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ORIGINAL RESEARCH

Remnant Cholesterol is Associated with Blood Pressure Control in US Adults with Hypertension: NHANES 2007–2018 Analysis

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Background: High blood pressure is a major risk factor for cardiovascular and renal diseases, and lipid metabolism disorders may affect blood pressure through mechanisms such as endothelial inflammation. Remnant cholesterol, a key component of triglyceride-rich lipoproteins, has been recognized as a causal factor for atherosclerosis and metabolic disorders. This study aims to investigate the relationship of remnant cholesterol with blood pressure control in the general US population.

Methods: A total of 3915 participants with self-reported hypertension from NHANES from 2007 to 2018 were included in this study. Demographic and behavior parameters, blood pressure, and blood samples were conducted. Remnant cholesterol was estimated as total cholesterol minus low-density lipoprotein cholesterol minus high-density lipoprotein cholesterol. Control of hypertension was defined as systolic blood pressure less than 140 mmHg and diastolic blood pressure less than 90 mmHg in participants with hypertension.

Results: The mean age was 56.98 ± 0.28 years, and 2021 (weighted percentage 51.34%) were female. Among all participants, 2650 participants had their blood pressure well controlled. In multivariate logistic regression, the associations between remnant cholesterol and blood pressure control were statistically significant after adjusting age, sex, race/ethnicity, education level, poverty income ratio, smoking and drinking status, metabolic equivalent, HbA1c, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (Model 1: OR=0.74, 95% CI: 0.57–0.95; Model 2: OR=0.72, 95% CI: 0.55–0.94; Model 3: OR=0.73, 95% CI: 0.56–0.93; Model 4: OR=0.60, 95% CI: 0.46–0.78). The subgroup analysis revealed generally consistent associations with the main results.

Conclusion: Remnant cholesterol is associated with blood pressure control. Targeting remnant cholesterol through lifestyle modifications or lipid-lowering therapies may improve blood pressure control in high-risk patients.

Keywords: remnant cholesterol, hypertension, blood pressure control, inflammation

Introduction

High blood pressure remains a leading modifiable risk factor for coronary heart disease, stroke, and end-stage renal disease,[1,2] with hypertension accounting for more cardiovascular disease deaths in the US than any other controllable risk factor.[3] Although substantial efforts have been made in the health system towards prevention and treatment among the general population, the global age-standardized mean blood pressure among adults has been largely unchanged since 1975.[4] In a series of cross-sectional surveys weighted to represent the adult US population, the proportion of adults with controlled blood pressure increased from 1999–2000 through 2007–2008 and remained stable until 2014. However, the proportion of adults with controlled blood pressure decreased from 2013–2014 through,2017−2018[5] highlighting an urgent need to identify novel factors influencing blood pressure management.

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Hypertension and dyslipidemia are closely intertwined in cardiovascular disease pathogenesis, with over 60% of hypertensive patients having hypercholesterolemia.[6] Lipid metabolism disorders drive chronic inflammation and endothelial dysfunction—key pathways impacting blood pressure regulation.[7–9] Meta-analysis and randomized placebo-controlled trials have shown that statins lowered blood pressure and reduced treatment-resistant hypertension.[10,11] Remnant cholesterol, which carries intermediate-density lipoprotein, very-low-density lipoprotein, and chylomicron remnants, has been gradually recognized as a powerful causative factor of atherosclerosis and metabolic disorders.[12–15] Shi et al showed that remnant cholesterol was associated with hypertension beyond low-density lipoprotein cholesterol.[16]

Notably, while remnant cholesterol's association with hypertension incidence is documented,[16] its relationship with blood pressure control in patients with established hypertension remains unstudied. Given the declining blood pressure control rate and the need for more targeted hypertension management strategies, investigating whether remnant cholesterol influences blood pressure control could deepen our understanding of lipid-related risks in hypertension and inform novel prevention and treatment approaches. This study thus aims to explore the association between remnant cholesterol and blood pressure control in a nationally representative sample of US adults with hypertension using data from the 2007–2018 National Health and Nutrition Examination Survey (NHANES).

