Clinical Interventions in Aging

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ORIGINAL RESEARCH

A Novel Scale System Based on the Frailty Index and Laboratory Indicators for the Short-Term Prognosis of Patients with Acute Myocardial Infarction: A Retrospective Cohort Study

Tianqing Cao[1,*], Fei Liu[2,*], Yan Yao[2], Danghong Sun[2], Rong Wang[3], Junxia Cao[3], Jie Meng[2], Ling Zhang[4], Weiming Li[1]

[1]Shanghai Tenth People's Hospital, Clinical Medical College of Nanjing Medical University, Nanjing, People's Republic of China; [2]Department of Cardiology, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu, People's Republic of China; [3]Department of Pulmonology, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu, People's Republic of China; [4]Department of Nursing, Changshu No.2 People's Hospital/Affiliated Changshu Hospital of Nantong University, Changshu, Jiangsu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Weiming Li; Ling Zhang, Email 18917683469@189.cn; nancy120312@163.com

Objective: Current scoring systems for short-term prognosis in patients with acute myocardial infarction (AMI) lack coverage of risk factors and have limitations in risk stratification. The aim of this study was to develop a novel assessment system based on laboratory indicators and frailty quantification to better infer short-term prognosis and risk indication in patients with AMI.

Methods: A total of 365 patients with MI from January 2022 to June 2023 in Northern Jiangsu Province Hospital were included. The primary endpoint was all-cause mortality and major adverse cardiac events (MACE) during follow-up. A novel scoring model ranging from 0 to 12 was constructed, and the predictive ability of this scoring system was evaluated using the area under the receiver operating characteristic curve (AUC).

Results: During follow-up, 68 patients experienced MACE. Five scoring indicators were selected through multivariate logistic regression analysis, resulting in a composite score with an AUC of 0.925, demonstrating good prognostic accuracy.

Conclusion: The novel prognostic assessment system, which integrates age, Stress Hyperglycemia Ratio (SHR), Neutrophil to Lymphocyte Ratio (NLR), lactate, and frailty score, exhibits good predictive value for short-term MACE in patients with acute myocardial infarction and may enable more accurate risk classification for future use in MI patient risk management.

Keywords: myocardial infarction, frailty index, major adverse cardiac events, prognosis, cohort study

Introduction

With the advancement of early revascularization and medical preventive strategies, especially the widespread use of percutaneous coronary intervention (PCI), the prognosis of patients with acute myocardial infarction (AMI) has been greatly improved. However, AMI remains one of the leading causes of morbidity and mortality globally, with adverse cardiac events such as heart failure persisting in the short-term prognosis of MI.

Frailty is commonly regarded as a state characterized by reduced physiological reserves and loss of resistance to stressors, manifested as poor physical activity, decreased muscle mass, poor nutritional status, and cognitive decline. Numerous studies have shown that frailty is a favorable predictor of adverse outcomes and mortality in patients with acute myocardial infarction.[1] The Fried frailty phenotype and Clinical Frailty Scale (CSF) are commonly used assessment tools for frailty, validated extensively in research and clinical practice.[2]

Received: 1 June 2024
Accepted: 6 September 2024
Published: 26 September 2024

Various scoring systems, such as the GRACE risk score, have been used to assess cardiovascular risk. Objective risk assessment helps to avoid the influence of subjective judgments by physicians on risk discrimination and plays an important role in personalized patient risk assessment and survival prediction.[3] As a guideline-recommended MI management risk model, the GRACE risk score is mainly used to predict mortality after 6 months but has limited predictive efficacy for short-term prognosis, and most current risk assessment models tend to be disease-related dimensions.[4] Indeed, biomarkers and laboratory indicators play an indispensable role in assisting timely diagnosis and accurate prediction of short-term prognosis. The levels of different biomarkers can reflect different pathological and physiological processes.[5] Various types of laboratory indicators have been used for cardiovascular disease risk prediction. For example, platelet count is an important parameter for the diagnosis, treatment, and prognosis assessment of circulatory failure-related diseases,[6] Short-term follow-up B-type natriuretic peptide (BNP) levels have been shown to be reliable predictors of short-term prognosis in acute coronary syndrome.[7] In addition, common prognostic risk factors include creatinine clearance, homocysteine, etc.[8–11] Imaging parameters, due to their simplicity, intuitiveness, non-invasiveness, and ease of acquisition, have also become potential predictors of prognosis in AMI patients,[12] All these provide possibilities for establishing a comprehensive evaluation system by integrating multiple indicators.

