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Association between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio and cerebral atherosclerotic stenosis: a retrospective study

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Abstract

Background Ischemic stroke (IS) is one of the leading causes of death and disability worldwide. Early identification of dyslipidemia associated with cerebral atherosclerosis is of great importance for reducing the risk of IS. The non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) is a novel lipid biomarker to assess atherosclerosis. The aim of this study is to investigate the association between NHHR and cerebral atherosclerotic stenosis using DSA imaging data, including intracranial/extracranial stenosis, anterior/posterior circulation stenosis, severe stenosis, and symptomatic stenosis.

Methods Patients who underwent DSA examination from July 2022 to December 2024 were included. Participants were divided into four groups based on NHHR levels. Univariable and multivariable logistic regression were applied to assess the association between NHHR and cerebral atherosclerotic stenosis, including intracranial and extracranial stenosis, anterior and posterior circulation stenosis, severe stenosis, and symptomatic stenosis. Restricted cubic splines (RCS) were applied to analyze and visualize the association between NHHR and cerebral atherosclerotic stenosis.

Results A total of 853 patients were included in the final analysis. After adjusting for covariables, compared to patients in the lower NHHR groups, those in the higher NHHR groups had a significantly higher occurrence rate of extracranial stenosis, posterior circulation stenosis, severe stenosis, and symptomatic stenosis. Multivariable-adjusted RCS showed a nonlinear association between NHHR and posterior circulation stenosis, and a linear positive association between NHHR and symptomatic stenosis.

Conclusions NHHR may serve as a lipid management indicator for patients with extracranial stenosis, posterior circulation stenosis, severe stenosis, or symptomatic stenosis. NHHR could be an independent risk factor for

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symptomatic stenosis, which can aid in risk stratification and treatment decision-making for cerebral atherosclerotic stenosis patients.

Keywords Ischemic stroke, Cerebral atherosclerotic stenosis, Dyslipidemia, Non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio, Digital subtraction angiography

Background

Ischemic stroke (IS) is one of the leading causes of death and disability worldwide, imposing a significant disease burden on patients, families, and society [1]. Large artery atherosclerotic stenosis is one of the primary etiologies of IS [2]. Studies have found that 15-20% of IS or TIA patients have 50% or more extracranial atherosclerotic stenosis and 8–50% of patients have intracranial atherosclerotic stenosis [3]. The pathogenesis of atherosclerosis involves several mechanisms, including vascular endothelial dysfunction, dyslipidemia and inflammation, among which dyslipidemia is considered to play a crucial role in the formation and progression of atherosclerosis. Early identification of dyslipidemia associated with cerebral atherosclerosis is of great importance for reducing the risk of IS.

In clinical practice, the primary monitoring biomarkers for dyslipidemia include cholesterol and triglycerides (TG), with low-density lipoprotein cholesterol (LDL-C) being the most widely used lipid parameter. However, studies have found that single plasma lipid, including LDL-C, have limitations in assessing IS risk. On the one hand, despite aggressive reduction of LDL-C levels, there remains a persistent residual risk [4].On the other hand, unlike its strongly positive association with coronary heart disease (CHD), the relationship between LDL-C and IS was controversial, as low LDL-C levels may be associated with increased risk of cerebral hemorrhage [5] and diabetes [6]. Therefore, there is a need to explore novel lipid parameters for IS to better guide IS risk stratification and dyslipidemia management.

The non-high-density lipoprotein cholesterol (non-HDL-C) to high-density lipoprotein cholesterol (HDL-C) ratio (NHHR) is a novel composite lipid parameter. Non-HDL-C refers to the content of cholesterol other than HDL-C, including LDL-C, intermediate-density lipoprotein cholesterol (IDL-C), very-low-density lipoprotein cholesterol (VLDL-C), and lipoprotein (a). Clinical studies found that in populations with well-controlled LDL-C levels, non-HDL-C was associated with the risk of atherosclerotic cardiovascular disease (ASCVD) and mortality [7]. Guidelines recommend non-HDL-C as a secondary treatment target for dyslipidemia [8]. HDL-C was found to have anti-atherosclerotic properties. Epidemiological studies also showed that HDL-C was negatively correlated with ASCVD risk [9]. NHHR, which combines the atherosclerotic risk factor (non-HDL-C) and the protective factor (HDL-C), was found to has advantages in assessing the risk of diseases such as diabetes mellitus (DM) [10], fatty liver [11], and metabolic syndrome [12]. NHHR has also demonstrated preliminary application value in cerebral atherosclerosis. Studies have found that NHHR is associated with carotid plaque stability [13], and is closely related to the degree of carotid stenosis in patients with acute ischemic stroke (AIS) [14].

Digital Subtraction Angiography (DSA) is the gold standard for cerebrovascular disease diagnosis. It can clearly display changes in vascular lumen diameter, quantitatively assess the degree of stenosis, and exclude other non-atherosclerotic diseases [15]. The aim of this study is to investigate the association between NHHR and cerebral atherosclerotic stenosis using DSA imaging data, including intracranial/extracranial stenosis, anterior/posterior circulation stenosis, severe stenosis, and symptomatic stenosis, and to provide insights for the early diagnosis and risk stratification of cerebral atherosclerotic stenosis.

Methods

Study population

This retrospective study included adult patients who underwent DSA examination at the Department of Neurology, Peking University People's Hospital from July 2022 to December 2024. The exclusion criteria were as follows: (1) presence or suspicion of cardiogenic embolism, such as atrial fibrillation; (2) concurrent other intracranial diseases, such as acute cerebral hemorrhage or subarachnoid hemorrhage, intracranial venous disease, aneurysm, arteriovenous malformation, or intracranial tumor; (3) cerebral artery stenosis caused by non-atherosclerotic diseases, such as moyamoya disease, cerebral artery dissection, or vasculitis; (4) comorbid hematologic diseases such as leukemia, acute infections, or severe liver or kidney dysfunction; (5) incomplete DSA imaging data or incomplete plasma lipid results (TC or HDL-C). This study was approved by the Medical Ethics Committee of the Peking University People's hospital (2024PHB503-001).

Clinical data collection

The following information of enrolled patients was collected: (1) Demographic data: age and gender. (2) Physical examination: body mass index (BMI) and mean arterial pressure (MAP). (3) Medical history: hypertension, DM, hyperlipidemia, CHD, stroke, peripheral artery disease (PAD), and smoking. (4) Medication: lipid-lowering

drugs, including statins and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, antiplatelet drugs, antihypertensive drugs, and antidiabetic agents. (5) Laboratory tests (obtained from the first fasting blood test conducted after admission): white blood cell count (WBC), neutrophil count (NEU), lymphocyte count (LYM), monocyte count (MON), red blood cell count (RBC), hemoglobin (HGB), platelet count (PLT), alanine aminotransferase (ALT), aspartate transaminase (AST), creatinine, uric acid, glucose, and lipid profile, including total cholesterol, TG, HDL-C, and LDL-C. NHHR was calculated using the following formula: NHHR = (TC - HDL-C) / HDL-C.

Imaging data collection and analysis

The DSA data of all patients were evaluated independently by two doctors who had more than 5 years of experiences in DSA image interpretation. Any disagreements between the two observers were resolved through consensus. The definition of intracranial/extracranial arteries were as follows: Intracranial arteries included the C6-C7 segments of the internal carotid artery (ICA), the M1-M2 segments of the middle cerebral artery (MCA), the A1-A2 segments of the anterior cerebral artery (ACA), the P1-P2 segments of the posterior cerebral artery (PCA), the basilar artery (BA), and the V4 segment of the vertebral artery (VA). Extracranial arteries included the subclavian artery (SA), the V1-V3 segments of the VA, the common carotid artery (CCA), and the C1-C5 segments of the ICA [16]. The definition of anterior/posterior circulation arteries were as follows: Anterior circulation arteries included the CCA, ICA, MCA, and ACA. Posterior circulation arteries included the PCA, BA, VA, and SA. The degree of arterial stenosis was assessed according to the Warfarin-Aspirin Symptomatic Intracranial Disease Study [17], and the calculation method was as follows: stenosis rate (%) = (1 - diameter at the narrowest point of the stenosis / diameter of the proximal normal vessel) × 100%. Severe stenosis was defined as a stenosis rate of 70–99% or occlusion. Symptomatic stenosis was defined as the occurrence of transient ischemic attack (TIA) and/or IS within 1 month prior to DSA [18]. The diagnosis of TIA and IS was based on the definitions of the International Classification of Diseases (ICD) (11th edition) [19].

