fasting plasma glucose (FPG) ≥ 7.0 mmol/L, or glycated hemoglobin (HbA1c) ≥ 6.5%, or previously diagnosis of diabetes, or using antidiabetic drugs. Prediabetes was defined as fasting plasma glucose (FPG) levels ranging from 5.6 mmol/L to 6.9 mmol/L or HbA1c levels between 5.7% and 6.4% [16]. Hypertriglyceridemia was defined as TG ≥ 1.7 mmol/L, and decreased HDL-C was defined as HDL-C < 1.0 mmol/L in men or < 1.30 mmol/L

in women [14]. The evaluation of liver-related disorders encompassed fatty liver disease (FLD), characterized by a fatty liver index (FLI) ≥ 60 [17], and hepatic fibrosis, characterized by a fibrosis-4 index (FIB-4) > 2.67 [18]. Urine albumin-to-creatinine ratio (UACR) ≥ 30 mg/g or estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 was considered renal function impairment, where the eGFR was calculated according to the modification of diet in renal disease (MDRD) Eqs. [19, 20]. Male hypogonadism was diagnosed by hypotestosteronemia (testosterone < 300 ng/dL). Female reproductive system abnormalities included menstrual thinning, infertility, and hyperandrogenemia. Hyperandrogenemia was defined as testosterone > 30 ng/dL or free androgen index > 5.0 [21]. To assess urinary incontinence, the grading of incontinence was defined by using two parameters [22], including incontinence frequency (less than monthly, several times per month, several times per week or per day) and urine leakage (count drops, splash, or more). The total score was obtained by multiplying the scores of the two parameters, ranging from 1 to 12 (1–2, mild incontinence; 3–6, moderate incontinence; 7–12, severe incontinence). Patients with a total score ≥ 1 were considered as exhibiting symptoms or signs of obesity-related urinary system disorders. Functional limitations in daily activities was assessed using modified Barthel Index, which evaluates domains including eating, bathing, dressing, personal hygiene, urine control, toilet use, transfer from chair to bed, walking, and the ability to walk up and down stairs. According to the score assessed with the Barthel index, patients can be divided into 5 groups: complete dependence (0–20), severe dependence (21–60), moderate dependence (61–90), mild dependence (91–99), and independent (100). Patients with score < 100 were considered as having daily activity limitation [23].

Definition of obesity stages

The guideline published by the AACE/ACE categorized obese patients into three stages [2]: (1) Stage 0: obesity without ORCs; (2) Stage 1: obesity with one or more mild-to-moderate ORCs; (3) Stage 2: obesity with one or more severe ORCs. The final stage of obesity was determined by the most severe stage among all associated complications. The NHANES provides information of 8 categories of ORCs recommended for routine screening and assessment in obesity, including prediabetes, type 2 diabetes (T2D), metabolic syndrome, hypertension, dyslipidemia, FLD, osteoarthritis, urinary incontinence, disability, and psychological disorder. The specific criteria utilized in this study for assessing obesity stages are described below and presented in tabular form in Table S2 [Additional file 1].

Definitions of overlapping assessment items in the two guidelines are not reiterated [2, 3], including prediabetes, T2D, hypertension, FLD, urinary incontinence and disability. Impaired fasting glucose (IFG) was defined as FPG levels ranging from 5.6 mmol/L to 6.9 mmol/L [16]. Impaired glucose tolerance (IGT) was defined as a 2-hour postprandial glucose level ≥ 7.8 mmol/L [16]. The presence of metabolic syndrome was ascertained if three of the following five criteria were met: (1)triglycerides (TG) ≥ 1.7 mmol/L; (2) HDL-C < 1.0 mmol/L in men and < 1.3 mmol/L in women; (3) Hypertension; (4) IFG or T2D; (5) abdominal obesity (WC ≥ 102 cm in men / ≥ 88 cm in women) [14]. Mental health status was assessed using the patient health questionnaire-9 (PHQ-9). This questionnaire tool has a scoring range of 0 to 27, reflecting the severity of depressive symptoms. The severity levels were classified as: no depression (0–4), mild depression (5–9), moderate depression (10–14), and moderately severe to severe depression (≥ 15) [24].

Assessment of body composition

Body composition was measured by using DEXA in the NHANES study. The appendicular skeletal muscle index (ASMI) was calculated as the ratio of appendicular skeletal muscle mass (ASM) to the square of height. Low muscle mass was defined as ASM < 20 kg or ASMI < 7 kg/m^2 in men, and ASM < 15 kg or ASMI < 5.5 kg/m^2 in women [25].

The Hologic APEX software was used to automatically segment and measure fat tissue. The visceral fat area (VFA) was defined as the measurement of abdominal visceral fat at the interspace between the fourth and fifth lumbar vertebrae. Visceral obesity was defined as VFA ≥ 100 cm^2 [26]. The visceral-to-subcutaneous fat ratio (VSR) was calculated as the ratio of abdominal visceral fat area to abdominal subcutaneous fat area. Elevated body fat was defined as BF ≥ 30% in men and ≥ 40% in women [27].

Assessment of other covariables

Several potential covariables, including age, gender, ethnicity, educational level, smoking habits, self-reported drug use and health status are considered in this study. Smoking history was defined as having smoked more than 100 cigarettes in one's lifetime. Alcohol consumption history was defined as daily intake of ≥ 3 drinks for men and ≥ 2 drinks for women [28]. According to the definition in the NHANES database, one standard drink is equivalent to approximately 355 mL of beer, 150 mL of wine, or 45 mL of liquor.

Statistical analysis

Given that complex sampling design employed by NHANES, prevalence estimates and models were

survey-weighted using the NHANES primary sampling unit, strata, and population weights to ensure national representativeness of the U.S. population. Weighted values for each cycle can be obtained directly from NHANES and the weighting procedure was conducted according to the NHANES analytic guideline (https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx). This study took "WTSAF2YR" as the weighted variable.