This study aimed to screen for risk factors associated with adverse cardiac events after acute myocardial infarction recovery, establish a novel scoring system based on the frailty index and laboratory indicators, and assess its impact on the short-term prognosis of patients with acute myocardial infarction.

Methods

Research Design and Participants

This study was a retrospective, single-center, observational study. A total of 723 patients hospitalized for ACS were consecutively screened, with the inclusion process depicted in Figure 1. The definition of acute myocardial infarction adhered to the fourth universal definition of myocardial infarction. Exclusion criteria included: 1) a diagnosis of chronic coronary syndrome upon admission; 2) age <18 years; 3) incomplete clinical information or short-term follow-up data. Ultimately, 365 patients were included and categorized into two groups based on short-term prognosis: those who experienced MACE and those who did not. The informed consents were obtained from the participants in this study. Besides, the study protocol of current study has been approved by the Ethics Committee of the Northern Jiangsu People's Hospital. This study was conducted in accordance with the Declaration of Helsinki, and the medical ethics committee approved this research.

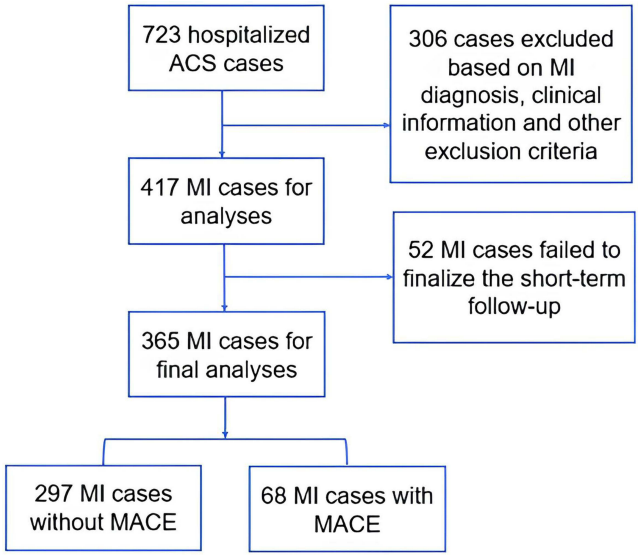

Figure 1 Patient selection process.

Data Collection and Definitions

Researchers obtained basic data on demographics, clinical characteristics, laboratory test results, and medication usage from electronic medical records. Demographics included age, gender, and Body Mass Index (BMI), calculated as weight (kg)/height $(m)^2$. Hypertension was defined as a self-reported history of hypertension, current use of antihypertensive drugs, or a diastolic blood pressure ≥80mmHg and/or systolic blood pressure ≥130mmHg on three or more occasions.[13] Current smokers or those who had quit smoking less than six months ago were considered smokers. Histories of diabetes, chronic kidney disease, chronic obstructive pulmonary disease(COPD), and hyperlipidemia were obtained from self-reports or clinical records. Particular attention was paid to the use of antihypertensive drugs, statins, anticoagulants, and antiplatelet agents. Blood samples taken within 24 hours of admission were used to determine complete blood count, liver function, lipid profile, and other biochemical indicators like lactate and SHR, all of which were conducted by the hospital's laboratory department. NLR is calculated as absolute ratio of peripheral neutrophil count to lymphocyte count, while platelet to lymphocyte ratio (PLR) is calculated as absolute ratio of peripheral platelet count to lymphocyte count. Systemic immune-inflammation index (SII) is calculated as peripheral platelet count × absolute neutrophils count / absolute lymphocytes count. SHR was calculated according to the following equation: SHR = admission glucose (mmol/L)/ (1.59× HbA1c [%]-2.59).

Frailty Assessment

Frailty was assessed using two common methods. The Frailty Phenotype (FP) consists of five criteria: weight loss, exhaustion, slow walking speed, low grip strength, and low physical activity. Meeting three or more criteria was considered frailty, 1–2 criteria pre-frailty, and 0 criteria no-frailty.[14] The Clinical Frailty Scale (CFS) involved researchers scoring patients based on their functional ability, mobility, and comorbidities, with scores ranging from 1 (very fit) to 9 (terminally ill).[15]

Endpoints

Follow-up data were obtained by the research institute using patient-provided identification and contact information, through electronic medical records, telephone follow-ups, and outpatient interviews. The primary endpoint was defined as Major Adverse Cardiac Events (MACE), a composite endpoint consisting of all-cause death, non-fatal myocardial infarction, readmission for heart failure, need for revascularization, and stroke.[16] A secondary endpoint includes arrhythmias and major bleeding events.

