

The predictive value of neutrophil–lymphocyte ratio combined with the Global Registry of Acute Coronary Events score for in-hospital adverse cardiovascular events in patients with acute ST-elevation myocardial infarction

Caoyang Fang^{1,2}, Zhenfei Chen^{1,2}, Jing Zhang², Xiaoqin Jin², Mengsi Yang²

¹Department of Cardiology, Hefei Second People's Hospital Affiliated to Bengbu Medical College, Anhui, Hefei, China, ²Department of Cardiology, The Second People's Hospital of Hefei, Hefei Hospital Affiliated to Anhui Medical University, Hefei, Anhui, China

Background: The research explores the predictive efficacy of the neutrophil-to-lymphocyte ratio (NLR) in conjunction with the Global Registry of Acute Coronary Events (GRACEs) score for in-hospital major adverse cardiovascular events (MACEs) among acute ST-segment elevation myocardial infarction (STEMI) subjects with primary percutaneous coronary intervention (PCI) history. **Materials and Methods:** Patients were categorized into MACE ($n = 58$) and non-MACE cohorts ($n = 184$) based on MACE occurrence events during hospitalization. The predictive value of the NLR, GRACE score, and their combination for in-hospital MACE events in STEMI subjects was assessed by the receiver operating characteristic curve (ROC). **Results:** NLR (8.99 [5.06, 12.01] vs. 5.15 [3.13, 7.66]) and GRACE scores (159.62 ± 43.39 vs. 116.96 ± 28.15) within MACE group notably surpassed the non-MACE group ($P < 0.05$). ROC curve analysis demonstrated that the area under the curve (AUC) for NLR in forecasting in-hospital MACE events was 0.72 (95% confidence interval [CI]: 0.645–0.795), with 0.655 sensitivity and 0.723 specificity, and optimal cutoff value was 7.01. The AUC for the GRACE score was 0.791 (95% CI: 0.717–0.865), with 0.862 sensitivity and 0.598 specificity, and the optimal cutoff value was 121.5. The combined AUC of NLR and GRACE score was 0.814 (95% CI: 0.745–0.884), with 0.707 sensitivity and 0.837 specificity. **Conclusion:** Both NLR and GRACE score independently predict in-hospital MACE events in STEMI patients post-PCI. Integration of the NLR and GRACE score enhances accuracy in forecasting in-hospital MACE event occurrences.

Key words: Acute ST-segment elevation myocardial infarction, Global Registry of Acute Coronary Events score, in-hospital major adverse cardiovascular events, neutrophil-to-lymphocyte ratio

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INTRODUCTION

The primary therapy for acute ST-segment elevation myocardial infarction (STEMI) involves myocardial perfusion early restoration. Currently, percutaneous coronary intervention (PCI) is the most practical method for treating STEMI. Characterized by rapid blood flow restoration and a reduced occurrence of reinfarction

or ischemia, primary PCI has markedly enhanced the prognosis and life quality in STEMI patients.^[1,2] Despite these advancements, mortality rates within STEMI patients undergoing emergency PCI vary from 2.7% to 8%.^[3] Thus, within acute myocardial infarction (AMI), effective risk stratification, early identification of high-risk individuals, and the implementation of tailored treatment approaches are imperative for optimizing patient outcomes.^[4]

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Address for correspondence: Dr. Zhenfei Chen, Department of Cardiology, The Second People's Hospital of Hefei, Hefei Hospital Affiliated to Anhui Medical University, West Side of The Intersection of Guangde Road and Leshui Road, Yaohai District, Hefei, Anhui - 230011, China. E-mail: 1601994492@qq.com

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The Global Registry of Acute Coronary Events (GRACE) score serves as a predictive tool for risk stratification at both admission and discharge in myocardial infarction patients. Research has demonstrated its effectiveness to forecast long-term mortality by all-cause within elderly STEMI patients.^[5] The GRACE score includes factors such as patient systolic blood pressure, cardiac injury markers, age, prehospital cardiac arrest, Killip grade, ST-segment changes on electrocardiogram (ECG), serum creatinine levels, and heart rate. However, its assessment is somewhat limited due to the exclusion of coronary angiography, troponin, a more sensitive indicator of myocardial cell damage, and inflammatory markers that indicate plate stability.^[6]