Statistical analysis

Participants were divided into four groups (Q1, Q2, Q3, Q4) based on NHHR quartiles. Baseline characteristics were analyzed according to NHHR quartiles. Continuous variables with normal distribution were expressed as mean ± standard deviation, and comparisons were performed using one-way analysis of variance (ANOVA). Continuous variables with non-normal distribution were expressed as median (interquartile range), and comparisons were performed using the Kruskal-Wallis test or Wilcoxon test. Categorical variables were expressed as percentages, and comparisons were performed using the chi-square test.

NHHR was analyzed as both a continuous variable and a categorical variable (with the first quartile of NHHR as the reference group). Univariable and multivariable logistic regression were applied to assess the association between NHHR and cerebral atherosclerotic stenosis, including intracranial and extracranial stenosis, anterior and posterior circulation stenosis, severe stenosis, and symptomatic stenosis. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. Three models were constructed: Model 1: unadjusted; Model 2: adjusted for age and gender; Model 3: adjusted for age, gender, BMI, MAP, hypertension, DM, smoking history, lipid-lowering drugs, uric acid, and glucose. Confounders were selected based on prior knowledge (risk factors for cerebral stenosis), univariate screening, and variance inflation factor (VIF) testing. The VIF was calculated for each variable, and variables with a VIF ≥ 5 were considered to have multicollinearity and were excluded from the model. Trend tests were performed by treating NHHR quartiles (Q1-Q4) as an ordinal variable (assigned values 1–4) in logistic regression models. P for trend was used to analyze the relationship between NHHR quartiles and cerebral artery stenosis. Restricted cubic splines (RCS) were applied to analyze and visualize the association between NHHR and cerebral atherosclerotic stenosis. Likelihood ratio tests compared models with 3–5 knots, and the optimal knot number was selected based on Akaike Information Criterion (AIC). P-values were two-sided, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using R software (version 4.4.0).

Results

Baseline characteristics

A total of 1,227 patients underwent DSA examination, of whom 853 were included in the final analysis. The recruitment process is shown in Fig. 1. Based on NHHR levels, the enrolled patients were divided into four groups: Q1 (0.4868–2.0090), Q2 (2.0112–2.5432), Q3 (2.5487–3.2222), and Q4 (3.2254–9.3875). The baseline characteristics were displayed by group (Table 1). Among the included patients, the median age was 66 years (59–71 years), and 34.74% were female. The median TC was 3.75 mmol/L (3.19–4.41 mmol/L), and the median HDL-C was 1.04 mmol/L (0.89–1.25 mmol/L). 760 (89.1%) had stenosis, and 93 (10.9%) had no stenosis. Compared with the other groups, patients in the highest NHHR quartile (Q4) had higher BMI and MAP, higher levels of RBC, HGB, uric acid, blood glucose, TC, TG, and LDL-C, lower HDL-C levels, and a higher proportion of smoking history. The NHHR among patients

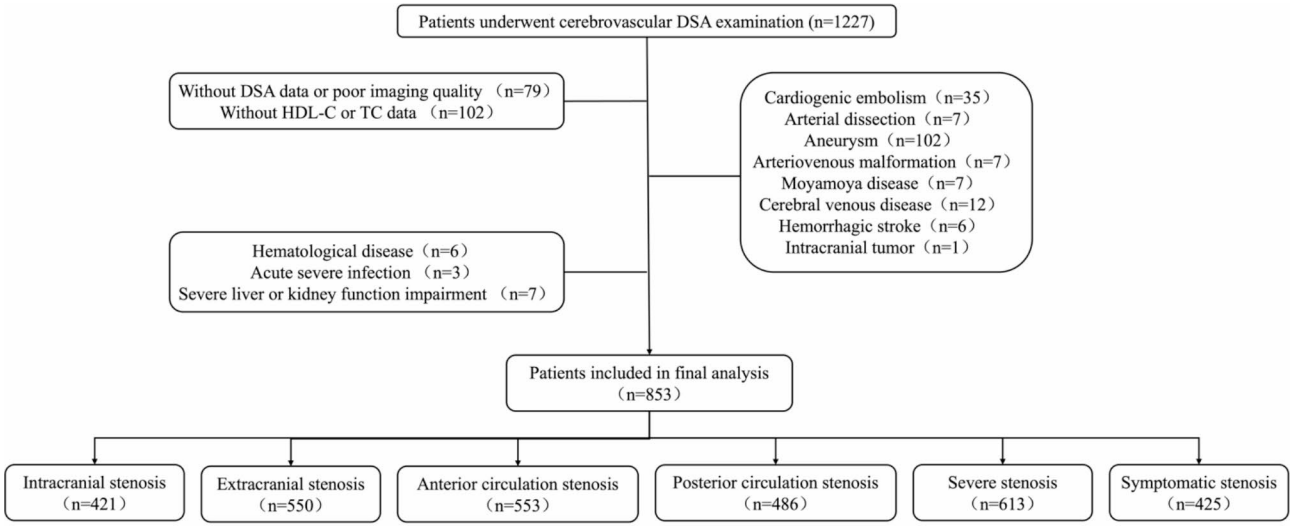

Fig. 1 A flowchart illustrating the participant recruitment process. Abbreviations: DSA, digital subtraction angiography; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol

with different stenosis status was shown by violin plots. NHHR was significantly higher in patients with symptomatic stenosis ($P = 0.0057$) (Fig. 2).

The association of NHHR with intracranial and extracranial stenosis

After adjusting for covariables (age, gender, BMI, MAP, hypertension, DM, smoking, lipid-lowering drugs, uric acid, and glucose), when NHHR was analyzed as a continuous variable, no significant association was observed between NHHR and intracranial stenosis or extracranial stenosis. When NHHR was analyzed as a categorical variable, compared to patients in the lower NHHR group (Q1), those in the higher NHHR groups (Q2 and Q4) had a significantly higher occurrence rate of extracranial stenosis. However, NHHR was not associated with intracranial stenosis (Table 2).

Multivariable-adjusted RCS showed no nonlinear association between NHHR and either intracranial stenosis or extracranial stenosis (Fig. 3).

The association of NHHR with anterior and posterior circulation stenosis

After adjusting for covariables, when NHHR was analyzed as a continuous variable, no significant association was observed between NHHR and anterior or posterior circulation stenosis. When NHHR was analyzed as a categorical variable, compared to patients in the lower NHHR group (Q1), those in the higher NHHR groups (Q2, Q3 and Q4) had a significantly higher occurrence rate of posterior circulation stenosis. However, NHHR was not associated with anterior circulation stenosis (Table 3).

Multivariable-adjusted RCS showed there was a nonlinear association between NHHR and posterior circulation stenosis (P for nonlinear = 0.006) (Fig. 4).

The association of NHHR with severe stenosis

After adjusting for covariables, when NHHR was analyzed as a continuous variable, no significant association was observed between NHHR and severe stenosis. When NHHR was analyzed as a categorical variable, compared to patients in the lower NHHR group, those in the higher NHHR group (2.0112–2.5432) had a significantly higher occurrence rate of severe stenosis (Table 4).

Multivariable-adjusted RCS showed no nonlinear association between NHHR and severe stenosis (Fig. 5).

The association of NHHR with symptomatic stenosis

After adjusting for covariables, when NHHR was analyzed as a continuous variable, NHHR was positively associated with the presence of symptomatic stenosis (OR, 1.31; 95% CI, 1.13–1.53; $P < 0.001$). When NHHR was analyzed as a categorical variable, compared to patients in the lower NHHR group (Q1), those in the higher NHHR group (Q2, Q3 and Q4) had a significantly higher occurrence rate of symptomatic stenosis (Table 5).

