

Higher Neutrophil to Lymphocyte Ratio at Admission is Association with Post-PCI Depressive Symptoms in Patients with ACS

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Background: Depression and elevated blood biomarkers of inflammation are common in patients with acute coronary syndrome (ACS) after percutaneous coronary intervention (PCI). Neutrophil to lymphocyte ratio (NLR) is an indicator of peripheral inflammation and has been proved to be associated with both ACS and depression.

Purpose: Our aim was to evaluate the possible association between NLR at admission and post-PCI depressive symptoms at 1 month.

Patients and Methods: A total of 224 patients with ACS who underwent PCI for the first time were recruited and completed 1-month follow-up. The 24-item Hamilton Depression Scale (HAMD-24) was used to measure depressive symptoms at 1 month after PCI. Logistic regression was used to analyze the relationship between different NLR levels and post-PCI depressive symptoms. A receiver operating characteristic (ROC) curve analysis was performed to assess the value of NLR for predicting post-PCI depressive symptoms and to determine its critical value.

Results: Of the 224 enrolled patients, 52 (23.2%) patients were diagnosed with depressive symptoms at 1 month after PCI. Patients with depressive symptoms showed significantly higher level of NLR at admission than patients without depressive symptoms (4.33 (3.26, 7.01) vs 2.57 (1.72, 3.91), $P < 0.001$). The proportion of depressive symptoms in post-PCI patients increases progressively along with NLR quartile. In the results of multivariate-adjusted logistic regression analysis, the odds ratio (OR) of post-PCI depressive symptoms was 12.028 (95% CI, 2.642–54.752) for the lowest quartile of NLR compared with the highest quartile. According to the receiver operating characteristic curve (ROC), the area under the curve (AUC) for predicting post-PCI depressive symptoms was 0.716 (95% CI, 0.641–0.791; $P < 0.001$), and the optimal cutoff of NLR levels was 3.235 (sensitivity: 76.9%, specificity: 66.9%).

Conclusion: Higher NLR levels at admission were associated with post-PCI depressive symptoms at 1 month, suggesting that NLR might be useful inflammatory markers to predict post-PCI depressive symptoms at 1 month.

Keywords: neutrophil to lymphocyte ratio, post-PCI depressive symptoms, acute coronary syndrome

Introduction

Depression is a common complication in patients with acute coronary syndrome (ACS) after percutaneous coronary intervention (PCI), which can occur at any time after PCI, with incidence rates ranging from 23% to 48%.¹ Some studies have reported that patients with ACS have the lowest incidence of depressive symptoms 3–5 days after PCI and the highest incidence of depressive symptoms 1 month after PCI.^{2,3} However, compared with the higher prevalence, the clinical screening, diagnosis and treatment of post-PCI depressive symptoms are obviously insufficient. Post-PCI depressive symptoms will not only reduce the therapeutic effect and increase the difficulty of treatment, it will also seriously affect the prognosis of PCI maneuvers. Previous studies revealed that a strong association between post-PCI depressive symptoms with poor cardiovascular outcome, increased mortality and lower quality of life.⁴ A prospective study found that the all-cause mortality of post-PCI patients with depressive symptoms increased by 77% compared with

those without depressive symptoms.⁵ Therefore, early diagnosis and timely treatment of post-PCI depressive symptoms are vital to reduce the incidence of major cardiovascular adverse events (MACEs) and improve the quality of life.

However, the potential pathogenesis of post-PCI depressive symptoms is still unclear. Previous studies have shown that the levels of interleukin (IL)-1 β , IL-18 and IL-6 in ACS patients are significantly increased, and PCI can further induce or promote the inflammatory response.⁶ In addition, we also observed that the levels of tumor necrosis factor (TNF)- α , IL-6 and IL-8 in cerebrospinal fluid of patients with depression increased significantly, and neuroinflammation was widely considered as a potential pathological mechanism of depression.⁷ In a word, ACS and depression are both related to inflammatory reaction. However, the above inflammatory indicators are often difficult to obtain in clinical practice. The neutrophil to lymphocyte ratio (NLR), an easily available marker of systemic inflammation, has been reported to be associated with various diseases, including cardiovascular diseases, psychiatric disorders, tumors, end-stage renal disease, peripheral artery disease, COVID-19, etc.⁸⁻¹⁵ but the detailed mechanisms have not been completely explored. Tahto et al found that NLR was significantly increased in patients with ACS, and NLR correlated significantly positive with the value of high sensitive troponin I (hs-TnI), creatine kinase MB (CK-MB) and C-reactive protein (CRP).¹⁶ Marazziti et al found that NLR levels were essentially higher in patients with major depression (MDD).¹⁷ Interestingly, We observed that the level of NLR increased significantly in both ACS and depression, and it is reported that many inflammatory markers in peripheral blood are highly correlated with inflammatory markers in cerebrospinal fluid, it is suggested that peripheral inflammatory signals may drive the inflammatory activity of central nervous system (CNS),¹⁸ it can be inferred that peripheral inflammation contributes, at least in part, to the development of post-PCI depressive symptoms. Up until now, there has been no study exploring the relationship between NLR and post-PCI depressive symptoms, so we assumed that the NLR could be used as a predictor of patients with post-PCI depressive symptoms. At present, the clinical diagnosis of post-PCI depressive symptoms mainly depends on the clinical manifestations and depression scale,¹⁹ and there is a lack of objective and accurate laboratory biochemical indicators. Therefore, the purpose of this study was to investigate the association between NLR at admission and post-PCI depressive symptoms and to further explore the predictive value of NLR in post-PCI depressive symptoms at 1 month.