All the information for the study population was summarized in accordance with tertiles of serum RC concentration. Continuous variables with normal distribution and with skewed distribution were expressed as mean ± standard deviation (SD) and median (interquartile range, IQR), respectively. Categorical variables were described as numbers (n) with weighted percentages (%). We utilized weighted linear regression analyses to evaluate trends across tertiles of RC concentration. Weighted multivariable logistic regression modeling was used to estimate the association of RC with preclinical/clinical obesity and obesity stages. Model 1 adjusted for basic demographic characteristics (age, gender, race, educational status, smoking status) and body composition (VSR, ASMI). Model 2 further adjusted for hypertension, T2D and the use of lipid-lowering drugs. Given the well-documented strong association between RC and TG in prior studies, model 3 further adjusted for TG on the basis of model 2. The dose-response relationships between serum RC levels and obesity phenotypes (preclinical/clinical obesity and obesity stages) were evaluated using restricted cubic spline (RCS) regression models, with multivariable adjustments consistent with those applied in model 3 as described above. To validate the robustness of our results, sensitivity analyses were further performed by excluding participants receiving lipid-lowering therapy. To assess potential multicollinearity among covariables, variance inflation factors (VIFs) was calculated. A VIF value greater than 5 was considered indicative of multicollinearity [29].

All analyses were two-sided and $P < 0.05$ was considered statistically significant. The statistical procedures were conducted using the "survey", "splines2", "rms", "ggplot2" R packages in R (4.4.1).

Results

Characteristics

General characteristics and body composition of participants are listed in Table S4 [Additional file 1]. A total of 3,207 participants were identified, including 1,662(53.76%) males and 1,545(46.24%) females, with a median age of 41(30,50) years. Subjects with higher RC concentration were more likely to report a history of hypertension, diabetes or prediabetes, cardiovascular diseases, use of lipid-lowering and anti-hypertension drugs. (all P values < 0.001). Only one patient in the T3 group had markedly elevated TG levels (≥ 4.5 mmol/L), with a measured value precisely at 4.5 mmol/L. Body composition measurements obtained via DEXA revealed that VFA, total abdominal fat area and VSR significantly increased with rising RC concentrations (all P values < 0.001). Subcutaneous fat area (SFA) ($P = 0.16$) and BF ($P = 0.10$) did not exhibit consistent trends with changes in RC levels. Muscle-related parameters (ASM and ASMI) showed an higher level in the group with higher RC concentrations.

RC and preclinical/clinical obesity

The prevalence of clinical obesity significantly increased with rising RC levels. In the T3 group of RC, 1,037 patients (96.74%) were identified as clinical obesity, while the proportion in the other two groups was approximately 85% [T1 group: 947 (84.72%); T2 group: 944 (85.65%)]. Except for the prevalence of ventricular systolic dysfunction ($P = 0.64$), urinary incontinence ($P = 0.68$), and reproductive abnormalities in females ($P = 0.98$), all other obesity-related clinical manifestations increased progressively with rising RC concentrations. Metabolic abnormalities(2,130, 62.30%) and renal impairment(1,219, 33.96%) were the first and second most common comorbidities, respectively, with their prevalence both peaking in the T3 group. Table 1 provides the prevalence of obesity-related clinical manifestations and preclinical/clinical obesity status stratified by tertiles of RC concentration.

The association between serum RC levels and preclinical/clinical obesity analyzed using logistic regression models is detailed in Fig. 2. The multivariable-adjusted ORs (95% CIs) among participants in the T3 group were 5.30(3.97–7.08) in model 1, 5.83(4.36–7.80) in model 2, 1.95(1.19–3.19) in model 3, respectively, compared with those in the T1 group. And the results from the analyses of individuals not using lipid-lowering medications indicated that, for per SD increase in RC in the fully adjusted model(model 3), the risk of progression from preclinical obesity to clinical obesity increased by 95% [OR (95% CI), 1.95(1.19–3.19)]. Results of RCS analyses indicated significant nonlinear dose-response association between RC levels and the risk of clinical obesity in both the overall population and the subgroup not receiving lipid-lowering therapy (P for nonlinearity < 0.001), sharing the same threshold at around a serum RC value of 0.51 mmol/L (Fig. 3).

RC and obesity stages defined by AACE/ACE guideline

The distribution of subjects across AACE/ACE obesity stages based on RC tertiles is shown in Table 2. Among all the obese patients included in this study, none were in stage 0. The majority of patients were in stage 1, comprising 1,578 (57.26%) patients. A total of 1,559(42.47%)

Table 1 Distribution of obesity related clinical manifestations and preclinical/clinical obesity across tertiles of serum RC concentration

Character	Tertiles of serum RC concentration			*P* for trend
	Tertile 1	Tertile 2	Tertile 3	
Cardiovascular (ventricular)				0.64
No	1060(99.18)	1064(99.19)	1047(98.68)	
Yes	10(0.82)	8(0.81)	18(1.32)	
Cardiovascular (arterial)				< 0.001
No	863(82.2)	816(78.78)	772(73.27)	
Yes	207(17.8)	256(21.22)	293(26.73)	
Metabolism				< 0.001
No	565(58.03)	420(46.15)	92(9.31)	
Yes	505(41.97)	652(53.85)	973(90.69)	
Liver				< 0.001
No	1036(96.61)	1013(94.05)	960(90.38)	
Yes	34(3.39)	59(5.95)	105(9.62)	
Renal				< 0.05
No	653(67.56)	666(64.18)	669(66.43)	
Yes	417(32.44)	406(35.82)	396(33.57)	
Urinary				0.68
No	840(78.74)	836(77.12)	833(77.81)	
Yes	230(21.26)	236(22.88)	232(22.19)	
Reproductive (female)				0.98
No	831(79.17)	923(84.75)	939(87.30)	
Yes	239(20.83)	149(15.25)	126(12.70)	
Reproductive (male)				< 0.001
No	537(54.7)	560(51.6)	614(59.87)	
Yes	533(45.3)	512(48.4)	451(40.13)	
Limitations of day-to-day activities				< 0.01
No	947(88.8)	908(83.98)	891(82.32)	
Yes	123(11.2)	164(16.02)	174(17.68)	
Obesity phenotypes				< 0.001
Preclinical obesity	123(15.28)	128(14.35)	28(3.26)	
clinical obesity	947(84.72)	944(85.65)	1037(96.74)	

