

The Association of Remnant Cholesterol with Obstructive Sleep Apnea and Coronary Heart Disease: A Cross-Sectional Study

Tiantian Wen¹, Bo He², Miaomiao Ma³, Liqun Ma²

¹Graduate School, Xinjiang Medical University, Urumqi, Xinjiang, 830000, People's Republic of China; ²Department of Cardiology, General Hospital of Xinjiang Military Command, Urumqi, Xinjiang, 830000, People's Republic of China; ³Cardiovascular Diagnosis and Treatment Center, The First People's Hospital of Yinchuan City, Yinchuan, Ningxia, 750000, People's Republic of China

Correspondence: Liqun Ma, Email mlq218@sina.cn

Background: Obstructive sleep apnea (OSA) is a significant risk factor for coronary heart disease (CHD), yet the precise pathophysiological mechanisms linking them remain incompletely understood. Remnant cholesterol (RC), as an atherogenic lipoprotein, is considered a key driver of residual cardiovascular risk. However, evidence regarding the role of RC in the association between OSA and CHD is still lacking.

Methods: In this single-center, cross-sectional study, we enrolled 368 consecutive patients with suspected coronary heart disease (CHD). All participants underwent overnight polysomnography (PSG) and were categorized into none/mild or moderate/severe obstructive sleep apnea (OSA) groups based on the apnea-hypopnea index (AHI). Coronary artery disease was assessed via angiography or computed tomography angiography (CTA), and its severity was quantified by the number of diseased vessels.

Results: Compared to the none/mild OSA group, patients with moderate/severe OSA had a significantly higher prevalence of CHD (73.0% vs. 15.2%, $p < 0.001$) and a greater proportion of multi-vessel disease ($p < 0.001$). AHI was strongly positively correlated with the number of diseased vessels (overall population $r = 0.612$, $p < 0.001$). Multiple Linear Regression identified AHI as an independent determinant of the number of diseased vessels ($\beta = 0.804$, $p < 0.001$). Logistic regression confirmed that the number of diseased vessels was an independent risk factor for moderate/severe OSA (OR=3.575, $p < 0.001$). While remnant cholesterol was not significantly correlated with AHI in the overall population ($r = -0.051$, $p = 0.327$), it showed weak negative correlations with the number of diseased vessels in males ($r = -0.120$, $p = 0.036$) and in the moderate/severe OSA subgroup ($r = -0.130$, $p = 0.035$), which may be influenced by residual confounding factors.

Conclusion: This study demonstrates a strong and significant independent association between OSA severity and the presence and severity of CHD. Although remnant cholesterol showed no global association with OSA severity, its weak inverse correlation with coronary disease in males and severe OSA patients suggests a potential complex role, warranting further investigation into its mechanisms within specific populations.

Keywords: remnant cholesterol, obstructive sleep apnea, coronary heart disease, severity, cross-sectional studies

Introduction

Obstructive sleep apnea (OSA) is a prevalent disorder characterized by recurrent upper airway collapse during sleep, leading to intermittent hypoxia and sleep fragmentation. Substantial evidence has established OSA as an independent risk factor for coronary heart disease (CHD). A landmark long-term study demonstrated that severe, untreated OSA significantly increases the risk of cardiovascular mortality and non-fatal events.¹ It is widely accepted that OSA promotes the initiation and progression of atherosclerosis through multiple interconnected pathways, primarily driven by intermittent hypoxia, including oxidative stress, systemic inflammation, and sympathetic activation.²

Among modifiable cardiovascular risk factors, dyslipidemia plays a central role. In recent years, remnant cholesterol (RC), the cholesterol content of triglyceride-rich lipoproteins, has gained significant attention for its pathogenic role.



Basic research indicates that RC particles can be directly taken up by macrophages in the arterial intima, promoting their transformation into foam cells, which is a crucial early step in atherosclerotic plaque formation.³ During this process, the degradation of triglycerides within the lipoproteins leads to the release of free fatty acids and monoacylglycerols, further triggering a local inflammatory cascade and accelerating plaque progression.⁴ A large prospective study involving over 73,000 participants from the Copenhagen General Population Study demonstrated that elevated remnant cholesterol levels, calculated from non-fasting lipid profiles, were significantly associated with an increased risk of ischemic heart disease; this association remained independent after multivariable adjustment, and Mendelian randomization analyses further supported a causal link between remnant cholesterol and ischemic heart disease.⁵ Concurrently, another large prospective cohort study based on the same community (the Copenhagen City Heart Study) found that non-fasting triglyceride levels, a major component of RC, were an independent and potent determinant of ischemic stroke risk in the general population.⁶ These clinical evidences, derived from the same high-caliber research platform, collectively confirm from both epidemiological and causal inference perspectives the central pathogenic role of RC and its related lipoproteins in atherosclerotic cardiovascular diseases.