Materials and Methods

Study Population

The National Health and Nutrition Examination Survey (NHANES) is a periodic, cross-sectional health and nutrition-related program examining about 5000 people across the United States annually conducted by the Centers for Disease Control and Prevention since 1960. With the program's complex, multistage, probability sampling design, estimates represent the US civilian population. We declare that all data is publicly available in the NHANES repository. The National Center for Health Statistics Ethics Review Board approved the NHANES study, and all participants provided written informed consent.[17] A total of 59842 participants were recruited in NHANES from 2007 to 2018. We excluded those with missing values on remnant cholesterol (total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol) (n=41945) and those without self-reported hypertension (n=12364). Then we excluded participants with missing values of other covariates (systolic blood pressure, diastolic blood pressure, education, smoking and drinking status, chronic kidney disease, diabetes mellitus, cardiovascular disease, poverty income ratio, body mass index, glycohemoglobin (HbA1c), fasting plasma glucose, metabolic equivalent, and estimated glomerular filtration rate (eGFR)) (n=1430). Participants without weights were also excluded (n=188). The final sample was 3915 for analysis (Figure 1).

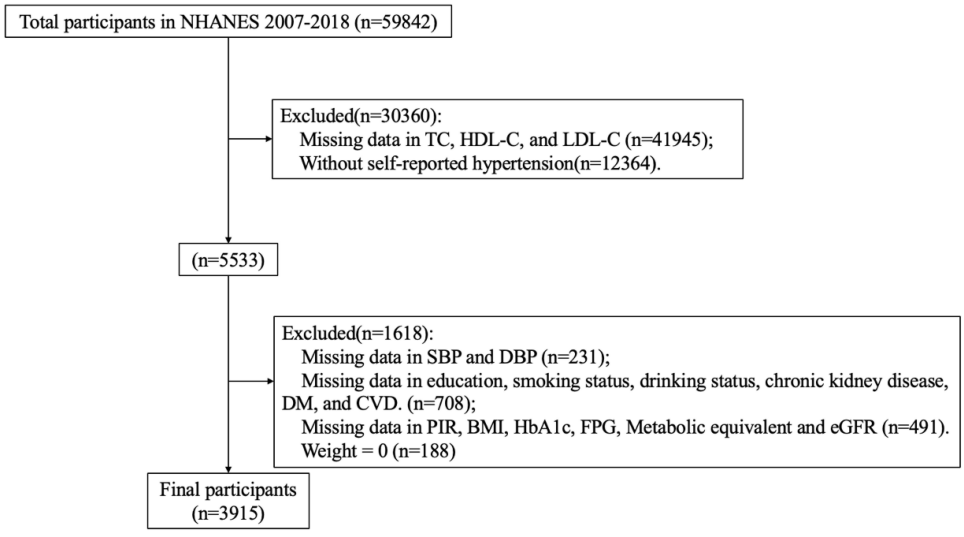

Figure 1 Flowchart of participant selection.

Abbreviations: NHANES, National Health and Nutrition Examination Survey; TC, Total Cholesterol; HDL – C, High-Density Lipoprotein Cholesterol; LDL – C, Low-Density Lipoprotein Cholesterol; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; DM, Diabetes Mellitus; CVD, Cardiovascular Disease; PIR, Poverty Income Ratio; BMI, Body Mass Index; HbA1c, Glycated Hemoglobin; FPG, Fasting Plasma Glucose; eGFR, Estimated Glomerular Filtration Rate.

Exposure and Outcome

The exposure is remnant cholesterol which was calculated as total cholesterol minus high-density lipoprotein cholesterol and low-density lipoprotein cholesterol.[18] The serum specimen collection took place in the mobile examination center and was processed, stored, and shipped to the University of Minnesota for analysis. The laboratory methods used to measure total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were described in detail on the NHANES website.[19–21]

The outcome was the control of hypertension which was defined as systolic blood pressure less than 140 mmHg and diastolic blood pressure less than 90 mmHg in participants with hypertension.[3] This definition was selected because it was widely employed in epidemiological studies using NHANES data from 2007 to 2018, ensuring consistency with previous analyses of this dataset—even though the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend a lower threshold (<130/80 mmHg) for the majority of patients.[22] Hypertension was self-reported in the mobile examination center and was assessed by trained interviewers. Average blood pressure was calculated by the following protocol recommended by NHANES: 1) The diastolic reading with zero was not used to calculate the diastolic average. 2) If all diastolic readings were zero, then the average would be zero. 3) If only one blood pressure reading was obtained, that reading was the average. 4) If there was more than one blood pressure reading, the first reading was always excluded from the average. All blood pressure determinations were taken in the mobile examination center.

