

A Predictive Model of New-Onset Atrial Fibrillation After Percutaneous Coronary Intervention in Acute Myocardial Infarction Based on the Lymphocyte to C-Reactive Protein Ratio

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Purpose: Lymphocyte to C-reactive protein ratio (LCR) is a recognized systemic inflammatory marker and novel prognostic indicator for several cancers. This study investigated the relationship between preoperative LCR and new-onset atrial fibrillation (NOAF) in patients with acute myocardial infarction (AMI) after percutaneous coronary intervention (PCI).

Patients and Methods: Patients with AMI (n=662) with no history of atrial fibrillation (AF) were enrolled and classified into NOAF and non-NOAF groups based on the occurrence of postoperative NOAF during hospitalization. Logistic regression models were used to analyze NOAF risk factors and to assess the association between preoperative LCR and NOAF incidence. We constructed a new nomogram from the selected NOAF risk factors, and tested its predictive performance, degree of calibration, and clinical utility using receiver operating characteristic and calibration curves, decision curve analysis, and clinical impact curves.

Results: Overall, 84 (12.7%) patients developed NOAF during hospitalization. The LCR was significantly lower in the NOAF group. Preoperative LCR accurately predicted NOAF after AMI and was correlated with increased NOAF risk. Age, body mass index, diabetes, serum albumin levels, uric acid levels, left atrium (LA) diameter, left ventricular ejection fraction, left circumflex artery stenosis > 50%, and Killip class II status were independent predictors of NOAF after AMI. In addition, a new nomogram combined with LCR was constructed to stratify the risk of NOAF in patients with AMI. The performance of the new nomogram was satisfactory, as shown by the receiver operating characteristic curve, calibration curve, decision curve analysis and clinical impact curve.

Conclusion: Preoperative LCR was an independent predictor of NOAF in patients with AMI after PCI. The novel nomogram combined with LCR could rapidly and individually identify and treat patients at a high risk of NOAF.

Keywords: C-reactive protein, acute myocardial infarction, atrial fibrillation, nomogram, left ventricular ejection fraction

Introduction

Atrial fibrillation (AF) is among the most common clinical arrhythmias, and new-onset atrial fibrillation (NOAF) is the most common complication after acute myocardial infarction (AMI), with an incidence rate of 6–21%.¹ NOAF increases in-hospital mortality and is associated with poor long-term prognosis.^{2,3} Although many factors play a role in the occurrence and development of NOAF, the exact mechanisms remain unclear.^{4,5} Therefore, early identification of AMI patients who are at a higher risk of developing NOAF is critical.

The lymphocyte to C-reactive protein ratio (LCR) is a recognized marker reflecting a systemic inflammatory state, and it has been identified as a novel prognostic indicator for gastric cancer,⁶ hepatocellular carcinoma,⁷ intrahepatic cholangiocarcinoma,⁸ gallbladder cancer,⁹ and colorectal cancer.¹⁰ It can also effectively predict the mortality rate of

hemodialysis patients.¹¹ Recent studies have revealed LCR as a potential independent predictor of poor prognosis in ST-segment elevation myocardial infarction (STEMI) patients after percutaneous coronary intervention (PCI).¹² This suggests that the relationship between lymphocytes and C-reactive protein is beginning to be evaluated as a marker of inflammation in cardiovascular events. Inflammation plays a crucial role in the occurrence and development of NOAF.¹³ Systemic immune- inflammation index¹⁴ and systemic inflammatory response index¹⁵ have been shown to be associated with the development of AF. The novel inflammatory marker fibrinogen- to-albumin ratio can also predict NOAF after PCI in patients with AMI.¹⁶ However, to the best of our knowledge, the value of LCR in predicting NOAF in AMI patients after PCI has not yet been studied.

Therefore, this study aimed to evaluate the value of LCR in predicting NOAF in AMI patients after PCI. Additionally, we developed a simple nomogram for clinicians to better predict the incidence of NOAF in AMI patients and optimize their clinical management.

Materials and Methods

Study Population

This single-center, retrospective study was performed at the Zhejiang Provincial People's Hospital (Hangzhou, China). We included 755 AMI patients without a history of AF who had undergone PCI at Zhejiang Provincial People's Hospital between January 2019 and January 2021. The included AMI patients met the diagnostic criteria of AMI set by the European College of Cardiology/American College of Cardiology.^{17,18} We excluded the following participants: (1) age < 18 years; (2) congenital heart disease or severe valvular heart disease; (3) severe liver insufficiency; (4) end-stage renal disease (estimated glomerular filtration rate [eGFR] < 15 mL/min/1.73 m²); (5) malignant tumor, severe infection, or hematological disease; (6) death during hospitalization; and (7) lack of data. Finally, 662 patients were included in the analysis (Figure 1).

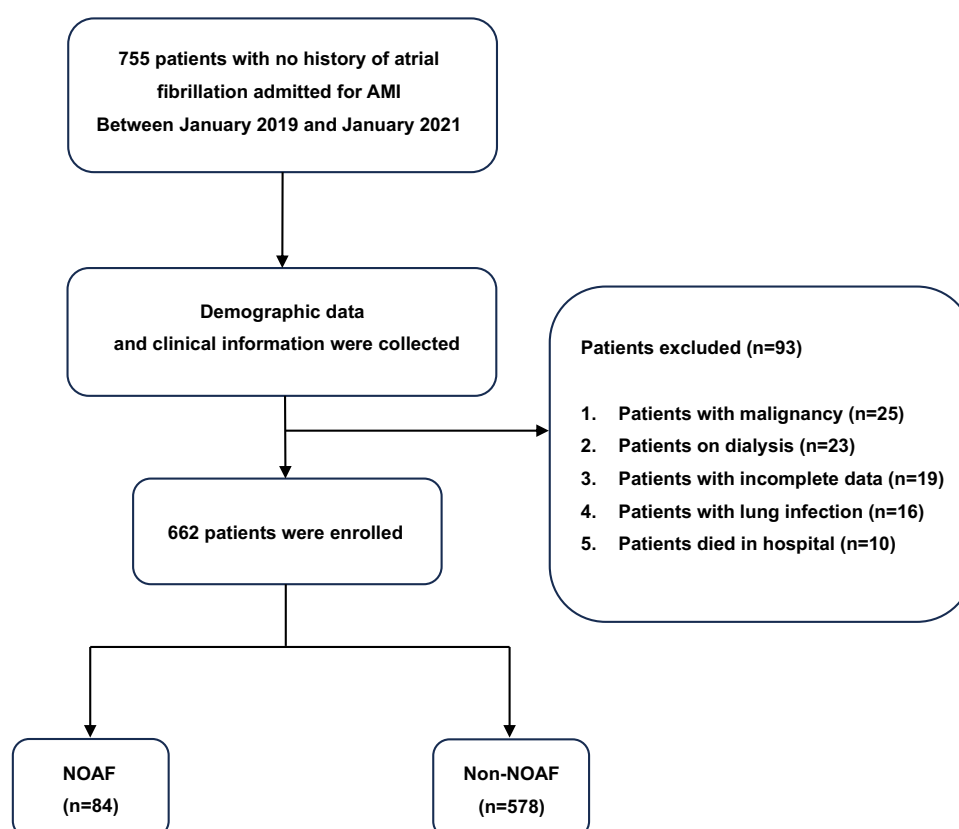


Figure 1 Flow chart of the study population.

