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Clinical study of a new nutritional index for predicting long-term prognosis in patients with coronary atherosclerotic heart disease following percutaneous coronary intervention

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Abstract

Background and Objective: Some patients continue to experience major adverse cardiovascular and cerebrovascular events (MACCE) after percutaneous coronary intervention (PCI) in frigid places. Indexes of inflammation and nutrition alone were shown to predict outcomes in patients with PCI. However, the clinical predictive value of mixed indicators is unclear. This study aimed to assess the predictive value of the albumin/neutrophil/lymphocyte ratio (NLR) on the long-term prognosis of patients with coronary heart disease (CHD) following percutaneous coronary intervention (PCI). **Methods:** A total of 608 post-PCI CHD patients were categorized into low- and high-index groups based on the optimal cut-off values for albumin and NLR. The primary outcome was a composite endpoint comprising all-cause mortality and major adverse cerebrovascular events. The secondary outcome was the comparison of the predictive efficiency of the new nutritional index, albumin/NLR, with that of albumin or NLR alone. **Results:** Over the five-year follow-up period, 45 patients experienced the composite endpoint. The incidence of endpoint events was significantly higher in the low-index group (12%) compared to the high-index group (4.9%). Receiver operating characteristic (ROC) curve analysis revealed that the albumin/NLR index had a larger area under the curve (AUC: 0.655) than albumin (AUC: 0.621) or NLR (AUC: 0.646), indicating superior predictive efficiency. The prognostic nutritional index had an AUC of 0.644, further supporting the enhanced predictive value of the albumin/NLR index over individual nutritional and inflammatory markers. **Conclusion:** The albumin/neutrophil/lymphocyte ratio is independently associated with the long-term prognosis of CHD patients post-PCI and demonstrates superior predictive efficiency compared to individual nutritional and inflammatory markers.

Keywords

coronary heart disease; percutaneous coronary intervention; malnutrition; inflammation; cardiovascular prognosis

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1 Introduction

According to mortality data from the Global Burden of Disease Study, coronary heart disease (CHD) remains the leading cause of death worldwide, contributing to high morbidity and mortality[1]. Especially in frigid zone, percutaneous coronary intervention (PCI) is an established procedure to restore blood flow by opening stenotic or obstructed vessels, alleviating patient's symptoms. However, some patients continue to experience recurrent myocardial infarction, cardiac death, stroke, and other major adverse cardiovascular and cerebrovascular events (MACCE) after PCI. Therefore, early identification of CHD patients at risk for poor prognosis post-PCI, coupled with timely intervention is crucial.

Numerous studies have demonstrated that malnutrition is prevalent among CHD patients and is closely linked to poor prognosis. Objective nutritional indicators, such as the prognostic nutritional index (PNI)[2-3], Geriatric Nutritional Risk Index (GNRI)[4-6], Controlling Nutritional Status (CONUT)[7-8], and Triglycerides × Total Cholesterol × Body Weight Index (TCBI)[9-10] have proven to be significant in assessing cardiovascular prognosis. Of these, the CONUT score Of these predict all-cause mortality and major cardiovascular events within one year more effectively than PNI and GNRI[11-12], although it is not yet widely adopted in clinical practice.

In addition to malnutrition, inflammation plays an important role in the progression of coronary atherosclerosis. The neutrophil/lymphocyte ratio (NLR), an emerging inflammatory marker, is strongly associated with prognosis in various cardiovascular diseases[13-14]. Given that both nutritional and inflammatory factors influence long-term prognosis in CHD patients after PCI, a new index—albumin/NLR—was developed. This index combines conventional nutritional indicators, such as body mass index (BMI), total cholesterol, albumin, and total lymphocyte counts, with the inflammatory marker NLR. The purpose of this study is to determine whether the albumin/NLR index correlates with the prognosis of CHD patients post- PCI and whether it offers superior prognostic value and clinical relevance compared to traditional markers.

