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Serum LDL-C/HDL-C ratio and the risk of carotid plaques: a longitudinal study

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Abstract

Background: Dyslipidemia contributes to an increased risk of carotid atherosclerosis. However, the association between the ratio of low-density lipoprotein cholesterol (LDL-C) to high-density lipoprotein cholesterol (HDL-C) and carotid plaque formation has not been well documented. This study aims to assess the role of LDL-C/HDL-C in the risk of carotid plaque formation in a Chinese population.

Methods: We followed 2,191 participants who attended the annual routine health examination. Cox proportional hazards regression, restricted cubic spline (RCS), and subgroup analysis were applied to evaluate the association between the LDL-C/HDL-C ratio and carotid plaques. The hazard ratio (HR) and 95% confidence interval (CI) were used to estimate the strength of the association.

Results: Among 2,191 participants, 388 had incident carotid plaques detected, with a median follow-up time of 1.05 years. Compared with subjects younger than 45 years, those aged 45 to 59 years (HR: 2.00, 95% CI: 1.55–2.58) and over 60 years (HR: 3.36, 95% CI: 2.47–4.58) had an increased risk of carotid plaque formation. Males (HR: 1.26, 95% CI: 1.01–1.56), diabetes (HR: 1.46, 95% CI: 1.06–2.01) and a high LDL-C/HDL-C ratio (HR: 1.22, 95% CI: 1.07–1.38) were significantly linked with the occurrence of carotid plaques. After adjusting for potential confounding factors, we observed that a high LDL-C/HDL-C ratio promoted carotid plaque events (HR: 1.30, 95% CI: 1.12–1.50). The RCS analysis revealed a significant nonlinear association. The association was stronger among females (P-interaction < 0.05).

Conclusion: A high LDL-C/HDL-C ratio could accelerate the occurrence of carotid plaques. Older men with diabetes and dyslipidemia are the critical target population. Women may be more likely to benefit from lipid-lowering interventions and thus avoid carotid plaque formation.

Keywords: Carotid plaque, Serum lipids, Lipid ratio, Longitudinal study

Introduction

Carotid atherosclerosis is a critical pathophysiological process in the progression of many cardiovascular diseases and is present in the early stage. In the long subclinical stage, the clinical manifestations and symptoms of patients depend on the presence of carotid plaques and their characteristics (stable plaques or vulnerable plaques) [1]. Carotid ultrasound can be used as a noninvasive method to study preclinical carotid atherosclerosis by detecting plaques and their characteristics [2]. Several studies have demonstrated that the formation of carotid plaques could increase the risk of ischemic strokes and other cardiovascular disease events, whose potential

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disease burden places enormous pressure on medical and socioeconomic systems [3–7]. Therefore, it is of great significance to identify risk factors for carotid plaque formation and provide interventions at the early stage for high-risk groups, resulting in decreased cardiovascular accidents.

Carotid plaques are formed by thickening of the arterial intima, blocking of the vascular lumen and tissue ischemia. Abnormal lipid metabolism and the inflammatory response can increase lipid deposition in the inner wall of blood vessels, consequently accelerating carotid plaque formation [8]. Dyslipidemia is generally defined as an increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) and a decline in high-density lipoprotein cholesterol (HDL-C) [9]. The unfavorable lipid profile has been linked to the acceleration of carotid plaque formation and premature subclinical atherosclerosis [10]. The causal relationship between high levels of LDL-C and the progression of carotid atherosclerosis has been verified [11, 12]. Nonetheless, even in patients with well-controlled LDL-C levels, there are quite a few residual risks of atherosclerosis that may be attributed to triglyceride-rich lipoprotein particles [13]. High serum TG concentrations have been independently associated with subclinical carotid atherosclerosis in women [10]. It is generally believed that the possible mechanism of the protective effect of elevated HDL-C on carotid plaque formation and stroke is that HDL can transport cholesterol from the periphery for delivery back to the liver, where it is metabolized or eliminated in bile [14]. Moreover, HDL has anti-inflammatory effects and prevents oxidation, thus protecting endothelial cell functions [15, 16]. However, some researchers have questioned the causality between HDL-C and adverse cardiovascular events based on Mendelian randomization and genome-wide association studies [17, 18]. Considering the levels of LDL-C and HDL-C, the LDL-C/HDL-C ratio can better possess a greater capacity for evaluating the extent of lipid accumulation.

