Relationship between the lymphocyte to C-reactive protein ratio and coronary artery disease severity

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Received May 30, 2023; Accepted November 23, 2023

DOI: 10.3892/etm.2023.12348

Abstract. Coronary atherosclerosis is a chronic systemic inflammatory disease. Laboratory parameters such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune inflammation index (SII) have been used to assess inflammation degree and coronary artery disease (CAD) severity. The lymphocyte-to-C-reactive protein ratio (LCR) is a new SII. However, its relationship with CAD development and severity is unclear. A total of 1,107 patients (479 in control group, 628 in CAD group) underwent coronary angiography. The routine and biochemical indices of the venous blood of patients were assessed before coronary angiography. LCR, SII, NLR and PLR were calculated and statistical analyses were performed. Propensity score matching (PSM) and a logistic regression model were used to analyze the relationship between LCR and CAD. After the PSM, 384 pairs of patients with or without CAD were successfully matched. After the median binary classification of all indicators, uni- and multivariate logistic regression analyses showed that platelet count was an independent risk factor and LCR was an independent protective factor. Using the same method, in the coronary heart disease severity group, 212 pairs were successfully matched and NLR and PLR were independent risk factors, while LCR was an independent protective factor. In conclusion, LCR is an independent protective factor against CAD development and severity.

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Abbreviations: BMI, body mass index; CAD, coronary artery disease; CRP, C-reactive protein; HDL-C, high-density lipoprotein; LCR, lymphocyte-to-C-reactive protein ratio; LDL-C, low-density lipoprotein; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PSM, propensity score matching; SII, systemic immune inflammation index; TC, total cholesterol; WBC, white blood cell

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Key words: CAD, Gensini score, LCR

Introduction

A total of 18,000,000 individuals die from cardiovascular diseases worldwide annually, accounting for 31% of all mortalities for any reason (1). Coronary artery disease (CAD) is caused by a narrowing of the coronary artery lumen due to atherosclerosis of the vessel wall. CAD is the main cause of death from cardiovascular disease, accounting for 45% of total mortality cases (2). Risk factors for CAD include hypertension, diabetes, smoking and hypercholesterolemia (3).

Studies have suggested that vascular inflammation plays an important role in the initiation, progression, plaque instability and eventual rupture of atherosclerosis (4,5). Therefore, various inflammatory biomarkers have attracted attention, including the systemic immune inflammation index (SII; calculated as neutrophils x platelets/lymphocytes), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Other studies have suggested that these inflammatory parameters can indicate CAD occurrence, development and severity (6-8). They can also be used as independent predictors of cardiovascular risk, all-cause mortality and CAD (9,10). Lymphocyte-to-C-reactive protein (CRP) ratio (LCR) is a novel immune system inflammatory indicator. Okugawa *et al* (11) found that LCR can predict the clinical prognosis of colorectal cancer. Zhang *et al* (12) found that LCR is associated with disease severity in patients with coronavirus disease 2019. Liu *et al* (13) found that LCR can predict the clinical prognosis of ST-segment elevation myocardial infarction. However, the association between LCR and CAD occurrence and progression remains unclear. Thus, the present study aimed to investigate the relationship between LCR and CAD.

Materials and methods

Participants. Patients who underwent concurrent coronary angiography at the Department of Cardiology, The 904th Hospital of Joint Logistics Support Force of People's Liberation Army (Wuxi, China) between January 2019 and December 2021 were included in the present study. Inclusion criteria of

this study were as follows: Patients who were hospitalized due to typical symptoms of chest tightness and chest pain, had suspected CAD and underwent improved percutaneous coronary angiography during hospitalization. The study exclusion criteria were as follows: i) Previous myocardial infarction, coronary intervention therapy or coronary artery bypass grafting; ii) acute cerebral infarction occurring within 6 months; iii) other heart diseases, such as congenital heart disease, valvular heart disease or great vascular disease; iv) presence of a malignant tumor, hematological disease or autoimmune disease; and v) complications of acute and chronic infectious diseases. CAD was diagnosed according to the American College of Cardiology/American Heart Association clinical guidelines for CAD: <50% stenosis of any of the following major coronary arteries, including the left main trunk, left anterior descending branch, left circumflex branch, right coronary artery or its major branches with a vessel diameter >1.5 mm (for example, diagonal branch, obtuse margin branch, posterior left ventricular branch and posterior descending branch) (14).