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation.

Definitions

NOAF was defined as a type of AF that occurred during postoperative hospitalization in patients without a previous history of AF. It was defined using AF episodes (≥ 30 seconds in duration) that were recorded using continuous telemetry, 12-lead electrocardiogram (ECG), or Holter monitoring throughout the duration of hospitalization. Further, LCR was defined as the lymphocyte count/C-reactive protein count in laboratory tests performed on the day of admission. Body mass index (BMI) was defined as weight (kg) divided by the square of the height (m). Coronary artery stenosis was defined as coronary angiography showing $\geq 50\%$ stenosis of any coronary artery (including the left main artery, left anterior descending branch, left circumflex branch, and right coronary artery). The Killip class was defined as follows: class I, no signs of heart failure; class II, the lungs had rales, but the scope of the rales was less than 1/2 the lung field; class III, the range of pulmonary rales was greater than 1/2 the lung field; and class IV, cardiogenic shock with varying degrees of hemodynamic change.¹⁹

Data Collection

The following clinical information was obtained from the patient's medical records: demographic data (age, sex, height, weight, BMI, heart rate, systolic blood pressure, diastolic blood pressure, current smoking and drinking status, and drug use); laboratory test results on the day of admission (leukocytes, neutrophils, monocytes, lymphocytes, C-reactive protein, LCR, platelets, red blood cells, hemoglobin, serum albumin, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, uric acid, eGFR, B-type natriuretic peptide [BNP], and cardiac troponin I [cTnI]); presence of comorbidities (hypertension, diabetes, history of stroke, history of coronary heart disease, and chronic obstructive pulmonary disease [COPD]); echocardiographic results (left atrium [LA] diameter and left ventricular ejection fraction [LVEF]); AMI type; coronary artery stenosis type; and Killip class. NOAF was recorded using continuous telemetry, ECG, or dynamic electrocardiography during postoperative hospitalization.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (version 25.0; SPSS Inc., Chicago, IL, USA) and R version 4.1.0 (The R Project for Statistical Computing, Vienna, Austria). GraphPad Prism (version 8.0.0) was used to create the graphics. The Kolmogorov–Smirnov test was used to evaluate the normality of the distribution for continuous variables, and those with a normal distribution were described as mean \pm standard deviation and analyzed by Student's *t*-test. Continuous variables with non-normal distributions were described as median (interquartile range [IQR]) and analyzed using the Mann–Whitney *U*-test. The classified variables were described as frequency (percentage) and analyzed by the χ^2 test or Fisher's exact test. Univariate and multivariate logistic regression models were used to determine the relationship between the variables and NOAF. Potential risk factors determined by the univariate analysis were tested using multicollinearity analysis. For variables with tolerances < 0.2 or a variance inflation factor (VIF) > 5 , more meaningful variables were incorporated into multivariate analysis according to experience to determine the independent risk factors related to NOAF after AMI. Furthermore, we divided the LCR levels into quartiles and performed the Mantel–Haenszel χ^2 test to evaluate whether the relationship between LCR levels and the incidence of NOAF was linear. Pearson's correlation coefficient was used to analyze the correlation between the two variables. Through logical regression analysis, the median value of the quartile was used as a quasi-continuous variable to calculate the P-value of the trend. The receiver operating characteristic (ROC) curve was used to determine the predictive performance of LCR for NOAF after AMI. We further evaluated the predictive performance of LCR using a subgroup analysis of AMI.

In this study, R version 4.1.0 was used to construct the novel nomogram. The ROC curve analysis was used to evaluate the predictive ability of the nomogram. The consistency between actual and predicted probabilities was evaluated using a calibration curve. Decision curve analysis (DCA) and clinical impact curves (CICs) were used to evaluate the clinical practicability of the novel nomograms. All statistical analyses were two-tailed with 95% confidence intervals (CI). A two-tailed P-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

The baseline data of all the patients are summarized in Table 1. A total of 662 AMI patients with no history of AF were included in this study, including 325 (49.1%) patients with STEMI and 337 (50.9%) patients without STEMI. Eighty-four (12.7%) patients developed NOAF during hospitalization, whereas 578 (87.3%) patients did not. Killip class > II was