Recent studies have shown that the LDL-C/HDL-C ratio can be used as a new biomarker to predict the risk of several diseases and has prognostic value. Zou et al. [19] concluded, based on a large sample of longitudinal cohorts, that the LDL-C/HDL-C ratio is an independent predictor of nonalcoholic fatty liver disease. A case–control study indicated that the LDL-C/HDL-C ratio was the main risk factor for ischemic strokes [20]. Kuang et al. [21] found that the LDL-C/HDL-C ratio also has some value in prediabetes risk assessment, and the accuracy was better than that of LDL-C and HDL-C. However, their predictive value is often applied only to subgroups of the whole population, such as nonobese people with normal lipids and patients with nonvalvular atrial fibrillation. Employing the LDL-C/HDL-C ratio as a biomarker for predicting carotid plaque occurrence is unclear. Our study aims to evaluate the relationship between the LDL-C/HDL-C ratio and carotid plaque formation in a large, longitudinal cohort of the Chinese population.

Methods

Study subjects

We recruited a group of Chinese adults who underwent a regular physical examination at the Health Management Center of the First Affiliated Hospital of Nanjing Medical University from January 2017 to December 2020. The inclusion criteria of subjects were: (a) individuals aged 18–85; (b) individuals with at least two annual physical examinations; and (c) individuals whose data including serum lipids and carotid ultrasonography could be obtained. Participants were excluded if they: (a) had a previous diagnosis of cancer, stroke, coronary heart disease, or myocardial infarction; (b) had plaques detected at baseline examination; (c) took lipid-lowering drugs, or (d) could not provide necessary demographic and clinical information. Ultimately, we recruited 2191 participants (1279 males and 912 females) and their complete information is in the analyses (Fig. 1).

Atherosclerosis assessment

A high-resolution B-mode ultrasound instrument was employed to identify carotid plaques bilaterally, which were divided into three parts of the carotid artery: the common carotid artery, the bifurcation, and the internal carotid artery [22]. The carotid plaque was described as an area whose thickness was over 1.5 mm as assessed from the media adventitia interface to the lumen-intima interface, or as a local wall whose thickness was at least 1.5 times that of the blood vessel walls surrounding it [2]. The incident carotid plaque was defined as carotid plaque newly detected during the follow-up period. Hyperechoic and isoechoic plaques were defined as stable plaques, and hypoechoic and mixed echoic plaques were defined as vulnerable plaques [22, 23]. All carotid plaque measurements followed a strict quality control procedure during image acquisition.

Assessment of demographic, behavioral, and clinical characteristics

A standard questionnaire was designed to collect demographic characteristics, medical history, and living habits. Body mass index (BMI) was calculated by taking a participant's weight (kg) and dividing it by his or her height squared (m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by clinical staff. After an overnight fast, venous blood samples were