Materials and Methods

Subjects

We included 224 consecutive patients who were admitted in the Department of Cardiovascular Medicine of Renhe Hospital affiliated to China Three Gorges University, diagnosed with ACS and treated with primary or elective PCI for the first time during the period from June 2020 to February 2022 into a prospective registry. ACS was diagnosed according to American College of Cardiology (ACC)/American Heart Association (AHA) guidelines.²⁰ The patients were included in the study if they met the following criteria: (1) age of 18 years or greater; (2) the ability and eagerness to provide informed consent; (3) Patients undergoing PCI for the first time due to ACS. The exclusion criteria were as follows for the participants: (1) patients with a history of depression or other psychiatric disorders and currently taking antipsychotic drugs; (2) patients with a family history of depression or other psychiatric disorders; (3) patients with malignant tumor or immune system disorders; (4) patients with severe hepatic or renal disease; (5) patients with an active infection history 2 weeks before PCI; (6) patients with blood system diseases; (7) patients lost to follow-up, died, and clinical data are incomplete (Figure 1). This study was approved by the Ethics Committee of the Renhe Hospital Affiliated to China Three Gorges University, where all participants signed an informed consent form before participation, and complied with the Helsinki Declaration.

Data Collection

Our researchers collected the patients' demographics (age, sex, BMI, marital status, education level), past medical history (hypertension, diabetes), personal history (smoking and drinking) and angiographic findings of patients at admission through the hospital electronic medical record system. The body mass index (BMI) is defined as the individual's body weight (kg) divided by the square of the height (m). The level of education is measured by the highest degree they receive and is divided into three grades, including below high school, high school and above. Marital status is divided