Notably, a close association exists between OSA and an atherogenic lipid profile. The distinctive pathophysiological alterations in OSA—the recurrent pharyngeal collapse leading to cycles of intermittent hypoxia and reoxygenation during sleep—can trigger a cascade of interrelated pathological responses. These include hemodynamic stress due to sympathetic activation, dysregulation of stress hormone metabolism such as cortisol, enhanced oxidative stress, and systemic inflammatory activation.^{7,8} These interconnected changes may interact and amplify each other, collectively disrupting normal lipid metabolism, for instance, by affecting hepatic very-low-density lipoprotein synthesis and secretion and reducing lipoprotein lipase activity, thereby specifically promoting the accumulation of triglyceride-rich lipoproteins and their remnants.⁹ However, existing evidence on the relationship between OSA and dyslipidemia remains inconsistent. While some studies have reported elevated triglyceride levels and decreased high-density lipoprotein cholesterol in OSA patients,¹⁰ others have suggested that the association may be largely confounded by obesity.⁹ The precise mechanisms underlying OSA-associated lipid disturbances are still not fully elucidated.¹⁰ This uncertainty underscores the need for a comprehensive evaluation of remnant cholesterol, a specific atherogenic remnant particle, in relation to both OSA severity and coronary atherosclerosis. Based on this, we propose a key scientific hypothesis: RC may play a significant mediating role in the pathological process leading to coronary artery lesions in OSA.

However, clinical studies that directly and simultaneously investigate the relationships among RC, OSA severity, and the anatomical severity of coronary atherosclerosis remain scarce, and existing findings are inconclusive. Therefore, this cross-sectional study aimed to systematically evaluate the associations of RC with the severity of both OSA and coronary artery lesions in a clinical cohort, intending to provide new epidemiological insights into the pathophysiology of OSA-associated cardiovascular risk.

Materials and Methods

Study Design and Settings

This was a single-center, cross-sectional study. A total of 368 consecutive patients with suspected coronary heart disease, who underwent both coronary angiography (or coronary CTA) and polysomnography between July 2017 and December 2024, were enrolled. Exclusion criteria were: 1) history of coronary artery bypass grafting; 2) severe hepatic or renal dysfunction; 3) active malignancy or autoimmune diseases; 4) recent acute infection or trauma; and 5) incomplete polysomnography data. The study was reviewed and approved by the Medical Ethics Committee of the General Hospital of Xinjiang Military Command (Approval No: 2026RR0101). All procedures were performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Written informed consent was obtained from all individual participants.

The sample size was estimated a priori. The primary aim was to examine the correlation between OSA severity, quantified by the AHI, and the extent of coronary artery disease. Based on the landmark cross-sectional analysis from the Sleep Heart Health Study, which established a strong, graded association between sleep-disordered breathing and prevalent cardiovascular disease,¹¹ we anticipated a statistically significant and clinically relevant association in our

cardiology-enriched cohort. We hypothesized a moderate correlation coefficient (ρ) of approximately 0.30 between AHI and the number of diseased vessels. Using G*Power 3.1 software (Heinrich Heine University Düsseldorf, Germany) for a two-tailed correlation test (Pearson), with an alpha error of 0.05 and a power ($1-\beta$) of 90%, the minimum required sample size was 112 participants. To ensure robust multivariable adjustment for potential confounders (eg., age, sex, BMI, diabetes) and to adequately power planned subgroup analyses (eg., by sex and OSA severity strata), we aimed to enroll at least 300 participants. The final consecutive cohort of 368 patients therefore provided sufficient statistical power for the primary and key secondary analyses. Given the non-normal distribution of key variables, nonparametric Spearman correlation was subsequently used for correlation analyses.

Data Collection

Baseline Characteristics

Baseline information, including age, sex, height, weight, body mass index (BMI), smoking history, alcohol consumption, history of hypertension, and diabetes mellitus, was collected by reviewing electronic medical records.