2 Methods

2.1 Study population

This was a single-center, observational, retrospective cohort study. The study population consisted of patients with CHD who underwent their first PCI for the first time at [blinded for review] between January 2015 and September 2017. The inclusion criteria were patients aged 18 to 80 years. The primary exclusion criteria were: (1) severe valvular heart disease; (2) severe congenital heart disease; (3) thyroid dysfunction; (4) liver and kidney failure; (5) systemic inflammatory disease, recent infection, or trauma; (6) hematologic disorders, including various types of anemia, leukemia, lymphoma, and other diseases; (7) malignancy; (8) arrhythmias with hemodynamic instability, such as atrial fibrillation or ventricular fibrillation. Based on these inclusion and exclusion criteria, 1006 patients were excluded, and 1043 patients were deemed eligible. Of these, 435 patients were further excluded due to incomplete data, leaving a final cohort of 608 patients. This study received approval by the Institutional Ethics Committee of the Fourth Affiliated Hospital of Harbin Medical University of China (NO.2023-31). Since this study was retrospective and all data analysis was conducted anonymously, there was no informed consent of patients.

2.2 Data sources

Basic patient information, including age, sex, height, weight, smoking history, and history of hypertension, diabetes, heart failure, stroke, myocardial infarction, and medication use, was collected from the electronic medical records at [blinded for review]. Data on total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), uric acid, creatinine, albumin, total lymphocytes, neutrophil count, and left ventricular ejection fraction (LVEF) were obtained from laboratory tests and cardiac Doppler ultrasonography after admission. The glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease equation[15]. Smoking history was defined as smoking within one year prior to the coronary intervention. Hypertension was defined as an average blood pressure ≥140/90 mmHg from three non-consecutive measurements without antihypertensive medication or in patients actively receiving antihypertensive therapy. Diabetes was diagnosed based on fasting blood glucose ≥7.0 mmol/L, 2-hour blood glucose ≥11.1 mmol/L during an oral glucose tolerance test, or hemoglobin A1c ≥6.5%. Data on the use of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), beta-blockers, and calcium channel blockers (CCBs) were also collected. All laboratory parameters were assessed through blood samples obtained prior to PCI, and LVEF was measured *via* echocardiography before the procedure.

2.3 Follow-up and endpoint events

Clinical follow-up was conducted for five years, involving a review of medical records and telephone contact. The primary outcome was a composite endpoint consisting of all-cause mortality and major adverse cardiovascular and cerebrovascular events (MACCE). The secondary outcome was the predictive accuracy of the new nutritional index, albumin/NLR, compared to individual indexes. All-cause mortality was defined as death from any cause. MACCE included cardiac death, nonfatal myocardial infarction, and stroke. In cases where multiple adverse events occurred in the same patient during follow-up, only the most severe event (all-cause death > nonfatal myocardial infarction > nonfatal ischemic stroke) was included in the analysis. If the same event recurred in a patient, only the first occurrence was considered for analysis.

2.4 Statistical analyses

All statistical analyses were performed using SPSS Software, version 25.0. The albumin/NLR ratio was treated as a continuous variable, and a receiver operating characteristic (ROC) curve was generated to determine the optimal cut-off value. Based on this cut-off, patients were categorized into low- and high-index groups. Quantitative data are presented as mean ± standard deviation for normally distributed variables, or as median and interquartile range for non-normally distributed variables. Categorical variables are expressed as percentages. Baseline characteristics and laboratory indicators were compared between the groups. Quantitative data meeting assumptions of independence, normality, and homogeneity of variance were compared using the t-test, while non-normally distributed data were assessed using the rank-sum test. Categorical variables were analyzed using the chi-squared test.

Kaplan–Meier analysis was used to evaluate the cumulative incidence of endpoint events, with the log-rank test used to assess differences between the two groups. A Cox proportional hazards regression model applied to examine the relationship between the albumin/NLR index and the endpoint event. Initially, a univariate analysis was performed, followed by a multivariate analysis for variables with $P < 0.05$ in the univariate analysis. A P-value of < 0.05 was considered statistically significant.