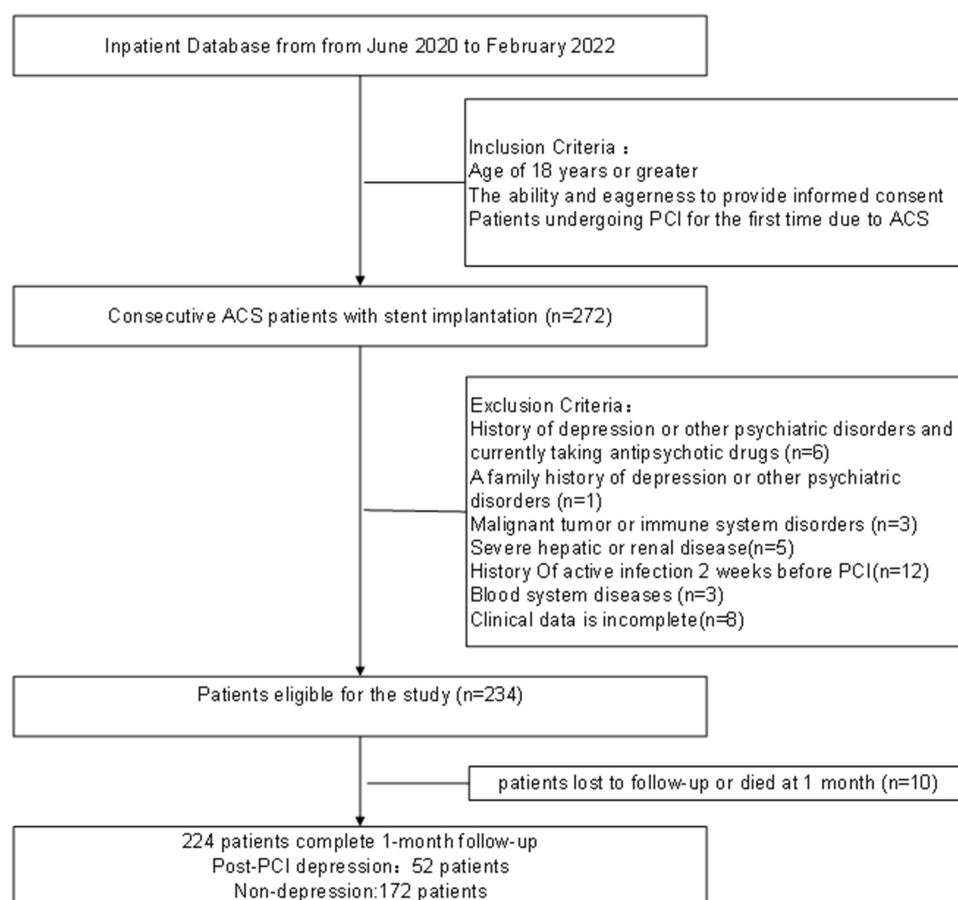


Figure 1 Study recruitment profile.

Abbreviations: ACS, acute coronary syndrome; PCI, percutaneous coronary intervention.

into married or unmarried, divorced and widowed. Smoking was defined as smoking at least 1 cigarette per day for the past 6 months. Drinking was defined as having at least one alcohol intake per week for the past 6 months. Hypertension is defined as measuring SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg three times on different days, or any history of hypertension and currently taking antihypertensive drugs. Diabetes is defined as fasting blood glucose (FBG) ≥ 7.0 mmol/L, glycated hemoglobin (HbA1c) $\geq 7.0\%$, or 2-h post-load glucose concentration ≥ 11.1 mmol/L, or any history of T2DM and currently taking hypoglycemic drugs. All patients were required to take aspirin for lifetime and a P2Y12 inhibitor for at least 1 year after PCI. Coronary angiography and PCI were performed using standard techniques. The severity of coronary artery was assessed by certified cardiologists using the Gensini scoring system through coronary angiography after admission.²¹ Patients were followed 1 month after PCI (See [Supplementary Materials](#)).

Blood Collection and Laboratory Test

Blood samples were collected from the patient's elbow vein on the day of admission or next morning after fasting for at least 8 hours by trained nurses, and collected in a 3 mL EDTA-K2 tube. Which were tested in our hospital's laboratory by the Sysmex XN-9000 (Sysmex, Kobe, Japan) Hematology Automated Analyzer, the examiner knows nothing about all clinical information. The NLR was calculated by another researcher by dividing neutrophil count by lymphocyte count.

Psychological Measurement

All psychological evaluations were conducted independently by two researchers trained by psychiatrists. At one-month follow-up, the severity of post-PCI depressive symptoms was measured by HAMD-24 through face-to-face interview or telephone interview. The Cronbach's coefficient of Chinese version of HAMD scale is larger than 0.8, and the test-retest

reliability and duplicate reliability larger than 0.7, indicating good internal consistency and stability. In addition, its content validity, criterion validity and construct validity are also acceptable.²² Patients having moderate or more depression (HAMD-24 scores >20) were diagnosed with clinically relevant post-PCI depressive symptoms. The diagnosis of post-PCI depressive symptoms was in accordance with the diagnostic criteria of depression in CCMD-3 published by the Chinese Society of psychiatry.²³ The full name of CCMD-3 is China's Classification and Diagnosis Standards of Mental Disorders 3 Edition, which is a diagnostic standard with China characteristics formulated with reference to the international diagnostic standards of mental disorders and the Diagnostic criteria for mental disorders in the United States.

Statistical Analysis

All statistical analyses were performed by SPSS22.0 statistical software (SPSS, Inc., Chicago, IL, USA). Continuous variables are presented as mean $\pm$ SD or as the median with the inter quartile range (IQR), Student's *t*-test and the Mann–Whitney *U*-test were used to compare continuous variables. Categorical variables are presented as the relative frequency with percentage. The Chi-square test was used to compare categorical variables.

To compare characteristics by quartile of NLR levels, one-way analysis of variance (ANOVA) or the Kruskal–Wallis was used to compare continuous variables and Pearson's Chi-square test or Fisher's exact test was used to compare categorical variables. Multivariable regression analyses were performed using 3 different models to assess the relationship between baseline NLR and incidence of post-PCI depressive symptoms at 1 month. The models were adjusted for variables with $P < 0.10$ in the univariate analysis and conventional confounding factors. Furthermore, we performed tests for linear trend by entering the median value of each quartile of NLR as a continuous variable in the models. A receiver operating characteristic (ROC) curve analysis was used to identify the cutoff point of NLR levels at admission for the diagnosis of post-PCI depressive symptoms at the 1-month follow-up. In this study, statistical significance was defined as a two-tailed $P < 0.05$.