Serological Parameters

Fasting venous blood samples were drawn from all participants the morning after admission, following an overnight fast of at least 8 hours. All blood samples were collected before polysomnography. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), and uric acid (UA) were measured using an automated biochemical analyzer. RC was calculated as: $RC = TC - HDL-C - LDL-C$.^{5,12}

Assessment of Coronary Artery Lesions

Coronary angiography or CTA results were independently assessed by two experienced cardiologists blinded to the sleep study results. The severity of coronary heart disease was quantified based on the number of diseased vessels, defined as: no disease, single-vessel disease, double-vessel disease, and multi-vessel (three or more) disease.¹³

All images were interpreted independently by two experienced cardiologists who were blinded to the sleep study results. The definition of a diseased vessel was a stenosis of $\geq 50\%$ in any major epicardial coronary artery, and this threshold was applied uniformly for both coronary angiography and CTA. In cases of disagreement, a consensus was reached by discussion.

Assessment of OSA Severity

All participants underwent overnight polysomnography. According to the American Academy of Sleep Medicine guidelines, patients were categorized based on the apnea-hypopnea index (AHI) into two groups: a none/mild OSA group ($AHI < 15$ events/hour) and a moderate/severe OSA group ($AHI \geq 15$ events/hour).¹⁴

Statistical Analysis

Statistical analyses were performed using SPSS software (version 26.0, IBM Corp). The normality of continuous variables was tested using the Shapiro–Wilk test. Normally distributed data were presented as mean $\pm$ standard deviation and compared using the independent samples *t*-test. Non-normally distributed data were presented as median (interquartile range) and compared using the Mann–Whitney *U*-test. Categorical variables were expressed as numbers (percentages) and compared using the Chi-square test.

Associations between variables were assessed using Spearman's rank correlation analysis. To investigate independent associations, the following regression analyses were conducted:¹ Multiple Linear Regression models were constructed with AHI and the number of diseased vessels as dependent variables, respectively. Referring to previous population-based studies on sleep issues,^{15,16} two models were built: Model 1 adjusted for age and sex; Model 2 further adjusted for BMI, hypertension, diabetes, smoking history, and LDL-C level.² Logistic regression analysis was performed with OSA severity (moderate/severe vs. none/mild) as the binary dependent variable. Additionally, subgroup analyses of the Spearman correlation between RC and the number of diseased vessels were conducted in different strata (eg., by sex, diabetes status). A two-sided *P*-value < 0.05 was considered statistically significant.

Ethical Considerations

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol received formal approval from the Medical Ethics Committee of the General Hospital of Xinjiang Military Command (Approval No: 2026RR0101). The ethics approval was obtained prior to the initiation of data analysis for this specific research project. It is important to clarify that the polysomnography and angiography procedures were part of the standard clinical evaluation for patients with suspected coronary heart disease. This study involved a retrospective analysis of de-identified clinical data and prospective collection of additional research variables under the approved protocol. Written informed consent was obtained from all individual participants included in the study, specifically covering the use of their clinical and polysomnographic data for research purposes.

Results

A total of 368 consecutive patients with suspected coronary heart disease were enrolled in this study. Based on AHI, 105 patients (28.5%) were categorized into the none/mild OSA group and 263 (71.5%) into the moderate/severe OSA group.

Descriptive Statistics

As shown in Table 1, compared to the none/mild OSA group, patients with moderate/severe OSA had a higher proportion of males, were older, had greater body weight and BMI, and exhibited a significantly higher prevalence of diabetes and

Table 1 Comparison of Baseline Characteristics Between Patients with None/Mild and Moderate/Severe Obstructive Sleep Apnea [n (%)/M (P25, P75)]

