

The Predictive Value of the Monocyte-to-Lymphocyte Ratio and Monocyte-to-Haematocrit Ratio for Cardiac Rupture Patients with Acute Myocardial Infarction: A Propensity Score Matching Analysis

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Background: Cardiac rupture (CR) is a serious complication of acute myocardial infarction (AMI). We aimed to explore the predictive value of blood cell parameters for identifying CR in patients with AMI using the introduction of propensity score matching (PSM).

Methods: This retrospective study enrolled patients who were diagnosed with AMI from January 2013 to May 2020. A total of 109 patients with CR were included, and 327 hospitalized non-CR patients were randomly selected at a 1:3 ratio. Based on the 1:1 nearest neighbour matching method by using SPSS, the covariances of the two groups were balanced. After PSM, the independent risk factors for CR were selected by using multivariate logistic regression analysis, and receiver operating characteristic (ROC) curve analysis was applied to evaluate the predictive value of blood cell parameters for CR. Ninety cases were matched successfully in each of the two groups.

Results: Among the 180 patients with AMI after PSM, the results of multivariate logistic regression analysis showed that the monocyte-to-lymphocyte ratio (MLR) (OR = 3.57, 95% CI: 1.28–9.97, P = 0.015) and monocyte-to-haematocrit ratio (MHR) (OR = 1.80, 95% CI: 1.02–3.20, P = 0.043) were independently related to the risk of CR. Additionally, the MLR (area under the curve (AUC): 0.74) and MHR (AUC: 0.73) were useful for distinguishing CR patients after PSM. To differentiate CR patients from the control subjects, the optimal cut-offs of the MLR and MHR were 0.61 (63% sensitivity and 80% specificity) and 2.06 (57% sensitivity and 81% specificity), respectively.

Conclusion: The blood cell parameters MLR and MHR were independently correlated with CR. Additionally, the MLR and MHR were useful to predict CR in patients with AMI.

Keywords: cardiac rupture, acute myocardial infarction, blood cell parameters, monocyte-to-lymphocyte ratio, inflammatory, monocyte-to-haematocrit ratio

Introduction

With the application of timely reperfusion therapy in patients with acute myocardial infarction (AMI), hospital mortality has decreased significantly. However, cardiac rupture (CR) is still one of the main causes of death in patients with AMI.^{1,2} CR is characterized by sudden onset and rapid progression.³ Therefore, it is of great clinical significance to identify patients with high-risk cardiac rupture early to actively prevent the occurrence of cardiac rupture and improve the prognosis of the patients.⁴

At present, the diagnosis of cardiac rupture is mainly based on clinical symptoms, signs, a combination of Doppler echocardiography and pericardiocentesis, and a lack of early predictive indicators.⁵ Blood cell analysis is a straightforward routine inspection method, and it is also the examination method with the highest utilization rate in clinical work. In recent years, many clinical studies have explored the relationships between various indicators of blood cell parameters and myocardial infarction.^{6,7} However, there is still a lack of research on the relationship between blood cell parameters and CR.

This study aimed to explore the relationship between these various indicators of blood cell parameters at admission and CR and identify the factors that can predict CR in the early stage.

Methods

Study Patients and Design

A retrospective collection of data from patients with AMI that were diagnosed at and admitted to the First Affiliated Hospital of Nanchang University and Jiangxi Provincial People's Hospital Affiliated to Nanchang University from January 2013 to May 2020 were divided into a CR group and a non-CR group. In this study, 109 patients with CR were included, and 327 hospitalized non-CR patients were randomly selected at a 1:3 ratio.

The inclusion criteria were as follows: (1) meeting the diagnostic criteria for AMI according to the definition of ACC/AHA;⁸ and (2) fitting the diagnosis of cardiac rupture (CR),⁹ which is confirmed by two professional cardiologists based on clinical symptoms and Doppler echocardiography or pericardial puncture. The exclusion criteria were as follows: (1) not diagnosed with CR due to AMI; (2) diagnosed with severe infection, liver and kidney disease, malignant tumours and haematological diseases; and (3) without complete clinical data.