Recent studies have established^[7,8] that the inflammatory response is central to the pathophysiological processes of unstable plaque rupture and local thrombosis in the coronary artery in acute coronary syndrome (ACS) subjects, resulting in myocardial ischemia and necrosis.^[9] Notably, the white blood cell (WBC) count within 24 h of admission serves as an independent indicator of death and major adverse cardiovascular events (MACE) in STEMI subjects.^[10,11] In addition, low lymphocyte levels are significantly linked to cardiovascular morbidity and mortality.^[12,13] An increase in blood neutrophils reflects the body's systemic inflammatory state. The neutrophil-to-lymphocyte ratio (NLR), encompassing changes in both lymphocyte and neutrophil counts, offers greater prognostic prediction in STEMI patients than in any single index. Elevated NLR values have been related to long-term survival in individuals with acute STEMI and non-STEMI (NSTEMI),^[14-17] also inhospital and 6-month survival of ACS patients.^[18] While numerous studies have focused on NLR impact and GRACE scores on the short- and long-term STEMI patients' prognosis, research on inhospital MACE following PCI in these patients is scarce. Hence, the primary aim for the investigation is to assess the predictive significance of both NLR and GRACE score in predicting MACE during hospitalization among patients with STEMI following primary PCI. The aim is to establish a straightforward, non-invasive, and cost-effective evaluation approach that offers meaningful insights for guiding clinical decision-making.

MATERIALS AND METHODS

Study design and participants

The retrospective study enrolled 242 STEMI patients undergoing PCI at Hefei Second People's Hospital from December 2019 to December 2021. Inclusion criteria comprised patients meeting the 2013 American College of Cardiology guidelines for STEMI diagnosis,^[19] exhibiting chest pain symptoms lasting over 30 min within 24 h before admission, and presenting an ECG indicating ST-segment elevation,

abnormal Q-waves, or new left bundle branch block. Elevated levels of serum biochemical markers, including 24-h creatine kinase isoenzyme and/or cardiac troponin T after chest pain begin, were also necessary for inclusion. Exclusion criteria encompassed patients with PCI history; or arrhythmia, valvular/congenital heart disease, cardiomyopathy, chronic heart failure; or chronic obstructive pulmonary disease, asthma; or chronic liver disease, hepatic insufficiency; or decompensated renal insufficiency; or autoimmune diseases, acute or chronic infections; or malignancy. For STEMI patients undergoing emergency PCI, pre-PCI treatment included 300 mg of aspirin, and oral clopidogrel (300–600 mg) or ticagrelor (180 mg). For elective subjects scheduled for PCI and lacking contraindications to long-term pre-PCI antiplatelet drugs, the prescribed treatment plan involved the oral administration of aspirin (300 mg) at least 24 h before the scheduled surgery. Simultaneously, patients were given oral clopidogrel (300 mg) or ticagrelor (180 mg). Stent placement followed conventional methods. During PCI, 100 U/kg of heparin was administered intravenously, with an additional 1000 U for procedures exceeding 1 h.

The utilization of platelet membrane glycoprotein IIb/IIIa receptor antagonists was measured at the surgeon's discretion, guided by clinical and coronary assessments. Following PCI, a postoperative regimen of dual antiplatelet therapy was initiated. This included daily aspirin (100 mg) in combination with either clopidogrel (75 mg) or ticagrelor (90 mg twice daily), with the therapy maintained for a minimum duration of 1 year. All methodologies applied followed ethical guidelines outlined within the Declaration of Helsinki. Study approval was from the Ethics Committee of the Second People's Hospital of Hefei (Approval No.: 2020-Ke-058). Due to its retrospective nature, informed consent was waived for all patients.