Variable	None/Mild Group (n=105)	Moderate/Severe Group (n=263)	z/ t/ χ^2 value	P value
Sex			12.956	<0.001***
Male	76 (72.4%)	231 (87.8%)		
Female	29 (27.6%)	32 (12.2%)		
Age, years	52.00 (44.00,60.50)	53.00 (47.00,64.00)	-2.151	0.031*
Height, m	1.70 (1.64,1.76)	1.70 (1.67,1.75)	-0.942	0.346
Weight, kg	76.00 (70.00,85.00)	81.00 (73.00,89.00)	-2.739	0.006**
BMI, kg/m²	26.78 (24.81,29.2)	27.72 (25.86,30.10)	-2.557	0.011*
Hypertension			2.284	0.131
No	31 (29.5%)	58 (22.1%)		
Yes	74 (70.5%)	205 (77.9%)		
Diabetes Mellitus			5.512	0.019*
No	85 (81.0%)	181 (68.8%)		
Yes	20 (19.0%)	82 (31.2%)		
Hyperlipidemia			0.671	0.413
No	81 (77.1%)	192 (73.0%)		
Yes	24 (22.9%)	71 (27.0%)		
CHD			101.894	<0.001***
No	89 (84.8%)	71 (27.0%)		
Yes	16 (15.2%)	192 (73.0%)		
Atrial Flutter			—	—
No	105 (100.0%)	263 (100.0%)		
Yes	0 (0.0%)	0 (0.0%)		
Atrial Fibrillation			0.367	0.545
No	103 (98.1%)	255 (97.0%)		
Yes	2 (1.9%)	8 (3.0%)		
COPD			0.197	0.657
No	102 (97.1%)	253 (96.2%)		
Yes	3 (2.9%)	10 (3.8%)		

(Continued)

Table 1 (Continued).

Variable	None/Mild Group (n=105)	Moderate/Severe Group (n=263)	z/ t/ χ^2 value	P value
Asthma				
No	105 (100.0%)	261 (99.2%)	0.803	0.370
Yes	0 (0.0%)	2 (0.8%)		

Note: Description: “*”: $P < 0.05$, “**”: $P < 0.01$, “***”: $P < 0.001$.

Abbreviations: BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease.

coronary heart disease (all $p < 0.05$). No significant differences were found in hypertension, hyperlipidemia, and other baseline characteristics between the two groups.

Regarding serological parameters (Table 2), the moderate/severe OSA group had higher fasting blood glucose but significantly lower levels of HDL-C and LDL-C (all $p < 0.05$). However, no statistical difference was observed in remnant cholesterol levels between the two groups ($p = 0.871$).

Regarding the severity of coronary artery lesions (Table 3), the moderate/severe OSA group had a significantly higher proportion of multi-vessel disease (16.7% vs. 4.8%) and a lower proportion of no disease (28.1% vs. 83.8%), with the difference being highly statistically significant ($p < 0.001$).

Correlation Analysis

Spearman correlation analysis (Table 4) revealed that in the overall population, AHI was strongly positively correlated with the number of diseased vessels ($r = 0.612$, $p < 0.001$), and also positively correlated with BMI and history of diabetes (all $p < 0.01$), but showed no significant correlation with RC ($r = -0.051$, $p = 0.327$). Conversely, the number of diseased vessels was strongly correlated with AHI and positively correlated with age and history of diabetes, but only showed a weak negative correlation with RC ($r = -0.107$, $p = 0.040$, Table 4).

Table 2 Comparison of Serological Parameters Between Patients with None/Mild and Moderate/Severe Obstructive Sleep Apnea [Mean $\pm$ SD/M (P25, P75)]

Variable	None/Mild Group (n=105)	Moderate/Severe Group (n=263)	t/ Z value	P value
TC, mmol/L	4.48 $\pm$ 1.08	4.35 $\pm$ 1.20	0.970	0.333
TG, mmol/L	1.70 (1.23,2.49)	1.75 (1.15,2.60)	-0.458	0.647
FBG, mmol/L	5.06 (4.71,5.80)	5.33 (4.78,6.15)	-2.097	0.036*
HDL-C, mmol/L	0.96 (0.88,1.17)	0.94 (0.82,1.11)	-2.081	0.037*
LDL-C, mmol/L	2.22 (1.80,2.76)	2.11 (1.52,2.59)	-2.033	0.042*
RC, mmol/L	1.12 (0.79,1.54)	1.08 (0.76,1.51)	-0.162	0.871
UA, μmol/L	350.56 $\pm$ 92.35	359.72 $\pm$ 95.81	-0.835	0.404

Note: Description: “*”: $P < 0.05$.

Abbreviations: FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; TC, total cholesterol; TG, triglycerides; UA, uric acid.

Table 3 Comparison of Coronary Heart Disease Severity Between Patients with None/Mild and Moderate/Severe Obstructive Sleep Apnea [n (%)]

Variable		None/Mild Group	Moderate/Severe Group	Z/ χ^2 value	P value
Number of Diseased Vessels	No disease	88 (83.8%)	74 (28.1%)	93.423	<0.001***
	Single-vessel	7 (6.7%)	78 (29.7%)		
	Double-vessel	5 (4.8%)	67 (25.5%)		
	Multi-vessel	5 (4.8%)	44 (16.7%)		

Note: Description: “***”: $P < 0.001$.

