Original Article
The correlation between PLR-NLR and prognosis in acute myocardial infarction

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Abstract: Objective: To explore the correlation between the prognosis of acute myocardial infarction (AMI) and the platelet to lymphocyte ratio (PLR)-neutrophil to lymphocyte ratio (NLR). Methods: A retrospective analysis was performed on the data of 300 patients with AMI admitted to our hospital between August 2016 and August 2019. The general data, data on the patients' major adverse cardiovascular and cerebrovascular events (MACCE), the global registry of acute coronary events (GRACE), and the different groups of patients' survival times were compared. Results: The area under the curve (AUC) of PLR was 0.810 [95% CI (0.751, 0.869), P < 0.001]. The AUC value of NLR was 0.882 [95% CI (0.839, 0.925), P < 0.001]. In our study, 102 patients were placed in the high PLR group, 198 patients were placed in the low PLR group, 126 patients were placed in the high NLR group, 174 patients were placed in the low NLR group, 174 patients were placed in PLR-NLR group 0, 24 patients were placed in PLR-NLR group 1, and 102 patients were placed in PLR-NLR group 2. The heart rates (HR) and brain natriuretic peptide (BNP) levels in Group 0 were the lowest among the three groups (P < 0.05), and the cTnI levels were observably lower than they were in Group 2 (P < 0.05). The patients' HR and BNP ratios in Group 1 were notably lower than the HR and BNP ratios in Group 2 (P < 0.05). The lowest incidence of MACCE was found in PLR-NLR Group 0. The number of intermediate-risk of patients in Group 0 was the lowest among the three groups. The order of the overall survival (OS) and the progression-free survival (PFS) of the three PLR-NLR Groups 0 were Group 0 > Group 1 > Group 2 (P < 0.001). The survival rate (SR) of the patients in PLR-NLR Group 0 was 100% within 2 years, which was significantly greater than the survival rates in Group 1 and Group 2 (P < 0.05). The SR of the patients in Group 0 was 98.8% within five years, which was also significantly higher than the survival rates in Groups 1 and 2 (P < 0.05). Conclusion: The PLR-NLR combination has an essential effect on the prognostic analysis of AMI. The incidence of MACCE increases with an increase in PLR-NLR.

Keywords: PLR, NLR, AMI, prognostic analysis

Introduction

Acute myocardial infarction (AMI) is a critical and acute illness in clinical practice, and its increasing incidence is closely related to lifestyle changes. It has become the biggest threat to human life with today's aging population, so evaluating the severity of AMI is of great significance in developing treatments for it. Although the GRACE, commonly used in clinical practice, plays a certain role in the evaluation of AMI, it is susceptible to many factors and still has certain limitations in the prognostic evaluation of AMI. Therefore, in order to improve our ability to identify high-risk patients and to treat them promptly, it is necessary to conduct a more in-depth analysis of the AMI related factors [1-3].

At present, many scholars have confirmed that the inflammatory response is of great importance in the development of atherosclerosis, and PLR and NLR are easy-to-obtain and effective coronary heart disease monitoring indicators. In recent years, many studies on the application of prognosis evaluation for various diseases have been conducted [4-6], yet there are still few studies that combine PLR and NLR to analyze the prognosis of AMI. Therefore, this study constructed a new PLR-NLR as an AMI treatment and prognosis evaluation model, aiming to explore the correlation between the combination of these two indicators and the prognosis of AMI. The research results are as follows.

Table 1. PLR-NLR grouping

Groups	Criterion	Number of Patients	Proportion (%)
PLR Grouping			
High PLR	PLR ≥ 169.8	102	34.0
Low PLR	PLR < 169.8	198	66.0
NLR Grouping			
High NLR	NLR ≥ 3.17	126	42.0
Low NLR	NLR < 3.17	174	58.0
PLR-NLR Grouping			
2	PLR ≥ 169.8 and NLR ≥ 3.17	102	34.0
1	PLR ≥ 169.8 or NLR ≥ 3.17	24	8.0
0	PLR < 169.8 and NLR < 3.17	174	58.0