Variables assessment

Global Registry of Acute Coronary Events scoring system

The GRACE score^[20] involves a variable scoring standard based on the patient's heart rate, cardiac marker damage, ECG ST-segment changes, age, prehospital cardiac arrest, serum creatinine, Killip classification, and systolic blood pressure. Scores were calculated for STEMI patients.

Major adverse cardiovascular events definition and grouping

MACEs encompassed the primary endpoint of cardiac death and secondary endpoints, including acute heart failure, myocardial reinfarction, and malignant arrhythmia. STEMI patients were categorized into the MACE group (58 cases), comprising 41 males 66.28 years old on average, and the non-MACE group (184 cases), including 146 males 60.63 years old on average, based on the occurrence of MACE events during hospitalization post-PCI.

General information

Detailed records of patients' baseline data were acquired in the hospital's electronic medical record system. The information comprised body mass index (BMI), history of diabetes and hypertension, family and smoking history, Killip classification, GRACE score, age, gender, and inhospital MACEs.

Laboratory and echocardiographic data

Two hours postemergency PCI, cubital venous blood was collected from all subjects. Biochemical indicators analyzed included uric acid, platelets, fasting blood glucose, total cholesterol, creatinine, neutrophils, lymphocytes, hemoglobin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides. Within 48 h postemergency PCI, an experienced sonographer conducted bedside cardiac color ultrasound examinations to observe cardiac ventricular wall motion and record left ventricle ejection fraction (LVEF).

Intervention-related data

Based on angiography results, experienced interventional physicians determined the culprit vessel, the number of diseased vessels, the number and dimensions of stents, and whether to use tirofiban, thrombus aspiration, or an intra-aortic balloon pump (IABP).

Statistical analysis

Statistical Package for the Social Sciences developed by IBM, USA was used for statistical analysis in this study. For measurement data, the Kolmogorov–Smirnov normality test determined distribution normality. Normally distributed data were presented as mean \pm standard deviation, intergroup comparisons utilized the independent samples *t*-test, while nonnormally distributed data were expressed as median *M* (P25, P75) and subjected to comparison through the Mann–Whitney *U*-test. Categorical data, presented as rates, underwent comparison by the Chi-square test. To discern the significance of the NLR and GRACE score as independent inhospital MACE following PCI predictors in STEMI patients, multivariable logistic regression was employed. Predicting capacities of the NLR, GRACE score, and their combination for inhospital MACE events post-PCI in STEMI individuals were evaluated using the area under the receiver operating characteristic (ROC), alongside sensitivity and specificity assessments. All statistical tests were two-sided, with statistical significance: $P < 0.05$.

RESULTS

Clinical baseline data comparison between cohorts

This research comprised 242 patients diagnosed with STEMI with PCI history. Based on the inhospital MACE occurrence, the participants were categorized into two cohorts:

the MACE cohort (58 cases, 24%) and the non-MACE cohort (184 cases, 76%). Clinical baseline data for both cohorts are presented in Table 1. Comparisons between the non-MACE and MACE cohorts revealed statistically significant differences. Patients in the MACE cohort were characterized by advanced age, elevated NLR, higher GRACE scores, increased neutrophil levels, and decreased lymphocyte levels ($P < 0.05$). In addition, notable variations were discovered in LVEF, Killip \geq grade 2, total cholesterol, fasting blood glucose, creatinine, LDL-C, and smoking history ($P < 0.05$). Nevertheless, no notable distinctions were noted in uric acid, diabetes, HDL-C, hypertension history, BMI, hemoglobin, gender, platelets, coronary heart disease family history, and triglycerides between two cohorts ($P > 0.05$).