Table 4 Spearman Correlation Analysis of Various Indicators with the Number of Diseased Coronary Vessels

Group	None/Mild Group		Moderate/Severe Group		Overall Population	
	r value	P value	r value	P value	r value	P value
Age, years	0.286	0.003**	0.192	0.002**	0.243	< 0.001***
Sex	-0.037	0.710	-0.036	0.558	-0.119	0.022*
Height, m	-0.035	0.726	-0.057	0.359	-0.027	0.600
Weight, kg	0.062	0.530	-0.017	0.786	0.072	0.171
BMI, kg/m ²	0.125	0.204	0.008	0.893	0.094	0.072
TC, mmol/L	-0.018	0.854	-0.181	0.003**	-0.171	0.001**
TG, mmol/L	0.022	0.822	-0.149	0.016*	-0.083	0.114
FBG, mmol/L	0.257	0.008**	0.011	0.865	0.106	0.042*
HDL-C, mmol/L	-0.066	0.501	-0.061	0.327	-0.104	0.047*
LDL-C, mmol/L	-0.019	0.851	-0.165	0.007**	-0.167	0.001**
Hypertension	0.073	0.462	0.008	0.893	0.063	0.228
Hyperlipidemia	-0.114	0.245	-0.117	0.059	-0.086	0.098
Diabetes	0.147	0.135	0.153	0.013*	0.197	< 0.001***
AHI, events/hour	-0.421	< 0.001***	0.538	< 0.001***	0.612	< 0.001***
AI, events/hour	-0.257	0.008*	-0.128	0.037*	0.171	0.001**
HI, events/hour	-0.392	< 0.001***	-0.083	0.179	0.115	0.027*
RC, mmol/L	-0.025	0.798	-0.130	0.035*	-0.107	0.040*
UA, μ mol/L	0.004	0.968	0.012	0.843	0.021	0.684
Atrial Fibrillation	-0.061	0.537	-0.030	0.627	-0.012	0.820
Atrial Flutter	-	-	-	-	-	-
COPD	0.065	0.512	-0.044	0.482	-0.017	0.741
Asthma	-	-	-0.068	0.275	-0.030	0.561
Spo2, %	0.077	0.436	0.058	0.349	-0.084	0.108
ODI, events/hour	-0.298	0.002**	-0.104	0.092	0.136	0.009**

Note: Description: ***: P < 0.05, **: P < 0.01, ***: P < 0.001.

Abbreviations: AHI, apnea-hypopnea index; AI, apnea index; BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HI, hypopnea index; LDL-C, low-density lipoprotein cholesterol; ODI, oxygen desaturation index; RC, remnant cholesterol; Spo2, peripheral oxygen saturation; TC, total cholesterol; TG, triglycerides; UA, uric acid.

Regression Analysis

To control for potential confounders, logistic regression analysis were performed. Multiple Linear Regression (Table 5) showed that after adjusting for age, OSA severity, various sleep parameters, and diabetes, AHI remained a strong

Table 5 Multiple Linear Regression Analysis of Factors Associated with the Number of Diseased Coronary Vessels

Model	Unstandardized Coefficients		Standardized Coefficient	t value	P value
	B	Std. Error			
Constant	-0.289	0.260		-1.111	0.267
Age, years	0.011	0.004	0.117	3.092	0.002**
OSA	-0.669	0.160	-0.193	-4.186	< 0.001***
Severity Group	0.327	0.148	0.137	2.214	0.027*
AHI, events/hour	0.041	0.003	0.804	12.792	< 0.001***
AI, events/hour	-0.024	0.003	-0.341	-7.362	< 0.001***
HI, events/hour	-0.026	0.005	-0.214	-5.007	< 0.001***
Diabetes Mellitus	0.262	0.091	0.109	2.879	0.004**

Note: Description: ***: P < 0.05, **: P < 0.01, ***: P < 0.001.

Abbreviations: AHI, apnea-hypopnea index; AI, apnea index; HI, hypopnea index; OSA, obstructive sleep apnea.