Table 2. Data group 1 general data comparison

Group	PLR-NLR			X^2/t	P
	0 (n=174)	1 (n=24)	2 (n=102)		
Sex				0.079	0.779
Male	104	13	52		
Female	70	11	50		
Average Age	61.84±12.51	61.74±12.52	62.01±12.31	0.114	0.909
Hypertension				0.049	0.825
Yes	64	10	40		
No	110	14	62		
Diabetes				0.000	0.982
Yes	54	9	38		
No	120	15	64		
Smoking History				0.385	0.535
Yes	56	8	41		
No	118	16	61		

Materials and methods

General data

300 patients with AMI admitted to our hospital between August 2016 and August 2019 were recruited as the study cohort. Group 0 (n=174), PLR-NLR Group 1 (n=24), and Group 2 (n=102) were established according to the optimal cut-off value (OCV). The Group 0 patients ranged in age from 49.33 to 74.35 years old, the PLR-NLR Group 1 patients ranged in age from 49.22 to 74.26 years old, and the Group 2 patients ranged in age from 49.70 to 74.32 years old. The patients in the three groups all had diabetes and hypertension, and they all had a history of smoking. The three groups baseline clinical data demonstrated no significant differences (P > 0.05), so the groups were comparable. See **Tables 1**, **2**.

Inclusion criteria

The inclusion criteria were as follows: ① ST-elevation myocardial infarction (ST-EMI): patients whose myocardial injury marker (troponin) levels were 99% beyond the upper limit of the normal level with dynamic changes, and patients who had myocardial ischemia. Patients with pain in the left sternum the lasted for more than 30 minutes, and the symptoms could not be relieved by medicines such as nitric acid, patients with an arched ST segment elevation in ECG (new arched ST segment elevation in V1-V3 leads with an amplitude ≥ 0.2 Mv, or an ST segment elevation in other leads with an amplitude ≥ 0.1 Mv), or emerging changes in the left bundle branch block, patients whose pathological Q waves appear in the corresponding leads of the ECG (shown as the Q wave of more than 2 adjacent leads ≥ 30 ms, with a depth of at least 1 mm), patients whose imaging diagnosis has an emerging loss of viable myocardium or an abnormal local ventricular wall motion. ② Non ST-elevation myocardial infarction: patients with symptoms of angina that last for more than 20 minutes, and the pain is above grade three, patients whose myocardial injury markers are positive. ③ This study obtained approval from the ethics committee of Guangdong Provincial Agricultural Central Hospital, and the patients signed the informed consent forms.

Exclusion criteria

The exclusion criteria of this study are as follows: ① Patients with a history of trauma surgery or a blood transfusion within the past 30 days. ② Patients who had acute infections or other cardiovascular diseases, etc. ③ Patients with a blood system disease. ④ Patients who-

se important clinical data was missing. ⑤ Patients who had recently taken steroids or who underwent radiotherapy and chemotherapy. ⑥ Patients undergoing immunotherapy.

Methods

Treatment method: All the AMI patients started taking clopidogrel bisulfate tablets (Shenzhen Salubris Pharmaceuticals Ltd., national approval number H20000542) on the day following their admission, one 75 mg tablet, once a day, and the medicine would be taken for more than one year. The patients also took aspirin (Guangdong Jiuming Pharmaceuticals Ltd., national approval number H44021139) for life, 100 mg/d. All the patients were administered a subcutaneous injection 6000 U/12 h of low molecular weight heparin for seven consecutive days, and they took statins for treatment [7-10].

Examination method: ① All the patients underwent an ECG examination immediately after their admission, and the ECGs were reviewed by two cardiologists; ② We collected a sample of the patients' cubital vein blood for a routine blood examination, and we exanimated their BNP and troponin levels, collected the patients' blood on an empty stomach to test their blood lipids, UA, and liver function, and the tests and report would be conducted and issued by the hospital [11-14].

Grouping method: An ROC curve was used for the clarification of the OCV of the two inflammation indicators, and the patients were put into different groups according to the OCV. The patients whose indicators were higher than the OCV were placed in the high numerical value group, and patients with indicators lower than the value were placed in the low numerical value group. If the patients' PLR and NLR were both higher than the value, they were placed in Group 2, but if only one value (PLR or NLR) was greater than the critical value, the patients were placed in Group 1. If both indicators were less than the value, the patients were placed in Group 0.

Research criteria

The criteria for this study were the general data, and the MACCE, GRACE, and survival times of the different groups of patients.