Interventional clinical data comparison

Table 1 presents the interventional data for both groups of patients. In the cohort experiencing MACE, the left main trunk was considered the culprit vessel in 6.9% of cases (four instances), a significantly higher rate in comparison to the non-MACE cohort ($P < 0.05$). Conversely, no notable disparities were discovered in the participation of the left circumflex artery, right coronary artery, and left anterior descending artery between the two cohorts ($P > 0.05$). The MACE cohort exhibited a higher prevalence of three-vessel disease and a lower occurrence of single-vessel disease, with these distinctions proving statistically notable ($P < 0.05$). Nevertheless, no statistical variance was found in the incidence of double-vessel disease between the cohorts ($P > 0.05$). Notably, the application of tirofiban and IABP implantation was more frequent in the MACE cohort, demonstrating a statistically notable disparity ($P < 0.05$). For procedural details, there were no differences in the number, length, and diameter of stents implanted between the two cohorts ($P > 0.05$).

Predictors of inhospital major adverse cardiovascular events

The logistic regression analysis results are detailed in Table 2. Owing to the synergistic relationship between GRACE and age, and between NLR and neutrophils and lymphocytes, the logistic regression analysis did not include age, neutrophil, and lymphocyte counts. Univariate logistic regression analysis suggested that smoking history, total cholesterol, fasting blood glucose, LDL-C, creatinine, LVEF, NLR, and GRACE scores were statistically notable ($P < 0.05$). Notable factors in univariate analysis were sent for multivariate logistic regression analysis, revealing that NLR (odds ratio [OR] = 1.096, 95% confidence interval [CI] 1.016–1.083, $P = 0.018$) and GRACE scores (OR = 1.031, 95% CI 1.017–1.045, $P < 0.05$) were inhospital MACE events independent predictors in STEMI patients post-PCI.

Table 1: Comparison of general clinical data between the major adverse cardiovascular events group and nonmajor adverse cardiovascular events group mean±standard deviation, M (P25, P75), number of cases, and percentage

Variables	MACE group (n=58)	Non-MACE group (n=184)	t/χ ² /Z	P
General clinical data				
Age (years)	66.28±14.89	60.63±13.83	2.662	<0.05*
Gender (male)	41 (70.7)	146 (79.3)	1.882	0.17
BMI (kg/m ²)	24.19±3.73	24.61±3.51	0.62	0.536
Diabetes	21 (36.2)	45 (24.5)	3.07	0.08
hypertension	36 (62.1)	97 (52.7)	1.558	0.212
Smoking	26 (44.8)	112 (60.9)	4.631	<0.05*
Family history of coronary heart disease	11 (19)	29 (15.8)	0.328	0.567
GRACE score	159.62±43.39	116.96±28.15	7.036	<0.05*
Killip grade II-IV	37 (63.79)	37 (20.1)	39.644	<0.05*
Laboratory data				
Neutrophils (×10 ⁹ /L), M (P ₂₅ , P ₇₅)	9.85 (6.82, 13.39)	7.36 (5.25, 9.61)	4.524	<0.05*
Lymphocytes (×10 ⁹ /L), M (P ₂₅ , P ₇₅)	1.13 (0.83, 1.6)	1.52 (1.07, 2.16)	2.984	<0.05*
NLR, M (P ₂₅ , P ₇₅)	8.99 (5.06, 12.01)	5.15 (3.13, 7.66)	5.051	<0.05*
Hemoglobin (g/L)	132.62±17.99	135.63±19.96	1.026	0.306
Platelets (×10 ⁹ /L), M (P ₂₅ , P ₇₅)	189.5 (146.5, 236)	199 (152.25, 242.75)	0.898	0.369
Triglycerides (mmol/L), M (P ₂₅ , P ₇₅)	1.29 (0.79, 1.97)	1.44 (1.04, 2.09)	1.521	0.128
Total cholesterol (mmol/L)	4.25±1.05	4.6±1.05	2.207	<0.05*
LDL-C (mmol/L)	2.71±0.91	2.97±0.89	1.978	<0.05*
HDL-C (mmol/L)	1.05±0.24	1.09±0.24	1.086	0.278
Creatinine (umol/L), M (P ₂₅ , P ₇₅)	79.4 (57.5, 110.58)	68 (56.58, 77.28)	3.164	<0.05*
Uric acid (umol/L)	387.16±128.12	356.11±106.54	1.84	0.067
Glucose (mmol/L), M (P ₂₅ , P ₇₅)	7.69 (6.1, 11.6)	6.14 (5.33, 8.04)	3.601	<0.05*
LVEF, M (P ₂₅ , P ₇₅)	54 (45.75.61)	60 (55, 64)	3.534	<0.05*
Interventional data				
Criminal vessel, n (%)				
LM	4 (6.9)	0	12.903	<0.05*
LAD	28 (48.28)	105 (58.7)	1.376	0.241
LCX	10 (17.2)	19 (10.3)	1.999	0.157
RCA	24 (41.38)	62 (33.7)	1.137	0.286
Number of diseased vessels				
Single	11 (18.97)	67 (36.41)	6.146	<0.05*
Two	19 (32.76)	61 (33.15)	0.003	0.956
Three	28 (48.28)	56 (30.43)	6.194	<0.05*
Stent implantation	48 (82.8)	168 (91.3)	3.358	0.067
Number of stents implanted, n (%)	1 (1.2)	1 (1.2)	0.074	0.941
Stent length, M (P ₂₅ , P ₇₅)	23 (18, 29)	23 (18, 29)	0.779	0.436
Stent diameter, M (P ₂₅ , P ₇₅)	2.75 (2.75, 3)	3 (2.75, 3)	0.44	0.66
Tirofiban	27 (46.6)	59 (32.1)	4.04	<0.05*
Thrombus aspiration	14 (24.1)	27 (14.7)	2.807	0.094
IABP	14 (24.1)	5 (2.7)	25.086	<0.05*
Inhospital MACE, n (%)				
Cardiogenic death	5 (8.62)	-	-	-
Myocardial reinfarction	1 (1.72)	-	-	-
Malignant arrhythmia	31 (53.45)	-	-	-
Acute heart failure	21 (36.21)	-	-	-