Table 6 Correlation of Remnant Cholesterol and Apnea-Hypopnea Index with the Number of Diseased Coronary Vessels in Different Subgroups

Group	Female		Male		Moderate/Severe OSA	
	r value	P value	r value	P value	r value	P value
AHI, events/hour	0.533	< 0.001***	0.605	< 0.001***	0.697	< 0.001***
RC, mmol/L	−0.012	0.926	−0.120	0.036*	−0.120	0.029*

Note: Description: ***: $P < 0.05$, ****: $P < 0.001$.

Abbreviations: AHI, apnea-hypopnea index; RC, remnant cholesterol.

independent determinant of the number of diseased vessels ($\beta = 0.804$, $p < 0.001$). Furthermore, logistic regression analysis confirmed that the number of diseased vessels was an independent risk factor for moderate/severe OSA (OR = 3.575, 95% CI: 2.506–5.099, $p < 0.001$).

Subgroup Analysis

We explored the relationship between RC and the number of diseased vessels across different subgroups (Table 6). The results indicated that RC had a statistically significant, albeit weak, negative correlation with the number of diseased vessels in males ($r = -0.120$, $p = 0.036$) and in patients with moderate/severe OSA ($r = -0.130$, $p = 0.035$). No significant association was observed in females or in the none/mild OSA group.

Discussion

This cross-sectional study examined the interrelationships among RC, OSA severity, and the extent of CHD. We confirmed a strong and significant independent association between OSA severity and CHD severity. Contrary to our initial hypothesis, RC was not a primary mediator of this link at the population level, although a weak inverse correlation was observed in male patients and those with moderate/severe OSA. While the individual associations linking OSA, CHD, and dyslipidemia are well-established, studies that directly integrate all three components remain scarce. Our study addresses this gap by simultaneously assessing polysomnography-defined OSA severity, angiography-quantified coronary atherosclerosis burden, and RC levels within the same cross-sectional sample.

The strong association between OSA and CHD identified in this study is highly consistent with the existing body of epidemiological and clinical evidence.¹ For instance, a large prospective cohort study based on the Sleep Heart Health Study, which followed 6,441 community-dwelling middle-aged and older adults for an average of 8.7 years, found that the presence of moderate/severe OSA (AHI ≥ 15 events/hour) at baseline was significantly associated with an increased risk of incident coronary heart disease and heart failure after adjusting for multiple potential confounders.¹⁷ This key finding—that OSA is an independent predictor of cardiovascular events—provides robust longitudinal support for our current cross-sectional observation of an association between OSA severity and CHD. Furthermore, a systematic review and meta-analysis by Xie et al, which synthesized data from multiple observational studies involving patients with cardiovascular or cerebrovascular diseases, confirmed that OSA is an independent predictor of major adverse cardiovascular events in patients with acute coronary syndrome.¹⁸ This finding is highly consistent with the conclusion drawn in our study that “OSA severity is an independent determinant of coronary artery lesion severity.” Our multiple regression models further confirmed that AHI remained an independent determinant of coronary lesion severity even after thorough adjustment for traditional cardiovascular risk factors. This strongly suggests that, beyond mechanisms mediated by traditional risk pathways, OSA may directly be associated with the progression of atherosclerosis through its unique pathophysiological mechanisms, such as intermittent hypoxia.²

Regarding remnant cholesterol, our findings differ from some previous studies. In the overall population analysis, we did not find a positive independent association between RC and AHI or the number of coronary lesions. However, several influential prospective studies, such as the work by Varbo et al, have indeed confirmed that RC is an independent and potentially causal risk factor for myocardial infarction.⁵ Furthermore, a community-based cohort study by Joshi et al also indicated that RC is significantly associated with the risk of incident coronary heart disease.¹² However, studies

specifically examining the direct link between RC and OSA are scarce and inconsistent. The lack of a positive independent association between RC and AHI or the number of diseased vessels in our overall analysis may indicate that RC is not a primary factor in the complex network of OSA-related CHD. The mechanism might be that OSA inflicts vascular damage through more immediate pathways like intense sympathetic activation, oxidative stress, and systemic inflammation, whose impacts on RC metabolism might be overshadowed by stronger metabolic compensatory mechanisms or exhibit non-linear relationships.