After admission, all patients were treated with 300 mg chewable aspirin and a 180-mg loading dose of ticagrelor. The demographic characteristics of all patients were collected, including hypertension, diabetes, smoking status, height and weight. The cohort consisted of 736 males and 371 females, and the median age was 64 years (range, 26-90 years). Body mass index [BMI; weight (kg)/height (m^2)] was also calculated. The present study was approved by the Ethics Committee of the 904th Hospital of Joint Logistic Support Force of People's Liberation Army, and all patients provided written informed consent (approval no. 2022-05-24).

Laboratory parameters. After admission, each patient fasted for 10-12 h. Venous blood was collected the next morning and subjected to routine blood marker and biochemical tests, including white blood cell (WBC) count and triglyceride, total cholesterol (TC), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), creatinine and CRP levels. LCR was calculated as lymphocyte count (103/μl)/CRP (mg/l). SII (neutrophils x platelets / lymphocytes), NLR and PLR were also calculated.

Angiography. Judkins-style coronary angiography was performed of each patient, and the degree of coronary stenosis was determined by at least two interventional cardiologists based on the angiography results (14). The Gensini score was used to determine coronary stenosis severity (15,16). The Gensini score evaluation criteria included coronary stenosis degree and lesion site scores. i) Coronary stenosis degree score: 1-25%, 1 point; 26-50%, 2 points; 51-75%, 4 points; 76-90%, 8 points; 91-99%, 16 points; and 100%, 32 points. ii) Lesion site score: Left trunk, 5 points; proximal left anterior descending branch, 2.5 points; middle left anterior descending branch, 1.5 points; aorta and first diagonal branch, 1 point; second diagonal branch, 0.5 point; distal left anterior descending branch, 1 point; proximal left circumflex branch, 2.5 points; middle left circumflex branch, 2.5 points; distal left circumflex branch, 1 point; blunt edge branch, 0.5 point; proximal segment of the right coronary artery, 1 point; middle segment of the right coronary artery, 1 point; distal segment of the right coronary artery, 1 point; distal segment of right coronary artery, 1 point; posterior descending branch, 1 point; and posterior branch of left ventricle, 0.5 point. The Gensini score is the sum of the coronary stenosis degree and lesion site scores as follows: 0 points, normal; 1-30 points, mild CAD; and ≥30 points, severe CAD.

Statistical analyses. Three ofmore experimental repeats were performed. The counting data are expressed as number of cases and percentage, while the non-normally distributed measurement data are expressed as median (interquartile range). The χ^2 test was used to examine counting data, while the non-parametric test (Mann-Whitney U test) was used to examine non-normally distributed measurement data. The Kolmogorov-Smirnov test was used to detect whether the data were normally distributed.

The propensity score matching (PSM) method was used to balance the clinical baseline data of the two groups, and the patients were included in the regression model variables by the logistic regression method, including sex, age, hypertension, diabetes, age, BMI and LDL-C and the 1:1 nearest neighbor matching method (caliper value=0.02) was adopted to facilitate matching accuracy. If the control group contained multiple observation objects that met the matching criteria, one participant was randomly selected. Pearson and Spearman correlation coefficients were used for the correlation analysis. The data were dichotomized according to the median and included in the univariate logistic regression analysis. The relevant influencing factors were screened according to the standard of P<0.1 and included in the multivariate logistic regression analysis to determine the independent risk factors for CAD and severe coronary artery stenosis. SPSS version 26.0 (IMB Corp.) was used to analyze the data. All comparisons were two-tailed and values of P<0.05 were considered to indicate a statistically significant difference.