Multivariable-adjusted RCS showed a linear association between NHHR and symptomatic stenosis (P for overall = 0.002) (Fig. 6).

Subgroup analyses were further conducted to evaluate the predictive value of NHHR for symptomatic stenosis across different populations. The results revealed that the positive association between NHHR and the incidence of symptomatic stenosis was more pronounced in specific subgroups: males (OR, 1.29; 95% CI, 1.08–1.54; $P = 0.005$), BMI < 28 kg/m² (OR, 1.40; 95% CI, 1.18–1.66;

Table 1 Baseline characteristics of patients categorized by NHHR quartiles

	Overall	Q1	Q2	Q3	Q4	*P*
	(*N* = 853)	(*N* = 213)	(*N* = 213)	(*N* = 213)	(*N* = 214)	
Age	66.00 (59.00, 71.00)	66.00 (60.00,72.00)	66.00 (59.00,72.00)	66.00 (59.00,71.00)	64.00 (58.00,69.00)	0.021*
Gender						0.192
Female	262 (30.72)	74 (34.74)	70 (32.86)	63 (29.58)	55 (25.70)	
Male	591 (69.28)	139 (65.26)	143 (67.14)	150 (70.42)	159 (74.30)	
BMI (kg/m^2)	24.80 (22.77, 27.17)	24.06 (22.03,25.95)	24.45 (22.86,26.71)	25.00 (22.83,27.68)	25.64 (23.69,28.05)	< 0.001*
MAP (mmHg)	98.67 (90.33, 107.00)	97.00 (90.00,106.00)	99.00 (90.67,106.00)	98.67 (90.33,106.33)	101.83 (91.67,110.00)	0.015*
Laboratory tests						
WBC(×10^9/μL)	6.30 (5.30, 7.40)	6.00 (5.20,7.00)	6.50 (5.07,7.60)	6.20 (5.30,7.40)	6.50 (5.50,7.60)	0.024*
NEU(×10^9/μL)	3.80 (3.00, 4.80)	3.70 (2.90,4.40)	3.90 (3.00,4.90)	3.70 (3.08,4.90)	3.99 (3.20,4.88)	0.136
LYM(×10^9/μL)	1.67 (1.30, 2.10)	1.60 (1.30,2.00)	1.60 (1.33,2.00)	1.70 (1.30,2.10)	1.70 (1.40,2.20)	0.020*
MON(×10^9/μL)	0.50 (0.40, 0.60)	0.40 (0.36,0.60)	0.50 (0.40,0.60)	0.50 (0.40,0.60)	0.50 (0.40,0.60)	0.050
RBC(×10^{12}/μL)	4.40 (4.12, 4.73)	4.26 (4.02,4.61)	4.39 (4.12,4.67)	4.45 (4.15,4.77)	4.50 (4.21,4.82)	< 0.001*
HGB(g/L)	138(129.00, 147.00)	134.00 (126.00,145.00)	137.50 (127.75,146.00)	140.00 (130.00,149.00)	141.00 (132.00,150.00)	< 0.001*
PLT(×10^9/μL)	209(175.00, 247.00)	193.00 (167.00,232.00)	209.00 (174.75,247.25)	214.50 (178.50,248.00)	213.00 (180.25,251.00)	0.018*
ALT(U/L)	19.00 (14.00, 28.00)	18.00 (14.00,27.00)	20.00 (15.00,26.00)	20.00 (14.00,30.00)	20.00 (15.00,27.75)	0.294
AST(U/L)	19.00 (16.00, 24.00)	20.00 (17.00,24.00)	19.00 (16.00,23.00)	19.00 (16.00,24.00)	19.00 (16.00,24.00)	0.556
Serum creatine (μmmol/L)	70.00 (60.00, 83.00)	69.00 (61.00,79.00)	69.00 (59.00,84.00)	71.00 (60.00,85.00)	72.00 (61.00,83.75)	0.369
Uric acid (μmmol/L)	332 (278.00, 396.00)	313.00 (268.00,360.00)	332.00 (273.00,388.00)	344.00 (278.00,407.00)	347.00 (282.00,427.00)	< 0.001*
Glucose (mmol/L)	5.45 (4.84, 6.84)	5.29 (4.70,6.40)	5.34 (4.81,6.54)	5.55 (4.83,6.85)	5.77 (4.94,7.61)	0.002*
TC (mmol/L)	3.75 (3.19, 4.41)	3.21 (2.74,3.81)	3.50 (3.09,4.03)	3.76 (3.30,4.29)	4.67 (4.01,5.44)	< 0.001*
TG (mmol/L)	1.30 (0.97, 1.76)	0.91 (0.75,1.19)	1.26 (0.99,1.56)	1.40 (1.09,1.79)	1.83 (1.33,2.50)	< 0.001*
HDL-C (mmol/L)	1.04 (0.89, 1.25)	1.27 (1.06,1.47)	1.06 (0.93,1.24)	0.97 (0.87,1.11)	0.94 (0.82,1.09)	< 0.001*
LDL-C (mmol/L)	2.08 (1.64, 2.63)	1.55 (1.23,1.86)	1.92 (1.63,2.26)	2.16 (1.89,2.58)	2.90 (2.40,3.41)	< 0.001*
Medical history						
Hypertension	611 (71.63)	143 (67.14)	155 (72.77)	160 (75.12)	153 (71.50)	0.317
DM	334 (39.16)	76 (35.68)	76 (35.68)	88 (41.31)	94 (43.93)	0.202
Hyperlipidemia	579 (67.88)	143 (67.14)	158 (74.18)	142 (66.67)	136 (63.55)	0.116
CHD	159 (18.64)	53 (24.88)	43 (20.19)	38 (17.84)	25 (11.68)	0.005*
Stroke	425 (49.82)	93 (43.66)	107 (50.23)	110 (51.64)	115 (53.74)	0.184
PAD	44 (5.16)	8 (3.76)	8 (3.76)	15 (7.04)	13 (6.07)	0.305
Smoking	326 (38.22)	73 (34.27)	74 (34.74)	77 (36.15)	102 (47.66)	0.012*
Medication						
Antihypertensive drugs	558 (65.42)	130 (61.03)	139 (65.26)	146 (68.54)	143 (66.82)	0.404
Antidiabetic drugs	320 (37.51)	72 (33.80)	76 (35.68)	83 (38.97)	89 (41.59)	0.353
Lipid-lowering drugs	787 (92.26)	201 (94.37)	200 (93.90)	196 (92.02)	190 (88.79)	0.124
Statins	759 (88.98)	197 (92.49)	191 (89.67)	189 (88.73)	182 (85.05)	0.104
PCSK9 inhibitor	15 (1.76)	5 (2.35)	3 (1.41)	5 (2.35)	2 (0.93)	0.593
Antiplatelet drugs	766 (89.80)	192 (90.14)	192 (90.14)	191 (89.67)	191 (89.25)	0.988
Stenosis status						
No stenosis	93 (10.90)	25 (11.74)	21 (9.86)	24 (11.27)	23 (10.75)	0.935
Intracranial stenosis	421 (49.36)	107 (50.23)	103 (48.36)	113 (53.05)	98 (45.79)	0.493
Extracranial stenosis	550 (64.48)	128 (60.09)	144 (67.61)	135 (63.38)	143 (66.82)	0.344
Anterior circulation stenosis	553 (64.83)	143 (67.14)	144 (67.61)	129 (60.56)	137 (64.02)	0.395
Posterior circulation stenosis	486 (56.98)	100 (46.95)	133 (62.44)	128 (60.09)	125 (58.41)	0.006*
Severe stenosis	613 (71.86)	144 (67.61)	165 (77.46)	152 (71.36)	152 (71.03)	0.150
Symptomatic stenosis	425 (49.82)	91 (42.72)	109 (51.17)	108 (50.70)	117 (54.67)	0.088

*$P < 0.05$. Abbreviations: BMI, body mass index; MAP, mean arterial pressure; DM, diabetes mellitus; CHD, coronary heart disease; PAD, peripheral arterial disease; WBC, white blood cell count; NEU, neutrophil count; LYM, lymphocyte count; MON, monocyte count; RBC, red blood cell count; HGB, Hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate transaminase; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9