*<0.05. BMI=Body mass index; LDL-C=Low-density lipoprotein cholesterol; HDL-C=High-density lipoprotein cholesterol; NLR=Neutrophil/lymphocyte ratio; LVEF=Left ventricular ejection fraction; LM=Left main coronary artery; LAD=Left anterior descending artery; LCX=Left circumflex artery; RCA=Right coronary artery; IABP=Intra-aortic balloon counterpulsation; MACE=Major adverse cardiovascular events

Predictive value of the neutrophil-to-lymphocyte ratio, Global Registry of Acute Coronary Events score, and their combination for inhospital major adverse cardiovascular events

The predictive value for inhospital MACE was analyzed using the ROC curve, as illustrated in Figure 1 and detailed in

Table 3. According to the ROC curve analysis, the area under the curve (AUC) for NLR was 0.72 (95% CI: 0.645–0.795, $P < 0.05$), exhibiting 0.655 sensitivity and 0.723 specificity, with an optimal cutoff value of 7.01. For the GRACE score, the AUC was 0.791 (95% CI: 0.717–0.865, $P < 0.05$), demonstrating 0.862 sensitivity and 0.598 specificity, with

Table 2: Logistic regression analysis of risk factors in major adverse cardiovascular events group

	Univariate logistic regression analysis				Multivariate logistic regression analysis			
	β	OR	95% CI	P	β	OR	95% CI	P
NLR	0.142	1.153	1.079–1.231	<0.001*	0.092	1.096	1.016–1.183	0.018*
GRACE score	0.037	1.037	1.026–1.049	<0.001*	0.03	1.031	1.017–1.045	<0.001*
Smoking	0.649	1.915	1.055–3.475	0.033*	0.128	1.137	0.536–2.41	0.738
Total cholesterol	-0.336	0.715	0.528–0.968	0.03*	0.055	1.056	0.739–1.51	0.764
LDL-C	-0.356	0.7	0.49–1.001	0.051	-	-	-	-
Creatinine	0.022	1.023	1.011–1.034	<0.001*	0.009	1.009	0.995–1.022	0.214
Glucose	0.095	1.1	1.029–1.176	0.005*	0.096	1.101	1.017–1.193	0.018*
LVEF	-0.072	0.93	0.898–0.963	<0.001*	-0.025	0.975	0.934–1.017	0.244