Data Collection

The general and hospitalization data of patients who met the requirements of the inclusion criteria were collected. General information included sex, age, previous diabetes, hypertension, stroke, smoking, alcohol consumption and other medical history. Hospitalization data consisted primarily of vital signs, drug use, coronary artery stenosis status, coronary revascularization and routine blood results for the first time after admission. The related indicators of blood cell parameters included white blood cell count (WBC), red blood cell count (RBC), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width (PDW), lymphocyte count (LY), monocyte count (MO), neutrophil count (NE), eosinophil count (EO), basophil count (BA), monocyte-to-lymphocyte ratio (MLR), monocyte-to-haematocrit ratio (MHR), and neutrophil-to-lymphocyte ratio (NLR).

The clinical symptoms of AMI manifest as severe chest pain with troponin elevation, new ischaemic changes on electrocardiogram, abnormal wall motion on Doppler echocardiography, and coronary angiography indicating the existence of thrombus.⁸ The diagnosis of CR was as follows: FWR was defined as the appearance of symptoms and signs of pericardial tamponade, electromechanical separation, a large amount of pericardial effusion and pericardial puncture with noncoagulable fluid; VSR was treated as a rough total systolic murmur with systolic tremor heard in the 4 to 5 intercostal spaces on the left edge of the sternum and a blood stream across the interventricular septum seen on echocardiography; PMR was based on a loud, rough systolic murmur heard at the apex of the heart and a large amount of mitral regurgitation or direct observation of papillary muscle rupture shown on echocardiography. Hypertension was described as systolic blood pressure (SBP) >140 mmHg, diastolic blood pressure (DBP) >90 mmHg without antihypertensive drugs, and/or the use of antihypertensive drugs.⁹ Diabetes mellitus was defined as fasting blood glucose over 7.0 mmol/L and/or the use of antidiabetic drugs.¹⁰ Previous stroke was described as clinical symptoms of a neurological impairment lasting more than 24 hours or a new infarct lesion detected by computed tomography or head magnetic resonance imaging.¹¹

Statistical Analysis

Data analysis of continuous and dichotomous variables was performed using SPSS software (version 25.0 for Windows, SPSS, Inc., Chicago, Illinois). The continuous variables in accordance with the normal distribution and the homogeneity

of variance were expressed as the mean±standard deviation, and the *T* test was applied for comparisons between the two groups. Otherwise, they were presented as median (interquartile range), and Mann–Whitney *U*-test was used for these continuous variables. Dichotomous variables are shown as frequencies (%) and were tested by χ^2 -test or Fisher exact test if necessary. The potential risk factors for CR were analysed by univariate logistic regression analysis. The indices with $P<0.05$ were selected and introduced into multivariate logistic regression analysis to identify the independent risk factors for CR. According to receiver operating characteristic (ROC) curve analysis, the predictive value of blood cell parameter-related indicators for CR was determined. An area under the curve (AUC) >0.70 was regarded as good predictive value. $P<0.05$ was considered to be statistically significant.

Based on the propensity score matching (PSM) method, the clinical baseline data of the two groups were balanced, and the regression model variables included age, sex, previous diabetes mellitus (DM), hypertension, stroke, smoking, alcohol consumption and systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate of the patients after admission. The propensity score of each patient was calculated by the 1:1 nearest matching method, and caliper matching was employed to limit the logarithmic standard deviation of the propensity score to 0.10 to prevent the difference between each pair of matched individuals.