Table 1 Patients Characteristics

Variables	NOAF n=84	Non-NOAF n=578	P-value
Demographic characteristics			
Age (years)	74.56 ± 11.04	60.55 ± 12.16	< 0.001
Male, n (%)	61 (72.6%)	466 (80.6%)	0.089
Weight (kg)	59.56 ± 11.05	68.52 ± 11.32	< 0.001
Height (cm)	165.19 ± 7.46	166.67 ± 7.02	0.085
BMI (kg/m ²)	21.71 ± 2.97	24.59 ± 3.32	< 0.001
Current smoker, n (%)	34 (40.5%)	256 (44.3%)	0.510
Current drinker, n (%)	20 (23.8%)	194 (33.6%)	0.074
Vital signs at admission			
Heart rate (bpm)	84.50 (75.00–97.50)	79.00 (70.00–89.00)	0.003
SBP (mmHg)	133.11 ± 27.06	141.02 ± 25.15	0.008
DBP (mmHg)	77.63 ± 14.54	84.80 ± 17.88	< 0.001
Comorbidities			
Hypertension, n (%)	58 (69.0%)	352 (60.9%)	0.151
Diabetes, n (%)	35 (41.7%)	144 (24.9%)	0.001
Coronary heart disease, n (%)	16 (19.0%)	70 (12.1%)	0.077
COPD, n (%)	4 (4.8%)	6 (1.0%)	0.033
Stroke, n (%)	9 (10.7%)	38 (6.6%)	0.167
Medications			
ACEI/ARB, n (%)	20 (23.8%)	140 (24.2%)	0.934
Beta-blocker, n (%)	6 (7.1%)	28 (4.8%)	0.530
Statin, n (%)	7 (8.3%)	54 (9.3%)	0.765
Laboratory findings			
WBC (10 ⁹ /L)	9.67 (7.02–11.53)	8.80 (7.09–11.44)	0.304
Lym (10 ⁹ /L)	1.10 (0.80–1.50)	1.59 (1.10–2.20)	< 0.001
Hs-CRP (mg/L)	10.25 (3.03–39.35)	3.10 (1.30–9.33)	< 0.001
LCR	0.10 (0.03–0.30)	0.50 (0.17–1.42)	< 0.001
Mon (10 ⁹ /L)	0.50 (0.33–0.60)	0.50 (0.35–0.60)	0.633
Neu (10 ⁹ /L)	7.65 (4.90–9.82)	6.12 (4.68–8.83)	0.036
RBC (10 ¹² /L)	4.13 ± 0.68	4.58 ± 0.60	< 0.001
Hb (g/L)	127.26 ± 22.87	142.72 ± 19.14	< 0.001
PLT (10 ⁹ /L)	188.50 (141.00–243.00)	192.00 (157.75–233.00)	0.258
Serum albumin (g/L)	34.26 ± 4.26	37.35 ± 3.36	< 0.001
TC (mmol/L)	4.17 ± 1.40	4.66 ± 1.23	0.001
TG (mmol/L)	1.07 (0.85–1.50)	1.38 (1.03–2.18)	< 0.001
HDL-C (mmol/L)	0.98 (0.84–1.12)	0.97 (0.83–1.14)	0.862
LDL-C (mmol/L)	2.34 (1.77–2.85)	2.74 (2.17–3.29)	< 0.001
Scr (umol/L)	95.85 (82.90–112.28)	81.60 (72.88–92.85)	< 0.001
Uric acid (umol/L)	389.50 (327.50–477.00)	355.00 (287.75–422.00)	0.001
eGFR (mL/min×1.73 m ²)	61.95 ± 22.38	78.07 ± 22.33	< 0.001
BNP (pg/mL)	551.15 (206.93–1278.65)	112.00 (48.18–243.20)	< 0.001
cTnl (ug/L)	2.50 (0.46–13.77)	1.47 (0.19–9.06)	0.069

(Continued)

Table I (Continued).

Variables	NOAF n=84	Non-NOAF n=578	P-value
Echocardiography results			
LA diameter (mm)	40.75 ± 5.31	37.45 ± 4.66	< 0.001
LVEF (%)	50.50 (42.25–58.00)	60.00 (55.00–64.00)	< 0.001
Type of AMI, n (%)			
STEMI	49 (58.3%)	276 (47.8%)	0.07
NSTEMI	35 (41.7%)	302 (52.2%)	0.07
Coronary artery stenosis > 50%, n (%)			
Left main	4 (4.8%)	44 (7.6%)	0.347
Left circumflex	74 (88.1%)	438 (75.8%)	0.012
LAD	52 (61.9%)	286 (49.5%)	0.033
RCA	57 (67.9%)	332 (57.4%)	0.07
Killip class > II, n (%)	31 (36.9%)	20 (3.5%)	< 0.001

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; BMI, body mass index; bpm, beats per minute; SBP, systolic blood pressure; DBP, diastolic blood pressure; RBC, red blood cell; WBC, white blood cell; Lym, lymphocyte; Mon, monocyte; Neu, neutrophil; Hb, hemoglobin; Plt, platelet; Hs-CRP, high-sensitivity C-reactive protein; LCR, lymphocyte to high-sensitivity C-reactive protein ratio; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Scr, serum creatinine; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; LA, left atrium; LVEF, left ventricular ejection fraction; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; LAD, left anterior descending artery; RCA, right coronary artery.

found in 31 patients (36.9%) in the NOAF group and in only 20 patients (3.5%) in the non-NOAF group ($P < 0.05$). There were 35 (41.7%) patients with diabetes and 4 (4.8%) patients with COPD in the NOAF group and 144 (24.9%) and 6 (1.0%) patients in the non-NOAF group, respectively. In the NOAF group, 74 patients (88.1%) had left circumflex artery stenosis > 50% and 52 patients (61.9%) had left anterior descending artery stenosis > 50%, while in the non-NOAF group, there were 438 patients (75.8%) and 286 patients (49.5%) respectively. Moreover, compared to patients in the non-NOAF group, those in the NOAF group were older; had a faster heart rate; had a larger LA diameter; and had higher levels of neutrophils, high-sensitivity C-reactive protein, serum creatinine, uric acid, and BNP ($P < 0.05$). Body weight, BMI, systolic blood pressure, diastolic blood pressure, lymphocyte and red blood cell counts, LCR, hemoglobin, serum albumin, total cholesterol, triglyceride, low-density lipoprotein cholesterol, eGFR, and LVEF were lower in the NOAF group than that in the non-NOAF group ($P < 0.05$). There were no statistically significant differences between the two groups with respect to sex, height, current smoking or drinking status, history of hypertension, stroke, coronary heart disease, current medication, white blood cells, neutrophils, platelet count, high-density lipoprotein cholesterol, cTnI, AMI type, or the proportion of patients with left main and right coronary artery stenosis > 50%.

Clinical Predictors of NOAF After AMI

The test variables were included in the univariate logistic regression analysis, and a multicollinearity analysis was performed. The results are shown in Table 2. The risk of NOAF was associated with a higher prevalence of type 2 diabetes (odds ratio [OR] = 2.153, 95% confidence interval [CI]: 1.342–3.455, $P < 0.001$) and COPD (OR = 4.767, 95% CI: 1.317–17.258, $P = 0.017$). Moreover, the risk of NOAF in patients with left circumflex artery stenosis > 50% (OR = 2.365, 95% CI: 1.190–4.703, $P = 0.014$), left anterior descending artery stenosis > 50% (OR = 1.659, 95% CI: 1.037–2.653, $P = 0.035$), and Killip class > II (OR = 16.319, 95% CI: 8.702–30.603, $P < 0.001$) was higher than that of patients with left circumflex artery stenosis ≤ 50%, left anterior descending artery stenosis ≤ 50%, and Killip class ≤ II, respectively. Further, continuous variables such as age, BMI, heart rate, systolic blood pressure, diastolic blood pressure, LCR, neutrophil count, red blood cell count, hemoglobin, albumin, total cholesterol, triglyceride, low-density lipoprotein cholesterol, serum creatinine, uric acid, eGFR, BNP, LA diameter, and LVEF were potential clinical predictors of NOAF after AMI. Multicollinearity analysis revealed multicollinearity between red blood cells and hemoglobin and between