3 Results

3.1 Determining the cut-off value using the ROC curve

The albumin/NLR ratio, treated as a continuous variable, was used as the test variable, with all-cause death and MACCE as the outcome variables. Based on the results of the ROC curve, the Youden index (sensitivity + specificity - 1) was calculated. The point corresponding to the maximum Youden index was identified as the optimal cut-off value. The best cut-off value was determined to be 17.9509, with an area under the curve (AUC) of 0.655, sensitivity of 0.661, and specificity of 0.578. Fig. 1 illustrates the division of patients into low- and high-index groups based on this cut-off value.

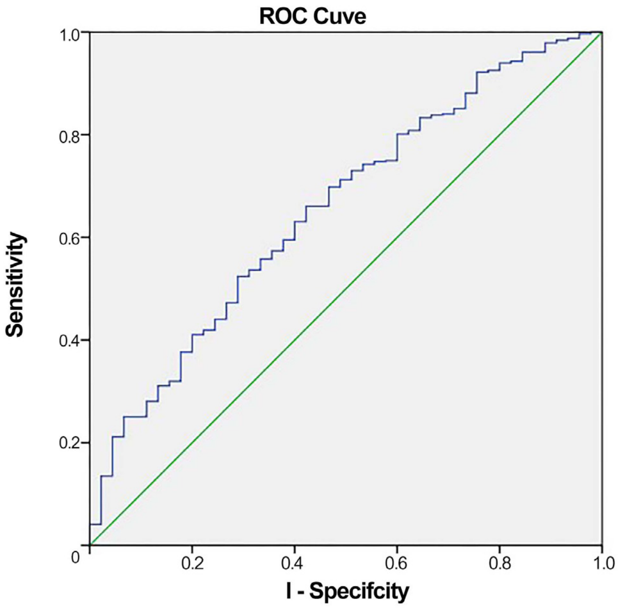

Fig. 1 Receiver operating characteristic (ROC) curve of the new nutritional index

3.2 Comparison of baseline patient data

Table 1 presents the baseline characteristics of the study population. A total of 608 patients were included, with 217 (35.7%) in the low-index group and 391 (64.3%) in the high-index group. The median age of the overall population was 59.5 years, with the low-index group being significantly older than the high-index group ($P < 0.001$). In the low-index group, 43 out of 217 patients (19.8%) had a history of heart failure, compared to 17 out of 391 patients (4.3%) in the high-index group ($P < 0.001$). The use of calcium channel blockers (CCBs) was significantly lower in the low-index group compared to the high-index group ($P < 0.05$). No significant differences were observed between the groups in terms of sex, hypertension, diabetes, stroke, history of myocardial infarction, or the use of ACE inhibitors/angiotensin II receptor blockers (ACEI/ARB) and beta-blockers.

3.3 Comparison of laboratory results and LVEF

Table 2 compares the laboratory indicators and cardiac ejection fractions between the low- and high-index groups. The low-index group had significantly lower triglyceride levels compared to the high-index group ($P = 0.004$). Additionally, the albumin levels, total lymphocyte count, and LVEF were significantly lower in the low-index group ($P < 0.001$), while the neutrophil count was significantly higher ($P < 0.001$). No statistically significant differences were observed between the two groups in terms of total cholesterol, LDL, HDL, uric acid, GFR, or BMI.

3.4 Kaplan–Meier survival curve and Log-rank analysis

During the five-year follow-up, 45 patients experienced all-cause mortality and major adverse cardiovascular and cerebrovascular events (MACCE). The incidence of endpoint events was significantly higher in the low-index group (12%) compared to the high-index group (4.9%). Kaplan–Meier analysis further demonstrated that the incidence of endpoint events following PCI was significantly greater in the low-index group than in the high-index group ($P = 0.001$) (Fig. 2).