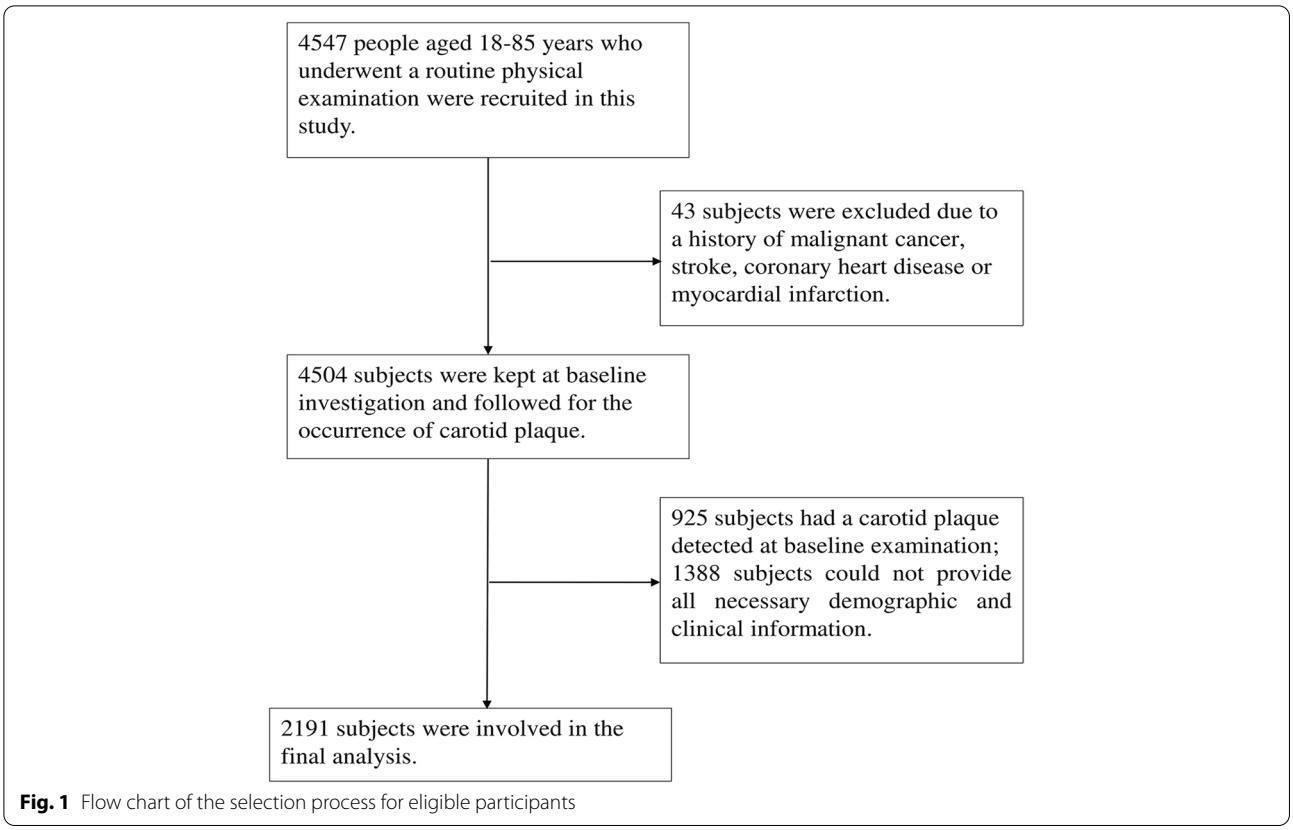

Fig. 1 Flow chart of the selection process for eligible participants

collected to conduct biochemistry tests. TC, TG, HDL-C, and LDL-C levels were calculated by standard enzymatic methods. Meanwhile, the glycated hemoglobin A1c (HbA1c) concentration was determined by ion-exchange high-performance liquid chromatography.

Definitions of variables

Smokers were identified as smoking one or more daily cigarettes for no less than 6 months. A former smoker was described as someone who quit smoking at least one year ago. Hypertension was identified by elevated blood pressure, either an SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg, and self-reported current consumption of antihypertensive drugs for hypertension [24]. Diabetes was defined following the American Diabetes Association 2020 criteria, which includes a fasting plasma glucose level of no less than 7.0 mmol/L or an HbA1c concentration of 6.5% or higher and a self-reported previous diagnosis of dieabetes [25]. Having a BMI over 25 kg/m^2 was considered as overweight, whereas a BMI exceeding 30 kg/m^2 was considered as obesity.