Nevertheless, the weak inverse correlation between RC and coronary disease observed in the subgroups of males and patients with moderate/severe OSA is a finding worthy of further exploration. Several plausible biological explanations may account for this counterintuitive phenomenon. Firstly, confounding by statin therapy is a primary consideration. Patients at high risk for CHD, such as males with moderate/severe OSA in our cohort, have a higher prevalence of statin use. Statins not only potently lower LDL-C but also moderately reduce triglycerides and consequently RC levels.¹⁹ Therefore, patients with more severe disease might exhibit lower RC levels due to more intensive lipid-lowering therapy, potentially creating a reverse false association. Secondly, systemic inflammation and metabolic consumption might play a role. Severe OSA coupled with extensive coronary disease represents a state of heightened systemic inflammation, characterized by elevated levels of inflammatory markers such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α).²⁰ This chronic inflammatory state might accelerate the turnover and clearance of triglyceride-rich lipoproteins, leading to relatively lower circulating RC levels.²¹ Finally, the hypothesis of residual risk redistribution should be considered. In patients with a very high OSA burden, the effects of more direct pathways of vascular injury, such as intermittent hypoxia, oxidative stress, and inflammation, might be so dominant that they overshadow the independent contribution of traditional lipid risk factors like RC, causing it to appear as a weak or even inverse correlate in statistical analyses.⁷ Furthermore, sex-specific differences in lipid metabolism, such as the influence of estrogen on lipid profiles, may partly explain why the inverse correlation was observed only in male patients, although this hypothesis requires further investigation.

Several limitations should be considered when interpreting our findings. First, the cross-sectional design precludes definitive causal inferences regarding the relationships among RC, OSA, and CHD, particularly for mediation analyses which require temporal precedence. While our regression models adjusted for key confounders, the temporal sequence cannot be established. Second, as a single-center study conducted in a cardiology setting, the generalizability of our findings to the general population or other ethnic groups may be limited. Third, we lacked detailed information on lipid-lowering medications (particularly statins and fibrates), which could significantly influence RC levels. This unmeasured confounding may partly explain the unexpected inverse correlation observed in some subgroups. Furthermore, while the sample size was adequately powered to detect the primary association between OSA and CHD severity, we did not perform a post-hoc power analysis for the mediation analysis. The null finding regarding RC should therefore be interpreted with caution, acknowledging that insufficient power could not be entirely ruled out. Additionally, the study period spanned from 2017 to 2024, during which clinical practices regarding lipid-lowering therapy and imaging modalities may have evolved. However, all patients were consecutively enrolled, minimizing selection bias. Finally, RC was calculated indirectly rather than measured directly via advanced lipoprotein profiling, which might introduce measurement error. Future prospective, multi-center studies with serial measurements of directly quantified RC and detailed medication records are warranted to confirm and extend our observations.

Conclusion

In this cross-sectional study, we identified a strong and significant independent association between OSA severity and the extent of coronary atherosclerosis, reinforcing OSA as a key contributor to coronary heart disease. Contrary to our hypothesis, RC was not a primary mediator in this relationship at the population level. However, a weak inverse correlation between RC and coronary disease severity in males and patients with moderate/severe OSA suggests a complex, context-dependent role for RC in OSA-related atherosclerosis. As one of the first studies to concurrently evaluate OSA severity, angiographic coronary burden, and RC, our findings underscore the importance of OSA management in cardiovascular care and highlight the need for further investigation into the nuanced interplay between dyslipidemia and sleep-disordered breathing in specific at-risk subgroups.

Data Sharing Statement

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

Ethics Statement

The study protocol was approved by the Medical Ethics Committee of the General Hospital of Xinjiang Military Command (Approval No: 2026RR0101). All participants provided written informed consent.

Acknowledgments

The authors thank all participants for their involvement in this study.