Results

Baseline Patient Characteristics

Among the 436 patients with AMI, the average age of the CR group was 70.20 ± 9.98 years old and that of the non-CR group was 62.35 ± 12.08 years old. This difference was statistically significant ($P<0.001$). In the comparisons between clinical characteristics, the SBP, HR, angiotensin-converting enzyme inhibitor (ACEI)/angiotensin-receptor blocker (ARB) and β -blocker treatment differed between CR patients and controls ($P<0.001$). The patients with CR had a significantly higher percentage of females than the patients in the non-CR group ($P=0.008$). In addition, the proportion of patients with emergency percutaneous coronary intervention (PCI) in the non-CR group was higher than that in the CR group, and the difference was statistically significant ($P<0.001$). Moreover, the results showed that patients in the CR group had a lower DBP and less statin treatment than those in the non-CR group (both $P<0.05$). Regarding previous DM, hypertension, stroke, smoking, drinking and culprit vessels, there were no statistically significant differences between the two groups (all $P>0.05$). Through evaluation by the PSM method, 90 pairs of patients in the two groups were successfully matched. There were no significant differences in the variables after matching, except for emergency PCI and ACEI/ARB treatment (Table 1).

The blood cell parameters of the study participants in the two groups after PSM are shown in Table 2. There were no significant differences between the two groups regarding the levels of MCV, MCH, MCHC, RDW, PLT, MPV, PCT, LY, NE, or BA (all $P>0.05$). The WBC, PDW, MO, MLR, MHR and NLR values were higher in the CR group than in the non-CR group ($P<0.05$). In contrast, compared with the CR group, the RBC, HGB, HCT and EO levels were significantly higher in the non-CR group ($P<0.05$).

The Results of Logistic Regression Analysis After PSM

According to the results of univariable logistic regression analysis after PSM, WBC (OR=1.08, 95% CI: 1.01–1.16, $P=0.035$), RBC (OR=0.52, 95% CI: 0.32–0.85, $P=0.008$), MHR (OR=2.32, 95% CI: 1.58–3.42, $P<0.001$), MLR (OR=6.64, 95% CI: 2.69–16.43, $P<0.001$) and emergency PCI (OR=0.46, 95% CI: 0.25–0.84, $P=0.011$) were risk factors for CR (Table 3). Moreover, the MLR (OR=3.57, 95% CI: 1.28–9.97, $P=0.015$) and MHR (OR=1.80, 95% CI: 1.02–3.20, $P=0.043$) levels were independent risk factors for CR in multivariate logistic regression analysis (Table 3).

The Results of ROC Curve Analysis

In the ROC curve analysis, the effective cut-off point of the MLR was at least 0.61 to predict CR with 64% sensitivity and 87% specificity (AUC=0.80, 95% CI: 0.73–0.87, $P<0.001$) before PSM (Figure 1A). In addition, a meaningful MLR result was also obtained after PSM (AUC=0.74, 95% CI: 0.65–0.83, $P<0.001$), with 63% sensitivity and 80% specificity, and the cut-off was also 0.61 (Figure 1B). Before and after PSM, the AUCs of MHR were 0.78 and 0.73, respectively,

Table 1 Comparison of Baseline Data Between Two Groups Before and After PSM

Factors	Before PSM			After PSM		
	Non-CR (n=327)	CR (n=109)	P-value	Non-CR (n=90)	CR (n=90)	P-value
Age, years	62.35±12.08	70.20±9.98	<0.001	71.03±11.42	70.01±10.09	0.525
Women, n (%)	93 (28.4%)	46 (42.2%)	0.008	35 (38.9%)	36 (40%)	0.879
Hypertension, (%)	180 (55%)	65 (59.6%)	0.403	48 (53.3%)	51 (56.7%)	0.653
DM, n (%)	77 (23.5%)	31 (28.4%)	0.305	20 (22.2%)	22 (24.4%)	0.724
Stroke, n (%)	19 (5.8%)	9 (8.3%)	0.367	3 (3.3%)	5 (5.6%)	0.718
Smoker, n (%)	143 (43.7%)	47 (43.1%)	0.911	37 (41.1%)	39 (43.3%)	0.763
Drinker, n (%)	75 (22.9%)	22 (20.2%)	0.550	13 (14.4%)	19 (21.1%)	0.242
SBP, mmHg	131.32±22.91	118.06±24.78	<0.001	122.83±22.93	119.98±24.88	0.424
DBP, mmHg	73 (65, 82)	70 (60.5, 77.5)	0.014	71 (63, 78)	70 (62, 77)	0.910
HR, beat/min	80 (68, 91)	88.5 (75, 109.5)	<0.001	88 (75, 98)	86 (72, 105)	0.882
ACEI/ARB treatment, n (%)	160 (48.9%)	16 (14.7%)	<0.001	34 (37.8%)	13 (14.4%)	<0.001
β-blocker treatment, n (%)	191 (58.4%)	42 (38.5%)	<0.001	45 (50%)	37 (41.1%)	0.231
Statin treatment, n (%)	321 (98.2%)	102 (93.6%)	0.035	87 (96.7%)	84 (93.3%)	0.494
Culprit vessels			0.236			0.747
LAD, n (%)	168 (51.4%)	35 (32.1%)		40 (44.4%)	29 (32.2%)	
LCX, n (%)	44 (13.5%)	14 (12.8%)		15 (16.7%)	14 (15.6%)	
RCA, n (%)	89 (27.2%)	14 (12.8%)		19 (21.1%)	12 (13.3%)	
Emergency PCI, n (%)	171 (52.3%)	38 (34.9%)	0.002	49 (54.4%)	32 (35.6%)	0.011