*<0.05. NLR=Neutrophil-to-lymphocyte ratio; LDL-C=Low-density lipoprotein cholesterol; LVEF=Left ventricular ejection fraction; OR=Odds ratio; CI=Confidence interval; GRACE=Global Registry of Acute Coronary Events

Table 3: Predictive value of the neutrophil-to-lymphocyte ratio and Global Registry of Acute Coronary Events scores on major adverse cardiovascular events

	Cutoff value	SE	AUC (95% CI)	P	Sensitivity (%)	Specificity (%)	Youden index
NLR	7.01	0.038	0.72 (0.645–0.795)	<0.001*	0.655	0.723	0.378
GRACE score	121.5	0.038	0.791 (0.717–0.865)	<0.001*	0.862	0.598	0.46
NLR+GRACE score	-	0.035	0.814 (0.745–0.884)	<0.001*	0.707	0.837	0.544

*<0.05. NLR=Neutrophil-to-lymphocyte ratio; AUC=Area under the curve; CI=Confidence interval; GRACE=Global Registry of Acute Coronary Events; SE=Standard error

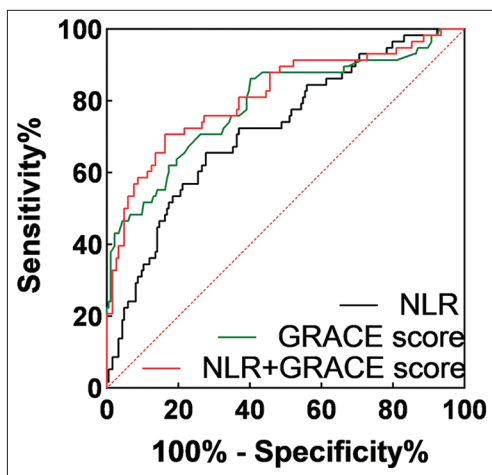


Figure 1: Receiver operating characteristic curves of the neutrophil-to-lymphocyte ratio and Global Registry of Acute Coronary Events scores predicting major adverse cardiovascular events

an optimal cutoff value of 121.5. The combined AUC for both NLR and GRACE score was 0.814 (95% CI: 0.745–0.884, $P < 0.05$), yielding 0.707 sensitivity and 0.837 specificity.

DISCUSSION

Recent studies have indicated that mental stress can lead to myocardial infarction without coronary artery occlusion.^[21] However, the current clinicopathologic understanding of STEMI primarily involves plaque rupture, bleeding, and thrombosis following coronary atherosclerosis, potentially leading to severe outcomes such as cardiogenic shock, sudden cardiac death, and acute heart failure if untreated.^[22–24] Early PCI effectively restores myocardial blood supply and is considered one of the best approaches

to ameliorate survival outcomes of acute STEMI patients.^[25] Hence, prompt and accurate risk stratification, coupled with reasonable treatment measures, is crucial for reducing cardiovascular events and enhancing patient prognosis.

The GRACE score is a widely recognized predictive tool for risk stratification at admission and discharge in myocardial infarction patients.^[26] This score, derived from a multicenter, prospective registry study involving nearly 100 hospitals in multiple countries, includes factors such as patient age, heart rate, serum creatinine, Killip grade, systolic blood pressure, ECG ST-segment changes, prehospital cardiac arrest, and cardiac injury markers. Research has demonstrated that the GRACE score can independently forecast 1-year postdischarge all-cause mortality in patients with AMI.^[27] However, its assessment may be limited due to the exclusion of coronary angiography results, troponin, a sensitive indicator of myocardial cell damage, and inflammatory markers indicating plaque stability. Overestimation of inhospital mortality risk in high-risk ACS patients can lead to potential overtreatment.^[6]