Table 2 Potential Clinical Predictors for NOAF After AMI

Predictors	Univariate Analysis			Multicollinearity Analysis	
	OR	95% CI	P-value	Tolerance	VIF
Age (years)	1.107	1.081–1.134	< 0.001	0.375	2.667
BMI (kg/m ²)	0.734	0.673–0.801	< 0.001	0.607	1.648
Heart rate (bpm)	1.022	1.009–1.035	0.001	0.735	1.361
SBP (mmHg)	0.987	0.978–0.997	0.008	0.438	2.285
DBP (mmHg)	0.975	0.961–0.989	0.001	0.395	2.529
Diabetes, n (%)	2.153	1.342–3.455	0.001	0.849	1.178
COPD, n (%)	4.767	1.317–17.258	0.017	0.926	1.080
LCR	0.214	0.113–0.405	< 0.001	0.880	1.136
Neu (10 ⁹ /L)	1.077	1.008–1.151	0.029	0.822	1.217
RBC (10 ¹² /L)	0.313	0.214–0.459	< 0.001	0.141	7.094
Hb (g/L)	0.964	0.953–0.975	< 0.001	0.134	7.481
Serum albumin (g/L)	0.797	0.745–0.852	< 0.001	0.617	1.620
TC (mmol/L)	0.694	0.560–0.859	0.001	0.109	9.144
TG (mmol/L)	0.437	0.292–0.653	< 0.001	0.420	2.379
LDL-C (mmol/L)	0.689	0.531–0.896	0.005	0.125	7.987
Scr (umol/L)	1.020	1.012–1.028	< 0.001	0.476	2.102
Uric acid (umol/L)	1.004	1.002–1.006	< 0.001	0.674	1.483
eGFR (mL/min×1.73 m ²)	0.969	0.959–0.980	< 0.001	0.399	2.506
BNP (pg/mL)	1.002	1.001–1.002	< 0.001	0.522	1.926
LA diameter (mm)	1.148	1.094–1.205	< 0.001	0.794	1.259
LVEF (%)	0.924	0.903–0.946	< 0.001	0.747	1.338
Left circumflex artery stenosis > 50%, n (%)	2.365	1.190–4.703	0.014	0.892	1.121
Left anterior descending artery stenosis > 50%, n (%)	1.659	1.037–2.653	0.035	0.905	1.105
Killip class > II, n (%)	16.319	8.702–30.603	< 0.001	0.755	1.325

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; BMI, body mass index; bpm, beats per minute; SBP, systolic blood pressure; DBP, diastolic blood pressure; RBC, red blood cell; Neu, neutrophil; Hb, hemoglobin; LCR, lymphocyte to C-reactive protein ratio; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; Scr, serum creatinine; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; LA, left atrium; LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; OR, odds ratio; CI, confidence interval; VIF, variance inflation factor.

total cholesterol and low-density lipoprotein cholesterol (tolerance < 0.200, VIF > 5). Therefore, we selected hemoglobin, low-density lipoprotein cholesterol, and other variables for the multivariate analysis. After adjusting for confounding factors, we found that a lower LCR was an important independent risk factor for NOAF after AMI (OR = 0.470, 95% CI: 0.234–0.942, P = 0.033). Simultaneously, multivariate analysis revealed other important predictors as follows: age (OR = 1.081, 95% CI: 1.038–1.127, P < 0.001), BMI (OR = 0.751, 95% CI: 0.661–0.852, P < 0.001), diabetes (OR = 2.406, 95% CI: 1.144–5.059, P = 0.021), serum albumin (OR = 0.888, 95% CI: 0.801–0.985, P=0.024), uric acid (OR = 1.007, 95% CI: 1.003–1.010, P < 0.001), LA diameter (OR = 1.234, 95% CI: 1.144–1.332, P < 0.001), LVEF (OR = 0.966, 95% CI: 0.934–0.999, P = 0.045), left circumflex artery stenosis > 50% (OR = 5.564, 95% CI: 1.794–17.257, P = 0.003), and Killip class > II (OR = 5.052, 95% CI: 1.909–13.371, P = 0.001) (Table 3).

LCR: A Good Predictor of NOAF After AMI

The ROC curve of LCR (Figure 2) could accurately predict the occurrence of NOAF after AMI (area under the curve [AUC] =0.756, 95% CI: 0.703–0.808). An LCR < 0.197 could distinguish patients at risk for NOAF with a sensitivity of 67.9% and specificity of 73.7% (maximum Youden index J, 0.416). Furthermore, its predictive ability was better than that of lymphocytes (AUC=0.698, 95% CI: 0.638–0.757) and CRP (AUC=0.712, 95% CI: 0.656–0.768) (Figure 2). Simultaneously, according to the AMI type, we analyzed the ROC curves of the two subgroups (Figure 3). Notably, LCR exhibited consistently good predictive performance in both the subgroups: AUC=0.786 (95% CI: 0.720–0.852) in the STEMI subgroup and AUC=0.735

Table 3 Independent Clinical Predictors for NOAF After AMI

Predictors	Multivariate Analysis		
	OR	95% CI	P-value
Age (years)	1.081	1.038–1.127	< 0.001
BMI (kg/m ²)	0.751	0.661–0.852	< 0.001
Diabetes, n (%)	2.406	1.144–5.059	0.021
LCR	0.470	0.234–0.942	0.033
Serum albumin (g/L)	0.888	0.801–0.985	0.024
Uric acid (umol/L)	1.007	1.003–1.010	< 0.001
LA diameter (mm)	1.234	1.144–1.332	< 0.001
LVEF (%)	0.966	0.934–0.999	0.045
Left circumflex artery stenosis > 50%, n (%)	5.564	1.794–17.257	0.003
Killip class > II, n (%)	5.052	1.909–13.371	0.001

Abbreviations: AMI, acute myocardial infarction; NOAF, new-onset atrial fibrillation; BMI, body mass index; LCR, lymphocyte to C-reactive protein ratio; LA, left atrium; LVEF, left ventricular ejection fraction; OR, odds ratio; CI, confidence interval.