Results

Baseline Characteristics According to Post-PCI Depressive Symptoms

This study enrolled 272 ACS patients treated with primary or elective PCI for the first time in Renhe Hospital Affiliated to China Three Gorges University from June 2020 to February 2022. Ultimately, 224 patients were included in the final analysis, excluding 6 cases with History of depression or other psychiatric disorders, 1 case with family history of depression or other psychiatric disorders, 3 cases with malignant tumor or immune system disorders, 5 cases with severe hepatic or renal disease, 12 cases with active infection history 2 weeks before PCI, 3 cases with blood system diseases, and 18 cases with incomplete data, lost to followed-up or died. Of all patients followed up, there were 165 (73.7%) males and 59 (26.3%) females, with an average age of (62.34 ± 10.54) years. Overall, the number of patients who were diagnosed with post-PCI depressive symptoms at the 1-month follow-up was 52 (23.2%).

The characteristics of included participants are shown in Table 1. Compared with subjects without post-PCI depressive symptoms, those with post-PCI depressive symptoms had higher proportions of female ($P < 0.001$), higher ages ($P = 0.007$), higher proportions of widowed and divorced ($P = 0.002$), higher proportions of hypertension history ($P = 0.001$), higher number of coronary lesions ($P < 0.001$), higher gensini score ($P < 0.001$), lower counts of lymphocyte ($P = 0.008$), higher levels of neutrophils ($P = 0.006$) and NLR ($P < 0.001$). In terms of BMI, education, history of diabetes, smoking, drinking, monocyte and platelet counts, there were no significant differences between the groups.

Baseline Characteristics of the Patients According to NLR Quartile

The patients were divided into four subgroups according to the quartile of NLR at admission: Quartile 1 ($n = 57$): ≤ 1.95 , Quartile 2 ($n = 56$): $1.96–2.84$, Quartile 3 ($n = 55$): $2.85–4.46$, Quartile 4 ($n = 56$): ≥ 4.47 . As shown in Table 2, we summarized the demographic, medical history, laboratory, and coronary angiography findings of the post-PCI patients by NLR quartile. The proportions of married, HAMD score, counts of Lymphocyte and Neutrophil among the patients with

Table 1 Patient Characteristics According to Post-PCI Depressive Symptoms

Variable	ALL (n=224)	Non-Depression (n=172)	Depression (n=52)	P-value
Demographic characteristics				
Age (year)	62.34±10.54	53.61±13.09	58.82± 12.89	0.007
BMI (kg/m ²)	22.44±3.59	22.58±3.69	21.95±3.20	0.266
Male, n (%)	165 (73.7)	137 (79.7)	28 (53.8)	<0.001
Married, n (%)	202 (90.2)	161 (93.6)	41 (78.8)	0.002
Education, n (%)				0.375
Below	168 (75.0)	125 (72.7)	43 (82.7)	
High school	44 (19.6)	37 (21.5)	7 (13.5)	
Above	12 (5.4)	10 (5.8)	2 (3.8)	
Medical history				
Hypertension, n (%)	132 (58.9)	91 (52.9)	41 (78.8)	0.001
Diabetes, n (%)	46 (20.5)	33 (19.2)	13 (25.0)	0.433
Smoking, n (%)	130 (58.0)	105 (61.0)	25 (48.1)	0.110
Drinking, n (%)	98 (43.8)	79 (45.9)	19 (36.5)	0.266
Laboratory findings				
Monocytes, 10 ⁹ /L, median (IQR)	0.40 (0.29, 0.51)	0.40 (0.30, 0.50)	0.35 (0.27, 0.55)	0.395
Neutrophils, 10 ⁹ /L, median (IQR)	4.52 (3.29, 6.62)	4.37 (3.13, 6.39)	5.60 (3.82, 7.40)	0.006
Lymphocytes, 10 ⁹ /L, median (IQR)	1.46 (1.05, 2.04)	1.57 (1.11, 2.32)	1.23 (0.99, 1.76)	0.008
Platelets, 10 ⁹ /L, median (IQR)	185.0 (154.25, 231.00)	187.50 (155.25, 230.0)	178.50 (149.25, 238.5)	0.867
NLR	2.84 (1.95, 4.48)	2.57 (1.72, 3.91)	4.33 (3.26, 7.01)	< 0.001
Coronary angiography				
Gensini score, median (IQR)	45.50 (32.00, 66.00)	41.0 (30.0, 57.88)	66.5 (48.50, 94.75)	< 0.001
Number of lesion, n (%)				< 0.001
Single-branch	63 (28.1)	56 (32.6)	7 (13.5)	
Double-branch	83 (37.1)	69 (40.1)	14 (26.9)	
Multi-branch	78 (34.8)	47 (27.3)	31 (59.6)	
HAMD score, median (IQR)	10.50 (7.00, 17.00)	9.00 (6.00, 12.75)	24.00 (22.00, 26.00)	< 0.001

Note: Data in bold indicates statistical significance (P<0.05).