General data

The general data, such as age, sex, hypertension, diabetes, and smoking history were included in Data Group 1. HR, BNP, troponin I peak (cTnI), blood lipids, UA and liver function were included in Data Group 2. Comparisons were conducted among the patients in the three PLR-NLR groups. The blood lipids included high-density lipoprotein cholesterol (HD L-C), total cholesterol (TC), low-density lipoprotein cholesterol (LD L-C), and triglycerides (TG).

MACCE

The numbers of the occurrences of acute left heart failure, new arrhythmia, cardiac death, and all-causes of death were collected, and a comprehensive calculation was conducted to determine their incidence.

GRACE

The measurement items included HR, systolic blood pressure, creatinine, the risk factors etc. According to the GRACE, the patients were divided into three grades: If the patient's score was below 108, the risk factor was considered low. If the patient's score was between 109 points and 140 points, it was considered an intermediate risk. If the patient's score was above 140 points, it was considered a high risk. We compared the patients' scores from the PLR Group, the NLR Group, and the PLR-NLR Group.

Survival times

The PFS, OS, and SR within 2 years and 5 years after the treatment were compared among the three PLR-NLR groups.

Statistical processing

The data obtained in this study were statistically analyzed and processed with SPSS 20.0. The research includes the count data and the measurement data, and chi-square tests and t tests were employed. When $P < 0.05$, a difference was considered statistically significant. In this study, GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to plot the data, and the OCV of PLR and NLR was determined using ROC curves. The survival analysis was carried out using the Kaplan-Meier meth-

Table 3. Data group 2 general data comparison

Group	PLR-NLR		
	0 (n=174)	1 (n=24)	2 (n=102)
HR (/min)	76.47±16.45	83.52±18.52*	89.61±13.09*,#
BNP (pg/ml)	340.71±68.41	380.56±67.51*	420.74±62.19*,#
CTnI (mg/L)	20.66±19.18	24.69±17.17	27.93±16.60*
Blood Lipids			
TC (mmol/L)	4.75±1.12	4.60±0.89	4.50±0.96
TG (mmol/L)	1.74±0.95	1.69±1.08	1.52±0.69
HDL-C (mmol/L)	1.05±0.24	1.05±0.36	1.10±0.25
LDL-C (mmol/L)	3.06±0.95	2.97±0.76	2.88±0.81
UA (mmol/L)	302.01±55.02	314.01±57.02	320.12±56.89
Liver Dysfunction			
Yes	34	7	22
No	140	17	80

Note: *indicated that P < 0.05 when compared with Group 0, #indicated that P < 0.05 when compared with Group 1.

Figure 1. Comparison of the MACCE among patients in the PLR-NLR groups. Note: the abscissa of **Figure 1** from left to right is acute left heart failure, new arrhythmia, cardiac death, total and all-cause deaths. In Group 0, the number of acute left heart failure, new arrhythmia, cardiac death, total and all-causes of death were 3, 4, 2, 9, and 2 respectively; the number of the above items in Group 1 were 2, 1, 2, 4 and 2 respectively; the number of the above items in Group 2 were 13, 21, 6, 40 and 28 respectively. * Indicated that P < 0.05 when the data between the two groups were compared, # indicated that P < 0.001 when the data between the two groups were compared.

od and the differences between groups were compared using log-rank tests.

Results

PLR-NLR grouping

Using the ROC curve analysis, the AUC was 0.810 [95% CI (0.751, 0.869), P < 0.001]. When the OCV of PLR was 169.8, the sensitivity was 73.2%, the specificity was 64.9%, and the PLR grouping of the patients was conducted based on that value. The AUC value of NLR was 0.882 [95% CI (0.839, 0.925), P < 0.001]. When the OCV of NLR was 3.17, the sensitivity was 78.1%, the specificity was 83.2%, and the PLR grouping of the patients was conducted based on that value, as shown in **Table 1**.
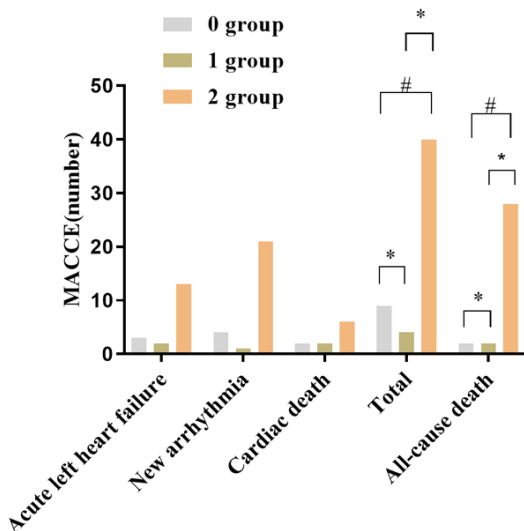
Comparison of the general data