Statistical analysis

Normally distributed continuous variables were expressed as the mean $\pm$ standard deviation, and comparisons among subgroups were analyzed by a *t test* or one-way ANOVA. Categorical variables were analyzed by a chi-squared test. Cox proportional hazard regression was performed to extensively identify the factors related to the incidence of carotid plaques. Stepwise multivariate analysis following the Akaike information criterion was employed to establish a nomogram [26]. The hazard ratio (HR) and 95% confidence interval (CI) were used to estimate the strength of the association. Meanwhile, the roles of HDL-C and LDL-C in the formation of carotid plaques were also assessed. Additionally, we compared the capacity of HDL-C, LDL-C, and the LDL-C/HDL-C ratio to forecast carotid plaque incidence by a receiver operating characteristic curve. Associations between the LDL-C/HDL-C ratio and the risk of carotid plaque formation were evaluated on a continuous scale with restricted cubic spline (RCS) curves. The count of knots was determined by assessing the AIC of the univariate models with 3, 4, and 5 knots. Probable linearity was identified by utilizing a likelihood ratio test comparing the model with only a linear item and the model with linearly added cubic spline items [27, 28]. Furthermore, stratified analyses by sex, age, hypertension, and diabetes were performed to examine the above association. The significance level α was set at 0.05, and a two-tailed test

was utilized. All statistical analyses were completed in R 4.1.2 (https://www.r-project.org/).

Results

Baseline characteristics of participants

We followed 2191 individuals for new carotid plaque occurrence, with a median follow-up duration of 1.05 years and interquartile range (IQR) of 0.96 to 1.99 years. A total of 388 (17.71%) subjects developed carotid plaques during this period, of which 129 were vulnerable plaques. As shown in Table 1, patients with carotid plaques were more likely to be male, older, current smokers, had a higher prevalence of hypertension and diabetes, and had increased BMI, HbA1c, LDL-C, LDL-C/HDL-C ratio, TG and non-HDL-C than patients without carotid plaques (all $P<0.05$).

Risk factors for carotid plaques

Univariate Cox regression analysis showed that male sex, old age, current smoking, hypertension, diabetes, BMI, SBP, DBP, HbA1c, and LDL-C/HDL-C ratio were significantly associated with carotid plaques (all $P<0.05$). Stepwise multivariate Cox regression analysis indicated that subjects whose LDL-C/HDL-C ratio was high were more likely to develop carotid plaques (HR: 1.22, 95% CI: 1.07–1.38). Additionally, males (HR: 1.26, 95% CI: 1.01–1.56) and patients diagnosed with diabetes (HR: 1.46, 95% CI: 1.06–2.01) were more likely to develop carotid plaques. Compared with subjects aged < 45 years, those aged 45 to 59 years (HR: 2.00, 95% CI: 1.55–2.58) and ≥ 60 years (HR: 3.36, 95% CI: 2.47–4.58) had a multifold increased risk of carotid plaque formation (Table 2).

LDL-C/HDL-C ratio and risk of carotid plaques

The relationship of the LDL-C/HDL-C ratio with the occurrence of carotid plaques is summarized in Table 3. No significant change existed in the main tendency of the LDL-C/HDL-C ratio on carotid plaque formation in all adjusted models. The LDL-C/HDL-C ratio increased by 1 mmol/L, and the risk of carotid plaque formation was