Covariates

The demographics questionnaires were asked, in the home, by trained interviews, including age, sex, race/ethnicity, education, and poverty income ratio.[23] The categorization of race/ethnicity was consistent with the NHANES. Education was reclassified into 1) less than high school, 2) high school, and 3) above high school. The Department of Health and Human Services poverty guidelines were used as the poverty measure to calculate the poverty income ratio.[24] Body mass index was calculated as weight in kg divided by square of height in meters. Smoking status was stratified into 3 strata: 1) never: smoked less than 100 cigarettes in life, 2) former: smoked more than 100 cigarettes in life and smoke not at all now, 3) now: smoked more than 100 cigarettes in life and smoke some days or every day. Alcohol use was stratified into: 1) never (had <12 drinks in lifetime); 2) former (had ≥12 drinks in 1 year and did not drink last year, or did not drink last year but drank ≥12 drinks in lifetime); 3) current mild drinker (≥1 drinks per day for females, ≥2 drinks per day for males); 4) current moderate drinker (≥2 drinks per day for females, ≥3 drinks per day for males, or binge drinking ≥2 and <5 days per month); 5) current heavy drinker (≥3 drinks per day for females, ≥4 drinks per day for males, or binge drinking on 5 or more days per month). The estimated glomerular filtration rate was calculated according to the Chronic Kidney Disease Epidemiology Collaboration Equation 2009 and chronic kidney disease was defined by KDIGO 2021 Clinical Practice Guideline. Hyperlipidemia was defined by triglycerides ≥150 mg/dl, total cholesterol ≥200 mg/dl, low-density lipoprotein ≥130 mg/dl or high-density lipoprotein <40 mg/dl (male) or 50 mg/dl (female). Diabetes mellitus was defined by one of the following criteria: 1) self-reported diabetes mellitus, 2) HbA1c ≥6.5%, 3) fasting glucose ≥7.0 mmol/l, 4) random blood glucose ≥11.1 mmol/l, 5) two-hour oral glucose tolerance test blood glucose ≥11.1 mmol/l, 6) use of anti-diabetes medication or insulin. Cardiovascular diseases (CVD) were defined by having at least one of the following self-reported diseases: 1) angina, 2) congestive heart failure, 3) stroke, 4) heart attack, and 5) coronary heart disease.

Statistical Analysis

The complex sampling design factors of NHANES, including clustering, stratification, and sample weights, were accounted for and appropriately calculated according to the NHANES Analytic Guidelines to produce estimates representative of the US population[15]. Participants who had missing values were excluded because the missing values of each covariate were less than 10%. Baseline characteristics were compared using the *t*-test, one-way ANOVA, or Wilcoxon test for continuous variables, and chi-square test or Kruskal–Wallis test for categorical variables. Continuous variables were presented as weighted means and standard errors, while categorical variables were expressed as numbers

and weighted percentages. Weighted univariable and multivariable logistic regressions were used to study the association between remnant cholesterol (as a continuous index or ordinal categorical index) and the odds of well-controlled hypertension after adjusting for potential confounders. Restricted cubic spline regression was used to examine the potential nonlinear relationships between the remnant cholesterol with well-controlled hypertension. Stratified analysis was applied by age strata, sex, antihypertensive medicine condition, and history of cardiovascular diseases, chronic kidney disease, hyperlipidemia, and diabetes mellitus to test subpopulations susceptible to demographic or medical history-related disparities. The significance of interactions was estimated by the P values for the production terms between remnant cholesterol and the stratified factors. A two-sided $P < 0.05$ was considered statistically significant. All analyses were performed with R software, version 4.2.3 (R Core Team, Vienna, Austria).

Results

Table 1 lists the weighted demographic baseline characteristics of the participants in the study according to current blood pressure status. Of the 3915 participants with hypertension involved in the final analyses, 2021 (weighted percentage 51.62%) were female, and the mean age was 56.98 ± 0.28 years. Among all, 2650 participants had their blood pressure well controlled, and the weighted controlled rate was 72.31%. Compared with those with uncontrolled hypertension, participants with well-controlled hypertension were younger and more likely to be white, have a higher poverty income ratio (indicating greater wealth), higher education levels, and be non-smokers. Regarding alcohol use, participants with well-controlled hypertension were more likely to be never drinkers or current mild drinkers and they had lower HbA1c, fasting plasma glucose, higher eGFR, and fewer comorbidities (eg, lower prevalence of diabetes mellitus, cardiovascular disease, and chronic kidney disease. Those with well-controlled blood pressure had lower remnant cholesterol than those without, though there was no statistically significant difference.