Statistical Analysis

All data were subjected to the Kolmogorov–Smirnov test for normality and the Levene test for homogeneity of variances. Quantitative data were expressed as mean ± standard deviation or median with interquartile range (IQR), and categorical variables as counts. The differences in baseline data between groups were compared using *t*-test, Kruskal–Wallis *H*-test, or Pearson chi-square test, depending on the variable type. Multivariate logistic regression models were employed to explore risk factors related to short-term prognosis and their odds ratios (OR) with 95% confidence intervals (CI). The discriminative ability of the novel evaluation system was assessed by the area under the receiver operating characteristic curve (AUC), with $P < 0.05$ considered statistically significant. Statistical analyses were performed using SPSS 26.0.

Results

Basic Characteristics

This study included 365 MI patients who met the inclusion and exclusion criteria, among which 68 cases (18.6%) experienced adverse cardiac events. Compared to patients who did not experience adverse cardiac events, the average age of those who did was significantly higher at 71.78 ± 11.33 years ($p< 0.001$, Table 1).

From the perspective of laboratory indicators, patients in the group that experienced adverse cardiac events had lower white blood cells and hemoglobin levels but higher levels of neutrophils, ALT, NLR, and SII. Lactate and SHR levels were significantly higher than in the group that did not experience adverse cardiac events, with these differences being

Table 1 Comparison of Basic Demographic and Clinical Characteristics of Patients According to the Occurrence of MACE

Parameters	Without MACE (n=297)	With MACE (n=68)	P
Demographic factors			
Age (years)	59.70±10.95	71.78±11.33	**< 0.001**
Gender (male/female)	191/106	41/27	0.577
BMI (kg/m^2)	25.72±3.43	25.40±3.10	0.477
Diabetes mellitus (Yes/No)	38/259	10/58	0.692
Hypertension (Yes/No)	154/143	29/39	0.181
Cigarette smoking (Yes/No)	89/208	26/42	0.195
Chronic kidney disease (Yes/No)	47/250	14/54	0.368
COPD (Yes/No)	63/234	10/58	0.313
Hyperlipidemia (Yes/No)	56/241	16/52	0.400
SBP (mmHg)	131.49±24.17	137.65±23.34	0.058
DBP (mmHg)	84.49±18.17	83.47±15.16	0.667
Drug use			
CaB (Yes/No)	108/189	19/49	0.206
ARB (Yes/No)	81/216	11/57	0.064
ACEI (Yes/No)	102/195	20/48	0.479
Statins (Yes/No)	44/253	12/56	0.577
Anticoagulant (Yes/No)	36/261	13/55	0.165
Antiplatelet (Yes/No)	27/270	12/56	0.050

Abbreviations: MACE, Major Adverse Cardiovascular Events; BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; CaB, Calcium Blocker; ARB, Angiotensin II Receptor Blocker; ACEI, Angiotensin-Converting Enzyme Inhibitor; bold font means p<0.05 and the result is statistically significant.

Table 2 Comparison of Laboratory Indicators and Frailty Scores in Patients According to the Occurrence of MACE

Parameters	Without MACE (n=297)	With MACE (n=68)	P
Laboratory examinations			
Neutrophils (10^9/L)	5.19±1.18	6.60±2.33	**< 0.001**
Lymphocytes (10^9/L)	1.33±0.25	1.23±0.16	**0.002**
PLT (10^9/L)	204.62±31.64	206.91±35.41	0.600
Hb (g/L)	129.76±11.88	118.03±8.33	**< 0.001**
NLR	4.07±1.32	5.45±2.09	**< 0.001**
PLR	159.13±40.32	158.22±37.95	0.865
SII	828.04±289.51	1047.24±482.54	**< 0.001**
ALT (U/L)	23.16±7.25	28.01±7.08	**< 0.001**
AST (U/L)	28.75±9.44	31.96±11.18	0.015
Triglycerides (mmol/L)	1.26±0.23	1.28±0.26	0.588
Total cholesterol (mmol/L)	4.34±0.90	4.43±0.88	0.440
LDL-C (mmol/L)	2.42±0.62	2.26±0.56	0.063
HDL-C (mmol/L)	1.47±0.12	1.34±0.31	0.432
Lactate (mmol/L)	3.15±1.12	5.35±1.99	**< 0.001**
SHR	0.99±0.13	1.07±0.28	**0.002**
Frailty status			
Frailty score	1.84±1.09	3.21±1.48	**< 0.001**
No frailty	34	4	**< 0.001**
Pre frailty	183	16	
Frailty	80	48	