Table 1 Baseline characteristics of subjects

Characteristics	Carotid plaque		*P*- value
	No ($n=1803$)	Yes ($n=388$)	
Gender			
Female, n(%)	778(43.15)	134(34.54)	**0.002**
Male, n(%)	1025(56.85)	254(65.46)	
Age (years), median (IQR)	44(38, 51)	51(45, 58)	**< 0.001**
< 45, n(%)	918(50.92)	83(21.39)	**< 0.001**
45–59, n(%)	732(40.60)	221(56.96)	
≥ 60, n(%)	153(8.49)	84(21.65)	
Smoking status			**0.004**
Never, n(%)	1524(84.53)	301(77.58)	
Current, n(%)	246(13.64)	78(20.10)	
Former, n(%)	33(1.83)	9(2.32)	
Hypertension, n(%)	389(21.58)	128(32.99)	**< 0.001**
Diabetes, n(%)	83(4.60)	44(11.34)	**< 0.001**
BMI (kg/m^2), median (IQR)	23.84(21.78, 26.06)	24.35(22.65, 26.45)	**0.001**
≥ 25 kg/m^2, n(%)	658(36.49)	158(40.72)	0.132
SBP (mmHg), median (IQR)	121.00(110.00, 132.00)	124.00(115.00, 135.00)	**< 0.001**
DBP (mmHg), median (IQR)	75.00(68.00, 84.00)	78.00(71.00, 86.00)	**< 0.001**
HbA1c(%)	5.40(5.20, 5.60)	5.50(5.30, 5.80)	**< 0.001**
TC (mmol/L), median (IQR)	5.38(4.81, 6.13)	5.51(4.79, 6.21)	0.302
LDL-C (mmol/L), median (IQR)	3.42(2.97, 3.94)	3.54(3.06, 4.03)	**0.012**
HDL-C (mmol/L), median (IQR)	1.33(1.13, 1.55)	1.26(1.10, 1.45)	**< 0.001**
LDL-C/HDL-C ratio, median (IQR)	2.61(2.05, 3.18)	2.81(2.36, 3.28)	**< 0.001**
TG (mmol/L), median (IQR)	1.33(0.94, 1.94)	1.41(1.01, 2.17)	**0.016**
Non-HDL-C (mmol/L), median (IQR)	4.04(3.47, 4.74)	4.14(3.54, 4.80)	**0.022**

Bold *P*-value indicates significance

Abbreviation: BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HbA1c* glycosylated hemoglobin, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *TG* triglyceride, IQR interquartile range

Table 2 Risk analysis of incident carotid plaque

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P*-value	HR(95%CI)	*P*-value
Gender				
Female	Reference		Reference	
Male	1.33(1.08, 1.64)	**0.008**	1.26(1.01, 1.56)	**0.040**
Age (years)				
< 45	Reference		Reference	
45–59	2.10(1.63, 2.71)	**< 0.001**	2.00(1.55, 2.58)	**< 0.001**
≥ 60	3.39(2.50, 4.59)	**< 0.001**	3.36(2.47, 4.58)	**< 0.001**
History of smoking				
Never	Reference			
Current	1.18(0.92, 1.51)	0.203		
Former	1.36(0.70, 2.63)	0.368		
Hypertension	1.50(1.21, 1.85)	**< 0.001**		
Diabetes	1.97(1.44, 2.70)	**< 0.001**	1.46(1.06, 2.01)	**0.021**
BMI (kg/m^2)	1.05(1.02, 1.08)	**0.003**		
≥ 25 kg/m^2	1.16(0.95, 1.43)	0.140		
SBP (per 20 mmHg increase)	1.25(1.11, 1.41)	**< 0.001**		
DBP (per 20 mmHg increase)	1.18(1.00, 1.40)	0.055		
HbA1c	1.38(1.21, 1.59)	**< 0.001**		
TC	1.03(0.94, 1.13)	0.551		
LDL-C/HDL-C ratio	1.29(1.15, 1.45)	**< 0.001**	1.22(1.07, 1.38)	**0.002**
TG	1.05(0.96, 1.16)	0.259		

Bold *P*-value indicates significance

Abbreviation: BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HbA1c* glycosylated hemoglobin, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *TG* triglyceride, *HR* hazard ratio, *CI* confidence interval

augmented by 30% in the completely adjusted model. Similar analysis steps were applied to explore HDL-C and LDL-C in the subsequent analysis. The results showed that LDL-C were positively correlated with new carotid plaque formation (HR: 1.50, 95% CI: 1.01–2.24), while HDL-C was negatively correlated with carotid plaque incidence (HR: 0.45, 95% CI: 0.28–0.73). In addition, an AUC (areas under the curve) was calculated to compare the capacity of HDL-C, LDL-C, and the LDL-C/HDL-C ratio to estimate the probability of carotid plaque occurrence. The AUCs of different lipoproteins were as follows: LDL-C: 0.541 < HDL-C: 0.568 < LDL-C/HDL-C ratio: 0.580 (Supplemental Table S1). We plotted the RCS to explore the nonlinear correlation between the LDL-C/HDL-C ratio and the hazard ratio of carotid plaque occurrence, as shown in Fig. 2 (*P* for nonlinearity = 0.010 in adjusted Model 3).