In Table 2, we first tested the association between remnant cholesterol and controlled hypertension with the univariate logistic regression model. When the remnant cholesterol was treated as a continuous or categorical variable, higher remnant cholesterol resulted in lower odds of blood pressure controlled, though there was no statistically significant difference. Because many kinds of factors influence hypertension control, we next synthesized the effects of remnant cholesterol and other variables on hypertension control using the multivariate logistic regression model. When the remnant cholesterol was treated as a continuous variable, the associations between remnant cholesterol and controlled hypertension were statistically significant in all four models after adjusting for several covariates including age, sex, race/ethnicity, education level, poverty income ratio, smoking and drinking status, metabolic equivalent, HbA1c, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (Model 1: OR=0.74, 95% CI: 0.57–0.95; Model 2: OR=0.72, 95% CI: 0.55–0.94; Model 3: OR=0.73, 95% CI: 0.56–0.93; Model 4: OR=0.60, 95% CI: 0.46–0.78). When the remnant cholesterol was treated as a categorical variable based on quartiles, compared with participants in the lowest quartile, those in the highest quartile of remnant cholesterol had lower odds for blood pressure control in all four models (Model 1: OR=0.74, 95% CI: 0.57–0.97; Model 2: OR=0.74, 95% CI: 0.56–0.98; Model 3: OR=0.75, 95% CI: 0.57–0.97; Model 4: OR=0.62, 95% CI: 0.47–0.83; all p for trend < 0.05).

As seen in Figure 2, the dose-response analysis with a restricted cubic spline model shows that the odds of blood pressure control went down with the increasing remnant cholesterol in most of the range (overall $p = 0.0179$; p for nonlinear = 0.453).

The subgroup analyses treating remnant cholesterol as a continuous variable (per unit increase) are shown in Figure 3. The odds of well-controlled hypertension decreased as the remnant cholesterol increased in the male subgroup (OR = 0.7094, 95% CI = 0.5147–0.9777), in the < 50 (OR = 0.6500, 95% CI = 0.4254–0.9933) and > 60 (OR = 0.6447, 95% CI = 0.4241–0.9801) years, in the hyperlipidemia (OR = 0.7463, 95% CI = 0.5600–0.9946) and cardiovascular disease (OR = 0.4987, 95% CI = 0.2863–0.8687) subgroups, and subgroups without chronic kidney disease (OR = 0.6829, 95% CI = 0.4862–0.9591) or diabetes mellitus (OR = 0.7285, 95% CI = 0.5352–0.9915). No significant associations were observed in the remaining subgroups. And no significant interactions were found between remnant cholesterol and any subgroups (all p for interaction >0.05).