(95% CI: 0.648–0.822) in the NSTEMI subgroup. We then divided LCR levels into quartiles to evaluate whether there was a linear relationship between LCR levels and the incidence of NOAF after AMI. The incidence was 3.0% in patients with an LCR > 1.207, 6.0% in patients with an LCR of 0.434–1.207, 14.5% in patients with an LCR of 0.137–0.434, and 27.3% in patients with an LCR < 0.137 (trend, $P < 0.001$), which was consistent with our assumption that LCR levels are associated with

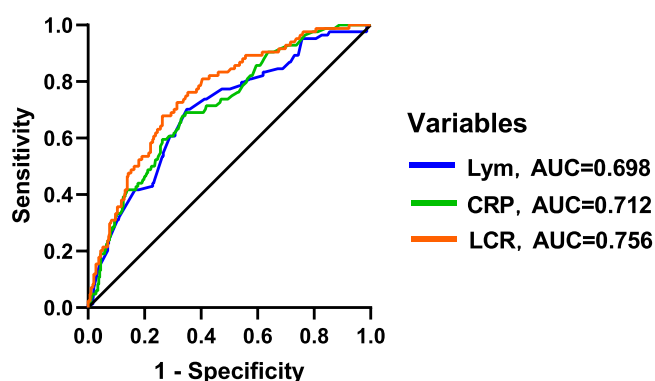


Figure 2 Receiver operating characteristic (ROC) curves of lymphocyte to C-reactive protein ratio (LCR), C-reactive protein (CRP) and lymphocyte (Lym).
Abbreviation: AUC, area under curve.

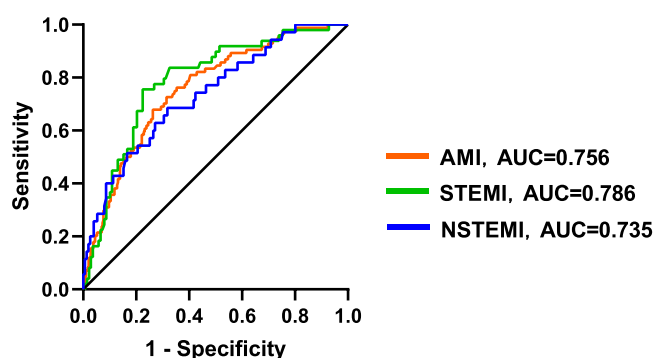


Figure 3 Receiver operating characteristic (ROC) curves of each subgroup of acute myocardial infarction (AMI).
Abbreviations: STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; AUC, area under curve.

an increased risk of NOAF (Table S1). Moreover, the Mantel–Haenszel χ^2 test revealed a linear relationship between the two parameters, $\chi^2 = 49.010$ ($P < 0.001$). Graphics were used to visualize the results, as shown in Figure S1. Pearson's correlation analysis revealed a decrease in the incidence of NOAF with an increase in LCR ($R = -0.272$, $P < 0.001$).

Nomogram for NOAF After AMI

In our study, age, BMI, diabetes, LCR, serum albumin, uric acid, LA diameter, LVEF, left circumflex artery stenosis $> 50\%$, and Killip class $> II$ were important predictors of NOAF after AMI (Table 3), and they were combined to construct a novel nomogram (Figure 4). The ROC curve was used to evaluate the performance of the model, and the AUC of the nomogram was 0.909 (95% CI: 0.875–0.944), indicating a good predictive performance (Figure 5). The calibration curve revealed a high fit between the predicted and observed risks of NOAF, with an average absolute error of 0.008 (Figure 6). DCA revealed that under the threshold probability of the main cohort, a greater net benefit could be obtained when using the predictive model to make clinical decisions, indicating the clinical practicability of the novel nomogram (Figure 7). Similarly, CIC confirmed that the predictive model had a high clinical efficacy rate (Figure 8).

Discussion

Our study analyzed the potential independent risk predictors of NOAF in 662 AMI patients treated with PCI at the Zhejiang Provincial People's Hospital (Hangzhou, China). After adjusting for the confounding factors, we found that age, BMI, diabetes, LCR, serum albumin levels, uric acid levels, LA diameter, LVEF, left circumflex artery stenosis $> 50\%$, and Killip class $> II$ (Table 3) were independently associated with NOAF in AMI patients. Among them, LCR exhibited a good ability to predict NOAF after AMI (AUC=0.756; 95% CI: 0.703–0.808); in addition, LCR exhibited good predictive ability in the AMI subgroup. Our results also revealed that the incidence of NOAF after AMI decreased with an increase in LCR at admission. Furthermore, we established a novel nomogram including LCR, which performed well in predicting the incidence of NOAF after AMI (AUC=0.909, 95% CI: 0.875–0.944). Calibration curves, DCA, and CICs revealed that our nomogram had excellent clinical effectiveness. To the best of our knowledge, this is the first study to build a nomogram incorporating LCR to predict NOAF in AMI patients.

NOAF is the most common complication after AMI, which prolongs the length of hospital stay and increases the in-hospital mortality of patients, and is also associated with poor long-term prognosis.^{2,3} The prevalence of NOAF in AMI

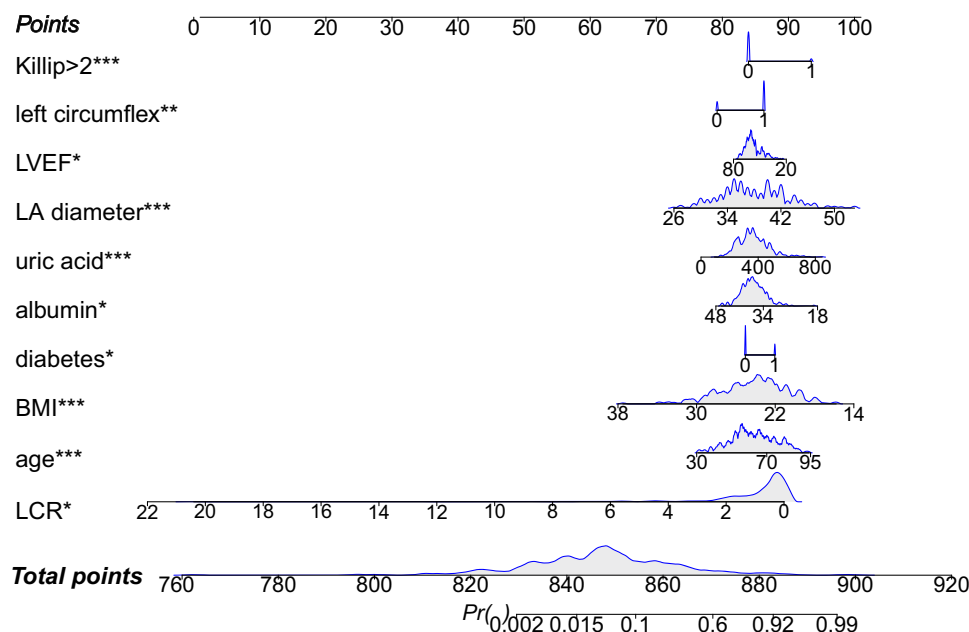


Figure 4 Nomogram for calculating risk score and predicting the incidence of new-onset atrial fibrillation (NOAF) in acute myocardial infarction (AMI) patients. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ with significant difference.