Subgroup analysis and interaction test

The results of subgroup analysis by different variables, including sex, age, hypertension, and diabetes, are shown in Table 4. The analysis demonstrated that the elevated LDL-C/HDL-C ratio contributes to carotid plaque occurrence, with HRs ranging from 1.27 to 1.40. However, there was no significant correlation between carotid plaque formation and the LDL-C/HDL-C ratio among males, participants over 60 years, and patients diagnosed with diabetes and hypertension. No interaction was found except in the analyses stratified by sex (*P* for interaction = 0.021).

Supplementary analysis

The AUC of lipid parameters (LDL-C, HDL-C, non-HDL-C, and LDL-C/HDL-C ratio) and the combined model (including LDL-C combined with HDL-C, LDL-C combined with LDL-C/HDL-C ratio, and HDL-C combined with LDL-C/HDL-C ratio) for predicting the presence of carotid plaques are shown in Supplemental Table S1. Baseline characteristics for patients with stable or vulnerable plaques are shown in Supplemental Table S2. The association between non-HDL-C and the risk of carotid plaque formation is shown in Supplemental Table S3. Moreover, stepwise multivariate analysis selected the LDL-C/HDL-C ratio, sex, age, and diabetes for nomogram construction (Supplemental Figure S1). Each variable was assigned a relevant point value for its role in the

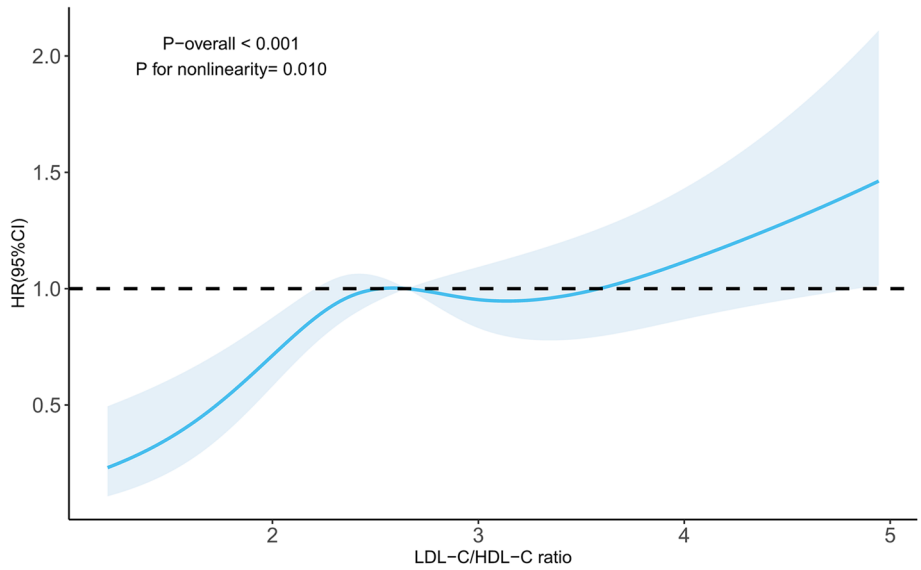

Fig. 2 Association between the LDL-C/HDL-C ratio and the risk of new-onset carotid plaques

Table 3 LDL-C/HDL-C ratio and risk of carotid plaque formation

Variables	Model 1 HR(95% CI)	Model 2 HR(95% CI)	Model 3 HR(95% CI)
LDL-C (mmol/L)	1.10(0.96, 1.26)	1.10(0.96, 1.25)	1.50(1.01, 2.24)
HDL-C (mmol/L)	0.59(0.40, 0.86)	0.62(0.42, 0.92)	0.45(0.28, 0.73)
LDL-C/HDL-C ratio	1.22(1.07, 1.38)	1.21(1.07, 1.38)	1.30(1.12, 1.50)

Model 1 was adjusted for age and sex. Model 2 was further adjusted for smoking status, hypertension, and diabetes based on Model 1. Model 3 was further adjusted for BMI, SBP, DBP, HbA1c, TC, and TG based on Model 2

Abbreviation: BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HbA1c* glycosylated hemoglobin, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *TG* triglyceride, *HR* hazard ratio, *CI* confidence interval

model. Total points can be calculated by the mathematical expression 52 (if age $\geq$ 60) + 9 (if male) + 16 (if diabetic) + 8* LDL-C/HDL-C ratio.