Results

Baseline characteristics of the unmatched group. A total of 1,107 patients [736 men, 371 women; median age, 64 years (55-70 years)] were included in the present study. According to the results of the coronary angiography, the patients were divided into normal control and CAD groups. The variables of sex, smoking history, hypertension, diabetes and age differed significantly between the two groups (P<0.05; Table I). After PSM, there were 384 cases in both groups with no statistically significant differences in characteristics such as sex, smoking history, hypertension, diabetes, or age (P>0.05; Table I). The absolute value of the standardized deviation after PSM was <0.1, indicating good matching (Fig. 1A). The CAD group was further divided into mild and severe CAD groups according to Gensini score (Table II; Fig. 1B).

Matched groups. After matching, the neutrophil, WBC and platelet counts as well as the SII, NLR and PLR were higher in the CAD vs. control group, whereas the HDL-C level and LCR were significantly lower in the CAD vs. control group (P<0.05; Table I). The neutrophil and platelet counts as well as the CRP level, SII, NLR and PLR were significantly higher in the severe CAD vs. mild CAD group after matching, whereas

Table I. Baseline characteristics of patients with and without coronary heart disease before and after matching.

Variable	Before matching			After matching		
	CAD(-) (n=479)	CAD(+) (n=628)	P-value	CAD(-) (n=384)	CAD(+) (n=384)	P-value
Men, n (%)	278 (58.04)	458 (72.93)	<0.001[a]	247 (64.32)	241 (62.76)	0.708
Smoking, n (%)	162 (34.11)	319 (51.12)	<0.001[a]	155 (40.36)	153 (39.84)	0.941
Hypertension, n (%)	310 (64.72)	453 (72.13)	0.010[a]	255 (66.41)	258 (67.19)	0.878
Diabetes mellitus, n (%)	89 (18.86)	189 (30.19)	<0.001[a]	85 (22.14)	87 (22.66)	0.931
Age, years	61 (54, 68)	65 (57, 72)	<0.001[a]	63 (56, 70)	64 (54.75, 70)	0.979
BMI, kg/m^2	24.80 (22.74, 27.00)	24.80 (22.49, 26.67)	0.220	24.77 (22.60, 26.99)	24.79 (22.32, 26.83)	0.472
LDL-C, mmol/l	2.3 0 (1.78, 2.79)	2.36 (1.78, 2.89)	0.301	2.30 (1.73, 2.79)	2.36 (1.78, 2.91)	0.236
LVEF, %	60 (60, 62)	60 (60, 62)	0.052	60 (60, 62)	60 (60, 62)	0.407
Triglyceride, mmol/l	1.43 (0.98, 2.00)	1.47 (0.99, 2.17)	0.425	1.45 (0.98, 1.96)	1.54 (1.00, 2.24)	0.087
TC, mmol/l	4.31 (3.65, 4.96)	4.26 (3.58, 4.93)	0.498	4.22 (3.63, 4.94)	4.27 (3.65, 4.98)	0.614
HDL-C, mmol/l	1.16 (1.01, 1.35)	1.10 (0.96, 1.26)	<0.001[a]	1.15 (1.00, 1.34)	1.11 (0.95, 1.28)	0.009[a]
CRP, mg/l	1.40 (0.70, 3.00)	2.00 (0.90,4.40)	<0.001[a]	1.40 (0.77, 2.92)	1.80 (0.90, 4.00)	0.001[a]
Creatinine, μmol/l	69 (59, 78)	74 (64, 85)	<0.001[a]	69 (62, 80)	71 (60, 82)	0.772
Hemoglobin, g/dl	13.70 (12.50, 14.90)	13.90 (12.70, 15.03)	0.302	13.80 (12.60, 15.00)	13.80 (12.70, 15.00)	0.848
Neutrophil, $10^3/\mu$l	3.60 (2.80, 4.55)	4.00 (3.12, 5.11)	<0.001[a]	3.59 (2.80, 4.46)	3.79 (3.00, 4.89)	0.012[a]
Lymphocyte, $10^3/\mu$l	1.7 0 (1.35, 2.10)	1.73 (1.38, 2.16)	0.317	1.76 (1.43, 2.16)	1.77 (1.41, 2.22)	0.761
White blood cell, $10^3/\mu$l	6.08 (5.01, 7.19)	6.48 (5.46, 7.89)	<0.001[a]	6.16 (5.04, 7.24)	6.28 (5.26, 7.78)	0.031[a]
Platelet, $10^3/\mu$l	192 (162, 229)	198 (166, 235)	0.051	184 (154, 217)	198 (164, 237)	0.002[a]
LCR	1.28 (0.50, 2.28)	0.90 (0.40, 1.81)	<0.001[a]	1.34 (0.54, 2.38)	0.96 (0.44, 1.98)	0.003[a]
SII, $10^3/\mu$l	389 (287, 575)	448 (314, 661)	<0.001[a]	360 (272, 504)	413 (296, 607)	<0.001[a]
NLR	2.08 (1.56, 2.81)	2.30 (1.67, 3.17)	<0.001[a]	1.99 (1.52, 2.59)	2.16 (1.62, 2.92)	0.019[a]
PLR	110 (88, 144)	112 (92, 142)	0.300	103 (85, 127)	110 (89, 137)	0.010[a]
Gensini score	0.00 (0.00,3.50)	18.50 (8.50, 36.00)	<0.001[a]	0.00 (0.00,3.00)	18.00 (8.75, 36.00)	<0.001[a]