Abbreviations: RC, remnant cholesterol

patients were in stage 2. As RC levels increased, there was a corresponding rising in the proportion of obese patients in stage 2 (24.09% in the T1 group,36.78% in the T2 group, 74.85% in the T3 group). According to the AACE/ACE obesity guideline for the definition of ORCs and their respective stages, it was observed that prediabetes, metabolic syndrome, and T2D ($n = 3,203$, 99.89%) was the most prevalent complication, followed by FLD ($n = 1,694$, 53.28%). The T3 group consistently exhibited the highest prevalence of severe ORCs. The prevalence and staging of the rest ORCs increased progressively with rising RC concentrations(P for osteoarthritis < 0.05, P for the other ORCs < 0.001).

The association between serum RC levels and obesity stages analyzed using logistic regression models is detailed in Fig. 4. Patients in the T3 group had higher risk of obesity stage progression than patients in the T1 group, with ORs (95% CI) of 9.70(5.24–17.96) in model 1, 9.48(5.07–17.74) in model 2, and 1.96(1.06–3.62) in model 3, respectively. The results obtained from the sensitivity analysis restricted to individuals not receiving lipid-lowering therapy demonstrated nearly identical to those derived from the overall population.

The RCS analyses revealed significant nonlinear dose-response association between RC and the risk of progression in obesity stages (P for nonlinearity < 0.001), and the serum RC threshold was remarkably equal to the cutoff value for distinguishing clinical obesity from preclinical obesity, approximately 0.51 mmol/L (Fig. 3).

Discussion

It is the first study to delve into the association between RC and adverse obesity phenotypes—preclinical/clinical obesity and obesity stages—evaluated via multi-organ functions. In contrast to prior studies that relied solely on BMI as the criterion for defining obesity, our analysis expanded the evaluation to incorporate comprehensive measurements of body size and body composition, thereby applying the new definition of obesity in practice.

This study demonstrated that elevated RC levels were associated with an increasing trend in visceral fat-related indicators, such as the VSR and VFA, while showing no significant association with BF or SFA. These findings suggested that RC is more closely associated with ectopic fat deposition, which marks the onset of morbid obesity [8, 30], rather than simple fat expansion. Traditionally, obesity has been viewed as a precursor to insulin resistance, which subsequently leads to hyperlipidemia. However, another hypothesis proposed that elevated RC levels preceded the development of insulin resistance [31], the core mechanism of morbid obesity. This insight pushes us early identification and intervention for obese patients exhibiting elevated RC level. Contrary to previous studies [32, 33], our findings indicated a positive association between RC and ASM as well as the ASMI. This discrepancy may be attributed to differences between study populations. Our research focused specifically on obese individuals, who are prone to intramuscular lipid deposition, including intramyocellular lipids (IMCL) and intermuscular adipose tissue (IMAT) [34, 35, 36]. However, DEXA has limitations in distinguishing between muscle and IMCL or IMAT, potentially leading to an overestimation of absolute muscle mass in obese individuals [37, 38]. Furthermore, this measurement error exhibits a dose-dependent relationship with anthropometric indices such as BMI and WC [39]. Moreover, RC is also significantly positively correlated with these indices [5], suggesting that abnormalities in lipid metabolism and the heterogeneity of fat distribution may synergistically amplify the measurement bias of DEXA in assessing lean tissue mass. This may explain the positive association between muscle mass and RC levels observed in our study.

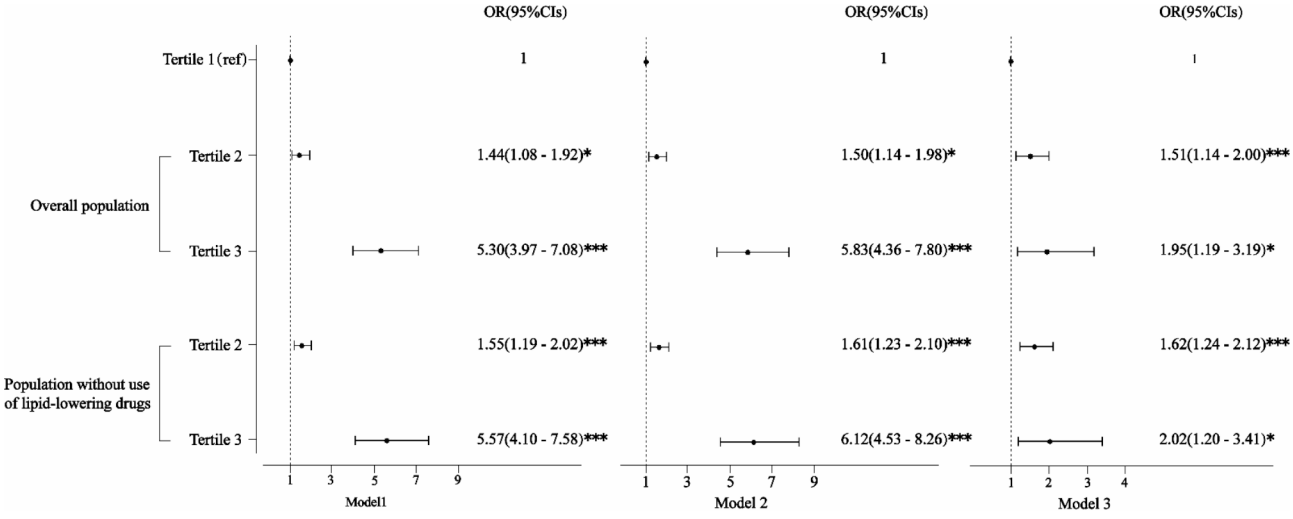

Fig. 2 Association between RC and preclinical/clinical obesity. Model 1: Adjusted for age, gender, race, educational status, smoke status, VSR and ASMI; Model 2: Adjusted for age, gender, race, educational status, smoke status, VSR, ASMI, hypertension, T2D and lipid-lowering drugs; Model 3: Additional adjusted for TG; *: $P < 0.05$; ***: $P < 0.001$. **Abbreviations**: Ref, reference; OR, odds ratio; CI, confidence interval