Abbreviations: BMI, body mass index; LCR, lymphocyte to C-reactive protein ratio; LA, left atrium; LVEF, left ventricular ejection fraction.

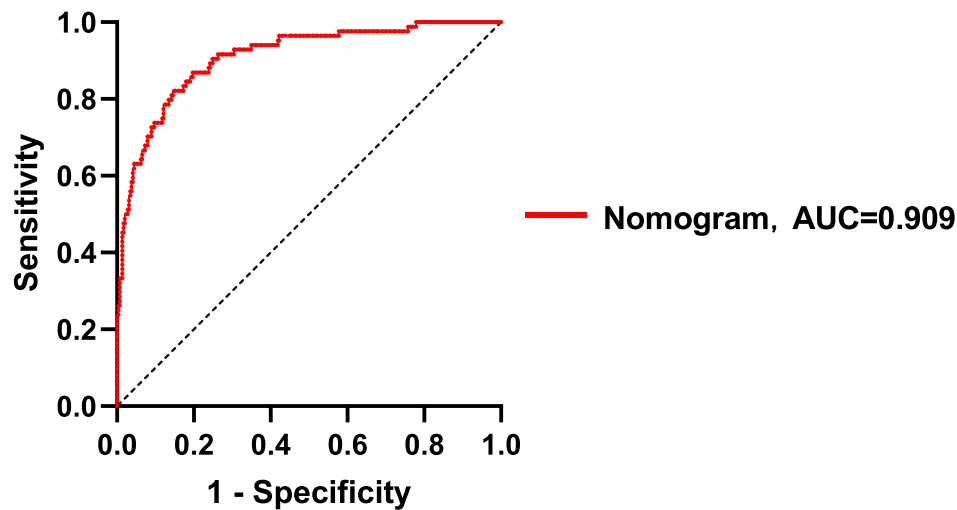


Figure 5 Receiver operating characteristic (ROC) curve for the nomogram to predict the incidence of new-onset atrial fibrillation (NOAF) in patients with acute myocardial infarction (AMI).

Abbreviation: AUC, area under curve.

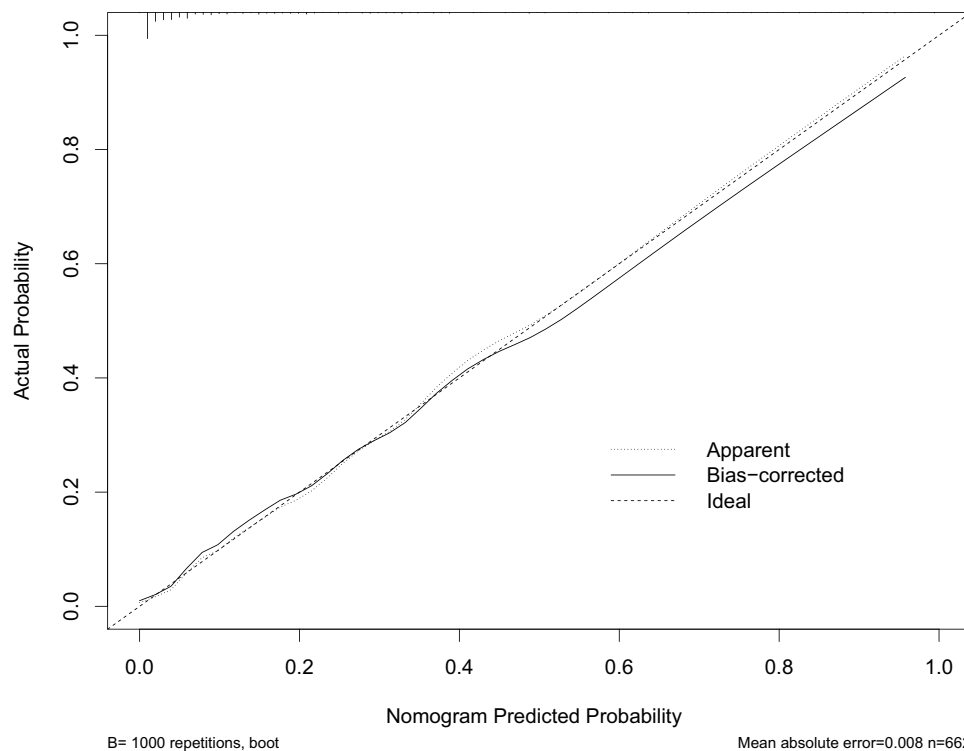


Figure 6 Calibration curve for the nomogram to predict the incidence of new-onset atrial fibrillation (NOAF) in patients with acute myocardial infarction (AMI).

patients is approximately 6–21%.¹ In our study, approximately 12.7% of AMI patients developed NOAF, which was consistent with previous research results.

Previous studies have found that the incidence of AF increases with age, and that advanced age is a clear risk factor for AF.²⁰ Other studies have found that older age is associated with an increased risk of NOAF in AMI patients,²¹ which aligns with the findings of our study.