Table 1 Characteristics of Participants

Characteristics	All (n=3915)	Uncontrolled Hypertension (n=1265)	Controlled Hypertension (n=2650)	*P* Value
Age (years)	56.98±0.28	60.96±0.45	55.45±0.36	< 0.0001
Sex, n (%)				0.45
Female	2021(51.34)	644(50.20)	1377(51.78)	
Male	1894(48.66)	621(49.80)	1273(48.22)	
Race/ethnicity, n (%)				< 0.0001
Non-Hispanic White	1817(71.33)	500(64.88)	1317(73.80)	
Non-Hispanic Black	952(13.02)	377(18.27)	575(11.00)	
Mexican American	435(5.01)	153(5.80)	282(4.70)	
Other Hispanic	364(4.08)	120(4.85)	244(3.79)	
Other Race - Including Multi-Racial	347(6.56)	115(6.20)	232(6.71)	
Poverty income ratio	2.99±0.05	2.80±0.08	3.06±0.06	0.003
Education, n (%)				< 0.001
Less than high school	995(17.43)	345(18.49)	650(17.03)	
Highschool	964(24.76)	349(29.64)	615(22.89)	
Above high school	1956(57.81)	571(51.87)	1385(60.08)	
BMI (kg/m2)	31.35±0.16	31.33±0.30	31.36±0.17	0.93
Metabolic equivalent (min/w)	3017.14±135.38	2972.63±208.89	3034.18±162.74	0.81
Smoking status, n (%)				0.01
Never	1988(49.49)	674(50.00)	1314(49.30)	
Former	1216(32.12)	390(34.88)	826(31.07)	
Now	711(18.38)	201(15.12)	510(19.63)	
Drinking status, n (%)				0.002
Never	594(11.65)	223(15.19)	371(10.29)	
Former	796(16.72)	269(19.03)	527(15.83)	
Mild	1430(40.32)	461(37.77)	969(41.30)	
Moderate	505(15.63)	141(13.04)	364(16.63)	
Heavy	590(15.68)	171(14.98)	419(15.95)	
SBP (mmHg)	129.42±0.42	151.84±0.54	120.83±0.25	< 0.0001
DBP (mmHg)	71.40±0.31	77.99±0.58	68.88±0.31	< 0.0001
Taking antihypertensive medicine, n (%)				0.03
Yes	3010(74.25)	989(75.62)	2021(73.73)	
No	415(11.01)	154(12.78)	261(10.34)	
Unknown	490(14.74)	122(11.61)	368(15.94)	
HbA1c, %	5.91±0.02	6.02±0.04	5.87±0.03	0.001
FPG (mmol/L)	6.36±0.05	6.59±0.09	6.27±0.05	0.002
TC (mmol/L)	4.95±0.02	5.10±0.04	4.90±0.03	< 0.001
LDL-C (mmol/L)	2.90±0.02	2.98±0.04	2.87±0.02	0.02
TG (mmol/L)	1.47±0.02	1.50±0.03	1.46±0.03	0.26
HDL-C (mmol/L)	1.37±0.01	1.43±0.02	1.35±0.01	0.002
Remnant cholesterol (mmol/L)	0.67±0.01	0.69±0.01	0.67±0.01	0.27
eGFR (mL/min/1.73m2)	85.46±0.50	82.26±0.71	86.69±0.66	< 0.0001
Chronic kidney disease, n (%)	1189(24.89)	507(36.25)	682(20.53)	< 0.0001
Hyperlipidemia, n (%)	3240(82.82)	1061(85.32)	2179(81.86)	0.03
Diabetes mellitus, n (%)	1424(29.86)	521(35.30)	903(27.78)	< 0.001
Cardiovascular disease, n (%)	838(18.60)	285(21.22)	553(17.60)	0.02

Note: Values are presented as weighted means standard error or frequency (weighted percentages) when appropriate.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol.

Table 2 Association Between Remnant Cholesterol and Controlled Hypertension

Remnant Cholesterol	Unadjusted	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Continuous per unit increase	0.88(0.70,1.11)	0.74(0.57,0.95)*	0.72(0.55,0.94)*	0.73(0.56,0.93)*	0.60(0.46,0.78)*
Categorical					
Quartile 1	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Quartile 2	0.92(0.70,1.20)	0.90(0.68,1.19)	0.92(0.69,1.21)	0.92(0.70,1.21)	0.86(0.65,1.15)
Quartile 3	0.98(0.77,1.25)	0.92(0.71,1.19)	0.93(0.71,1.22)	0.93(0.72,1.22)	0.85(0.64,1.13)
Quartile 4	0.86(0.67,1.10)	0.74(0.57,0.97)*	0.74(0.56,0.98)*	0.75(0.57,0.97)*	0.62(0.47,0.83)*
p for trend	0.301	0.034	0.034	0.034	0.001

Notes: *P* < 0.005. Model 1 adjusted for age, sex and race/ethnicity. Model 2 further adjusted for education, poverty income ratio, smoking status, drinking status, and metabolic equivalent. Model 3 further adjusted for HbA1c. Model 4 further adjusted for high-density lipoprotein cholesterol and low-density lipoprotein cholesterol.
Abbreviations: CI, confidence interval; OR, odds ratio.