RC exhibited a consistent trend with the prevalence of multiple obesity-related clinical manifestations and activity limitations according to our results. The 2025 clinical obesity guideline emphasized the classification and diagnosis of preclinical/clinical obesity based on clinical manifestations (symptoms/signs) directly induced by obesity itself, providing a more objective and intuitive framework for clinicians and patients to understand obesity status and select personalized treatment strategies [3]. Unlike previous studies that predominantly focused on metabolic phenotype to identify obese individuals at high cardiovascular risk, the definition of clinical obesity characterized obesity as a persistent disease affecting various organs and tissues, distinguishing it from metabolically unhealthy obesity, which is limited to metabolic dysregulation [3]. However, completing a comprehensive assessment of all 18 clinical manifestations is a cumbersome process. Our study results demonstrated that the number of patients with clinical obesity significantly increased with rising RC levels, with the proportion reaching up to 96.74% in the highest tertile of RC. These findings suggested that RC may serve as a convenient and effective biomarker for rapidly identifying a high-risk group prone to clinical obesity. Importantly, this association remained significant even after adjusting for various risk factors, including age, gender, race, educational status, smoking status, VSR, ASMI, history of hypertension, TG levels and the use of lipid-lowering drugs. Notably, when TG was included as a confounding factor in model 3, the estimated effect in the T3 group was significantly reduced compared to model 1 and 2, despite the P-value indicating statistical significance. In contrast, the change of OR in the T2 group compared to the T1 group remained almost negligible across all the models. This observation may be explained by the fact that RC represents the cholesterol content of triglyceride-rich lipoproteins (TRL), which tends to exhibit strong collinearity with TG. High plasma concentrations of RC, formed when TRL undergo partial TG depletion by lipoprotein lipase, are well-recognized for their potent atherogenic properties [40, 41]. In this context, it has been suggested that plasma RC, rather than plasma TG, is an independent risk factor for the development of cardiovascular disease [40, 41, 42]. Our findings aligned with this conclusion, demonstrating that RC predicts clinical obesity independently of TG levels. Therefore, it is imperative to prioritize the assessment of serum RC levels, irrespective of TG concentration.

According to the obesity stages definition of AACE/ACE obesity guideline [2], none of the 3,207 patients included in this study were classified at stage 0. This finding aligns with a previous study applying the AACE/ACE of obesity in a Venezuelan population of 1,320 individuals, which reported that only approximately 3.1% of patients were classified at stage 0 [43]. The mild discrepancy in the prevalence of stage 0 obesity between the two studies may be attributed to the fact that the Venezuelan study assessed only three ORCs as defined by the 2016 AACE/ACE guideline [2], whereas our study employed a more comprehensive evaluation. Both studies collectively suggested that nearly all obese patients exhibit at least one mild-to-moderate or severe complication, indicating that maintaining a complication-free stage is likely to be challenging or transient for obese individuals. This conclusion is further supported by a meta-analysis summarizing 17 studies [44], underscoring the importance of proactive stage assessment and intervention in obese patients to prevent stage progression and promote stage reversal. Previous studies have highlighted that elevated