[a]P<0.05. Values are presented as number (%) or median (interquartile range). CAD, coronary artery disease; BMI, body mass index; LVEF, left ventricular ejection fraction; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein; LCR, lymphocyte/C-reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

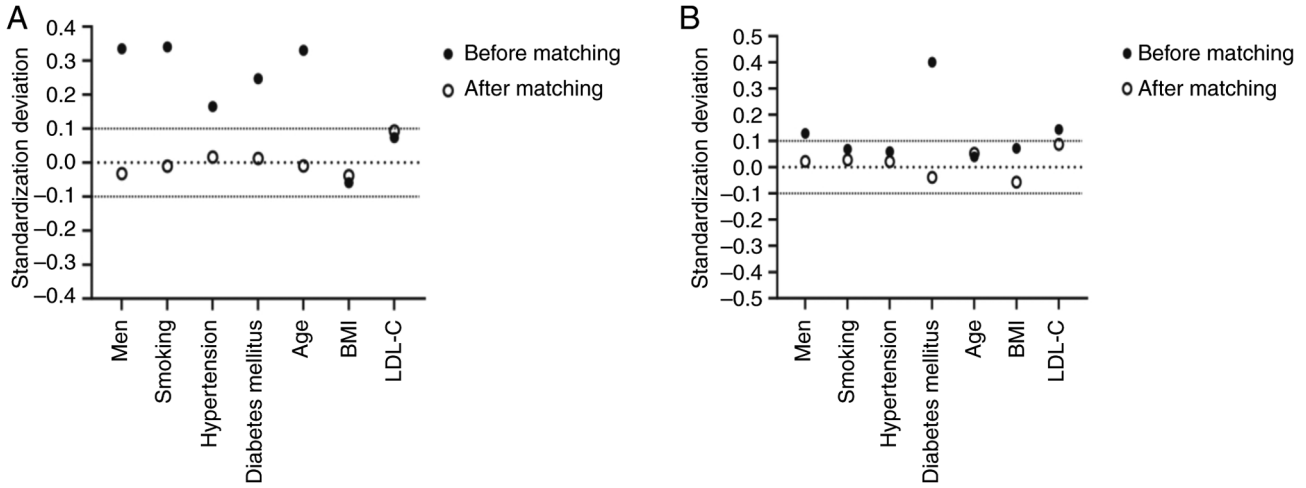

Figure 1. Standardized differences before vs. after propensity score matching (A) with or without coronary heart disease and (B) by coronary heart disease severity. BMI, body mass index; LDL-C, low-density lipoprotein cholesterol.