Abbreviations: BMI, body mass index; NLR, neutrophil to lymphocyte ratio; IQR, inter-quartile range; HAMD, Hamilton depression scale.

Table 2 Baseline Characteristics of Post-PCI Patients in NLR Quartiles

Variables	All Patients	NLR Quartiles				
		Quartile 1 (≤ 1.95)	Quartile 2 (1.96–2.84)	Quartile 3 (2.85–4.46)	Quartile 4 (≥4.47)	P-value
Demographic characteristics						
Age (year)	62.34±10.54	60.81±11.11	60.98±11.07	65.47±8.18	62.18±11.05	0.070
BMI (kg/m ²)	22.44±3.59	22.64±3.30	22.48±3.57	22.12±3.57	22.49±3.96	0.892
Male, n (%)	165 (73.7)	43 (75.4)	39 (69.6)	42 (76.4)	41 (73.2)	0.858
Married, n (%)	202 (90.2)	56 (98.2)	51 (91.1)	45 (81.8)	50 (89.3)	0.032
Education, n (%)						0.069
Below	168 (75.0)	43 (75.4)	36 (64.3)	40 (72.7)	49 (87.5)	
High school	44 (19.6)	12 (21.1)	15 (26.8)	13 (23.6)	4 (7.1)	
Above	12 (5.4)	2 (3.5)	5 (8.9)	2 (3.6)	3 (5.4)	
Medical history						
Hypertension, n (%)	132 (58.9)	31 (54.4)	36 (64.3)	36 (65.5)	29 (51.8)	0.348
Diabetes, n (%)	46 (20.5)	9 (15.8)	13 (23.2)	10 (18.2)	14 (25.0)	0.319
Smoking, n (%)	130 (58.0)	36 (63.2)	32 (57.1)	35 (63.6)	27 (48.2)	0.313
Drinking, n (%)	98 (43.8)	25 (43.9)	26 (46.4)	29 (52.7)	18 (32.1)	0.171
Laboratory findings						
Monocytes, 10 ⁹ /L, median (IQR)	0.40 (0.29, 0.51)	0.41 (0.33, 0.55)	0.38 (0.27, 0.48)	0.41 (0.32, 0.51)	0.35 (0.27, 0.54)	0.148
Neutrophils, 10 ⁹ /L, median (IQR)	4.52 (3.29, 6.62)	3.17 (2.56, 4.63)	3.87 (3.19, 4.61)	4.66 (3.61, 6.13)	7.27 (5.45, 8.49)	< 0.001

(Continued)

Table 2 (Continued).

Variables	All Patients	NLR Quartiles				
		Quartile 1 (≤ 1.95)	Quartile 2 (1.96–2.84)	Quartile 3 (2.85–4.46)	Quartile 4 (≥ 4.47)	P-value
Lymphocytes, $10^9/L$, median (IQR)	1.46 (1.05, 2.04)	2.5 (1.85, 3.55)	1.58 (1.39, 2.02)	1.27 (1.00, 1.74)	1.00 (0.68, 1.29)	< 0.001
Platelets, $10^9/L$, median (IQR)	185.0 (154.25, 231.00)	177.0 (150.0, 224.0)	191.0 (157.25, 223.75)	193.0 (140.0, 242.0)	182.0 (155.50, 235.25)	0.878
NLR, median (IQR)	2.84 (1.95, 4.48)	1.42 (1.21, 1.70)	2.31 (2.13, 2.66)	3.65 (3.22, 3.95)	7.12 (5.53, 9.66)	< 0.001
Coronary angiography						
Gensini score, median (IQR)	45.50 (32.00, 66.00)	44.0 (32.0, 61.5)	42.0 (29.75, 59.38)	46.0 (32.00, 65.00)	56.0 (32.75, 76.00)	0.195
Number of lesion, n (%)						0.302
Single-branch	63 (28.1)	16 (28.1)	17 (30.4)	13 (23.6)	17 (30.4)	
Double-branch	83 (37.1)	26 (45.6)	22 (39.3)	21 (38.2)	14 (25.0)	
Multi-branch	78 (34.8)	15 (26.3)	17 (30.4)	21 (38.2)	25 (44.6)	
HAMD score, median (IQR)	10.50 (7.00, 17.00)	7.00 (5.00, 10.00)	8.00 (6.00, 11.75)	14.00 (8.00, 20.00)	17.00 (13.00, 24.00)	< 0.001

Note: Data in bold indicates statistical significance ($P < 0.05$).