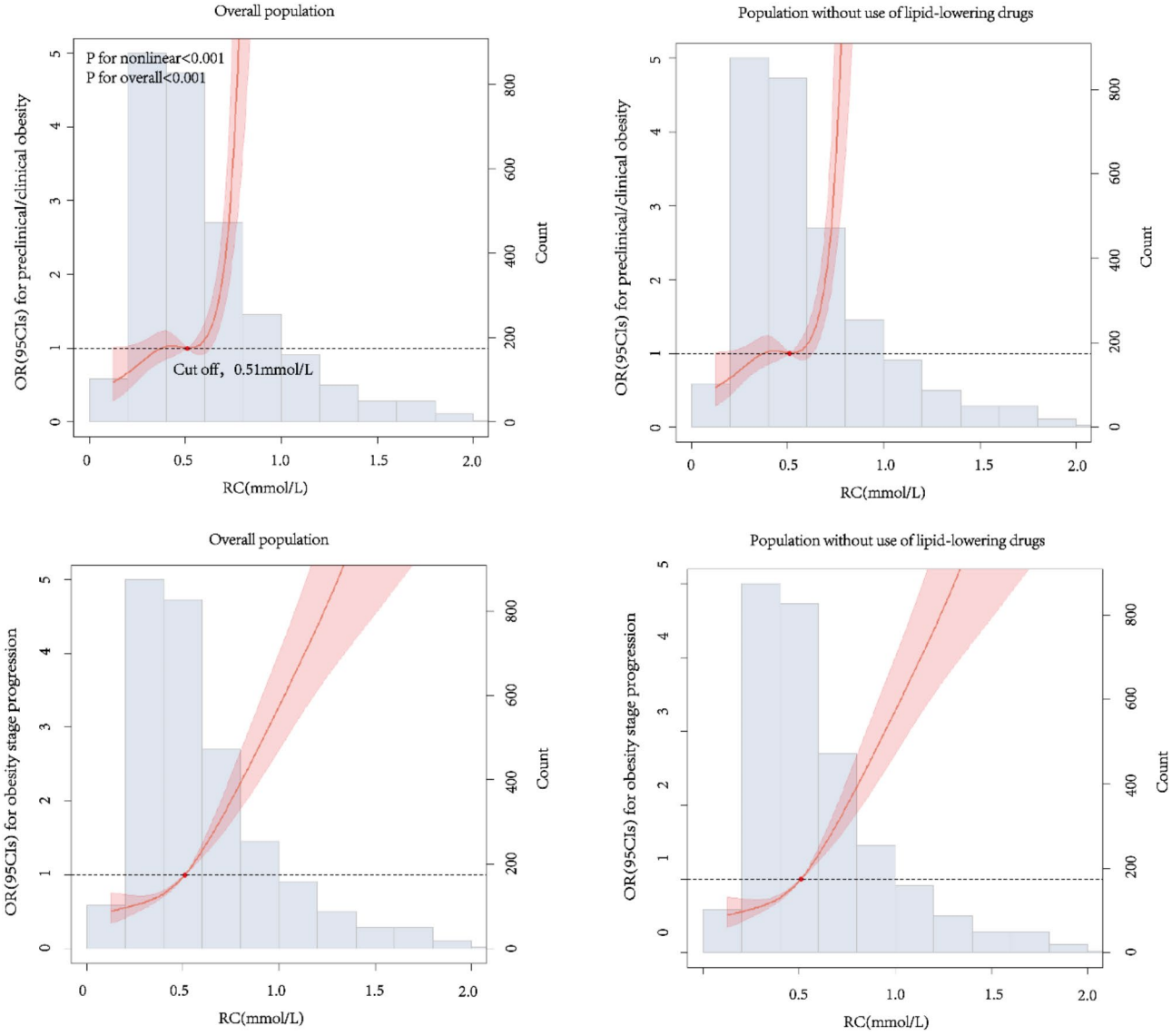

Fig. 3 Nonlinear associations of RC with obesity phenotypes and population distribution histograms by RC concentration. **Abbreviations**: RC, remnant cholesterol; OR, odds ratio; CIs, confidence intervals

RC levels are closely associated with various ORCs, such as renal insufficiency, sleep apnea syndrome, and atherosclerosis [5, 9, 10, 11, 12, 45, 46, 47]. Additionally, some studies have analyzed the mediating role of RC in metabolic diseases, suggesting that RC may contribute to the development of these comorbidities [48, 49, 50]. Consistent with these findings, our study demonstrated that patients in the T3 group of RC concentration exhibited a higher prevalence as well as more advanced stages of ORCs compared to other groups, indicating that RC independently predicted the progression of obesity stages. Therefore, RC has the potential to provide a comprehensive assessment of the obesity phenotypes, reflecting multi-system health status, rather than merely serving as an indicator of blood lipid levels.

To figure out the dose-response association between RC and adverse obesity phenotypes (clinical obesity, progression of obesity stages), we implemented RCS regression analyses, which revealed their nonlinear association. Specifically, the relationships between RC levels and both clinical obesity and the progression of obesity stages exhibited "J"-shaped curves, with a pivotal inflection point at an RC level of 0.51 mmol/L. It can be argued that the risk for adverse obesity phenotypes will escalate abruptly when RC concentration continue to ascend at 0.51 mmol/L. Although our cross-sectional analysis does not allow for the establishment of a direct causal relationship, it is reasonable to speculate that RC may predict the conversion of obesity to an adverse phenotype. Therefore, we suggest obese individuals to be cognizant of their RC

Table 2 Distribution of ORCs and obesity stages across tertiles of serum RC concentration

Character	Tertiles of serum RC concentration			*P* for trend
	Tertile 1	Tertile 2	Tertile 3	
Prediabetes, metabolic syndrome, and type 2 diabetes				< 0.001
Stage 0	1(0.05)	3(0.29)	0(0.00)	
Stage 1	927(89.55)	836(80.8)	675(65.89)	
Stage 2	142(10.4)	233(18.91)	390(34.11)	
Hypertension				< 0.001
Stage 0	846(81.02)	783(75.77)	711(67.25)	
Stage 1	44(5.30)	70(7.07)	33(2.77)	
Stage 2	180(13.68)	219(17.16)	321(29.98)	
Hypertriglyceridemia/Dyslipidemia				< 0.001
Stage 0	858(81.88)	723(69.75)	159(14.36)	
Stage 1	131(12.12)	184(16.14)	271(26.15)	
Stage 2	81(6.00)	165(14.11)	635(59.49)	
Non-alcoholic fatty liver disease				< 0.001
Stage 0	753(71.13)	526(49.1)	234(20.48)	
Stage 1	304(27.78)	532(50.18)	824(78.28)	
Stage 2	13(1.08)	14(0.73)	7(1.24)	
Osteoarthritis				< 0.05
Stage 0	1053(97.92)	1058(98.11)	1032(96.42)	
Stage 1	16(2.02)	12(1.8)	26(2.94)	
Stage 2	1(0.06)	2(0.09)	7(0.64)	
Stress and urge urinary incontinence				0.53
Stage 0	840(78.74)	836(77.12)	833(77.81)	
Stage 1	216(19.75)	216(21.35)	201(19.71)	
Stage 2	14(1.51)	20(1.53)	31(2.48)	
Disability/Immobility				< 0.001
Stage 0	947(88.8)	908(83.98)	891(82.32)	
Stage 1	119(10.95)	148(14.98)	158(16.38)	
Stage 2	4(0.24)	16(1.05)	16(1.31)	
Psychological disorder/Stigmatization				< 0.001
Stage 0	1013(95.34)	998(93.43)	949(89.24)	
Stage 1	49(4.05)	62(5.89)	100(9.3)	
Stage 2	8(0.61)	12(0.68)	16(1.45)	
Obesity stages				< 0.001
Stage 0	0(0)	0(0)	0(0)	
Stage 1	737(73.45)	629(62.58)	339(32.46)	
Stage 2	333(26.55)	443(37.42)	726(67.54)	

Abbreviations: RC, remnant cholesterol

levels at an earlier stage, potentially necessitating a recalibration of the reference values to more accurately reflect the metabolic risks in this population.