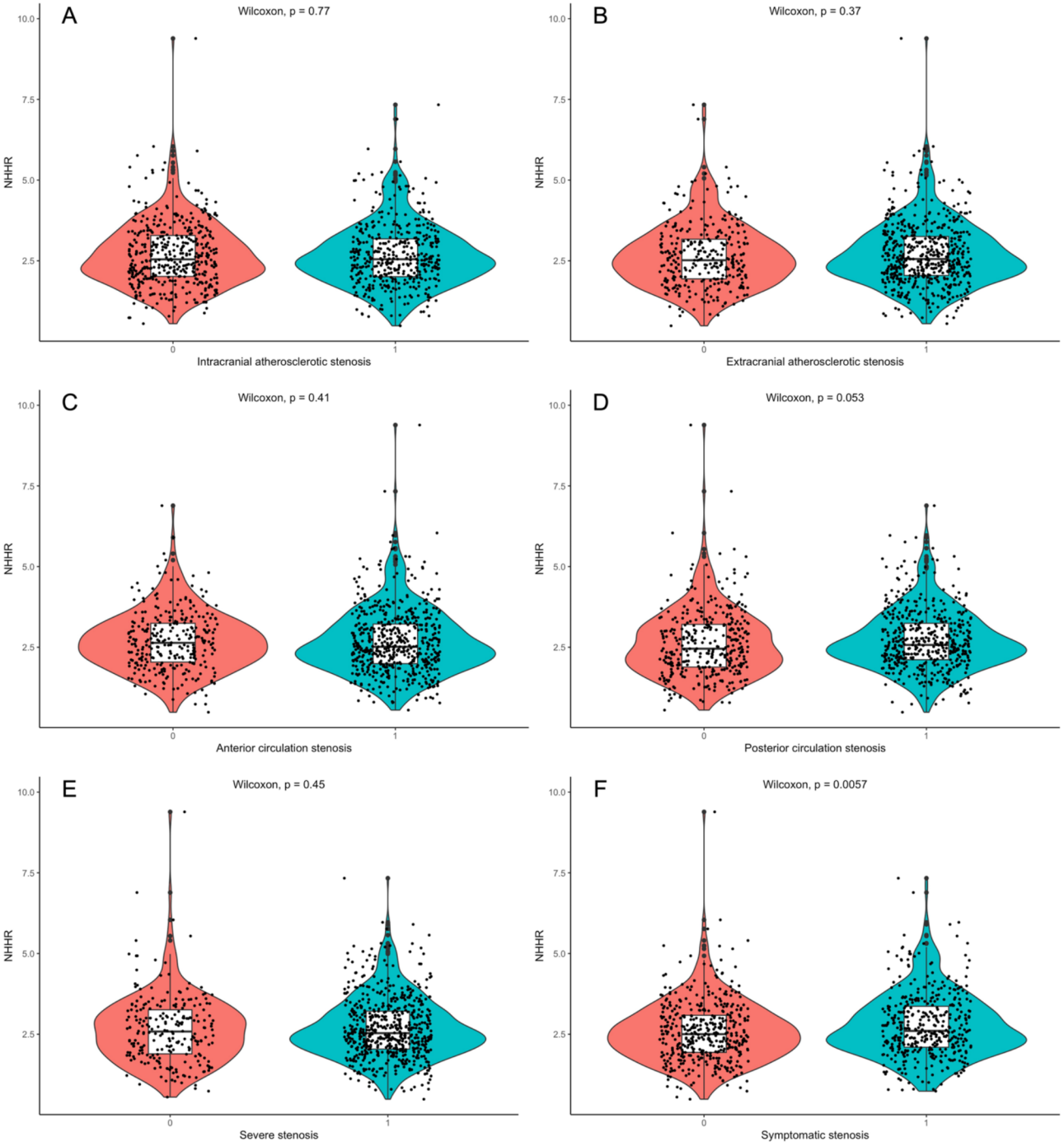

Fig. 2 The violin plots demonstrating the distribution of the NHHR among patients in different groups. **A**. With and without intracranial stenosis; **B**. With and without extracranial stenosis; **C**. With and without anterior circulation stenosis; **D**. With and without posterior circulation stenosis; **E**. With and without severe stenosis; **F**. With and without symptomatic stenosis. Abbreviations: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

$P < 0.001$), individuals with hypertension (OR, 1.36; 95% CI, 1.13–1.64; $P = 0.001$), TC < 5.2 mmol/L (OR, 1.29; 95% CI, 1.08–1.54; $P = 0.006$), TG < 1.7 mmol/L (OR, 1.37; 95% CI, 1.12–1.69; $P = 0.003$), non-HDL-C < 4.1 mmol/L (OR, 1.32; 95% CI, 1.10–1.60; $P = 0.003$), and HDL-C ≥ 1 mmol/L (OR, 1.44; 95% CI, 1.13–1.84; $P = 0.003$). These findings suggest that NHHR may have enhanced predictive utility in these populations. Additionally, significant positive associations between elevated NHHR and symptomatic stenosis incidence were consistently observed across other subgroups stratified by age, diabetes mellitus, smoking, statins use, and LDL-C levels, indicating

Table 2 Association of NHHR with intracranial and extracranial stenosis

	Model 1		Model 2		Model 3	
	OR (95%CI)	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Intracranial stenosis						
NHHR	0.98 (0.86 ~ 1.12)	0.791	0.96 (0.83 ~ 1.10)	0.522	0.90 (0.78 ~ 1.05)	0.182
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	0.93 (0.63 ~ 1.36)	0.698	0.92 (0.63 ~ 1.34)	0.656	0.84 (0.56 ~ 1.25)	0.383
Q3	1.12 (0.77 ~ 1.64)	0.561	1.09 (0.74 ~ 1.60)	0.656	0.96 (0.64 ~ 1.43)	0.844
Q4	0.84 (0.57 ~ 1.22)	0.359	0.79 (0.54 ~ 1.16)	0.226	0.66 (0.44 ~ 1.00)	0.053
P for trend	0.97 (0.86 ~ 1.09)	0.572	0.95 (0.84 ~ 1.07)	0.386	0.90 (0.79 ~ 1.02)	0.106
Extracranial stenosis						
NHHR	1.06 (0.92 ~ 1.22)	0.418	1.12 (0.97 ~ 1.31)	0.132	1.17 (0.99 ~ 1.37)	0.059
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	1.39 (0.93 ~ 2.06)	0.107	1.46 (0.96 ~ 2.22)	0.080	1.54 (1.01 ~ 2.35)	0.048*
Q3	1.15 (0.78 ~ 1.70)	0.485	1.21 (0.80 ~ 1.83)	0.363	1.30 (0.85 ~ 1.99)	0.224
Q4	1.34 (0.90 ~ 1.99)	0.149	1.51 (0.99 ~ 2.30)	0.054	1.69 (1.09 ~ 2.63)	0.019*
P for trend	1.07 (0.95 ~ 1.22)	0.276	1.11 (0.97 ~ 1.27)	0.119	1.15 (1.01 ~ 1.33)	0.048*

*$P < 0.05$. Model 1: unadjusted; Model 2:adjusted for age and gender; Model 3:adjusted for age, gender, body mass index, mean arterial pressure, hypertension, diabetes mellitus, smoking, lipid-lowering drugs, uric acid, glucose. Abbreviations: OR, odds ratio; CI, confidence interval; NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