Abbreviations: PSM, propensity score matching; DM, diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker; PCI, percutaneous coronary intervention; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery.

Table 2 Comparison of Blood Cell Parameters Between Two Groups After PSM

Variables	Non-CR (n=90)	CR (n=90)	P-value
WBC, ×10 ⁹ /L	9.66 (7.71, 12.95)	11.13 (9.28, 14.09)	0.009
RBC, ×10 ¹² /L	4.25±0.64	3.98±0.65	0.007
HGB, g/L	128.67±19.91	122.57±20.96	0.047
HCT, L/L	0.39±0.06	0.37±0.06	0.035
MCV, fL	91.34±5.47	93±6.56	0.066
MCH, pg	30.35±2.27	30.87±2.56	0.155
MCHC, g/L	332.08±13.88	331.92±13.24	0.939
RDW, %	13.43±1.48	13.46±1.31	0.902
PLT, ×10 ⁹ /L	203.2±66.81	217.61±81.55	0.196
MPV, fL	11.14±1.24	10.73±1.65	0.063
PCT, %	0.23±0.06	0.23±0.08	0.699
PDW, %	13.4 (12, 16)	15.7 (12.7, 16.35)	0.015
LY, ×10 ⁹ /L	1.33 (0.84, 1.82)	1.16 (0.73, 1.50)	0.126
MO, ×10 ⁹ /L	0.45 (0.34, 0.74)	0.8 (0.52, 1.05)	<0.001
NE, ×10 ⁹ /L	7.83 (5.92, 10.55)	8.77 (6.95, 11.99)	0.053
EO, ×10 ⁹ /L	0.03 (0.01, 0.06)	0 (0, 0.03)	0.003
BA, ×10 ⁹ /L	0.02 (0.01, 0.03)	0.01 (0, 0.03)	0.313
MLR	0.41 (0.25, 0.58)	0.75 (0.44, 1.45)	<0.001
MHR, ×10 ⁹ /L	1.24 (0.86, 1.94)	2.20 (1.33, 3.21)	<0.001
NLR	6.42 (3.93, 10.89)	9.25 (5.11, 13.51)	0.025

Abbreviations: PSM, propensity score matching; WBC, white blood cell count; RBC, red blood cell count; HGB, haemoglobin; HCT, haematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; RDW, red blood cell distribution width; PLT, platelet count; MPV, mean platelet volume; PCT, plateletcrit; PDW, platelet distribution width; LY, lymphocyte count; MO, monocyte count; NE, neutrophil count; EO, eosinophil count; BA, basophil count; MLR, monocyte-to-lymphocyte ratio; MHR, monocyte-to-haematocrit ratio; NLR, neutrophil-to-lymphocyte ratio.