This study has several strengths that deserve emphasis. Firstly, this is the first study to explore the association between RC and obesity phenotypes defined by two of the most authoritative guidelines for obesity diagnosis and phenotype assessment [3]. Our results demonstrated that RC can serve as a simple and effective initial screening indicator for adverse obesity phenotypes, enabling rapid and efficient identification of high-risk population in clinical practice, particularly well-suited for primary care settings or resource-limited healthcare environments. Moreover, it facilitates the implementation of obesity guidelines, ultimately improving patient outcomes. Secondly, unlike prior studies that primarily focused on single system disorder, our research provides a comprehensive evaluation of clinical manifestations and staging of ORCs, thereby offering a more systematic reflection of the obesity phenotypes. Thirdly, we employed the latest diagnostic criteria for obesity to identify the population in this study, rather than relying solely on BMI as done in previous literature. This approach ensures that our study captured a unique cohort that has not been previously investigated. Additionally, we utilized data from the NHANES, which employs a stratified, multistage probability design to ensure nationally representative sampling, administered by well-trained research personnel. Furthermore, we employed rigorous statistical methods, including multivariable adjustment and sensitivity analyses, to enhance the reliability and robustness of our findings.

Several limitations of the current study should be recognized also. Firstly, the observational nature of this research precludes us from establishing a causal link between RC and obesity phenotypes. Secondly, although we have undertaken multiple adjustments to minimize the influence of confounders, there may still be unmeasured potential variables that could impact the results. Lastly, the indirect calculation of RC in our study might lead to an overestimation its value compared to direct measurement [48], particularly when TG levels are excessively high [13]. However, in our study, only one patient had a TG level ≥ 4.5 mmol/L, with a concentration of exactly 4.5 mmol/L, which is at the borderline. Therefore, it is reasonable to assume that LDL-C levels of the majority of participants were minimally affected by TG concentrations. Additionally, blood samples were collected in the morning after an overnight fast of at least eight hours to minimize the influence of recent food intake on lipid profiles. This approach is particularly critical for TG levels, as they are highly susceptible to dietary effects, thereby enhancing the standardization and reliability of the measurements. Furthermore, in the model 3 of logistic regression analyses, TG was included as a covariable to minimize its potential impact on the results. In summary, although the indirect calculation of LDL-C may introduce some bias, the measures described above suggest that the findings of this study were likely minimally affected by TG levels. Nonetheless, the indirect calculation of RC is an affordable and accessible method that could provide valuable data for clinical management. Further research is needed to address these limitations and deepen our understanding of the relationship between RC and obesity phenotypes.

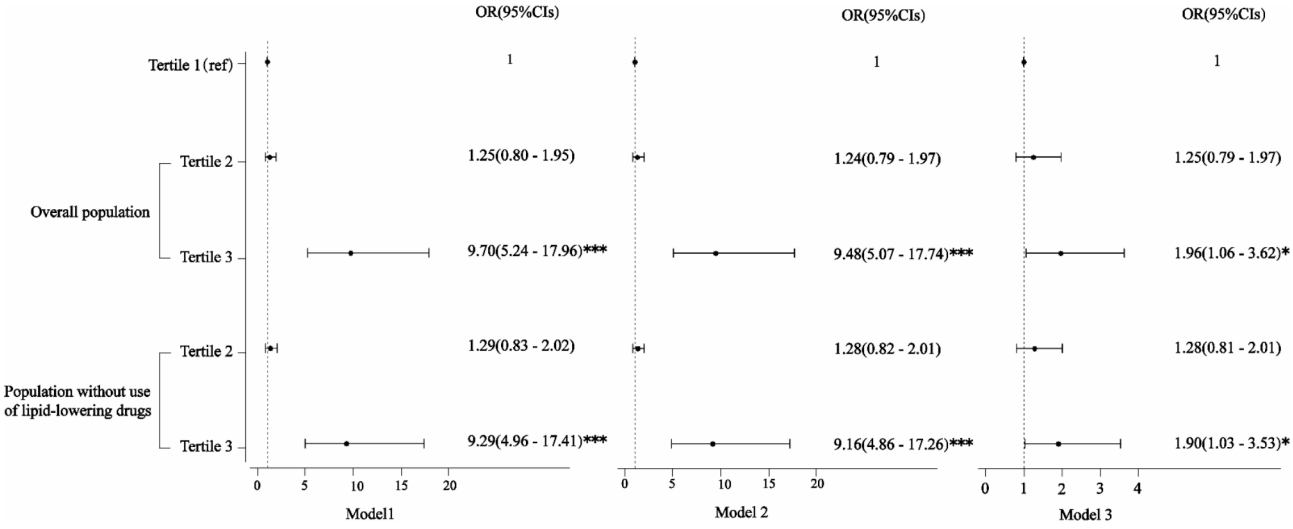

Fig. 4 Association between RC and the progression of obesity stages. Model 1: Adjusted for age, gender, race, educational status, smoke status, VSR and ASMI; Model 2: Overall population, adjusted for age, gender, race, educational status, smoke status, VSR, ASMI, hypertension, T2D and lipid-lowering drugs; Model 3: Additional adjusted for TG; *: $P < 0.05$; ***: $P < 0.001$. **Abbreviations**: Ref, reference; OR, odds ratio; CIs, confidence intervals

Conclusion

In conclusion, our study has identified a positive and independent association between RC concentration and adverse obesity phenotypes. In addition to routine blood lipid monitoring, it is advisable to incorporate RC assessment into the clinical management of obese patients. This approach will enable early detection and intervention for high-risk individuals and facilitate the adoption of guidelines in clinical practice, thereby improving patient outcomes and reducing the burden of obesity.