Discussion

This study provided novel insight into the relationship between the LDL-C/HDL-C ratio and carotid plaque formation in Chinese adults. We proved that the LDL-C/HDL-C ratio was positively associated with the risk of carotid plaque formation, and RCS analysis showed a nonlinear relationship between the LDL-C/HDL-C ratio and carotid plaque formation. Subgroup analyses further identified an interaction between sex and the LDL-C/HDL-C ratio in predicting carotid plaque formation.

Vascular endothelial inflammation caused by dyslipidemia is a crucial event in the pathogenesis of atherosclerosis [29]. A prospective cohort study on a low-income Chinese population revealed that high concentrations of LDL-C were positively associated with the risk of carotid plaque formation, especially in women [30]. HDL can prevent atherosclerosis by protecting the vascular endothelium and reversing cholesterol transport function [31]. Yin et al. found that low levels of HDL-C (< 1.04 mmol/L) were significantly associated with unstable carotid plaques in populations with a high risk of stroke [32]. A case–control study involving 187 patients with severe carotid artery stenosis revealed that the LDL-C/HDL-C ratio was an independent risk factor for vulnerable plaque [33]. However, the study of Yang et al. [34], a cross-sectional study with comparatively few subjects, did not demonstrate causality. These findings were consistent with the results of the present study. Although participants with a high LDL-C/HDL-C ratio have normal or even high levels of HDL-C, HDL may lose its antioxidant effects or acquire proinflammatory features and become dysfunctional, thereby inducing atherosclerotic progression [35]. In addition, the LDL-C/HDL-C ratio has been reported to be closely related to HDL particle distribution. An elevated LDL-C/HDL-C ratio can prohibit HDL maturation and the process of reverse cholesterol transport, consequently promoting atherosclerotic progression [36, 37]. Therefore, monitoring the LDL-C/HDL-C ratio is of great significance to identify high-risk groups for carotid plaque formation.

Older age and diabetes mellitus are known risk factors for carotid plaque formation and atherosclerosis [38, 39]. The metabolic disorders that accompany diabetes, such as chronic hyperglycemia, dyslipidemia, and insulin

Table 4 Subgroup analysis

Variables	Model 1 HR(95% CI)	Model 2 HR(95% CI)	Model 3 HR(95% CI)	*P* for interaction
Gender				**0.021**
Female	1.43(1.25, 1.62)	1.42(1.24, 1.62)	1.40(1.21, 1.62)	
Male	1.07(0.90, 1.27)	1.12(0.94, 1.33)	1.13(0.95, 1.36)	
Age (years)				0.928
< 60	1.32(1.16, 1.49)	1.28(1.12, 1.47)	1.28(1.11, 1.47)	
≥ 60	1.26(0.95, 1.68)	1.24(0.92, 1.66)	1.26(0.93, 1.72)	
Hypertension				0.075
No	1.35(1.19, 1.53)	1.32(1.16, 1.52)	1.30(1.13, 1.50)	
Yes	1.01(0.79, 1.29)	1.04(0.81, 1.34)	1.03(0.80, 1.33)	
Diabetes				0.900
No	1.31(1.16, 1.47)	1.28(1.13, 1.46)	1.27(1.11, 1.45)	
Yes	0.86(0.59, 1.26)	0.96(0.65, 1.42)	0.98(0.66, 1.46)	

Model 1, crude model. Model 2 adjusted for sex and age. Model 3 was further adjusted for hypertension, diabetes, and smoking status based on Model 2