Table 3 Predictors of CR in Multivariable Logistic Regression Analysis After PSM

Variables	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
WBC	1.08 (1.01–1.16)	0.035	0.93 (0.83–1.05)	0.228
RBC	0.52 (0.32–0.85)	0.008	0.79 (0.41–1.54)	0.494
PDW	1.01 (0.95–1.07)	0.843	–	–
MHR	2.32 (1.58–3.42)	<0.001	1.80 (1.02–3.20)	0.043
MLR	6.64 (2.69–16.43)	<0.001	3.57 (1.28–9.97)	0.015
NLR	1.03 (0.99–1.07)	0.108	–	–
Emergency PCI	0.46 (0.25–0.84)	0.011	1.02 (0.45–2.33)	0.959

Abbreviations: CR, cardiac rupture; PSM, propensity score matching; WBC, white blood cell count; RBC, red blood cell count; PDW, platelet distribution width; MHR, monocyte-to-haematocrit ratio; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PCI, percutaneous coronary intervention.

which were helpful to distinguish CR patients. In addition, an MHR value >1.66 was identified as an effective cut-off point for CR (69% sensitivity and 76% specificity) before PSM (Figure 2A). The optimal cut-off of MHR was 2.06 (57% sensitivity and 81% specificity) after PSM (Figure 2B).

Discussion

CR is one of the most serious complications of AMI, and it usually occurs suddenly. Moreover, it is difficult to manage by medical and surgical treatment, and it has a high fatality rate.³ We found that among the blood cell parameters, an increase in the MLR and MHR were independently associated with the risk of CR. According to the results of ROC curve analysis, the MLR and MHR were useful to predict CR in patients with AMI.

The MLR and MHR could be new markers that are useful for evaluating CR after combining monocytes and lymphocytes and monocytes and haematocrit, respectively. The use of these parameters combined can provide more cumulative information than each marker alone. Previous studies have shown that a high monocyte count or low lymphocyte count is closely related to adverse cardiovascular events in patients with coronary heart disease.¹²