Abbreviations

ASM	Appendicular skeletal muscle mass
ASMI	Appendicular skeletal muscle index
ALB	Albumin
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
AACE/ACE	American Association of Clinical Endocrinologists and the American College of Endocrinology
BMI	Body mass index
BF	Body fat percentage
DBP	Diastolic blood pressure
DEXA	Dual-energy X-ray absorptiometry
eGFR	Estimated glomerular filtration rate
FLI	Fatty liver index
FLD	Fatty liver diseases
FIB-4	Fibrosis 4 score
FPG	Fasting plasma glucose
GGT	Gamma-glutamyl transferase
HDL-C	High density lipoprotein-cholesterol
HbA1c	Glycated hemoglobin
IDL	Intermediate-density lipoproteins
IQR	Interquartile range
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IMCL	Including intramyocellular lipids
IMAT	Intermuscular adipose tissue
LDL-C	Low-density lipoprotein-cholesterol
MDRDEs	Modified diet in renal disease equations
NHANES	National Health and Nutrition Examination Survey
ORCs	Obesity-related comorbidities
PHQ-9	Patient health questionnaire-9
RC	Remnant cholesterol
RCS	Restricted cubic spline
SBP	Systolic blood pressure
SFA	Subcutaneous fat area
TG	Triglycerides
TC	Total cholesterol
TRL	Triglyceride-rich lipoproteins
T2D	Type 2 diabetes
T	Tertile
UACR	Urinary albumin to creatinine ratio
VLDL	Very low-density lipoproteins
VFA	Visceral fat area
VSR	Visceral-to-subcutaneous fat ratio
WC	Waist circumference
WHtR	Waist-to-height ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02550-5.

Supplementary Material 1

Acknowledgements

We extend our sincere gratitude to the teams of National Health and Nutrition Examination Survey for their data provision.

Author contributions

Tian Yu for study concept and design and drafting of the manuscript; Tian Yu, Lu Fang and Shaohua Liu for analysis and interpretation of data; Tian Yu, Tingting Du and Zhelong Liu statistical analysis and technical support; Tian Yu, Lu Fang and Shaohua Liu for obtained data; Tingting Du and Zhelong Liu for study supervision. All authors have read and approved the final manuscript.

Funding

This work was supported by Noncommunicable Chronic Diseases-National Science and Technology Major Project[grant number 2024ZD0532300], Clinical Medical Education Teaching Reform Research Project of Hubei Provincial Health Commission [grant numbers HBJG-220045] and Sen-Mei China Diabetes Research Fund [grant number Z-2017-26-1902].

Data availability
Publicly available datasets were analyzed in this study. This data can be found at: all data for this study can be obtained from NHANES (https://www.cdc.gov/nchs/nhanes/index.htm).

Declarations

Ethics approval and consent to participate
Ethics approval and consent to participate The NHANES study was approved by the National Center for Health Statistics Ethics Review Board. All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Division of Endocrinology, Department of Internal Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[2]Hubei Clinical Medical Research Center for Endocrinology and Metabolic Diseases, Hubei, China
[3]Branch of National Clinical Research Center for Metabolic Diseases, Hubei, China
[4]Key Laboratory of Vascular Aging, Tongji Hospital of Tongji Medical College, Ministry of Education, Huazhong University of Science and Technology, Wuhan 430030, China

Received: 24 February 2025 / Accepted: 27 March 2025
Published online: 09 April 2025

References

1. Trends in adult. body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016;387:1377–96.
2. Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, et al. American association of clinical endocrinologists and American college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract. 2016;22(Suppl 3):1–203.
3. Rubino F, Cummings DE, Eckel RH, Cohen RV, Wilding J, Brown WA, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol; 2025.
4. Garvey WT, Garber AJ, Mechanick JI, Bray GA, Dagogo-Jack S, Einhorn D, et al. American association of clinical endocrinologists and American college of endocrinology position statement on the 2014 advanced framework for a new diagnosis of obesity as a chronic disease. Endocr Pract. 2014;20:977–89.
5. Choi YJ, Jo YE, Kim YK, Ahn SM, Jung SH, Kim HJ, et al. High plasma concentration of remnant lipoprotein cholesterol in obese children and adolescents. Diabetes Care. 2006;29:2305–10.
6. Vekic J, Stefanovic A, Zeljkovic A. Obesity and dyslipidemia: A review of current evidence. Curr Obes Rep. 2023;12:207–22.
7. Ginsberg HN, Packard CJ, Chapman MJ, Borén J, Aguilar-Salinas CA, Averna M, et al. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European atherosclerosis society. Eur Heart J. 2021;42:4791–806.
8. Nakajima K, Tokita Y, Tanaka A, Hypothesis. Postprandial remnant lipoproteins are the causal factors that induce the insulin resistance associated with obesity. Clin Chim Acta. 2018;485:126–32.
9. Varbo A, Benn M, Smith GD, Timpson NJ, Tybjaerg-Hansen A, Nordestgaard BG. Remnant cholesterol, low-density lipoprotein cholesterol, and blood pressure as mediators from obesity to ischemic heart disease. Circ Res. 2015;116:665–73.
10. Tong J, Li X, Liang X, Tang F, Ren Y, Hao G, et al. The relationship of remnant cholesterol and abdominal obesity in children: A cross-sectional study. Front Cardiovasc Med. 2022;9:929560.
11. Fang Z, Zhu L, Chen Y, Jin Y, Yao Y. Elevated remnant cholesterol was associated with the increased metabolically unhealthy obesity risk in Chinese youth. Asia Pac J Clin Nutr. 2024;33:389–96.
12. Varbo A, Freiberg JJ, Nordestgaard BG. Remnant cholesterol and myocardial infarction in normal weight, overweight, and obese individuals from the Copenhagen general population study. Clin Chem. 2018;64:219–30.
13. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499–502.
14. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American heart association/national heart, lung, and blood Institute scientific statement. Circulation. 2005;112:2735–52.
15. Schneider HJ, Friedrich N, Klotsche J, Pieper L, Nauck M, John U, et al. The predictive value of different measures of obesity for incident cardiovascular events and mortality. J Clin Endocrinol Metab. 2010;95:1777–85.
16. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011;34(Suppl 1):S62–9.
17. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006;43:1317–25.
18. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol. 2006;6:33.
19. Peng J, Zhang Y, Zhu Y, Chen W, Chen L, Ma F, et al. Estimated glucose disposal rate for predicting cardiovascular events and mortality in patients with non-diabetic chronic kidney disease: a prospective cohort study. BMC Med. 2024;22:411.
20. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study group. Ann Intern Med. 1999;130:461–70.
21. Sir-Petermann T, Codner E, Pérez V, Echiburú B, Maliqueo M, Ladrón DGA, et al. Metabolic and reproductive features before and during puberty in daughters of women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2009;94:1923–30.
22. Wu JM, Matthews CA, Vaughan CP, Markland AD. Urinary, fecal, and dual incontinence in older U.S. Adults. J Am Geriatr Soc. 2015;63:947–53.
23. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J. 1965;14:61–5.
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606–13.
25. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:16–31.
26. Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. Physiol Rev. 2013;93:359–404.
27. Fitch AK, Bays HE. Obesity definition, diagnosis, bias, standard operating procedures (SOPs), and telehealth: an obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obes Pillars. 2022;1:100004.
28. Bellentani 28RV, Cortez-Pinto S, Day H, Marchesini C. G. A position statement on NAFLD/NASH based on the EASL 2009 special conference. J Hepatol 2010; 53: 372– 84.
29. Yu H, Jiang S, Land KC. Multicollinearity in hierarchical linear models. Soc Sci Res. 2015;53:118–36.
30. Pazos F. Range of adiposity and cardiorenal syndrome. World J Diabetes. 2020;11:322–50.
31. Cohn JS, Johnson EJ, Millar JS, Cohn SD, Milne RW, Marcel YL, et al. Contribution of apoB-48 and apoB-100 triglyceride-rich lipoproteins (TRL) to postprandial increases in the plasma concentration of TRL triglycerides and retinyl esters. J Lipid Res. 1993;34:2033–40.
32. Li J, Lin Y. Association between residual cholesterol and sarcopenia in American adults. Front Endocrinol (Lausanne). 2024;15:1461961.
33. Jang SY, Hwang SY, Jang A, Kim KJ, Yu JH, Kim NH, et al. Association of remnant cholesterol with sarcopenia in Korean adults: a nationwide population-based study using data from the KNHANES. Front Endocrinol (Lausanne). 2024;15:1391733.
34. Goodpaster BH, Thaete FL, Kelley DE. Thigh adipose tissue distribution is associated with insulin resistance in obesity and in type 2 diabetes mellitus. Am J Clin Nutr. 2000;71:885–92.