Abbreviations: BMI, body mass index; NLR, neutrophil to lymphocyte ratio; HAMD, Hamilton Depression Scale; IQR, inter-quartile range.

different quartiles of NLR were significantly different (all $P < 0.05$). Other baseline characteristics have no significant difference according to the NLR quartile.

In addition, we compared the proportion of depressive symptoms among PCI patients stratified by NLR quartiles. The proportion of post-PCI depressive symptoms increased with ascending quartiles of NLR (P for trend < 0.001). The numbers of patients with post-PCI depressive symptoms at 1 month follow-up were 4 (7.02%) in quartile 1, 8 (14.29%) in quartile 2, 18 (32.73%) in quartile 3 and 22 (39.29%) in quartile 4 respectively (Figure 2).

Association Between NLR Level and Depressive Symptoms After PCI

In unadjusted multivariate logistic regression analyses, the ORs for the post-PCI depressive symptoms risk of patients in quartiles 2, 3 and 4 compared with those in quartile 1 were 2.208 (0.625, 7.802), 6.446 (2.017, 20.602) and 8.574 (2.717,

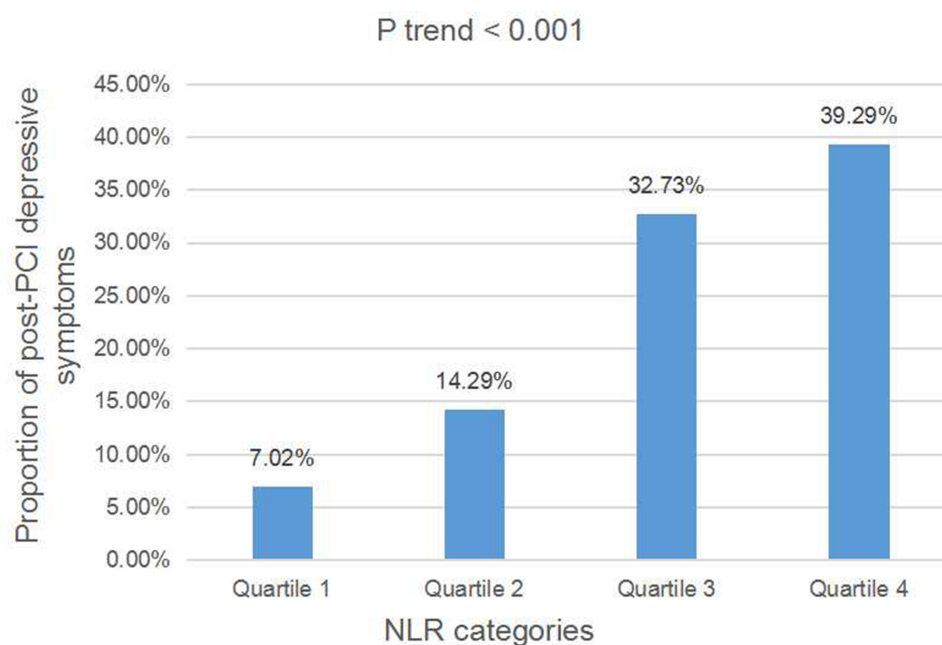


Figure 2 The proportion of post-PCI depressive symptoms for the quartiles of NLR at admission.

Abbreviations: NLR, neutrophil to lymphocyte ratio; PCI, percutaneous coronary intervention.

Table 3 Multivariate Adjusted Odds Ratios for the Association Between NLR Levels and Post-PCI Depressive Symptoms

	OR (95% CI) ^a				P-value for Trend ^b
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Unadjusted	1.000 (reference)	2.208 (0.625, 7.802)	6.446 (2.017, 20.602)	8.574 (2.717, 27.053)	<0.001
P-value		0.219	0.002	<0.001	
Model 1 ^c	1.000 (reference)	2.102 (0.575, 7.685)	6.826 (2.039, 22.852)	9.633 (2.915, 31.838)	<0.001
P-value		0.262	0.002	<0.001	
Model 2 ^d	1.000 (reference)	2.310 (0.482, 11.063)	8.420 (1.868, 37.950)	12.208 (2.698, 55.241)	<0.001
P-value		0.295	0.006	0.001	
Model 3 ^e	1.000 (reference)	2.255 (0.466, 10.920)	8.580 (1.882, 39.118)	12.028 (2.642, 54.752)	<0.001
P-value		0.312	0.005	0.001	