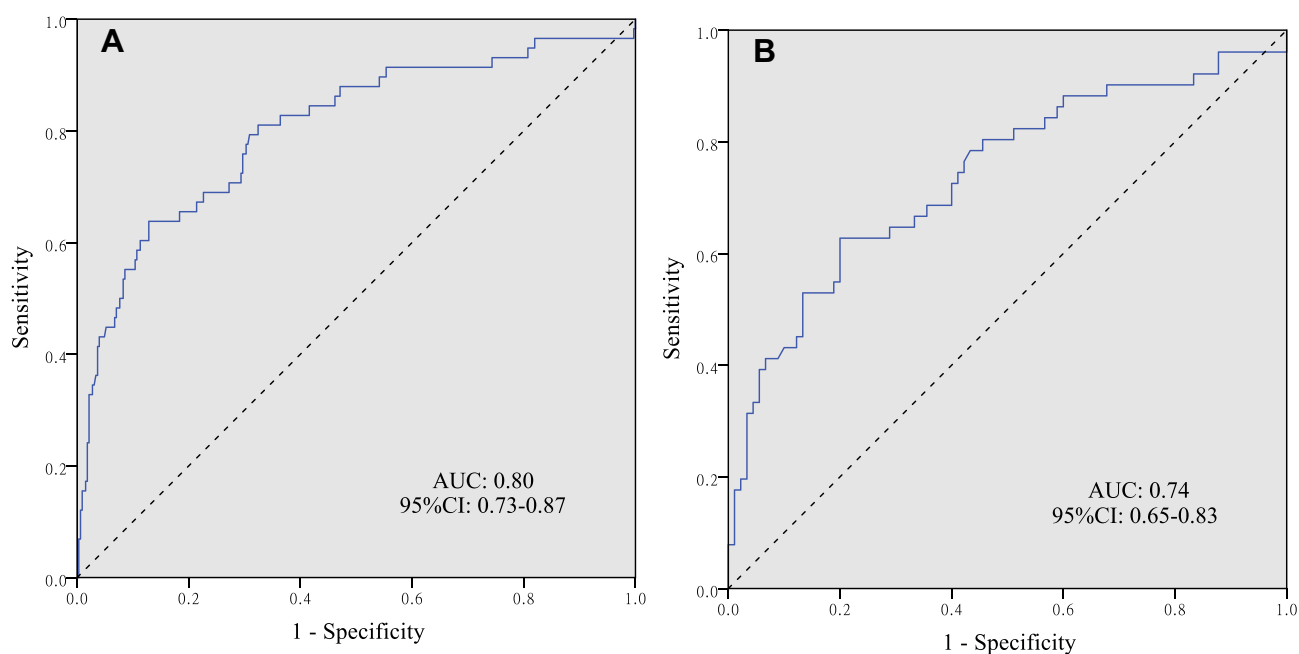


Figure 1 (A) Receiver operating characteristic (ROC) curve of MLR for predicting CR patients with AMI before PSM. (B) Receiver operating characteristic (ROC) curve of MLR for predicting CR patients with AMI after PSM.

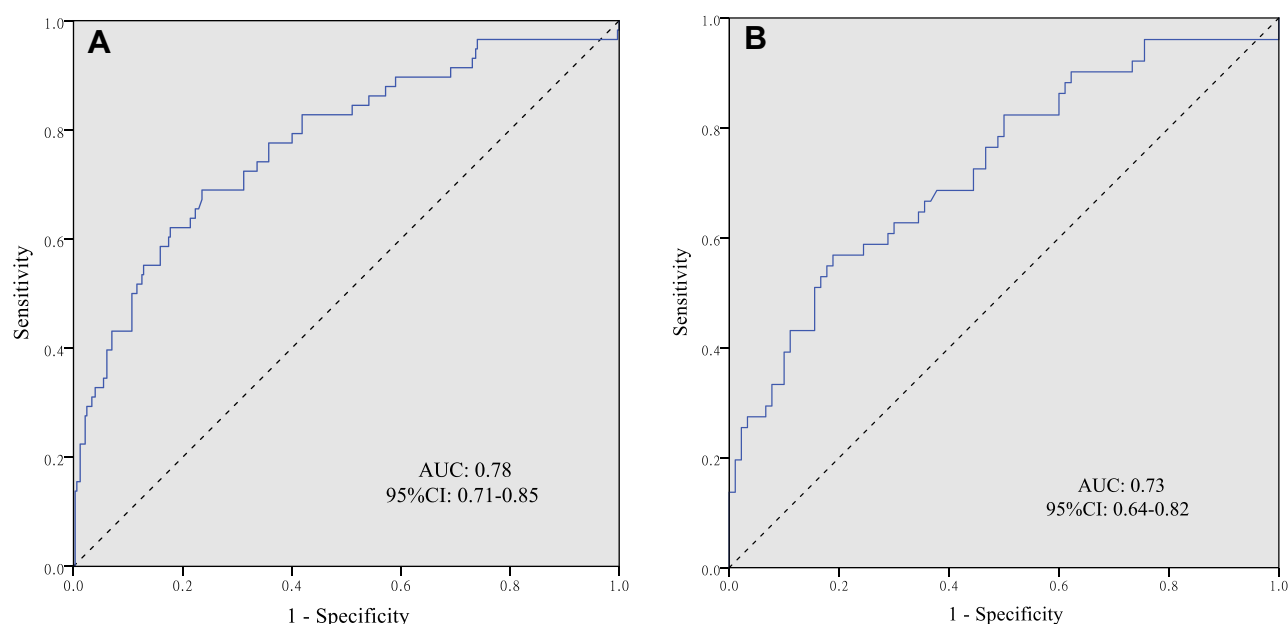


Figure 2 (A) Receiver operating characteristic (ROC) curve of MHR for predicting CR patients with AMI before PSM. (B) Receiver operating characteristic (ROC) curve of MHR for predicting CR patients with AMI after PSM.