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. All authors have read and agreed to the published version of the manuscript.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet*. 2005;365(9464):1046–1053. doi:10.1016/S0140-6736(05)71141-7
2. Drager LF, McEvoy RD, Barbe F, Lorenzi-Filho G, Redline S. Sleep apnea and cardiovascular disease: lessons from recent trials and need for team science. *Circulation*. 2017;136(19):1840–1850. doi:10.1161/CIRCULATIONAHA.117.029400
3. Sniderman A, Couture P, de Graaf J. Diagnosis and treatment of apolipoprotein B dyslipoproteinemias. *Nat Rev Endocrinol*. 2010;6(6):335–346. doi:10.1038/nrendo.2010.50
4. Goldberg IJ, Eckel RH, McPherson R. Triglycerides and heart disease: still a hypothesis? *Arterioscler Thromb Vasc Biol*. 2011;31(8):1716–1725. doi:10.1161/ATVBAHA.111.226100
5. Varbo A, Benn M, Tybjaerg-Hansen A, Jørgensen AB, Frikke-Schmidt R, Nordestgaard BG. Remnant cholesterol as a causal risk factor for ischemic heart disease. *J Am Coll Cardiol*. 2013;61(4):427–436. doi:10.1016/j.jacc.2012.08.1026
6. Freiberg JJ, Tybjaerg-Hansen A, Jensen JS, Nordestgaard BG. Nonfasting triglycerides and risk of ischemic stroke in the general population. *JAMA*. 2008;300(18):2142–2152. doi:10.1001/jama.2008.621
7. Drager LF, Polotsky VY, Lorenzi-Filho G. Obstructive sleep apnea: an emerging risk factor for atherosclerosis. *Chest*. 2011;140(2):534–542. doi:10.1378/chest.10-2223
8. Jun J, Reinke C, Bedja D, et al. Effect of intermittent hypoxia on atherosclerosis in apolipoprotein E-deficient mice. *Atherosclerosis*. 2010;209(2):381–386. doi:10.1016/j.atherosclerosis.2009.10.017
9. Adedayo AM, Olafiran O, Smith D, et al. Obstructive sleep apnea and dyslipidemia: evidence and underlying mechanism. *Sleep Breath*. 2014;18(1):13–18. doi:10.1007/s11325-012-0760-9
10. Meszaros M, Bikov A. Obstructive sleep apnoea and lipid metabolism: the summary of evidence and future perspectives in the pathophysiology of osa-associated dyslipidaemia. *Biomedicine*. 2022;10(11). doi:10.3390/biomedicine10112754
11. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the sleep heart health study. *Am J Respir Crit Care Med*. 2001;163(1):19–25. doi:10.1164/ajrccm.163.1.2001008
12. Joshi PH, Khokhar AA, Massaro JM, et al. Remnant lipoprotein cholesterol and incident coronary heart disease: the Jackson Heart and Framingham offspring cohort studies. *J Am Heart Assoc*. 2016;5(5). doi:10.1161/JAHA.115.002765
13. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. *J Am Coll Cardiol*. 1999;33(6):1756–1824. doi:10.1016/s0735-1097(99)00126-6
14. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(3):479–504. doi:10.5664/jcsm.6506

15. You Y. Accelerometer-measured physical activity and sedentary behaviour are associated with C-reactive protein in US adults who get insufficient sleep: a threshold and isotemporal substitution effect analysis. *J Sports Sci.* **2024**;42(6):527–536. doi:10.1080/02640414.2024.2348906
16. You Y, Ding H, Tang M, et al. Dose-response relationship between leisure-time physical activity and metabolic syndrome in short sleep US adults: evidence from a nationwide investigation. *Appl Physiol Nutr Metab.* **2025**;50:1–10. doi:10.1139/apnm-2024-0347
17. Gottlieb DJ, Yenokyan G, Newman AB, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the sleep heart health study. *Circulation.* **2010**;122(4):352–360. doi:10.1161/CIRCULATIONAHA.109.901801
18. Xie W, Zheng F, Song X. Obstructive sleep apnea and serious adverse outcomes in patients with cardiovascular or cerebrovascular disease: a PRISMA-compliant systematic review and meta-analysis. *Medicine.* **2014**;93(29):e336. doi:10.1097/MD.0000000000000336
19. Mach F, Baigent C, Catapano AL, et al. ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J.* **2019**;41(1):111–188.
20. Arnardottir ES, Mackiewicz M, Gislason T, Teff KL, Pack AI. Molecular signatures of obstructive sleep apnea in adults: a review and perspective. *Sleep.* **2009**;32(4):447–470. doi:10.1093/sleep/32.4.447
21. Feingold KR, Grunfeld C, et al. Effect of Inflammation and Infection on Lipids and Lipoproteins. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, editors. *Endotext*. South Dartmouth (MA): MDText.com, Inc, Copyright © 2000–2025MDText.com, Inc.; **2000**.

Vascular Health and Risk Management

Publish your work in this journal

Vascular Health and Risk Management is an international, peer-reviewed journal of therapeutics and risk management, focusing on concise rapid reporting of clinical studies on the processes involved in the maintenance of vascular health; the monitoring, prevention and treatment of vascular disease and its sequelae; and the involvement of metabolic disorders, particularly diabetes. This journal is indexed on PubMed Central and MedLine. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/vascular-health-and-risk-management-journal>

Dovepress
Taylor & Francis Group