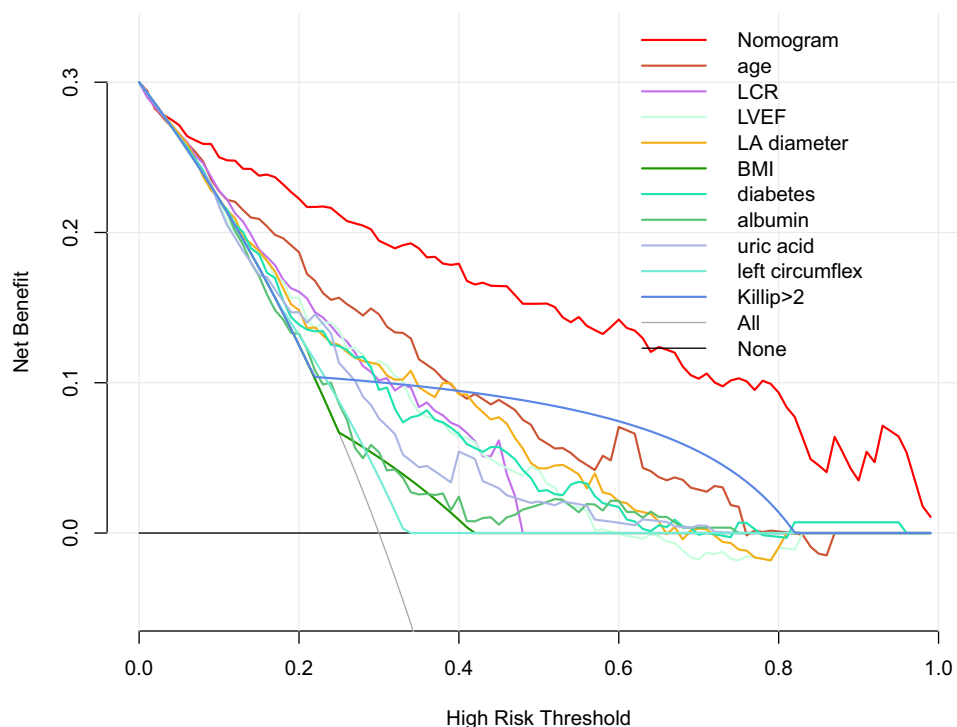


Figure 7 Decision curve analysis (DCA) for the incidence of new-onset atrial fibrillation (NOAF) in patients with acute myocardial infarction (AMI), demonstrating the net benefit of using the nomogram.

Abbreviations: LCR, lymphocyte to C-reactive protein ratio; LVEF, left ventricular ejection fraction; LA, left atrium; BMI, body mass index.

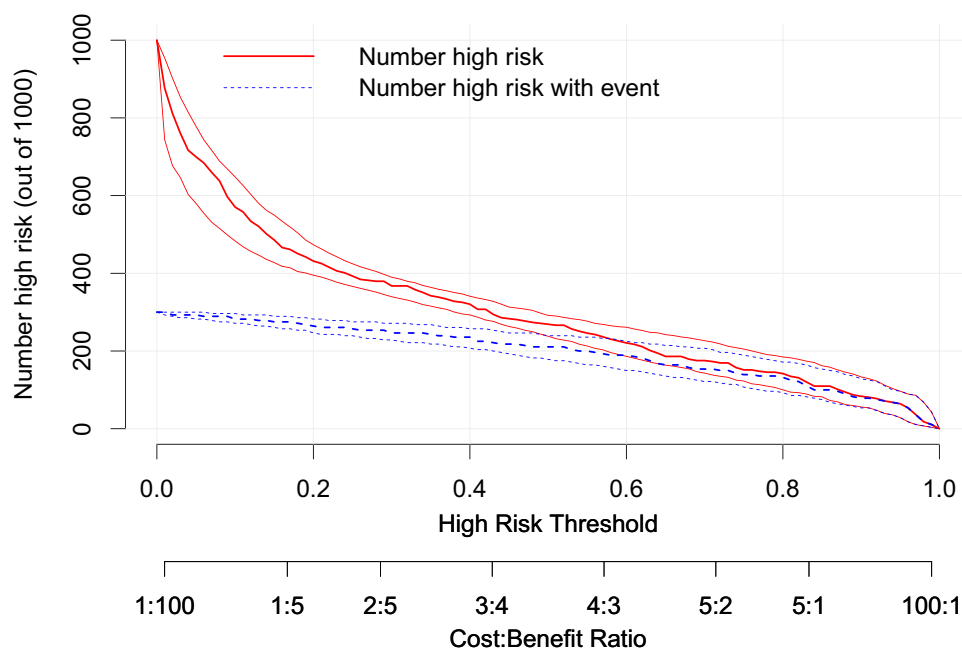


Figure 8 Clinical impact curve (CIC) for the incidence of new-onset atrial fibrillation (NOAF) in patients with acute myocardial infarction (AMI), demonstrating the net benefit of using the nomogram.

BMI is an important standard used internationally to measure the degree of obesity in humans. Numerous studies have shown that elevated BMI is associated with an increased short- and long-term risk of developing AF, both in healthy populations and in patients with diabetes.^{22–25} However, some studies have concluded that in patients with advanced heart failure, obesity is not only associated with increased mortality but may also be associated with higher survival rates.²⁶ Among patients with stable coronary artery disease and those with acute coronary syndrome undergoing PCI, patients who are obese may have a more favorable prognosis.^{27,28} In a cohort study, Liu et al²⁹ found a negative correlation between BMI and NOAF after AMI; that is, a lower BMI was associated with a higher risk of NOAF. Our results also support this “obesity paradox”.

It is well known that diabetes is significantly associated with a higher risk of developing AF,^{30,31} and the risk of developing AF increases by 3% for each additional year of treatment in patients with diabetes.³² Similar to previous findings, we found that after adjusting for confounding factors, diabetes was still an independent predictor of NOAF in AMI patients, which may be due to hyperglycemia directly reducing parasympathetic activity, resulting in cardiac autonomic neuropathy with relatively high sympathetic nervous system activity.^{33,34} Concurrently, diabetic patients are often complicated by metabolic syndrome, which causes myocardial inflammation, myocardial steatosis, and endothelial dysfunction, resulting in atrial structure and electrical remodeling and eventually, NOAF.³⁵

Serum albumin is a protein that reflects the nutritional status of an individual. Previous studies found that low albumin levels increased the risk of coronary heart disease.³⁶ Other studies have revealed that low albumin levels may be associated with the occurrence and development of AF.³⁷ A recent meta-analysis found a negative linear relationship between serum albumin levels and the risk of AF,³⁸ which was similar to our results. We clearly recognized the anti-inflammatory properties of albumin. Lower albumin levels may have a negative effect on anti-inflammatory properties and oxidative stress; thus, albumin plays a role in the occurrence and development of NOAF.³⁹