Abbreviations: MACE, Major Adverse Cardiovascular Events; PLT, Platelet Count; Hb, Hemoglobin; NLR, Neutrophil to Lymphocyte Ratio; PLR, Platelet to Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; LDL-C, Low-Density Lipoprotein Cholesterol; HDL-C, High-Density Lipoprotein Cholesterol; SHR, Stress Hyperglycemia Ratio; bold font means p<0.05 and the result is statistically significant.

statistically significant. Additionally, the frailty score in the group that experienced adverse cardiac events was significantly higher than in the group without adverse cardiac events, with a higher prevalence of pre-frail and frail patients, indicating a statistically significant difference (Table 2).

Model Construction

A multivariate logistic regression model analysis was conducted on the indicators that showed significant differences between the two groups of patients, calculating the odds ratios to explore their correlation with adverse cardiac event outcomes (Table 3). The results indicated that laboratory indicators with statistical significance included the NLR, lactate levels, and SHR. Additionally, age and frailty were identified as independent risk factors for poor prognosis in patients with acute myocardial infarction, showing a significant correlation with the primary outcomes. The predictive value of a combined diagnosis, as shown by the multivariate joint diagnostic ROC curve plotted based on the multivariate regression predicted probabilities, was significantly higher than that of individual indicators, with the largest area under the curve (Figure 2).

Based on the Youden index, indicators with potential impact on adverse cardiac events were grouped by their cutoff values, with the group below the cutoff value serving as the reference group. Using the multivariate logistic regression model, the partial regression coefficients for each risk factor were calculated (Table 4). The results showed that all indicator values were positively correlated with adverse outcomes.

Model Validation

Statistically significant partial regression coefficient estimates were converted into the nearest integer values to establish a risk scoring model. Each potential impact indicator was assigned stratified integer values, which were then summed to calculate each patient's score. This formed a new scale scoring system for predicting short-term prognosis in patients with acute myocardial infarction, (Table 5) including indicators such as age, NLR, lactate, stress hyperglycemia ratio, and frailty score.

The scoring results were reclassified into low-risk (0–4), middle-risk (5–8), and high-risk (9–12) groups (Table 6). The endpoint outcomes served as the gold standard for evaluating the diagnostic performance of this new quantitative scoring system by calculating the area under the receiver operating characteristic curve (AUC).

As shown, the AUC was 0.925 ($p < 0.01$) (Figure 3), indicating that this new scoring scale has a good predictive value for adverse cardiac events in the short-term prognosis of patients with acute myocardial infarction.

Discussion

In this study, we developed a new scoring scale based on laboratory indicators and frailty scores for predicting short-term prognosis in patients with acute myocardial infarction, demonstrating good predictive ability for the incidence and risk stratification of adverse cardiac events. This scoring scale incorporates five readily available indicators at admission: age,

Table 3 Multivariate Logistic Regression for Selecting Predictive Factors for MACE in MI Patients

Parameters	Odds Ratio	95% CI	P
Age	1.12	1.07 to 1.17	**<0.001**
NLR	2.47	1.39 to 4.56	**0.003**
SII	1.00	0.99 to 1.00	0.087
ALT	1.05	0.99 to 1.12	0.105
AST	1.04	0.99 to 1.09	0.153
Lactate	2.72	1.98 to 3.97	**<0.001**
SHR	13.02	1.41 to 160.10	**0.033**
Frailty	2.36	1.64 to 3.53	**<0.001**

Abbreviations: NLR, Neutrophil to Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; SHR, Stress Hyperglycemia Ratio; bold font means p<0.05 and the result is statistically significant.