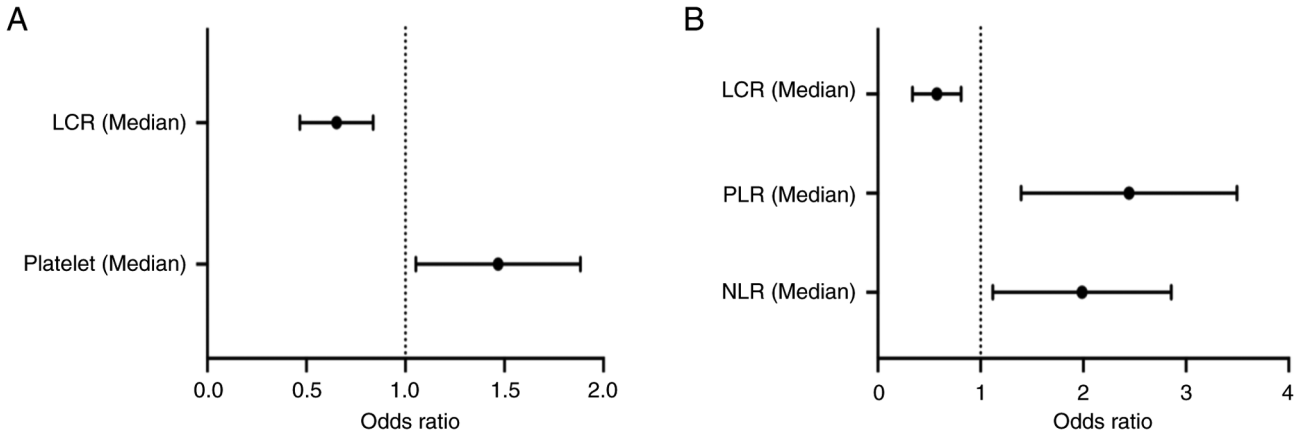

Figure 2. Multivariate logistic regression analysis after propensity score matching of patients (A) with or without coronary heart disease and (B) by coronary heart disease severity. LCR, lymphocyte-to-C-reactive protein ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune inflammation index.

the lymphocyte count and LCR were significantly lower in the severe CAD vs. mild CAD group (P<0.05; Table II).

After the PSM analysis, the risk factors for CAD were explored. As shown in Table III, the results of the univariate logistic regression analysis suggested that HDL-C level, CRP level, neutrophil count, platelet count, LCR, SII, NLR and PLR were possible risk factors for CAD (P<0.1). However, LCR was strongly correlated with CRP level (r=-0.831, P<0.001) (data not shown), and single risk factors were not as stable as combined risk factors; therefore, CRP level was excluded from further analysis. HDL-C level, neutrophil and platelet counts, LCR, SII, NLR and PLR were included in the multivariate logistic analysis. Platelet count [odds ratio (OR), 1.429; 95% confidence interval (CI), 1.074-1.902; P=0.014] was an independent risk factor for CAD, while LCR (OR, 0.635; 95% CI, 0.477-0.845; P=0.002) was an independent protective factor for CAD (Table III; Fig. 2A). The univariate logistic regression analysis showed that HDL-C, CRP, lymphocytes, platelets, LCR, SII, PLR and PLR were correlated with CAD severity. Similarly, LCR was strongly correlated with CRP level (r=-0.739, P<0.001), which was then excluded from the further analysis.

The remaining factors were included in the multivariate logistic analysis, and the results suggested that NLR (OR, 1.862; 95% CI, 1.189-2.914; P=0.007) and PLR (OR, 2.295; 95% CI, 1.478-3.564; P<0.001) were independent risk factors for CAD severity. LCR (OR, 0.541; 95% CI, 0.354-0.825; P=0.004) was an independent protective factor against severe CAD (Table IV; Fig. 2B).