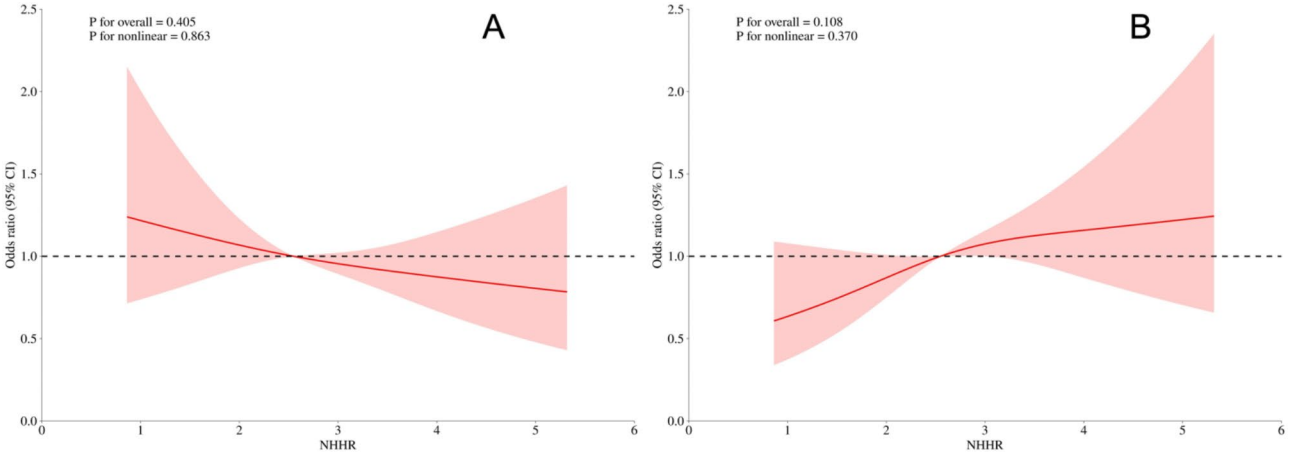

Fig. 3 Restricted cubic spline regression analysis for association of NHHR with intracranial and extracranial stenosis. **A**. Intracranial stenosis; **B**. Extracranial stenosis. Abbreviations: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

robust predictive consistency of NHHR in these populations (Fig. 7).

Discussion

In this study, we included 853 patients who underwent DSA examination to evaluate the relationship between NHHR and cerebral atherosclerotic stenosis, including intracranial/extracranial stenosis, anterior/posterior circulation stenosis, severe stenosis, and symptomatic stenosis. The results indicated that compared to patients in the lower NHHR groups, those in the higher NHHR groups had a significantly higher occurrence rate of extracranial stenosis, posterior circulation stenosis, severe stenosis, and symptomatic stenosis. A nonlinear association was observed between NHHR levels and posterior circulation stenosis, while a linear positive association was found between NHHR levels and symptomatic stenosis.

We found that NHHR was associated with the distribution, severity, and symptomatic status of cerebral atherosclerotic stenosis, further demonstrating the value of NHHR as an assessment indicator for atherosclerotic diseases. NHHR is a novel composite lipid parameter that integrates the non-HDL-C and HDL-C. Research has shown that, in addition to LDL-C, other non-HDL-C components also contribute to atherosclerosis. VLDL and VLDL remnants can enter the arterial wall, damage endothelial cell surfaces, be absorbed by macrophages, generate non-oxidatively modified foam cells, release cytokines, induce inflammation, and promote the

Table 3 Association of NHHR with anterior and posterior circulation stenosis

	Model 1		Model 2		Model 3	
	OR (95%CI)	***P***	**OR (95%CI)**	***P***	**OR (95%CI)**	***P***
Anterior circulation stenosis						
NHHR	0.98 (0.85 ~ 1.13)	0.793	1.00 (0.86 ~ 1.15)	0.956	1.00 (0.86 ~ 1.17)	0.950
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	1.02 (0.68 ~ 1.53)	0.918	1.03 (0.68 ~ 1.54)	0.904	1.04 (0.69 ~ 1.58)	0.849
Q3	0.75 (0.51 ~ 1.12)	0.158	0.76 (0.51 ~ 1.13)	0.170	0.76 (0.50 ~ 1.15)	0.190
Q4	0.87 (0.58 ~ 1.30)	0.498	0.89 (0.60 ~ 1.33)	0.576	0.91 (0.59 ~ 1.39)	0.660
P for trend	0.93 (0.82 ~ 1.06)	0.263	0.94 (0.83 ~ 1.06)	0.318	0.94 (0.82 ~ 1.08)	0.377
Posterior circulation stenosis						
NHHR	1.11 (0.96 ~ 1.27)	0.154	1.16 (1.01 ~ 1.34)	0.046*	1.12 (0.96 ~ 1.30)	0.145
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	1.88 (1.28 ~ 2.76)	0.001*	1.98 (1.33 ~ 2.96)	< 0.001*	1.89 (1.26 ~ 2.83)	0.002*
Q3	1.70 (1.16 ~ 2.50)	0.007*	1.82 (1.22 ~ 2.70)	0.003*	1.69 (1.12 ~ 2.54)	0.012*
Q4	1.59 (1.08 ~ 2.33)	0.018*	1.76 (1.18 ~ 2.62)	0.005*	1.60 (1.06 ~ 2.42)	0.027*
P for trend	1.14 (1.01 ~ 1.29)	0.035*	1.18 (1.04 ~ 1.34)	0.012*	1.14 (1.00 ~ 1.30)	0.051

*$P < 0.05$. Model 1: unadjusted; Model 2:adjusted for age and gender; Model 3:adjusted for age, gender, body mass index, mean arterial pressure, hypertension, diabetes mellitus, smoking, lipid-lowering drugs, uric acid, glucose. Abbreviations: OR, odds ratio; CI, confidence interval; NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

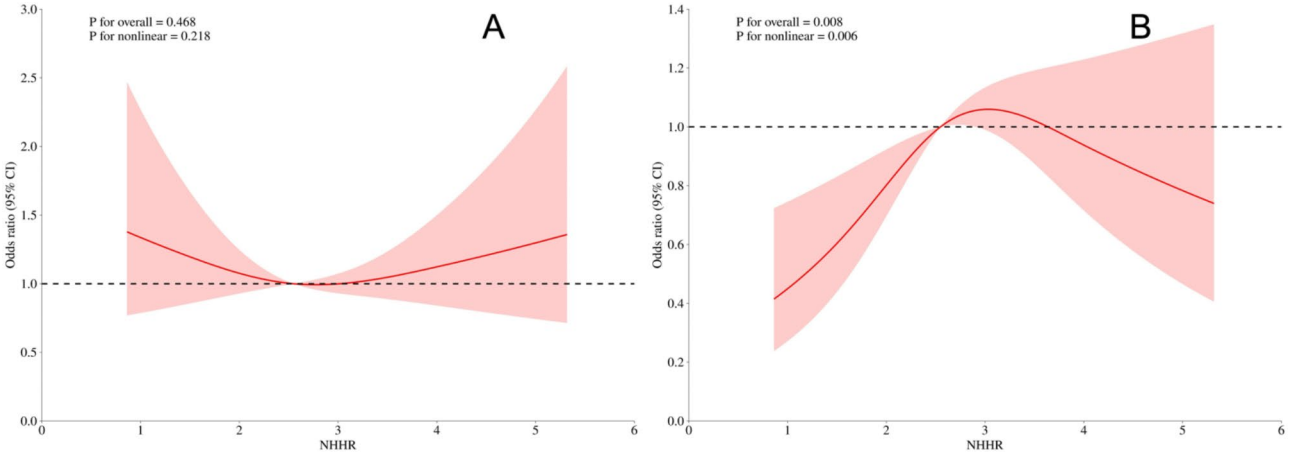

Fig. 4 Restricted cubic spline regression analysis for association of NHHR with anterior and posterior circulation stenosis. **A**. Anterior circulation stenosis; **B**. Posterior circulation stenosis. Abbreviations: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

Table 4 Association of NHHR with severe stenosis

Severe stenosis	**Model 1**		**Model 2**		**Model 3**	
	OR (95%CI)	***P***	**OR (95%CI)**	***P***	**OR (95%CI)**	***P***
NHHR	1.05 (0.90 ~ 1.22)	0.569	1.03 (0.88 ~ 1.21)	0.699	1.02 (0.87 ~ 1.21)	0.798
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	1.65 (1.07 ~ 2.53)	0.023*	1.66 (1.07 ~ 2.58)	0.024*	1.65 (1.05 ~ 2.60)	0.029*
Q3	1.19 (0.79 ~ 1.80)	0.400	1.16 (0.76 ~ 1.77)	0.495	1.14 (0.73 ~ 1.76)	0.567
Q4	1.17 (0.78 ~ 1.77)	0.443	1.12 (0.73 ~ 1.71)	0.607	1.07 (0.68 ~ 1.67)	0.779
P for trend	1.02 (0.89 ~ 1.17)	0.763	1.00 (0.87 ~ 1.15)	0.979	0.99 (0.85 ~ 1.14)	0.851