Current studies^[7,8] have confirmed that the inflammatory response is central to the pathophysiology of unstable plaque rupture and local thrombosis in the coronary arteries of ACS patients, resulting in myocardial ischemia and necrosis. Notably, the WBC count within 24 h of admission serves as an independent death and MACEs predictor within STEMI subjects.^[10,11] Similarly, low lymphocyte levels are significantly related to cardiovascular morbidity and mortality.^[12,13] NLR, which accounts for alterations in both lymphocyte and neutrophil counts, offers greater predictive value for the prognosis of STEMI patients than

any single indicator. A meta-analysis has shown that NLR can predict both in-hospital adverse events and long-term outcomes post-PCI in STEMI patients.^[28] Therefore, the research focuses on STEMI individuals to search inflammatory markers' prediction capability, namely, the NLR and GRACE score, which are related to the occurrence, progression, and plaque stability of atherosclerosis, in the incidence of in-hospital MACE events post-PCI.

Study results suggested that the NLR and GRACE scores were higher within the MACE cohort in comparison to the non-MACE cohort, aligning with the aforementioned discoveries.^[29,30] Univariate logistic regression analysis, using in-hospital MACE as the dependent variable, identified LVEF, total cholesterol, NLR, fasting blood glucose, creatinine, smoking history, LDL-C, and GRACE score as risk factors for in-hospital MACE events in STEMI patients. Subsequent multivariate logistic regression analysis revealed that the GRACE score, NLR, and fasting blood glucose were independent predictors of in-hospital MACE in these patients. Given that the NLR and GRACE scores within 24 h of admission independently forecast MACE events in STEMI patients, they are also likely to forecast in-hospital MACE events occurrence. ROC curve analysis demonstrated that AUC for NLR in predicting in-hospital MACE events was 0.72 (95% CI 0.645–0.795, $P < 0.001$), with 0.655 sensitivity and 0.723 specificity, and optimal cutoff value as 7.01; for the GRACE score, AUC was 0.791 (95% CI 0.717–0.865, $P < 0.001$), with 0.862 sensitivity and 0.598 specificity, and optimal cutoff value as 121.5; when combining the NLR and GRACE score, AUC was 0.814 (95% CI 0.745–0.884, $P < 0.001$), with 0.707 sensitivity and 0.837 specificity. According to these results, the combined NLR and GRACE score outperforms a single index in both sensitivity and specificity, indicating its strong predicting capability for in-hospital MACE events within STEMI subjects.

This study is not without limitations. First, as single-center retrospective research with a relatively small sample size, it may contain biases. Second, it focused solely on the predictive value of the NLR and GRACE scores for in-hospital MACE events in STEMI patients, lacking long-term follow-up. Future multicenter, large-scale, prospective trials are needed to further explore the long-term prognostic factor role of combining the NLR with GRACE score in STEMI patients post-PCI.

CONCLUSION

In summary, NLR and GRACE scores on admission significantly predict in-hospital MACE in STEMI patients post-PCI. Therefore, their combination can be instrumental in identifying high-risk patients with poor prognoses, allowing for early adjuvant therapy. NLR, as a simple,

noninvasive, cost-effective biomarker, when combined with the GRACE score, provides a novel, valuable reference for the evaluation, treatment, and STEMI patients' prognosis.

Authors' contributions

ZFC and JZ participated in the conceptualization of the study, its execution, draft revision, and approval of the final manuscript, and concurred on all aspects of the work. CYF contributed to the conceptualization, drafting, and revision of the manuscript, approved the final version, and agreed on all aspects of the study. MSY and XQJ were involved in the acquisition, analysis, and interpretation of the data for the study.

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EC Approval No.: This study has been approved by the Second People's Hospital of Hefei Ethics Committee (Approval No.: 2020-ke-058).

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Conflicts of interest

There are no conflicts of interest.

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