3.5 Cox regression analysis

Univariate Cox proportional hazards regression analysis was conducted to investigate the association between baseline characteristics and the occurrence of all-cause mortality and MACCE. The univariate analysis revealed that age, history of hypertension, history of heart failure, history of myocardial infarction, history of ACE inhibitor/angiotensin II receptor blocker (ACEI/ARB) use, GFR, LVEF, and the new nutritional index were significantly associated with endpoint events (Table 3). Multivariate Cox proportional hazards regression indicated that patients

Table 1 Comparison of general characteristics between the low- and high-index groups

Characteristics	Total (*N* = 608)	Low-index group (*N* = 217)	High-index group (*N* = 391)	*P*-value
Age, years	59.50 (52.25, 66.00)	61.00 (55.00, 69.00)	58.00 (52.00, 65.00)	< 0.001
Sex				
Male	406 (66.8)	147 (67.7)	259 (66.2)	0.706
Female	202 (33.2)	70 (32.3)	132 (33.8)	0.294
Smoking				
Yes	235 (38.7)	88 (40.6)	147 (37.6)	0.473
No	373 (61.3)	129 (59.4)	244 (62.4)	0.527
Other comorbidities				
Hypertension	343 (56.4)	117 (53.9)	226 (57.8)	0.355
Diabetes mellitus	158 (26.0)	59 (27.2)	99 (25.3)	0.615
Heart failure	60 (9.9)	43 (19.8)	17 (4.3)	< 0.001
Stroke	117 (19.2)	45 (20.7)	72 (18.4)	0.486
Myocardial infarction	45 (7.4)	17 (7.8)	28 (7.2)	0.761
Drug use				
ACEI/ARB	221 (36.3)	88 (40.6)	133 (34.0)	0.108
Beta receptor antagonist	336 (55.3)	128 (59.0)	208 (53.2)	0.169
CCB	203 (33.4)	59 (27.2)	144 (36.8)	0.016

Values are presented as number (%), unless otherwise stated; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; CCB, calcium channel blocker.

Table 2 Comparison of routine laboratory indices and left ventricular ejection fraction (LVEF) between the low- and high-index groups

Characteristics	Total (*N* = 608)	Low-index group (*N* = 217)	High-index group (*N* = 391)	*P*-value
Laboratory parameters				
Triglycerides	1.60 (1.21, 2.30)	1.51 (1.18, 2.03)	1.67 (1.25, 2.50)	0.004
Total cholesterol	4.51 (3.81, 5.31)	4.50 (3.86, 5.17)	4.53 (3.80, 5.36)	0.320
LDL	2.72 (2.16, 3.30)	2.75 (2.18, 3.28)	2.72 (2.16, 3.30)	0.728
HDL	1.07 (0.94, 1.26)	1.04 (0.92, 1.22)	1.09 (0.95, 1.26)	0.058
Trioxypurine	343.45 (288.75, 404.75)	348.20 (289.30, 406.60)	341.60 (288.60, 403.00)	0.726
GFR	91.72 (79.15, 105.93)	92.23 (75.22, 108.01)	91.27 (80.19, 105.48)	0.790
Serum albumin	43.78 ± 3.42	42.24 ± 3.59	44.63 ± 3.00	< 0.001
Neutrophil count	4.07 (3.21, 5.18)	5.34 (4.28, 6.44)	3.57 (2.93, 4.36)	< 0.001
Lymphocyte count	1.95 (1.55, 2.40)	1.51 (1.18, 1.85)	2.19 (1.79, 2.59)	< 0.001
Healthy nutritional status				
BMI	25.35 (23.18, 27.46)	25.18 (22.55, 27.55)	25.35 (23.44, 27.43)	0.351
Imageological examination				
LVEF, %	59.00 (57.00, 60.00)	58.00 (56.00, 60.00)	59.00 (58.00, 60.00)	< 0.001

LVEF, left ventricular ejection fraction; LDL, low-density lipoprotein; HDL, high-density lipoprotein; GFR, glomerular filtration rate; BMI, body mass index.

in the low-index group had a 1.179-fold increase in the risk of endpoint events compared to those in the high-index group (hazard ratio: 2.179, 95% confidence interval: 1.163-4.080, *P* = 0.015). The new nutritional index, albumin/NLR, was associated with the incidence of all-cause mortality and MACCE after PCI, with lower values indicating an increased risk of long-term adverse outcomes.