Discussion

CAD is the leading cause of morbidity and mortality worldwide (17). CAD is a multifactorial disease for which dyslipidemia, abnormal blood glucose levels, smoking and genetic susceptibility are all risk factors. Atherosclerosis is the leading cause of CAD (5). In recent years, atherosclerosis has been increasingly recognized as a chronic inflammatory disease of the arterial wall (18) and an active inflammatory process instead of a simple passive injury caused by lipid infiltration (19). Vascular inflammation plays an important role in plaque formation, progression and even rupture and can have serious consequences such as local thrombosis and hypoxia-related myocardial injury (20).

Table II. Baseline characteristics of two groups of patients with coronary heart disease severity before and after matching.

Variable	Before matching			After matching		
	Mild CAD (n=399)	Severe CAD (n=229)	P-value	Mild CAD (n=212)	Severe CAD (n=212)	P-value
Men, n (%)	283 (70.93)	175 (76.42)	0.162	157 (74.06)	159 (75)	0.911
Smoking, n (%)	198 (49.87)	121 (53.3)	0.458	109 (51.42)	112 (52.83)	0.846
Hypertension, n (%)	284 (71.18)	169 (73.8)	0.540	154 (72.64)	156 (73.58)	0.913
Diabetes mellitus, n (%)	91 (22.92)	98 (42.79)	<0.001[a]	87 (41.04)	83 (39.15)	0.766
Age, years	65 (57, 71)	65 (56, 72)	0.651	65 (57, 71)	65 (56, 72)	0.525
BMI (kg/m^2)	24.8 (22.60, 26.45)	24.80 (22.32, 26.99)	0.522	24.80 (22.79, 26.68)	24.66 (22.32, 26.83)	0.563
LDL-C (mmol/l)	2.33 (1.75, 2.82)	2.42 (1.81, 2.99)	0.066	2.37 (1.90, 2.79)	2.42 (1.82, 2.98)	0.355
LVEF (%)	60 (60, 62)	60 (60, 62)	0.727	60 (60, 62)	60 (60, 62)	0.356
Triglyceride (mmol/l)	1.46 (0.95, 2.16)	1.49 (1.03, 2.19)	0.455	1.53 (1.02, 2.42)	1.46 (1.02, 2.19)	0.527
TC (mmol/l)	4.26 (3.56, 4.93)	4.27 (3.63, 4.93)	0.59	4.34 (3.69, 4.94)	4.29 (3.69, 4.93)	0.861
HDL-C (mmol/l)	1.14 (0.98, 1.30)	1.05 (0.91, 1.20)	<0.001[a]	1.13 (0.97, 1.26)	1.06 (0.91, 1.20)	0.003[a]
CRP (mg/l)	1.70 (0.90, 3.40)	2.60(1.30, 6.50)	<0.001[a]	1.70(0.90, 3.32)	2.45 (1.28, 6.43)	<0.001[a]
Creatinine (μmol/l)	73 (63, 84)	75 (64, 86)	0.326	73.5 (63, 86)	75 (64, 86)	0.757
Hemoglobin, g/dl	139 (128, 151)	138 (125, 149)	0.245	139 (129, 151)	139 (125, 151)	0.377
Neutrophil, $10^3/\mu$l	3.89 (3.00, 4.88)	4.12 (3.37, 5.49)	0.003[a]	3.84 (3.02, 4.87)	4.10 (3.39, 5.43)	0.004[a]
Lymphocyte, $10^3/\mu$l	1.75 (1.38, 2.16)	1.7 0(1.38, 2.18)	0.600	2.00 (1.62, 2.42)	1.71 (1.39, 2.11)	<0.001[a]
White blood cell, $10^3/\mu$l	6.43 (5.32, 7.73)	6.59 (5.70, 8.24)	0.016[a]	6.70 (5.51, 7.88)	6.56 (5.69, 8.23)	0.373
Platelet, $10^3/\mu$l	198 (164, 235)	197 (167, 232)	0.992	182 (155, 222)	197 (169, 230)	0.007[a]
LCR	1.04 (0.49, 2.13)	0.69 (0.25, 1.33)	<0.001[a]	1.17 (0.58, 2.39)	0.7 (0.26, 1.38)	<0.001[a]
SII, $10^3/\mu$l	433(302, 624)	479 (340, 696)	0.017[a]	342 (256, 483)	480 (345, 681)	<0.001[a]
NLR	2.19 (1.63, 3.05)	2.52 (1.84, 3.31)	0.004[a]	1.88 (1.44, 2.47)	2.52 (1.85, 3.28)	<0.001[a]
PLR	113 (92, 140)	112 (93, 146)	0.770	94 (79, 110)	112 (90, 147)	<0.001[a]
Gensini score	12.00 (7.00, 18.00)	48.00 (36.00, 66.00)	<0.001[a]	11.50 (6.00, 18.00)	48.00 (36.00, 66.00)	<0.001[a]