No significant differences were detected in the patients' general clinical data in the different PLR-NLR groups (P > 0.05), as shown in **Table 2**. There were also no significant differences in the blood lipid, UA, and liver function levels among the patients in the different PLR-NLR groups (P > 0.05). However, the HR and BNP of Group 0 were the lowest among the three groups (P < 0.05), and the cTnI of Group 0 was much smaller than it was in Group 2 (P < 0.05). The patients' HR and BNP in Group 1 were markedly lower than they were in Group 2 (P < 0.05), as shown in **Table 3**.

MACCE

The patients in PLR-NLR Group 0 had the lowest MACCE incidence, accounting for only 5.1%, and their all-causes of death accounted for only 1.1%. The incidence of MACCE in Group 1 was 16.7%, and all-causes of death 8.3%, showing a remarkable difference from Group 0 (P < 0.05). The incidence of MACCE in Group 2 was 40.0%, and the all-cause death rate was 27.5%. Compared with Group 0, the difference was significant (P < 0.001), and in Group 1, the difference was also significant (P < 0.05), as shown in **Figure 1**.

GRACE

The intermediate-risk rate (P < 0.05) and the high-risk rate (P < 0.001) of the patients in the

Table 4. Comparison of GRACE among patients of different groups [n (%)]

Groups	Number of Patients	Low-Risk	Intermediate-Risk	High-Risk
PLR Groups				
High PLR	102	11 (10.8)	40 (39.2)	51 (50.0)
Low PLR	198	98 (49.5)#	54 (27.3)*	46 (23.2)#
NLR Groups				
High NLR	126	10 (7.9)	55 (43.7)	61 (48.4)
Low NLR	174	64 (36.8)#	60 (34.5)	50 (28.7)#
PLR-NLR Groups				
2	102	12 (11.7)	40 (39.2)	50 (49.0)
1	24	4 (20.8)	9 (37.5)	11 (45.8)
0	174	69 (39.7)^,&	64 (36.8)	41 (23.6)^,&

Note: *Indicated that P < 0.05 when the data in the same group were compared, #indicated that P < 0.001 when the data in the same group were compared; ^indicated that P < 0.05 when compared with Group 0, &indicated that P < 0.05 when compared with Group 1. Rounding-off was adopted in the percentage calculation.

Figure 2. Survival time of patients of PLR-NLR groups. Note: In the picture, the abscissa from left to right is PFS and OS. PFS of PLR-NLR Group 0 was (25.5±1.2) months, the OS was (35.2±2.3) months; the PFS of PLR-NLR Group 1 was (19.2±1.6) months, the OS was (29.1±2.1) months; the PFS of PLR-NLR Group 2 was (10.4±1.2) months, the OS was (23.2±1.7) months. * indicated that P < 0.001.

Low PLR Group were significantly lower than corresponding rates in the High PLR Group, and the low-risk rate of the patients in the Low PLR Group was much higher than it was in the High PLR Group (P < 0.001); The low-risk rate of the patients in the Low-NLR Group was significantly higher than it was in the High-NLR Group (P < 0.001), and the high-risk rate of the Low-NLR Group was markedly lower than it was in the High-NLR Group (P < 0.001). In the PLR-NLR groups, the low-risk rate of the patients in Group 0 was the highest, and it was markedly greater than the rates in groups 1 and 2 (P < 0.05), and the high-risk rate of the patients in Group 0 was observably lower than the rates in groups 1 and 2 (P < 0.05). The intermediate risk rate of Group 0 was the lowest among the three groups, as shown in **Table 4**.

Survival times

The order of the patients' PFS and OS in the PLR-NLR Groups was Group 0 > Group 1 > Group 2, with significant differences between each group (P < 0.001), as shown in **Figure 2**. In addition, the SR of the patients in PLR-NLR Group 0 was 100% within 2 years and 98.8% within five years, which was observably better than it was in groups 1 and 2 (P < 0.05). The SR of the patients in Group 1 was 91.6% within five years, which was significantly greater than the 72.5% of Group 2 (P < 0.05), as shown in **Figures 2**-**4**.