3.6 Comparison of prediction efficiency of each index

The AUC is widely used to assess the accuracy of diagnostic tests. When comparing the performance of multiple diagnostic tests, the ROC curve with the largest AUC is considered to have superior diagnostic performance[16]. In this study, the AUC of the new nutritional index was 0.655, which is greater than that of albumin (AUC: 0.621) and the NLR (AUC: 0.646). This indicates that the diagnostic efficiency of the new nutritional index is higher than that of albumin and NLR alone. Additionally, the AUC of the PNI was 0.644, suggesting that the new nutritional index may be more effective in predicting the prognosis of patients with coronary heart disease after PCI compared to individual nutritional indices.

4 Discussion

Coronary artery disease (CAD) is a major global health concern, representing the leading cause of death and disability associated with cardiovascular diseases especially in frigid zone. Its primary

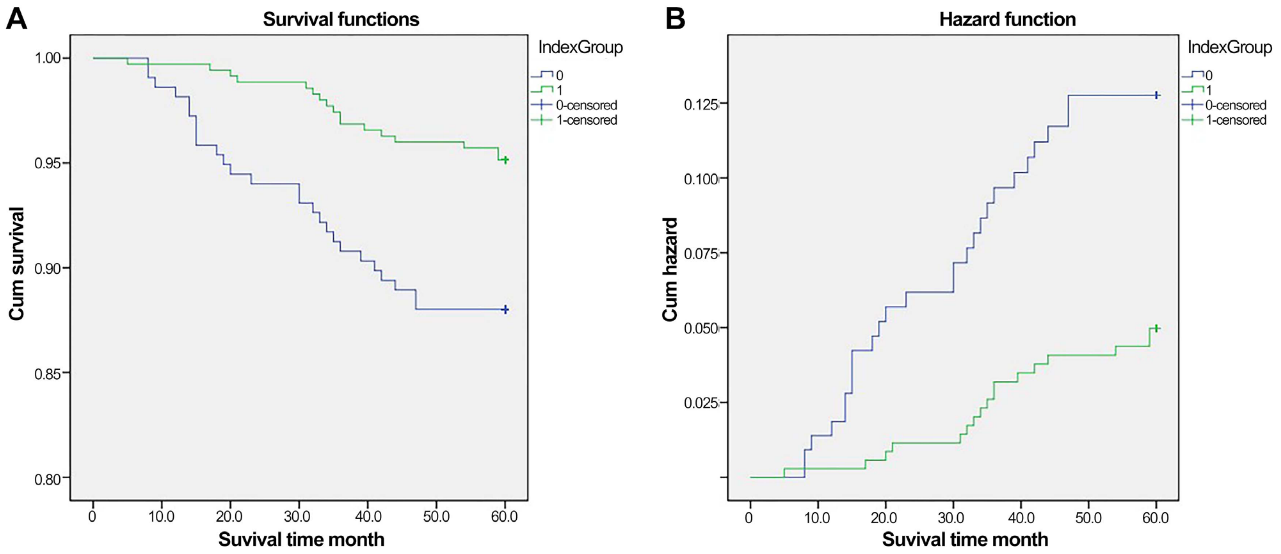

Fig. 2 Kaplan–Meier and cumulative hazard curves.

(A) The Kaplan–Meier curve displays survival time (in months) on the horizontal axis and the cumulative survival rate on the vertical axis. (B) The cumulative risk curve shows time to event (in months) on the horizontal axis and the cumulative incidence of all-cause mortality and major adverse cardiovascular and cerebrovascular events (MACCE) on the vertical axis. Log-rank analysis indicates a significant difference ($P = 0.001$).

Table 3 Cox proportional hazards regression analysis for all-cause mortality and MACCE

Variables	**Single-factor analysis**			**Multiple-factor analysis**		
	HR	**95% CI**	***P*-value**	**HR**	**95% CI**	***P*-value**
Age	1.509	1.026-1.094	< 0.001	1.038	1.003-1.074	0.033
Hypertension	0.512	0.269-0.976	0.042	0.662	0.326-1.345	0.254
Heart failure	2.375	1.144-4.930	0.020	1.092	0.405-2.942	0.862
Myocardial infarction	0.265	0.131-0.535	< 0.001	0.415	0.179-0.961	0.040
ACEI/ARB	0.364	0.201-0.661	0.001	0.531	0.275-1.026	0.059
GFR	0.974	0.960-0.988	< 0.001	0.988	0.973-1.002	0.091
LVEF	0.932	0.894-0.971	0.001	0.977	0.922-1.036	0.433
Low-index group	2.584	1.430-4.670	0.002	2.179	1.163-4.080	0.015