[a]P<0.05. Values are presented as number (%) or median (interquartile range). CAD, coronary artery disease; BMI, body mass index; LVEF, left ventricular ejection fraction; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein; LCR, lymphocyte/C-reactive protein; SII systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Table III. Multivariate logistic regression analysis of patients with or without coronary heart disease after propensity score matching.

	Univariate analysis				Multivariable analysis			
Variable	P-value	OR	95% CI		P-value	OR	95% CI	
HDL-C (median)	0.061	0.762	0.574	1.012				
CRP (median)	<0.001	1.858	1.396	2.474				
Neutrophil (median)	0.037	1.353	1.019	1.797				
Platelet (median)	0.012	1.441	1.085	1.915	0.014	1.429	1.074	1.902
LCR (median)	0.002	0.631	0.475	0.839	0.002	0.635	0.477	0.845
SII (median)	0.009	1.457	1.096	1.935				
NLR (median)	0.083	1.284	0.967	1.705				
PLR (median)	0.017	1.411	1.063	1.875				

CI, confidence interval; OR, odds ratio; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein; LCR, lymphocyte/C-reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil/lymphocyte; PLR, platelet/lymphocyte.

Table IV. Multivariate logistic regression analysis of coronary heart disease severity group after propensity score matching.

	Univariate analysis				Multivariable analysis			
Variable	P-value	OR	95%CI		P-value	OR	95%CI	
HDL-C (median)	0.012	0.611	0.416	0.896				
CRP (median)	0.001	1.910	1.299	2.810				
Lymphocyte (median)	<0.001	0.422	0.286	0.623				
Platelet (median)	0.020	1.576	1.074	2.312				
LCR (median)	<0.001	0.382	0.258	0.566	0.004	0.541	0.354	0.825
SII (median)	<0.001	2.616	1.768	3.870				
NLR (median)	<0.001	3.074	2.069	4.567	0.007	1.862	1.189	2.914
PLR (median)	<0.001	3.337	2.241	4.969	<0.001	2.295	1.478	3.564

CI, confidence interval; OR, odds ratio; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein; LCR, lymphocyte/C-reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil/lymphocyte; PLR, platelet/lymphocyte.

The immune system is divided into innate and adaptive systems. Neutrophil and platelet counts are important indicators of innate immunity (21,22), whereas lymphocytes primarily mediate adaptive immunity (23). NLR, PLR and SII reflect the balance between innate and adaptive immunity well (24-26). The NLR, PLR and SII are correlated with CAD severity and prognosis (6). In patients with cancer, LCR is a novel systemic inflammation indicator with a stronger predictive effect compared with other indicators, such as NLR and PLR (11). After PSM, the present study balanced the traditional risk factors for cardiovascular disease, including sex, smoking history, hypertension, diabetes, age, BMI and LDL-C. Platelet count and a lower LCR were risk factors for CAD, whereas PLR, NLR and a lower LCR were risk factors for severe CAD.