Monocytes are the main component of the innate immune system and participate in the process of endogenous inflammation.¹³ Monocytes can migrate from blood to tissue in response to body signals. Then, they can differentiate into inflammatory dendritic cells, macrophages and foam cells, and activate the secretion of proinflammatory cytokines, the production of matrix metalloproteinases and reactive oxidizing substances. This allows for the accumulation of a large number of inflammatory cells that can infiltrate into the infarcted area, which aggravates the damage to myocardial cells in ischaemic area and microcirculation disorders. This then leads to the destruction and dissolution of myocardial cell membrane structure, fibrin cytoskeleton and even cell death.¹⁴ After ischaemic injury, the combination of TNF- α secreted by macrophages and receptors on the cell surface can amplify an inflammatory cascade in the cardiomyocytes of the infarcted area. This can further lead to the activation of transcription factors that aggravate the fragmentation and degradation of the myocardial collagen fibre structure and can even increase the incidence of CR.¹⁵ The level of lymphocytes represents cellular immunity and humoral immunity in the body.¹⁶ In the inflammatory state, the induction and adhesion of chemokines can lead to a large amount of lymphocyte infiltration, and effector T cells are recruited into infarcts to release proinflammatory transmitters. The immune system also produces a group of regulatory T lymphocytes with anti-inflammatory effects.¹⁷ Therefore, the main function of lymphocytes is to inhibit the inflammatory response of the body. Gary found that the MLR increased the risk of severe limb ischaemia and other vascular events in peripheral arterial occlusive disease.¹⁸ A recent study has shown that the MLR is associated with adverse hospital outcomes in patients with ST-elevation myocardial infarction (STEMI) undergoing PCI.¹⁹ Ji's research showed that the MLR can predict the severity of CAD through the SYNTAX score.²⁰ Fan et al reported that a high MLR in AMI patients treated with PCI was independently related to the risk of 6-month death.⁶ In a study of 306 patients, Wang found that the MLR was an independent predictor of major adverse cardiovascular events in STEMI patients.⁷ Patients with low haematocrit levels might be at a high risk of decreased oxygen supply, which could aggravate myocardial necrosis. Toss et al²¹ reported that haematocrit was associated with the risk of myocardial infarction in young Swedish men. Kosiborod's study showed that among anaemic patients with heart failure after myocardial infarction, a decrease in haematocrit is associated with a marked decline in health status.²² In addition, emergency PCI is treated as an effective measure to prevent CR by reducing the area of myocardial infarction at present.^{23–25} In this study, the number of patients with emergency PCI in the non-CR group was markedly higher than that in the CR group. Moreover, in univariable logistic regression analysis, emergency PCI was a protective factor for CR. This study took the lead in exploring the relationship between the MLR,

MHR and CR. The results indicated that the MLR and MHR were independently related to the risks of CR and could be used as effective predictors. Therefore, the MLR and MHR could be useful as conventional, efficient, rapid and inexpensive biomarkers, and they may provide new insights for the screening and treatment of high-risk CR patients.

This study is a retrospective analysis, which has bias in statistics. In addition, due to the small sample size, it is impossible to analyse the types of cardiac rupture in subgroups. Thus, further in-depth and high-quality studies are needed. This study illustrates that the results obtained for the MLR and MHR indicate a possible relationship between inflammatory parameters and CR. It may provide a theoretical reference for front-line clinicians to identify high-risk CR patients early. Furthermore, in addition to the revascularization of culprit arteries as preventive measure, it is available to control inflammation in the development of CR in the future.

Ethical Approval

This research was an anonymous retrospective study, which was approved by the ethics committees of the First Affiliated Hospital of Nanchang University and Jiangxi Provincial People's Hospital Affiliated to Nanchang University. This study was conducted in accordance with the Declaration of Helsinki. And informed consent was waived by the ethics committees due to the retrospective nature of the study. We confirm that the privacy of the participants was preserved, and the data was anonymized and maintained with confidentiality. The patient data accessed complied with relevant data protection and privacy regulations.

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Disclosure

The authors declared that there were no potential conflicts of interest with the research, authorship, and publication of this article.

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