Discussion

Our study is the first to investigate the association between remnant cholesterol and blood pressure control. In this cross-sectional analysis of 3,915 participants with self-reported hypertension from the NHANES 2007–2008 to 2017–2018 cycles, those with well-controlled blood pressure (systolic blood pressure <140 mmHg and diastolic blood pressure

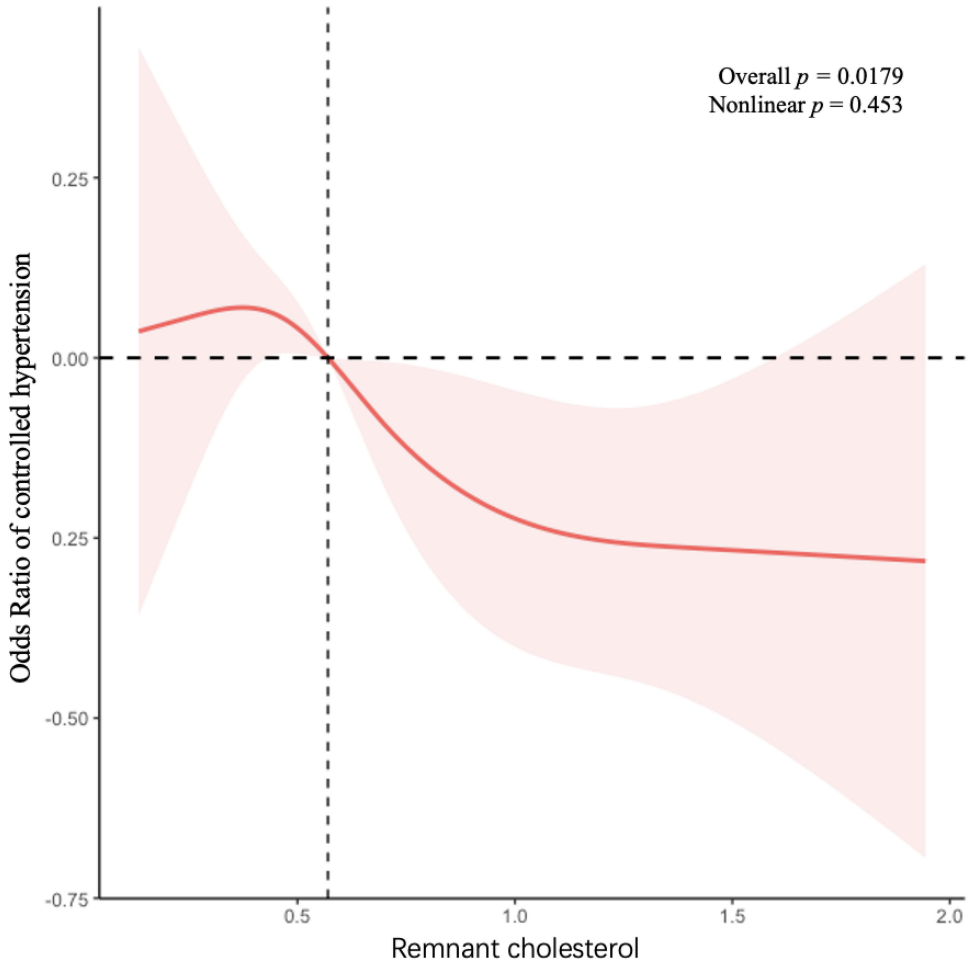

Figure 2 Dose-response relation between remnant cholesterol and blood pressure control.
Abbreviations: OR, odds ratio; CI, Confidence Interval.