*$P < 0.05$. Model 1: unadjusted; Model 2:adjusted for age and gender; Model 3:adjusted for age, gender, body mass index, mean arterial pressure, hypertension, diabetes mellitus, smoking, lipid-lowering drugs, uric acid, glucose. Abbreviations: OR, odds ratio; CI, confidence interval; NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

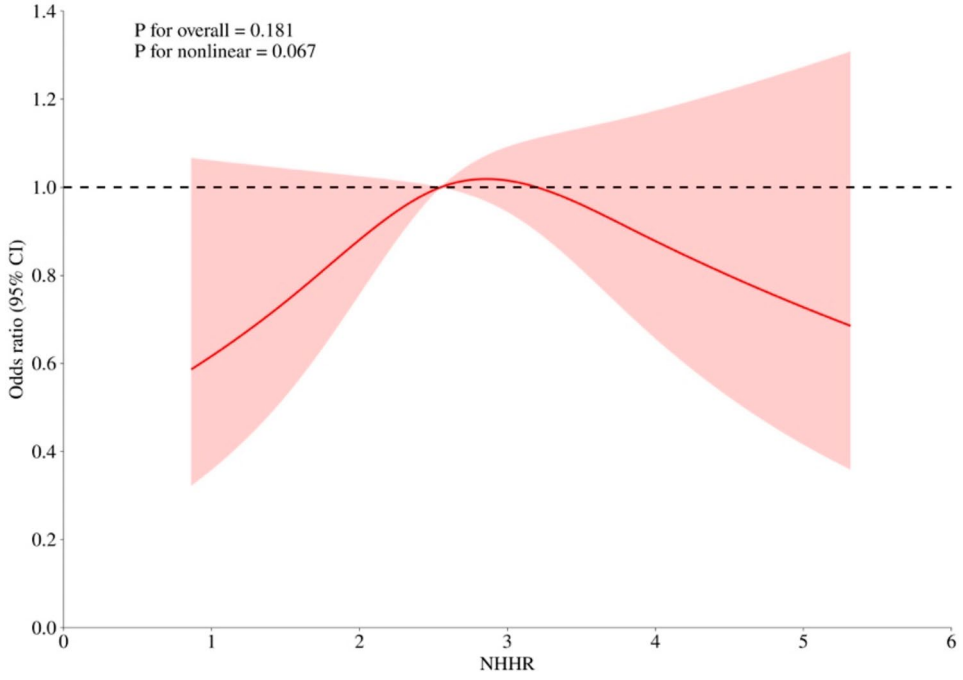

Fig. 5 Restricted cubic spline regression analysis for association of NHHR with severe stenosis. Abbreviations: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

Table 5 Association of NHHR with symptomatic stenosis

Symptomatic stenosis	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
NHHR	1.23 (1.07 ~ 1.41)	0.004*	1.23 (1.07 ~ 1.42)	0.004*	1.31 (1.13 ~ 1.53)	< 0.001*
NHHR quartiles						
Q1	Reference		Reference		Reference	
Q2	1.41 (0.96 ~ 2.06)	0.081	1.41 (0.96 ~ 2.07)	0.081	1.51 (1.02 ~ 2.23)	0.042*
Q3	1.38 (0.94 ~ 2.02)	0.099	1.37 (0.93 ~ 2.02)	0.108	1.54 (1.03 ~ 2.29)	0.035*
Q4	1.62 (1.10 ~ 2.37)	0.014*	1.61 (1.09 ~ 2.37)	0.016*	1.84 (1.22 ~ 2.78)	0.004*
P for trend	1.15 (1.02 ~ 1.30)	0.021*	1.15 (1.02 ~ 1.30)	0.025*	1.20 (1.06 ~ 1.37)	0.005*

*$P < 0.05$. Model 1: unadjusted; Model 2:adjusted for age and gender; Model 3:adjusted for age, gender, body mass index, mean arterial pressure, hypertension, diabetes mellitus, smoking, lipid-lowering drugs, uric acid, glucose. Abbreviations: OR, odds ratio; CI, confidence interval; NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

formation of atherosclerosis [20]. Elevated Lp(a) levels may promote atherosclerosis and thrombosis by interfering with fibrinolysis, binding to macrophages, increasing arterial wall inflammation, and impairing endothelial cell function [21]. In contrast, HDL-C exerts protective effects through mechanisms such as reverse cholesterol transport, reducing LDL oxidation, protecting the endothelium, anti-inflammatory actions, antioxidant stress, and anti-apoptosis [22]. Previous studies found that NHHR showed advantages in metabolic diseases, cardiovascular diseases, and cerebrovascular diseases assessment compared to traditional lipid parameters. Wang Z et al. found that the prevalence of hyperuricemia increased with higher NHHR levels, and NHHR is an independent risk factor for hyperuricemia [23]. A large cohort study revealed a positive association between NHHR and the risk of diabetes, with every 1-unit increase in NHHR associated with an 18% increase in diabetes risk. Compared to HDL-C, TC, TG, LDL-C, and non-HDL-C, NHHR is a better predictor of diabetes risk [24]. Jiayin You et al. analyzed 930 patients with chest discomfort undergoing coronary angiography and found that elevated NHHR levels were associated with an increased risk of coronary heart disease and acute coronary syndrome [25].

This study found that NHHR was positively correlated with extracranial stenosis but showed no significant association with intracranial stenosis, suggesting that dyslipidemia may be more closely related to extracranial stenosis. A study based on population health examination data found that as NHHR levels increased, the prevalence of carotid plaques detected by carotid ultrasound

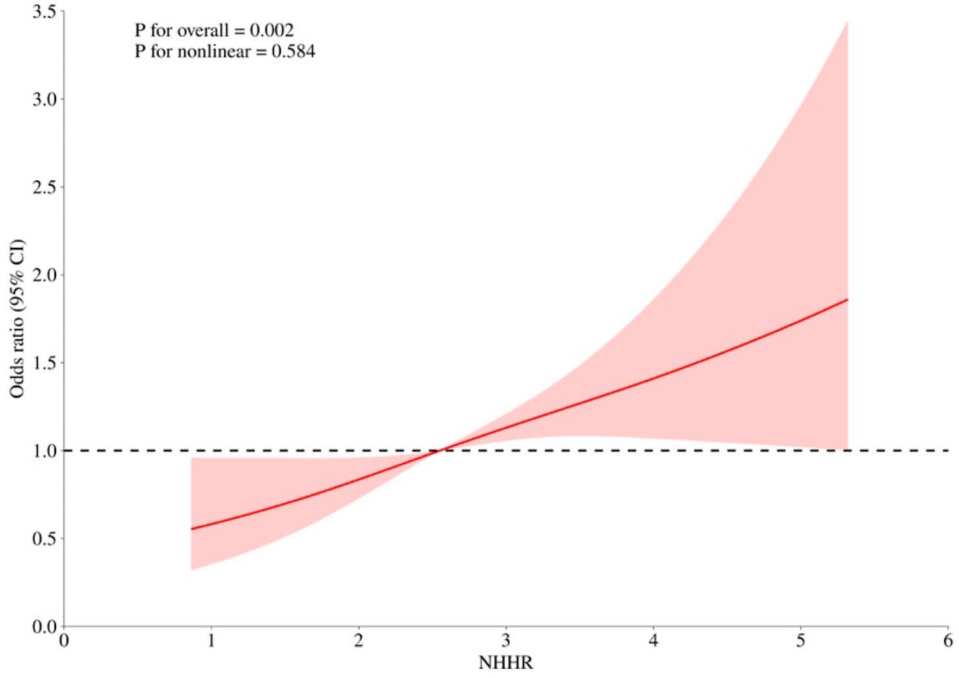

Fig. 6 Restricted cubic spline regression analysis for association of NHHR with symptomatic stenosis. Abbreviations: NHHR, non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio

significantly rose [13]. Epidemiological studies also indicated differences in risk factors between intracranial and extracranial stenosis. A meta-analysis found that dyslipidemia and smoking were more strongly associated with extracranial stenosis [26]. This result can be explained by the following possible mechanisms: Firstly, extracranial arteries generally have a larger diameter than intracranial arteries, with thicker arterial wall rich in elastic fibers, higher distal resistance, and more susceptible to systemic blood pressure fluctuations. These factors may lead to lower wall shear stress and longer blood flow retention, promoting lipid deposition and plaque formation under the vascular endothelium. In contrast, intracranial arteries have thinner walls, lack an external elastic layer, and have lower distal resistance and relatively stable blood flow [26]. Secondly, the adventitia of extracranial arteries contains abundant vasa vasorum, providing pathways for lipid and inflammatory cell infiltration. Oxidized LDL promotes plaque progression by activating inflammatory pathways, while intracranial arteries lack vasa vasorum, limiting lipid deposition [27]. Additionally, animal experiments showed that mildly oxidized LDL impaired vasomotor function in extracranial arteries but has no effect on intracranial arteries, suggesting that intracranial arteries are relatively resistant to dyslipidemia, possibly due to differences in antioxidant content in the arterial walls [28]. Furthermore, In rabbits that received a high-fat diet, markers of vascular endothelial damage, such as α-smooth muscle actin and tropomyosin 1 (TPM1), were significantly increased in extracranial arteries compared to intracranial arteries, while the expression of the anti-inflammatory factor heat shock protein (HSP70) was reduced [29].

We also found that compared to patients in the lower NHHR group, those in the higher NHHR groups had a significantly higher occurrence rate of posterior circulation stenosis, while no significant association was observed between NHHR and anterior circulation stenosis. This suggests that dyslipidemia may be more closely associated with posterior circulation stenosis than with anterior circulation stenosis. Previous studies have reported similar findings. For example, the WASID cohort study found that patients with severe stenosis in the posterior circulation, particularly in the basilar artery, had a higher prevalence of hyperlipidemia compared to those with anterior circulation stenosis [30]. A study containing 610 patients with AIS found that posterior circulation infarction was associated with a higher proportion of dyslipidemia, including elevated TG levels, reduced HDL-C levels, and an increased TG/HDL-C ratio, compared to anterior circulation infarction [31]. Additionally, other studies have shown that patients with posterior circulation stenosis tend to be older, and have a higher prevalence of hyperlipidemia compared to those with anterior circulation stenosis [32]. The closer association between dyslipidemia and posterior circulation stenosis may be attributed to several factors. Firstly, in terms of hemodynamics, the blood flow velocity is slower in the posterior

Subgroups	*P* _value	HR (95% CI)	*P* _for_interaction
Overall	<0.001*	1.31 (1.13 ~ 1.53)	
Gender			0.933
Female	0.144	1.26 (0.93 ~ 1.70)	
Male	0.005*	1.29 (1.08 ~ 1.54)	
Age			0.232
<65	0.003*	1.40 (1.12 ~ 1.76)	
≥65	0.048*	1.24 (1.00 ~ 1.54)	
BMI			0.075
<28kg/m^2	<0.001*	1.40 (1.18 ~ 1.66)	
≥28kg/m^2	0.759	0.94 (0.64 ~ 1.38)	
Hypertension			0.344
0	0.211	1.19 (0.91 ~ 1.56)	
1	0.001*	1.36 (1.13 ~ 1.64)	
Diabetes mellitus			0.768
0	0.030*	1.26 (1.02 ~ 1.55)	
1	0.006*	1.39 (1.10 ~ 1.76)	
Smoking			0.672
0	0.033*	1.26 (1.02 ~ 1.55)	
1	0.022*	1.31 (1.04 ~ 1.64)	
Statins			0.321
0	0.037*	1.67 (1.03 ~ 2.72)	
1	0.005*	1.26 (1.07 ~ 1.49)	
Total cholesterol			0.908
<5.2mmol/L	0.006*	1.29 (1.08 ~ 1.54)	
≥5.2mmol/L	0.394	1.21 (0.78 ~ 1.89)	
Triglyceride			0.177
<1.7mmol/L	0.003*	1.37 (1.12 ~ 1.69)	
≥1.7mmol/L	0.381	1.13 (0.86 ~ 1.47)	
LDL-C			0.511
<2.6mmol/L	0.029*	1.27 (1.02 ~ 1.59)	
≥2.6mmol/L	0.014*	1.52 (1.09 ~ 2.12)	
non-HDL-C			0.827
<4.1mmol/L	0.003*	1.32 (1.10 ~ 1.60)	
≥4.1mmol/L	0.334	1.26 (0.79 ~ 2.02)	
HDL-C			0.185
≥1mmol/L	0.003*	1.44 (1.13 ~ 1.84)	
<1mmol/L	0.093	1.21 (0.97 ~ 1.51)	

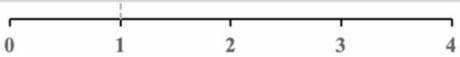

Fig. 7 Forest plot of subgroup analysis on the association between NHHR and symptomatic stenosis. Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol

circulation than in the anterior circulation, which may facilitate lipid deposition [33, 34]. Furthermore, autopsy studies revealed that the internal elastic lamina (IEL) proportion of the arterial area was larger in the posterior circulation compared to the anterior circulation. In the early stages of atherosclerosis, lipid deposition primarily occurs in the IEL, and the higher IEL proportion reflects greater lipid deposition [35]. Additionally, high-resolution magnetic resonance vessel wall imaging studies found that low-signal plaques, indicative of lipid-rich necrotic cores, are more common in posterior circulation atherosclerotic plaques compared to anterior circulation [36]. This study also identified a nonlinear association between NHHR and posterior circulation stenosis. Previous studies had similar findings of nonlinear relationships between NHHR and disease risks. For example, a "J"-shaped association was observed between NHHR and the risk of diabetic nephropathy [37]. And NHHR showed a U-shaped association with all-cause mortality and an L-shaped association with cardiovascular mortality in patients with diabetes and prediabetes [38]. The U-shaped association suggests a potential threshold effect of NHHR on posterior circulation stenosis. The underlying mechanisms may be as follows: As NHHR increases, elevated non-HDL-C levels promote lipid deposition in the subendothelial space through apoB binding to vascular proteoglycans, while reduced HDL-C impairs cholesterol efflux capacity, exacerbating macrophage-mediated lipid uptake. At this stage, the rate of lipid deposition surpasses the protective clearance capacity of HDL-C, leading to continuous plaque progression [208,209]. However, when NHHR rises further, compensatory anti-inflammatory responses may be triggered. Additionally, other metabolic factors (e.g., insulin resistance) could participate in posterior circulation atherosclerosis at higher NHHR levels, thereby masking the isolated impact of lipid ratios.

This study found an association between NHHR and severe stenosis. In patients who have no vascular evaluation, NHHR may potentially indicate underlying severe cerebral artery stenosis. Previous studies found that dyslipidemia was significantly associated with severe cerebral artery stenosis [30]. In AIS patients carotid ultrasound examinations revealed a positive association between NHHR and the degree of carotid plaque stenosis [14]. This may be related to the progression of plaques due to non-HDL-C damaging endothelial cells, promoting lipid deposition, enhancing inflammation, and the reduced protective effects of HDL-C. Identifying factors associated with severe stenosis is important because patients with severe stenosis have a higher rate of recurrent stroke. NHHR may help to identify severe stenosis and promote early lipid management to reduce the risk of IS.

Additionally, this study found that NHHR is positively correlated with symptomatic stenosis, suggesting that NHHR may serve as a potential predictive marker for symptomatic cerebral atherosclerotic stenosis and could aid in screening high-risk populations for IS. Asymptomatic stenosis patients with persistently elevated NHHR may benefit from intensified follow-up or early intervention. Symptomatic stenotic plaques often exhibit more unstable features [39, 40], and the association between NHHR and symptomatic stenosis may be related to its regulatory effects on atherosclerotic plaque stability. Previous studies have also identified elevated NHHR as a potential predictor for unstable carotid plaques [13, 14]. NHHR likely influences plaque stability through dual pathways: on one hand, non-HDL-C is phagocytosed by macrophages to form foam cells, expanding the plaque lipid core; on the other hand, reduced HDL-C weakens its protective functions, including cholesterol efflux, anti-inflammatory, and antioxidant effects, thereby promoting plaque burden and instability. Additionally, Lp(a) may exacerbate thrombotic risk by inhibiting fibrinolysis, ultimately leading to symptomatic ischemic events [8, 21, 22, 41].