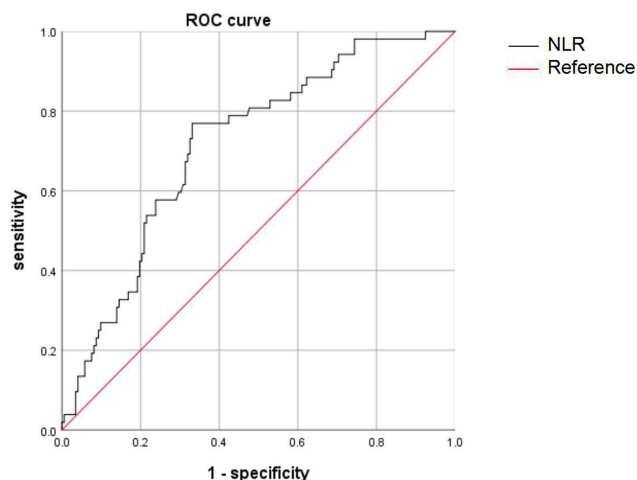
Notes: ^aReference OR (1.000) is the Quartile 4 of NLR. ^bTest for trend based on variable containing median value for each quartile. ^cModel 1: adjusted for age, sex. ^dModel 2: adjusted for covariates from Model 1 and further adjusted for variables with $P < 0.05$ in univariate analysis (married, Hypertension, Gensini score, Number of lesion). ^eModel 3: adjusted for covariates from Model 2 and further adjusted for conventional confounding factors (smoking, diabetes).

Abbreviations: OR, odds ratio; CI, confidence level.

27.053), respectively. After adjusting for conventional factors and significant variables in the univariate analyses, including age, sex, marital status, hypertension, Gensini score, number of lesion, diabetes and smoking, patients in the highest quartile had elevated risk of post-PCI depressive symptoms compared to patients in the lower quartile (Model 1: OR = 9.633, 95% CI 2.915–31.838, P for trend <0.001; Model 2: OR = 12.208, 95% CI 2.698–55.241, P for trend <0.001; Model 3: OR = 12.028, 95% CI 2.642–57.752, P for trend <0.001) (Table 3).

ROC Curves for Predicting of Post-PCI Depressive symptoms

According to the ROC curve, the area under the curve for predicting post-PCI depressive symptoms with NLR was 0.716 (95% CI, 0.641–0.791; $P < 0.001$). By calculating the Jorden index, the optimal cutoff of NLR levels as an indicator for the prediction of post-PCI depressive symptoms was 3.235, with a sensitivity of 76.9% and a specificity of 66.9% (Figure 3).

**Figure 3** ROC curves for predicting of post-PCI depressive symptoms.

Abbreviations: NLR, neutrophil to lymphocyte ratio; ROC, receiver operating characteristic.

Discussion

As far as we know, this is the first study exploring the prospective association between NLR levels and the development of post-PCI depressive symptoms. In our study, we found that higher levels of NLR at admission were significantly related to post-PCI depressive symptoms of patients at 1 month follow-up. After adjusting for potential confounders, individuals in the highest quartile of NLR had a 12.028-fold (95% CI: 2.642–57.752) higher risk of post-PCI depressive symptoms than those with the lowest quartile of NLR. Furthermore, our findings revealed that the NLR level has a high accuracy in predicting the depressive symptoms of patients with ACS after PCI.

In addition, the incidence of post-PCI depressive symptoms at 1-month follow-up was 23.2%, which was consistent with the results of the previous studies.³ The diagnosis of post-PCI depressive symptoms is a dynamic process, with different manifestations in different time stages, and the conclusions of different studies are quite different, which may be related to the timing of post-PCI depressive symptoms determination, psychological assessment methods, and different criteria for evaluation.²⁴ The gensini scores reflect the severity of coronary artery stenosis. Our results showed that gensini scores were risk factors for the development of post-PCI depressive symptoms, which was broadly consistent with the recent studies.²⁵