Discussion

AMI is a disease with a rapid onset and an extremely high fatality rate. It has now surpassed cancer as the most significant threat to human health. Therefore, research on the disease has never stopped in clinical practice. The clinical manifestations of the disease are plaque ruptures occurring in the coronary arteries, the activation of platelet aggregations or thromboses, which leads to artery stenosis and occlusion, and the patients' myocardial blood flow drops sharply, resulting in a critical condition [15-18]. With the continuous popularization of coronary interventional surgery, the therapeutic effect of AMI has also been improved. However, the various serious complications it brings still puts patients at risk. Therefore, an in-depth study of a prognostic analysis is imperative. The GRACE has certain advantages in evaluating the prognosis of AMI
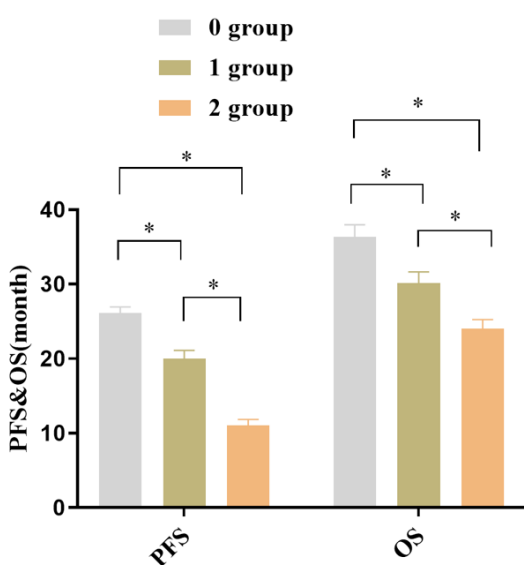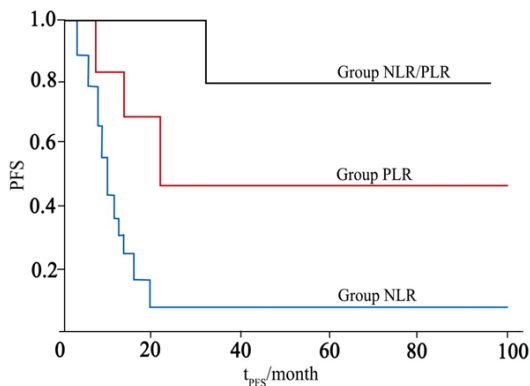
Figure 3. Progression-free survival (PFS) curve.

Figure 4. Overall survival (OS) curve.

patients, but there are also limitations that cannot be ignored. Various methods must be adopted to support the prognostic determination of AMI patients. The enhancement of the inflammatory response and the activation of the inflammatory cells are the pathological basis for the formation of lesions. Therefore, it helps to monitor atherosclerosis through the inflammatory response. In addition, leukocyte subsets have become classic markers of the inflammatory response in cardiovascular diseases. Similarly, lymphocytes decrease in AMI, which may be a physiological stress response to myocardial ischemia or infarction. Lymphocyte apoptosis and the release of proinflammatory cytokines lead to a significant decrease in lymphocytes under acute stress. When the number of neutrophils is significantly increased or continues to be high after surgery, and the number of lymphocytes is significantly reduced or continues to be low, this suggests a poor clinical prognosis. Postoperative NLR is a useful indicator for predicting the occurrence of major adverse cardiovascular events in AMI patients. Postoperative PLR has a certain predictive value for the occurrence of major adverse cardiovascular events in AMI. NLR, which integrates two types of inflammatory cells, has a higher predictive value for AMI, and it is more instructive than the use of the inflammatory cells alone, evidence that has been widely used in clinical practice to study the prognosis of AMI. However, few studies on PLR, which is also an indicator of the inflammatory response, or on the prognosis of AMI have been conducted. Therefore, this study constructed a new PLR-NLR model and analyzed the evaluation performance of these two indicators using the AUC. The results indicate
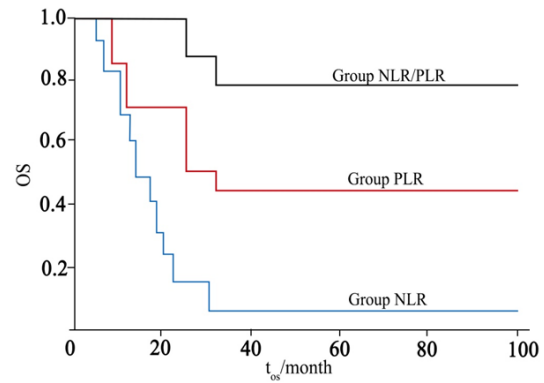
that the AUC was 0.810 [95% CI (0.751, 0.869), $P < 0.001$]. When the OCV of PLR was 169.8, the sensitivity was 73.2% and the specificity was 64.9%. The AUG value of NLR is 0.882 [95% CI (0.839, 0.925), $P < 0.001$]. When the NLR OCV was 3.17, the sensitivity was 78.1%, and the specificity was 83.2%. These two indicators are highly sensitive in AMI and of great importance for predicting a prognosis.