35. Gallagher D, Kuznia P, Heshka S, Albu J, Heymsfield SB, Goodpaster B, et al. Adipose tissue in muscle: a novel depot similar in size to visceral adipose tissue. Am J Clin Nutr. 2005;81:903–10.
36. Miljkovic I, Zmuda JM. Epidemiology of myosteatosis. Curr Opin Clin Nutr Metab Care. 2010;13:260–4.
37. Schautz B, Later W, Heller M, Müller MJ, Bosy-Westphal A. Total and regional relationship between lean and fat mass with increasing adiposity–impact for the diagnosis of sarcopenic obesity. Eur J Clin Nutr. 2012;66:1356–61.
38. Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. Proc Nutr Soc. 2015;74:355–66.
39. Fosbøl MØ, Zerahn B. Contemporary methods of body composition measurement. Clin Physiol Funct Imaging. 2015;35:81–97.
40. Twickler TB, Dallinga-Thie GM, Cohn JS, Chapman MJ. Elevated remnant-like particle cholesterol concentration: a characteristic feature of the atherogenic lipoprotein phenotype. Circulation. 2004;109:1918–25.
41. Zilversmit DB. Atherogenic nature of triglycerides, postprandial lipidemia, and triglyceride-rich remnant lipoproteins. Clin Chem. 1995;41:153–8.
42. Saeed A, Feofanova EV, Yu B, Sun W, Virani SS, Nambi V, et al. Remnant-Like particle cholesterol, Low-Density lipoprotein triglycerides, and incident cardiovascular disease. J Am Coll Cardiol. 2018;72:156–69.
43. Nieto-Martínez R, González-Rivas JP, Ugel E, Brajkovich I, Risquez A, Garvey WT, et al. Application of the Aace/ace advanced framework for the diagnosis of obesity and cardiometabolic disease staging in a general population from 3 regions of Venezuela: the Vemsols study results. Endocr Pract. 2018;24:6–13.
44. Čermáková E, Forejt M. Metabolically healthy obesity and health risks - a review of meta-analyses. Cent Eur J Public Health. 2024;32:3–8.
45. Tian F, Xiang QY, Zhang MY, Chen YQ, Lin QZ, Wen T, et al. Changes in non-fasting concentrations of blood lipids after a daily Chinese breakfast in overweight subjects without fasting hypertriglyceridemia. Clin Chim Acta. 2019;490:147–53.
46. Yan P, Xu Y, Miao Y, Bai X, Wu Y, Tang Q, et al. Association of remnant cholesterol with chronic kidney disease in middle-aged and elderly Chinese: a population-based study. Acta Diabetol. 2021;58:1615–25.
47. Zhou Y, Gong W, Yan Y, Wang X, Zheng W, Que B, et al. Prognostic implications of obstructive sleep apnea in patients with unstable angina stratified by remnant cholesterol and triglyceride: a prospective cohort study. BMC Cardiovasc Disord. 2024;24:549.
48. Varbo A, Freiberg JJ, Nordestgaard BG. Extreme nonfasting remnant cholesterol vs extreme LDL cholesterol as contributors to cardiovascular disease and all-cause mortality in 90000 individuals from the general population. Clin Chem. 2015;61:533–43.
49. Nakajima K, Nakano T, Tanaka A. The oxidative modification hypothesis of atherosclerosis: the comparison of atherogenic effects on oxidized LDL and remnant lipoproteins in plasma. Clin Chim Acta. 2006;367:36–47.
50. Bernelot MS, Verweij SL, Schnitzler JG, Stiekema L, Bos M, Langsted A, et al. Remnant cholesterol elicits arterial wall inflammation and a multilevel cellular immune response in humans. Arterioscler Thromb Vasc Biol. 2017;37:969–75.

Publisher's note