P for interaction based on Model 3

Abbreviation:HR hazard ratio, *CI* confidence interval

resistance, lead to impaired function of vascular endothelial cells, smooth muscle cells, and platelets, which predisposes patients to carotid plaques [40–42]. Researchers have reported a higher prevalence and incidence of carotid plaques in men than in women [30]. Possible reasons include the sex-specific nature of genes involved in inflammation and endothelial function [43] and sex differences in carotid bifurcation anatomy [44]. The subgroup analysis in our study also suggested that females were more likely to benefit from such lipid-regulating measures, thereby reducing the risk of carotid plaque occurrence. This is consistent with Lin et al. [30], who showed that controlling LDL-C is essential for alleviating atherosclerosis in women. This may be related to the fact that there are more risk factors for carotid plaque formation in men, and comprehensive intervention in many aspects is needed. Smoking has been proven to be closely associated with the risk of carotid plaque formation, particularly in current smokers [45, 46], but current smoking was not significant in our study, either through univariate analysis or multivariate analysis. This may be because our study did not collect pack-years of smoking (burden) or the number of cigarettes smoked per day (intensity) [46]. Therefore, clinicians should reinforce monitoring of this ratio to avoid carotid plaques, especially in elderly men with diabetes. Among the females, lowering the lipid ratio had an additional benefit in reducing the risk of carotid plaque formation.

A significant strength of this research was that it was conducted with a comparatively large sample size, prospective study design, and took into account the involvement of other potential risk factors. In addition, we conducted a comprehensive analysis of the relationship between the LDL-C/HDL-C ratio and carotid plaque formation and provided more reliable evidence for the prevention of carotid plaques in the general population.

Limitations

Our study inevitably had certain limitations. First, the participants were recruited from one center, and the conclusions should be replicated and verified in other populations. Second, we failed to collect data on exercise habits and dietary intake, which are considered modifiable factors for carotid plaque formation [47, 48]. Finally, medications, especially lipid-lowering drugs, could also affect the development of carotid plaques [49, 50]. However, we excluded subjects with a previous diagnosis of stroke, coronary heart disease, and myocardial infarction and those with carotid plaques at baseline, which are primary indications for lipid-lowering therapy [51]. Excluding those potential drug users at baseline could mitigate the effect to some extent.

Future directions

Risk thresholds for the LDL-C/HDL-C ratio should be established in large cohorts, identifying those at high risk for primary stroke prevention. In addition, the association between the LDL-C/HDL-C ratio and the transition from stable to vulnerable carotid plaques will further enhance clinical practice value.

Conclusion

A high LDL-C/HDL-C ratio could accelerate the occurrence of carotid plaques. Older men with diabetes and dyslipidemia should be the critical intervention population. Women are more likely to benefit from lipid-lowering interventions and thus avoid carotid plaque formation.

Abbreviations

HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; RCS: Restricted cubic spline; HR: Hazard ratio; CI: Confidence interval; TC: Total cholesterol; HbA1c: Glycated hemoglobin A1c; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBG: Fasting blood glucose; TC: Total cholesterol; TG: Triglyceride; AUC: The area under the curve.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-022-02942-w.

Additional file 1: Supplemental Table S1. AUC with the 95% CI of serum lipoproteins and LDL-C/HDL-C ratio for predicting carotid plaques. **Supplemental Table S2.** Baseline characteristics for patients with plaques. **Supplemental Table S3.** Non-HDL-C and risk of carotid plaques. **Supplemental Figure S1.** A nomogram was used to predict the risk of carotid plaques among a Chinese population.

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Not applicable.

Authors' contributions

ZW, XL, QW, QZ, and JW conceived, initiated, and led the study. ZW, XL, QW, BT and BQ collected the data. ZW, XL, and QW analyzed the data with input from all the authors. ZW, XL, and QW prepared the manuscript. QZ and JW revised the manuscript. All authors reviewed and approved the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed according to the convention of the Declaration of Helsinki, 1964. The research protocol was approved by the ethics committee or review committee of the First Affiliated Hospital of Nanjing Medical University, and all subjects signed the informed consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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