As we all know, neuroinflammation is recognized as one of the most important pathogenesis of psychiatric or neurological disorders. Accumulating evidence shows that peripheral inflammation can induce central neuroinflammation and is closely related to the pathogenesis and progression of psychiatric or neurological disorders.²⁶ The NLR serves as a marker of peripheral inflammation and has been proved to be related to the diagnosis and prognosis of a variety of psychiatric or neurological disorders. Chen et al found that increased NLR is associated with post-stroke depression (PSD), $\text{NLR} \geq 3.701$ were independently associated with the development of PSD.²⁷ Hou et al also found that elevated NLR is associated with an increased risk of mild cognitive impairment (CI) in patients with cerebral small vessel disease (CSVD).²⁸ In addition to NLR, other peripheral inflammatory markers such as systemic immune inflammatory index (SII), platelet-lymphocyte ratio (PLR), mean platelet volume (MPV) and platelet distribution width (PDW) also have been widely studied. Oyama and Pasqui et al found that SII, PLR, MPV and PDW can predict the occurrence of postoperative delirium (POD).^{29,30} However, the relationship between peripheral and central neuroinflammation is not completely clear. It is reported that acute myocardial infarction induced peripheral inflammation, such as $\text{TNF}\alpha$, $\text{IL-1}\beta$ and IL-6 , increases blood-brain barrier (BBB) permeability by affecting endothelial cells. These peripheral inflammatory cells and inflammatory cytokines may reach the CNS passing through a disrupted BBB and activate microglia, and the triggered microglia release nitric oxide (NO), prostaglandin E2 (PGE2), reactive oxygen species (ROS), and cytokines such as $\text{IL-1}\beta$, IL-6 , and $\text{TNF-}\alpha$, which may induce neuroinflammation to impair the function of limbic system areas and lead to depressive symptoms.^{31,32}

Neutrophils are usually the first immune cells to be recruited to the site of inflammation. They can not only remove pathogens and debris by phagocytosis, but also release a variety of pro-inflammatory factors to activate other types of inflammatory cells. Lymphocytes also play an important role in inflammation. Sheng et al found that the neutrophil count and proportion at 24 hours after PCI in patients with ACS were significantly higher than those before PCI, while platelet and lymphocyte counts were significantly decreased.³³ Additionally, a recent study also reported that the absolute counts of neutrophils, intermediate monocytes and CD4^+ (helper) T cells were significantly increased in the depressed group.³⁴ In view of that decreased lymphocyte and increased neutrophil count are both found in post-PCI patients and depression subjects, which might partly explain the increased NLR levels observed in post-PCI depression patients. Aydin et al found that patients with higher HAMD score had significantly higher NLR levels compared to patients with lower HAMD score, and NLR more than 1.57 was an independent predictor of severe or very severe depression.³⁵ As our research shows, post-PCI patients with higher NLR values at admission were inclined to have depressive symptoms, the best cut-off value for NLR at admission was 3.235 in predicting post-PCI depressive symptoms, with sensitivity of 76.9% and specificity of 66.9%. Consequently, the NLR, which reflects the immune response and systemic inflammation based on peripheral neutrophil and lymphocyte, could be adopted as an easily available predictor for the occurrence of post-PCI depressive symptoms. In addition, Luo et al found that the normal reference interval for NLR among healthy

adults is (0.88–4.0).³⁶ In our study, the median NLR for patients with post-PCI depressive symptoms was 4.33 (3.26–7.01), which was significantly higher than that in healthy subjects.

Our study had several limitations. First, NLR levels were examined only once at admission, and we cannot assess the relationship between dynamic changes in NLR and post-PCI depressive symptoms. Second, our follow-up period of 1 month may be too short for us to explore the long-term effects of NLR on depressive symptoms after PCI. Follow-up visits were performed at 3 days, 1 month, 3 months, and 6 and 12 months after PCI is necessary. Finally, this is a single-center-based prospective study. We need to be cautious in generalizing this conclusion, larger sample size and multi-center research are needed in the future to support our findings and apply them clinically. Despite these limitations, this study will provide a scientific basis for further understanding the pathogenesis and pathological process of post-PCI depressive symptoms, and provide objective laboratory biochemical indicators for clinicians to predict the risk of post-PCI depressive symptoms.

Conclusion

Our current research shows that the higher NLR level at admission is significantly related to the development of post-PCI depressive symptoms at 1 month follow-up. The NLR measured at admission can be used as a potential diagnostic biomarker to predict post-PCI depressive symptoms.

Data Sharing Statement

The authors confirm that the data supporting the findings of this study are available within the article and its [Supplementary Materials](#).

Ethics Statement

This study was approved by the Ethics Committee of the Renhe Hospital Affiliated to China Three Gorges University (2021YJ22), and complied with the Helsinki Declaration.

Acknowledgments

This study was supported by the Scientific Research Project of Hubei Provincial Health Committee (WJ2021F061).

Disclosure

The authors declare that they have no conflicts of interest in this study.

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