MACCE, major unconscionable cerebrovascular events; HR, hazard ratio; CI, confidence interval; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction.

pathogenesis is linked to atherosclerosis of the coronary arteries. Atherosclerosis is characterized by a specific inflammatory state, where inflammation can both indirectly and directly promote its development through mechanisms such as endothelial dysfunction, lipid metabolism disorders, and oxidative stress[17]. Previous studies have shown that inflammation is associated with decreased albumin levels, and lower serum albumin is linked to a higher risk of mortality[18]. Low albumin levels may also indicate malnutrition. Given the relationship between inflammation and nutrition, inflammatory-protein indicators could serve as valuable predictors of prognosis in cardiovascular disease.

Malnutrition is associated with a poor prognosis in CHD patients following PCI through various mechanisms. Albumin, the most abundant circulating protein in the plasma, plays a crucial role in antioxidant activity due to its numerous binding sites and free radical trapping properties[19]. Lapenna *et al.*[20] found that reduced serum albumin levels correlate with oxidative damage to atherosclerotic plaques and the severity of atherosclerosis. Albumin levels not only reflect nutritional status but also indicate acute-phase reactions. It serves as a serological marker of malnutrition associated with inflammation and exerts pro-inflammatory effects on vascular endothelium and lipoprotein structures[21]. Studies have reported that low serum albumin levels are linked to an increased risk of atherosclerosis[22], cardiovascular death[23], and all-cause death[24]. The pathological decrease in albumin levels in CAD may be related to the diminished antioxidant, anti-inflammatory, and antiplatelet aggregation activities, resulting in impaired endothelial function, increased blood viscosity, oxidative stress, and elevated levels of key platelet mediators of s, which contribute to coronary artery stenosis[25]. Consequently, improving albumin levels may mitigate the risk of cardiovascular disease and inflammatory status of patients, potentially lowering mortality rates[26].

Inflammation and oxidative stress are pivotal in the pathogenesis of cardiovascular diseases, prompting numerous studies on inflammatory markers. Currently, several inflammatory indices, including C-reactive protein (CRP) and the neutrophil-to-lymphocyte ratio (NLR), have emerged as prognostic markers for patients with CAD. CRP, a classical downstream effector of various inflammatory pathways, promotes inflammation by stimulating the secretion of pro-inflammatory cytokines[27]. Research confirms a correlation between elevated CRP levels and the severity of coronary heart disease, as well as an increased likelihood of future cardiovascular events[28]. Eldrup, *et al.*[29] demonstrated that high CRP levels are associated with an elevated risk of unstable angina, myocardial infarction, and mortality in patients with stable CAD. Additionally, a study by Li *et al.* highlighted that baseline CRP levels remain an independent predictor of long-term MACCE in patients undergoing coronary revascularization, even with comprehensive statin and antiplatelet therapy[30]. Similarly, a meta-analysis involving 18,715 individuals found a significant association between elevated CRP levels and an increase in multiple adverse outcomes, including all-cause and cardiovascular mortality, in patients with acute myocardial infarction undergoing PCI[31]. Atherosclerosis is characterized as a unique inflammatory state, with neutrophils reflecting this inflammatory status and lymphocyte counts indicating immune capacity. Low lymphocyte percentages have been significantly associated with CAD and serve as predictors of poor prognosis[32]. Previous studies have shown that elevated white blood cell counts predict an increased risk of death or myocardial infarction in CAD patients; however, an increase in neutrophils coupled with a decrease in lymphocytes is more strongly correlated with poorer long-term outcomes than white blood cell count alone, suggesting that specific white blood cell components provide better prognostic value[33]. The NLR, which combines neutrophil and lymphocyte counts, offers enhanced prognostic predictive capability for CAD. A meta-analysis of over 16,000 patients with acute coronary syndrome found that a high NLR at admission was associated with an increased risk of MACCE, hospitalization, and long-term mortality[13]. Studies indicate that a pre-PCI NLR is significantly associated with long-term outcomes in patients with stable coronary heart disease, with higher NLR values correlating with increased all-cause and cardiovascular mortality[14]. Therefore, the NLR demonstrates significant predictive value for CAD prognosis, with higher values indicating a poorer outlook. Additionally, previous research has shown that lipid-lowering therapies (such as statin and ezetimibe combinations) can influence CD4+ lymphocytes, thereby interfering with the body's immune-inflammatory system and potentially delaying the progression of atherosclerosis[34].