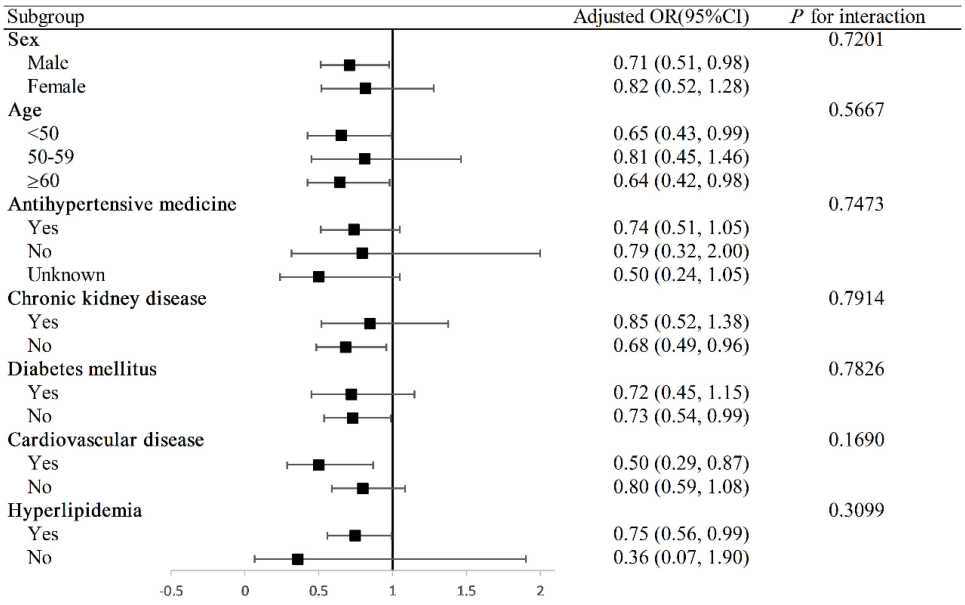

Figure 3 Subgroup analyses of the associations between remnant cholesterol as a continuous variable (per unit increase) and blood pressure control.
Abbreviations: OR, odds ratio; CI, Confidence Interval.

<90 mmHg) had lower remnant cholesterol levels compared to those who did not achieve the recommended control level, although the difference was not statistically significant. This initial observation laid the foundation for our subsequent multivariate analyses, highlighting the potential link between remnant cholesterol and blood pressure management in established hypertension—an unstudied dimension in prior lipid-hypertension research. A prior study has explored the relationship between remnant cholesterol and hypertension, focusing on the development of new-onset hypertension in a smaller, regional cohort, which fills a key gap in understanding the early, causal links between remnant cholesterol and hypertension pathogenesis—providing foundational evidence that remnant cholesterol may contribute to the initiation of high blood pressure, whereas our study builds on this by exploring its role in the management of existing disease.[16] This sequential focus (onset vs control) creates a more comprehensive narrative of how remnant cholesterol impacts hypertension across its clinical trajectory.

In this national representative analysis, we found that elevated remnant cholesterol level was associated with lower odds of well-controlled hypertension independent of multiple risk factors, including low-density lipoprotein cholesterol. Regarding baseline characteristics, the higher prevalence of mild drinkers among participants with controlled hypertension may be explained by the "J-shaped" alcohol-cardiovascular health relationship.[25] In our study, mild alcohol intake (≥1 drink/day for females, ≥2 drinks/day for males) correlates with slightly better vascular regulation—possibly via reduced sympathetic nervous system activity or improved endothelial function—vs abstinence or heavy drinking. Conversely, heavy alcohol use (≥3 drinks/day for females, ≥4 drinks/day for males, or frequent binge drinking) raises blood pressure by increasing sodium retention and activating the renin-angiotensin-aldosterone system, likely accounting for the overrepresentation of heavy drinkers in the uncontrolled hypertension group. The stratified analysis suggested that the direction of the relationship between remnant cholesterol and blood pressure control was consistent with that in the total study population. Besides traditional low-density lipoprotein cholesterol, remnant cholesterol needs more attention.

The univariate logistic regression results aligned with the above baseline characteristics, reflecting the trend: "higher remnant cholesterol correlates with lower odds of blood pressure control." Participants with well-controlled hypertension already exhibited numerically lower remnant cholesterol levels than those with uncontrolled hypertension, along with other favorable profiles (eg, younger age, higher education, lower HbA1c). Race/ethnicity and age disparities in hypertension control persisted and were discussed for a long time. Hypertension control was lower in black than white adults with hypertension.[5,6] Hypertension control was more likely among those aged 45–64 years compared to those aged 18–44 years and 75 years or older. Though neither the baseline difference nor the univariate association reached

statistical significance—likely due to confounding by factors like race/ethnicity and age disparities in hypertension control (eg, lower control rates in Black adults and older populations)—these consistent trends supported the need for further multivariate adjustment to isolate the effect of remnant cholesterol. Next, we explore the association between remnant cholesterol and blood pressure control with multivariate regression models to mitigate confounding effects. After adjusting for basic demographic confounding factors such as age, sex, and race/ethnicity, we found statistically significant odds for higher remnant cholesterol levels with a higher incidence of uncontrolled blood pressure. This relationship remained after adjusting for additional risk factors including education level, poverty income ratio, smoking and drinking status, metabolic equivalent, and HbA1c. Considering low-density lipoprotein cholesterol and high-density lipoprotein cholesterol were associated with blood pressure control as mentioned above, we further adjusted for those two risk factors in model 4. The result showed that remnant cholesterol was associated with blood pressure control beyond low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels. The subgroup analysis revealed generally consistent associations with the main results. No significant associations were observed in some subgroups. For example, the absence of association in subgroups with chronic kidney disease or diabetes mellitus might stem from reduced sample sizes in these subgroups or confounding by advanced comorbidities (eg, impaired renal function, insulin resistance) that modulate the relationship between remnant cholesterol and blood pressure.