Subgroup analyses revealed that NHHR demonstrated stronger predictive value for symptomatic stenosis in males, non-obese individuals, and individuals with hypertension. Monitoring NHHR levels could provide actionable insights for optimizing lipid management strategies in these subgroups. In males, this predictive advantage may relate to sex hormone regulatory mechanisms. Estrogen exerts anti-atherosclerotic effects by improving endothelial function, reducing inflammation and oxidative stress, and modulating apoptosis [42]. The absence of estrogen-mediated vascular protection in males may heighten susceptibility to lipid metabolic imbalances. Furthermore, male atherosclerotic plaques are more prone to unstable morphologies, including larger lipid cores, intraplaque hemorrhage, and heightened inflammation [43], which may accelerate plaque progression and increase IS risk. In non-obese populations, NHHR's predictive superiority may reflect a greater dependence of atherosclerosis progression on lipid metabolic disturbances. Obesity drives insulin resistance and chronic low-grade systemic inflammation [44], alongside endothelial dysfunction and impaired vasomotor regulation. In contrast, non-obese individuals typically exhibit fewer complex metabolic disturbances and preserved vascular function [45], allowing lipid imbalances to dominate atherosclerotic progression with reduced confounding. Obesity also impairs HDL particle functionality, diminishing anti-inflammatory and antioxidant capacities [46], whereas non-obese individuals retain more intact HDL-mediated cholesterol efflux and endothelial protection, enhancing NHHR's ability to reflect lipid metabolic

equilibrium. For hypertensive populations, NHHR's predictive strength may arise from synergistic interactions between hypertension and lipid dysregulation. Hypertension increases endothelial mechanical stress, disrupts endothelial barrier integrity, and promotes subendothelial lipid deposition. Concurrently, it amplifies inflammation and oxidative stress, accelerating LDL oxidation and plaque destabilization [47]. Notably, NHHR remained predictive of symptomatic stenosis even in populations with well-controlled traditional lipid parameters (TC, TG, non-HDL-C, HDL-C). This suggests NHHR may capture residual atherosclerotic risk not reflected by conventional lipid metrics. Combining NHHR with traditional indicators could improve risk stratification for symptomatic cerebral stenosis and identify high-risk individuals for IS.

Previous studies have shown that elevated NHHR is associated with an increased risk of unstable carotid plaques [13], and is a potential predictor of carotid plaque vulnerability in patients with AIS [14], which is consistent with our study. Imaging-based studies revealed that patients with symptomatic stenosis usually showed unstable plaques, and dyslipidemia may influence plaque stability, thereby linking it to symptomatic stenosis. Ruijing Xin et al. used magnetic resonance imaging to compare plaque characteristics between symptomatic and asymptomatic sides of bilateral carotid plaques and found that the symptomatic side had a greater plaque burden, more intraplaque hemorrhage and thrombosis, and a higher incidence of fibrous cap rupture compared to the asymptomatic side [40]. Yue Zhang et al. used ^{18}F-FDG PET/MR to study the morphological and metabolic features of symptomatic and asymptomatic carotid atherosclerotic plaques and found that the symptomatic group had a significantly higher proportion of high-risk features, including plaque burden, luminal stenosis, maximum necrotic core area, and maximum intraplaque hemorrhage area, compared to the asymptomatic group [39]. Dyslipidemia plays a crucial role in the formation and progression of plaques. Oxidized LDL can be engulfed by macrophages to form foam cells, contributing to the lipid core, while HDL-C can reduce lipid deposition and endothelial inflammation through reverse cholesterol transport, anti-inflammatory, and antioxidant effects. Lipid-lowering drugs can enhance plaque stability and reduce the recurrence rate of stroke. Imaging studies such as ultrasound have shown that statins can reduce the lipid content of plaques, decrease plaque burden, and enhance plaque stability [48]. A study of cilostazol treatment for symptomatic intracranial stenosis found that changes in symptomatic intracranial stenosis status were associated with HDL-C levels [49].

The strength of this study was that we explored the relationship between NHHR and cerebral atherosclerotic stenosis, and found that NHHR was more closely related to extracranial stenosis and posterior circulation stenosis. NHHR may be an independent risk factor for symptomatic cerebral arterial stenosis, and NHHR may potentially indicate underlying severe stenosis. However, this study also has some limitations. At first, the retrospective study design cannot establish a causal relationship between NHHR and cerebral artery stenosis. Secondly, a single-center study may be subject to bias. Future multicenter prospective studies are needed to determine the causal relationship between NHHR and cerebral atherosclerotic stenosis and to generalize the findings to the entire population. Additionally, as DSA is an invasive procedure, patients undergoing this examination are often those who have been suspected of having cerebral arterial stenosis through non-invasive tests such as carotid ultrasound and computed tomographic angiography, and usually have more severe stenosis. This selection bias also explains why there are more patients with severe stenosis included in this study. Moreover, DSA cannot assess plaque composition. In the future, combining imaging examinations such as carotid ultrasound and high-resolution magnetic resonance vessel wall imaging could provide more information on atherosclerotic plaque characteristics, and further explore the relationship between NHHR and cerebral atherosclerosis. Furthermore, in the future, other outcomes such as stroke occurrence, recurrence, and all-cause mortality can be analyzed, which could better reveal the relationship between NHHR, cerebral atherosclerotic stenosis, and ischemic stroke.

Conclusions

In this study, we found that NHHR was associated with extracranial stenosis, posterior circulation stenosis, severe stenosis, and symptomatic stenosis, suggesting that NHHR could serve as a lipid management indicator for patients with these conditions. The study showed a linear positive association between NHHR and symptomatic stenosis, indicating that NHHR might be an independent risk factor for symptomatic stenosis, which can aid in risk stratification and treatment decision-making for cerebral atherosclerotic stenosis patients.

Abbreviations

ALT	Alanine Aminotransferase
AST	Aspartate Transaminase
AIS	Acute Ischemic Stroke
BA	Basilar Artery
BMI	Body Mass Index
CCA	Common Carotid Artery
CHD	Coronary Heart Disease
CI	Confidence Interval
DM	Diabetes Mellitus
DSA	Digital Subtraction Angiography
HDL-C	High-Density Lipoprotein Cholesterol
HGB	Hemoglobin

ICA	Internal Carotid Artery
IS	Ischemic Stroke
LDL-C	Low-Density Lipoprotein Cholesterol
LYM	Lymphocyte Count
MAP	Mean Arterial Pressure
MCA	Middle Cerebral Artery
MON	Monocyte Count
NEU	Neutrophil Count
NHHR	Non-High-Density Lipoprotein Cholesterol To High-Density Lipoprotein Cholesterol Ratio
OR	Odds Ratio
PAD	Peripheral Arterial Disease
PCA	Posterior Cerebral Artery
PCSK9	Proprotein Convertase Subtilisin/Kexin Type 9
PLT	Platelet Count
RBC	Red Blood Cell Count
SA	Subclavian Artery
TC	Total Cholesterol
TG	Triglyceride
TIA	Transient Ischemic Attack
WBC	White Blood Cell Count
VA	Vertebral Artery

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Author contributions
Yating Han and Tao Zheng: manuscript writing, analysis, interpretation of results, editing, and revising. Zunjing Liu: research design, interpretation of results, and manuscript writing and editing. Yuting Gao, Mengyuan Qiu, Yida Wang, Shenjie Li, Mengmeng Guo: data sorting, interpretation of results, and editing. Zunjing Liu: senior author. All authors contributed to the manuscript and approved the submitted version.

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Data availability
The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval
This study was approved by the Medical Ethics Committee of the Peking University People's hospital (2024PHB503-001). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Competing interests
The authors declare no competing interests.

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