The new nutritional index developed in this study, which integrates both nutritional and inflammatory factors, demonstrated superior predictive value for the prognosis of patients with CAD following PCI, consistent with the study's objectives. Malnutrition is a complex condition characterized by protein reserve depletion, inadequate caloric intake, and diminished immune defense[35], and it serves as an independent risk factor affecting CAD prognosis. Previous studies have shown that cardiac rehabilitation in CAD patients after PCI can significantly reduce hospitalization and mortality rates[36]. Nutritional prescription, one of the five major components of cardiac rehabilitation, is vital for improving outcomes in these patients. This highlights the importance of addressing not only traditional inflammatory markers but also the nutritional status of patients with CAD post-PCI. In the present study, the implementation of this new nutritional index for assessing comprehensive nutritional and inflammatory status enabled the identification of patients at risk for poor outcomes. This facilitated early intensifications in anti-inflammatory therapy and cardiac rehabilitation, particularly through targeted nutritional interventions, which are crucial for enhancing patient prognosis. In clinical practice, intensive anti-inflammatory therapies, such as statins, ezetimibe, and PCSK9 inhibitors, combined with nutritional interventions, can be utilized to lower inflammation levels and improve the nutritional status of patients.

In this study, the use of calcium channel blockers (CCBs) in the low-index group was significantly lower than that in the high-index group ($P < 0.05$). While several trials have demonstrated the effectiveness of CCBs in treating patients with coronary heart disease, they have not shown a mortality benefit[37]. This difference in medication usage does not impact the anticipated results of this study. Although only baseline information collected at the time of patient admission was utilized, many large studies[38-39] have similarly relied on single test indices without tracking changes in these indices during the follow-up period. Despite not capturing changes in patient status over time, these studies have still yielded valuable results.

This study has several limitations. First, it was a small-scale, single-center, retrospective observational study. Future research should involve large-scale, multicenter, prospective cohort studies to further investigate the impact of improved nutritional and inflammatory status on the prognosis of patients with CHD after PCI. Second, due to the retrospective nature of this study, comprehensive surgical information, such as collateral blood vessels, degree of stenosis, and number of stents, which may significantly influence patient prognosis, was not fully obtainable. Lastly, incomplete follow-up data may have introduced selection bias. Therefore, further large-scale, multicenter prospective studies are necessary to validate the relationship between the new nutritional index and the prognosis of patients with CHD after PCI.

5 Conclusion

In conclusion, the new nutritional index, which incorporates albumin and the NLR demonstrates greater predictive efficiency than individual nutritional and inflammatory markers in assessing the prognostic of patients with coronary heart disease following PCI. This new index not only predicts patient outcomes but also holds significant clinical utility. Specifically, a value below 17.9509 indicates an elevated risk of poor prognosis, highlighting the need for early intervention in these patients.

Author contributions

Study design: Li Y; Experiment implementation and statistical analysis: Yu Y W; Manuscript writing and revision: Chen J Y, Chu X Q; Sample collection: Yuan Y W; Clinical data collection and Table and figure preparation: Chu X Q. All authors approved the final version of this manuscript.

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Ethical approval

This study received approval by the Institutional Ethics Committee of the Fourth Affiliated Hospital of Harbin Medical University of China. (NO.2023-31).

Informed consent

Since this study was retrospective and all data analysis was conducted anonymously, there was no informed consent of patients.

Conflict of interest

We have no conflicts of interest to this work.

Data availability statement

All data used during the study are available from the corresponding author by request.

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