Lipid metabolism plays an important role in cardiovascular disease. And dyslipidemia is a promising modifiable target for cardiovascular disease. Controlling cholesterol particle concentrations is fundamental to the management of atherosclerotic cardiovascular disease.[8,26] In recent years, studies suggest that even when low-density lipoprotein and high-density lipoprotein are in the optimal range, lipid metabolism remains a residual risk of cardiovascular disease.[27,28] The potent effect of remnant cholesterol on cardiovascular disease has been gradually recognized.[29,30] In a large-scale Mendelian randomization study including a combined sample of958434participants, Navarese et al showed a robust genetic causal association between remnant cholesterol and cardiovascular outcomes, including coronary artery disease, myocardial infarction, and stroke.[31] They suggested that remnant cholesterol should be considered an independent marker of risk for atherosclerotic cardiovascular disease in addition to low-density lipoprotein. Besides atherosclerotic cardiovascular disease, hypercholesterolemia treatment has a link to hypertension. In a meta-analysis of 40 randomized placebo-controlled studies, patients randomized to statins had a reduction in systolic blood pressure compared to the placebo group. Gupta et al showed that patients with hypertension randomized to atorvastatin had a lower risk of treatment-resistant hypertension than those randomized to placebo.[10,11] More recently, one study showed that remnant cholesterol was associated with hypertension and type 2 diabetes. These positive associations remained even when total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein were at normal levels.[32] Shi et al also identified that remnant cholesterol was associated with hypertension beyond low-density lipoprotein cholesterol in the general US adult population.[16] This association remained beyond increased triglyceride levels.

The potential mechanism explaining the correlation between remnant cholesterol and blood pressure control may be correlated with inflammation. Remnant cholesterol is cholesterol that is carried within the very-low-density lipoprotein, intermediate-density lipoprotein, chylomicrons, and chylomicron remnants.[33] Medium-sized remnant cholesterol can enter into the intima. Moreover, the remnant cholesterol that enters into the intima may get trapped preferentially to low-density lipoprotein cholesterol due to its larger molecular size.[34–36] Remnant cholesterol is also more difficult to return to the arterial lumen. Lipoprotein lipase either at the endothelial surface or within the arterial intima may degrades remnant cholesterol, leading to the liberation of free fatty acid and monoacylglycerols, which are toxic to endothelium and will generate inflammation in the intima.[18,37–39] Impaired endothelial function and inflammation result in dysregulation of blood pressure.

This study has several limitations that should be noted. First, this was a cross-sectional study with a single national representative data, the present finding of the relationship between remnant cholesterol and blood pressure control may preclude a conclusion about causality and the interpretation of the finding to other counties with different demographics may be limited. Second, due to the limitations of the database, those parameters were measured only once and hypertension was self-reported. This may misconduct the finding. Third, remnant cholesterol was estimated as done previously. Labor-intensive and relatively expensive ultracentrifugation and with nuclear magnetic resonance spectroscopy may be more precise to measure remnant cholesterol.

Cutting-edge strategies such as artificial intelligence (AI) may enhance the detection and management of remnant cholesterol for blood pressure control. For example, AI models can integrate multiple biomarkers (including remnant cholesterol) and clinical data to predict blood pressure control outcomes.[40] Besides, targeted therapies aimed at the metabolic modulation of triglyceride-rich lipoproteins (TRLs) hold promising potential for future clinical application.

Conclusion

Remnant cholesterol was independently associated with blood pressure control in a representative national sample of adults in the US. Our findings may provide new insight for the management of blood pressure and support for further prospective studies to clarify the causality of the relationship.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Declarations

The National Center for Health Statistics (NCHS) Ethics Review Board approved the NHANES study, and all participants provided written informed consent. For our study using publicly available NHANES data, the Ethics Committee of Peking Union Medical College Hospital determined that it is exempt from additional ethical approval in accordance with Item 2 of Article 32 of the Measures for *Ethical Review of Life Science and Medical Research Involving Human Subjects* (issued on February 18, 2023, China).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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