Increasing studies have found that there is an association between uric acid levels and cardiovascular diseases, including AF.^{40,41} When the baseline uric acid level is low, a slight increase in uric acid level can lead to an increased incidence of AF in women. In men, an increase in uric acid level ($\Delta\text{UA} \geq 0.3$ mg/dL) was significantly associated with the incidence of AF when the baseline uric acid level was ≥ 6.5 mg/dL.⁴² Wang et al found that uric acid level was an independent risk factor for NOAF in older adult patients with acute non-STEMI.⁴³ Similar to the findings of previous studies, we found that after excluding confounding factors such as age, high uric acid levels still promoted the occurrence of NOAF after AMI. Inflammation, oxidative stress, and fibrosis may be the molecular mechanisms of uric acid-induced AF.⁴⁴

Reportedly, LA diameter can be used to predict the occurrence and progression of AF.^{45–47} In our study, LA diameter in the NOAF group was significantly larger than that in the non-NOAF group, which was consistent with the results of a retrospective study by Li et al⁴⁸ in 4713 AMI patients without a history of AF, wherein LA diameter enlargement was significantly associated with increased risk of NOAF even after adjusting for confounding risk factors. The left atrial myocardium is the substrate for the occurrence and maintenance of AF,⁴⁹ however, after progressive expansion and remodeling of the left atrial myocardium, the diameter of the LA increases, which indicates increased susceptibility to AF. Furthermore, LVEF was an independent predictor of NOAF after AMI in this study, which was consistent with previous studies.^{50,51}

In our study, left circumflex artery stenosis $> 50\%$ was an independent risk factor for NOAF after AMI, which has been poorly studied. Kang et al reported in their study that AF was more common in older adult AMI patients with left circumflex artery involvement.⁵² The underlying mechanisms are unclear. When this vessel is large and compromised in its proximal third, it causes probably transient or permanent mitral insufficiency that acutely overloads the LA and I speculate this would be the most probable mechanism for the incidence of NOAF when left circumflex artery stenosis $> 50\%$.⁵³ Moreover, it is plausible that the LA is involved when the left circumflex artery is occluded, and that atrial ischemia may promote the occurrence of AF.⁵⁴ Restoration of the sinus rhythm by reversal of left atrial ischemia has been reported in a patient with NOAF and proximal left circumflex occlusion.⁵⁵ However, the effect of early revascularization on NOAF in AMI patients requires further investigation.

Killip classes are a diagnostic criterion for evaluating cardiac function in AMI patients. Compared with Killip classes I and II, Killip classes III and IV represent worse cardiac function. In our study, Killip class $> \text{II}$ was an independent risk

factor for NOAF, which was consistent with the results of previous studies.^{52,56–58} A higher Killip class may reflect more severe cardiovascular disease in these patients.

The inflammatory response after myocardial infarction is critical for cardiac repair.⁵⁹ However, inflammation also plays an important role in the development and progression of NOAF after myocardial infarction.⁶⁰ Lymphocytes are involved in the inflammatory response during AMI,⁶¹ which reflects the inflammatory response and stress stages of the body. In myocardial infarction, the body is in a state of stress, and elevated levels of catecholamines and cortisol lead to increased lymphocyte apoptosis, resulting in a decrease in lymphocyte count.⁶² Furthermore, decreased lymphocyte count has been associated with poor prognosis in patients with chronic coronary artery disease,⁶³ unstable angina,⁶⁴ and STEMI.⁶⁵ Moreover, CRP, which is a typical inflammatory marker, is involved in the pathogenesis of myocardial infarction. It promotes atherosclerosis and plaque rupture by activating the complement system and inducing endothelial dysfunction, which eventually leads to myocardial infarction.⁶⁶ High CRP levels are reportedly a good predictor of death in patients with acute coronary syndrome.⁶⁷ CRP levels were also identified as useful for predicting NOAF.⁶⁸ Therefore, LCR, which represents the ratio of the lymphocyte count to CRP level, can better reflect the degree of inflammation and the immune status of the body during myocardial infarction. Compared to lymphocytes or CRP alone, LCR can more accurately predict adverse events after PCI in patients with myocardial infarction.¹² However, research on the value of LCR in predicting NOAF after PCI in AMI patients remains limited. We found that a negative correlation between LCR and NOAF after PCI in AMI patients persisted even after adjusting for the influence of confounding factors. In the subgroup analysis, the predictive performance of LCR for NOAF in the STEMI group (AUC = 0.786, 95% CI: 0.720–0.852) was better than that in the NSTEMI group (AUC = 0.735, 95% CI: 0.648–0.822), which may be due to a greater inflammatory response in STEMI.⁶⁹ Additionally, the LCR levels correlated with the risk of NOAF. A lower LCR correlated with a more intense inflammatory response as well as more severe damage to the immune status, and a higher incidence of NOAF.

Nomograms are widely used to predict individual probabilities of clinical events by integrating multiple variables.⁷⁰ In this study, we constructed a novel nomogram combining LCR and nine other risk factors for NOAF. Our nomogram exhibited a high clinical predictive performance and was a practical fit. Furthermore, DCA and CICs revealed greater net benefits and extremely high clinical efficiencies when the predictive model was used to make clinical decisions. The nomogram could identify patients who were truly at a high risk of NOAF and facilitate early intervention in these patients to improve clinical outcomes.

Limitations

First, this was a single-center retrospective study with a small sample size that might not have been representative of the entire population. Therefore, the association between LCR and NOAF after AMI requires further verification in a large multicenter study. Moreover, some patients were not included because of missing data, which resulted in a selection bias. Second, although we adjusted for confounding factors, other factors that were not included, such as myocardial injury markers, might also have played a role. Third, although AMI patients with lower preoperative LCR levels were more likely to develop AF after PCI, we did not explore whether anti-inflammatory therapy could reduce the risk of NOAF in these patients. In the future, anti-inflammatory therapies may be used to explore this relationship in AMI patients. Finally, we did not perform external validation of the nomogram; therefore, external validation is required to determine the applicability of the model to other patient populations.

Conclusion

A low preoperative LCR may be an independent risk factor for NOAF after PCI in AMI patients. Moreover, the novel nomogram constructed in this study exhibited a satisfactory predictive effect for NOAF, which will help develop individualized primary prevention programs for AMI patients.

Ethics Approval and Informed Consent

This study protocol was reviewed and approved by the Institutional Review Committee of the Zhejiang Provincial People's Hospital, registration number: QT2023256. Informed consent was waived due to the retrospective nature of the

study. At the same time, patient data was anonymized or maintained with confidentiality and this study was in line with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the report has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could appear to influence the work reported in this paper.

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