The PLR grouping, NLR grouping, and PLR-NLR grouping of the patients were conducted according to the OCV. The results of this paper are as follows: There were no apparent differences in the PMH, blood lipids, UA, or the liver function of the patients in the different PLR-NLR groups ($P > 0.05$), but the HR and BNP in Group 0 were much smaller than they were in groups 1 and 2 ($P < 0.05$), and the cTnI level was significantly lower than it was in group 2 ($P < 0.05$). Lower HR and BNP levels in the patients were observed in Group 1 than in Group 2 ($P < 0.05$). This indicated that the higher the PLR-NLR overall score, the worse the patient's general data, and the more severe the symptoms. In terms of MACCE, the patients in PLR-NLR Group 0 had the lowest MACCE incidence, accounting for only 5.1%, and their all-causes of death only accounted for 1.1%. The incidence of MACCE in Group 1 was 16.7%, and the all-causes of death accounted for 8.3%, which was much different from Group 0 ($P < 0.05$). The incidence of MACCE in Group 2 was 40.0%, and the all-causes of death accounted for 27.5%. It was quite a notable difference in the contrast with Group 0 ($P < 0.001$). A significant difference was obtained in the comparison with Group 1 ($P < 0.05$). This indicated

that the MACCE of the patients based on the PLR-NLR grouping increased with the overall PLR-NLR score. In terms of GRACE, a notable lower intermediate-risk rate of the patients in the Low PLR Group was seen in contrast with the High PLR Group ($P < 0.05$), and the results also showed a far lower high-risk rate than the High PLR Group ($P < 0.001$). In the comparison with the High-NLR Group, the patients' low-risk rate in the Low-NLR Group was significantly higher ($P < 0.001$), and the high-risk rate was notably lower ($P < 0.001$). In the PLR-NLR groups, the patients' low-risk rate in Group 0 was the highest among these three groups ($P < 0.05$), and a much lower high-risk rate of patients was seen in Group 0 than in groups 1 and 2 ($P < 0.05$). The intermediate-risk rate of Group 0 was the lowest among the three groups. It indicated that the risk coefficient of Group 0 was the lowest, followed by Group 1, and it was the highest in Group 2. In terms of survival times, the order of the PFS and OS of patients in the PLR-NLR Groups were as follows: Group 0 > Group 1 > Group 2, and their differences were absolutely enormous ($P < 0.001$). The SR of the patients of PLR-NLR Group 0 within 2 years was 100% and five years with 98.8%, far exceeding the results of groups 1 and 2 ($P < 0.05$). The SR of the patients in Group 1 was 91.6% within five years, which was prominently higher than the 72.5% of Group 2 ($P < 0.05$). It indicated that the SR of patients decreased with the increase of the PLR-NLR overall scores. Scholar Hyeon-Cheol Gwon et al. used an ROC curve to obtain the OCV of PLR and NLR, and employed this value as the basis for patient classification and concluded that patients with high scores were along with a higher incidence of MACCE and a lower SR. The results obtained in this study were consistent with these findings [19].

In summary, PLR-NLR has a higher correlation with the prognosis of AMI. The higher the score, the higher the incidence of MACCE. The more high-risk patients in the GRACE, the lower the SR of patients. Therefore, this model should be employed in clinical practice.

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Disclosure of conflict of interest

None.

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