LCR is the ratio of lymphocytes to CRP level, and a decreased lymphocyte count and increased CRP level can downregulate LCR (13). Atherosclerotic plaques are characterized by the infiltration of monocytes/macrophages and lymphocyte cells that migrate from the blood to the lower arterial endothelium, thereby reducing the number of lymphocytes in the circulating blood when plaques form (27). This has been confirmed in lymphocyte-deficient mice, in which the atherosclerotic burden induced by a high-cholesterol diet can be reduced by 80% (28). In clinical studies, Horne *et al* (19) found that WBC count is an independent predictor of prognosis of patients with CAD. However, a high neutrophil or low lymphocyte count has a stronger predictive power, and a low lymphocyte count increases the risk of cardiovascular disease. Similarly, Adamstein *et al* (10) reported the protective effect of a high lymphocyte count on atherosclerosis.

Although mechanistic studies suggest that lymphocytes can be both atheroprotective and atherogenic, the lymphopenia-induced effect of atherosclerosis may reflect a more general process such as frailty (29,30). CRP, a part of the innate immunity that aggregates or binds to ligands to activate the classical complement pathway, also binds to the phospholipids of damaged cells and subsequently activates the complement system in a limited manner, enhancing the uptake of these

cells by macrophages, which have atherogenic properties (31). A previous study suggests that plasma CRP levels can predict the risk of vascular disease with a predictive ability as high as that of TC or HDL-C (20). In the CANTOS trial, decreased CRP levels were closely associated with reduced rates of cardiovascular events and all-cause mortality (31). Platelets are involved in various vascular inflammation-related diseases, including atherosclerosis, myocardial infarction and autoimmune diseases (32). NLR and PLR can be used to assess CAD development and severity before coronary angiography (33). In the present study, LCR was closely related to CAD occurrence and severity.

The present study had several limitations. First, only patients initially diagnosed with CAD were included, while those previously diagnosed with CAD were excluded. Therefore, the results can be applied to only a narrow population. Second, only a single blood sample was collected from patients after admission, and the LCR was not regularly assessed. Therefore, the long-term predictive effect of LCR remains unclear. Thirdly, the present study did not further explore the predictive efficacy of LCR compared with traditional inflammatory biomarkers NLR and PLR in predicting CAD and severe coronary artery stenosis. Therefore, the aforementioned issues will be further improved in future research. Finally, this was a single-center study with a small sample size. Subsequent multicenter studies will aim to include more patients to provide high-quality clinical evidence.

In conclusion, LCR, a simple and easy-to-acquire indicator in clinical studies, is an independent protective factor against CAD occurrence. It is also related to CAD severity and an independent protective factor against severe CAD. LCR determinations may guide the early screening and assessment of CAD severity.

Acknowledgements

The authors would like to thank Professor Gangjun Zong and Professor Yehong Liu from Department of Cardiology, The 904th Hospital of Joint Logistic Support Force of People's Liberation Army for their assistance in manuscript editing and language polishing.

Funding

This study was supported by the Natural Science Foundation of Jiangsu Province (grant no. BK20201139), the Major Project of Jiangsu Provincial Health Commission (grant no. ZD2021020) and the Wuxi Science and Technology Development Fund (grant no. Y20212011).

Availability of data and materials

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

Authors' contributions

KC, YHL and GJZ conceived and designed the study. KC, BDX, TY, LC and GYW contributed to the data acquisition. KC and YHL performed the statistical analyses. KC and YHL drafted the manuscript. All authors have read and approved the final manuscript. KC, YHL and GJZ confirm the authenticity of all the raw data.

Ethics approval and consent to participate

This study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the 904th Hospital of the Joint Logistic Support Force of People's Liberation Army (approval no. 2022-05-24). All participants provided written informed consent prior to participating.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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