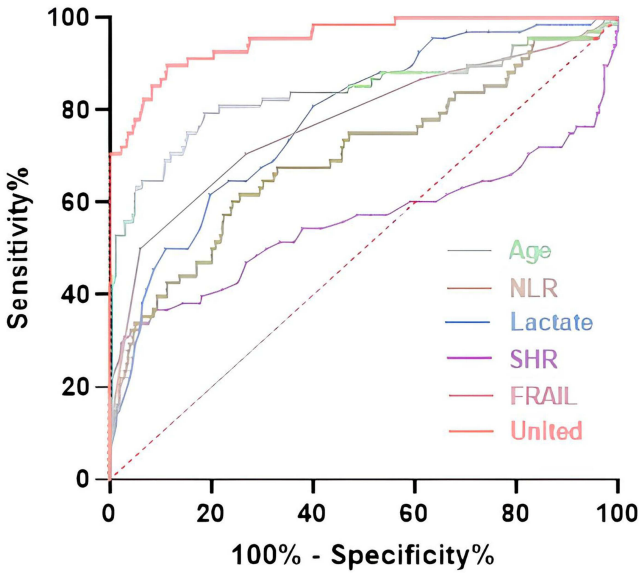

Figure 2 Multivariate joint diagnosis of ROC curves.

NLR, lactate, SHR, and frailty score, making it easily applicable in clinical practice. It classifies patients into low, medium, and high risk, exhibiting excellent discriminative power for predicting adverse cardiac event outcomes and risk stratification in patients with acute myocardial infarction.

Age is one of the significant risk factors for the onset and progression of coronary artery disease, and numerous studies have indicated its crucial impact on the short-term prognosis of AMI patients.[17] The IMRS risk score can predict short-term mortality in STEMI patients, with age being a major component of IMRS.[18] Similarly, in this experiment, *t*-test analysis revealed a statistical difference in age between the MACE and non-MACE groups (Table 1).

The acute exacerbation of ASC is closely related to the inflammatory response, which dominates and participates in the entire process of coronary artery progression. Stress hyperglycemia, secondary to the inflammation and neuroendocrine disorder caused by severe illnesses, is closely associated with poor prognosis in AMI patients. Various experiments and clinical studies have shown that acute hyperglycemia can trigger vascular inflammation, exacerbating myocardial damage, and high glucose levels may lead to an increase in MCP-1 and its inducible proteins, affecting cardiac recovery post-PCI in AMI patients.[19] Furthermore, stress hyperglycemia can cause an increase in the levels of the novel biomarker Cyr61 for myocardial ischemia and damage, reflecting underlying mechanisms possibly related to sympathetic activation, inflammation, and increased ischemia.[20] This study demonstrates that SHR has a more significant and stable predictive value for the short-term prognosis of MI patients compared to the diabetic status.

Table 4 Multivariate Logistic Regression Analysis for Predicting MACE with Weighted Scores in MI Patients

Parameters	Estimate	95% CI	P
Age	1.72	0.86 to 2.64	**0.001**
NLR	1.93	0.97 to 2.95	**0.001**
Lactate	3.45	2.51 to 4.55	**<0.001**
SHR	1.98	0.98 to 3.04	**0.001**
Frailty	3.18	2.17 to 4.32	**<0.001**

Abbreviations: NLR, Neutrophil to Lymphocyte Ratio; SHR, Stress Hyperglycemia Ratio; bold font means p<0.05 and the result is statistically significant.

Table 5 Contents of the New MACE Prediction Scale for MI Patients

Parameters	Classifications	Scores
Age	< 65 years	0
	≥ 65 years	2
NLR	< 5.673	0
	≥ 5.673	2
Lactate	< 4.080	0
	≥ 4.080	3
SHR	< 1.145	0
	≥ 1.145	2
Frailty	0 to 2	0
	3 to 5	3
Total score	12	

Abbreviations: NLR, Neutrophil to Lymphocyte Ratio; SHR, Stress Hyperglycemia Ratio.

Table 6 Correlation Between Staging of the New Evaluation System and Incidence of MACE in MI Patients

Parameters	Without MACE (n=297)	With MACE (n=68)	P
Low risk	281	20	**<0.001**
Middle risk	16	29	
High risk	0	19	

Abbreviations: MACE, Major Adverse Cardiovascular Events; bold font means p<0.05 and the result is statistically significant.

(Table 3) A large-scale study by ZENG G et al also confirmed that high SHR is an independent risk factor for poor cardiac outcomes in AMI, serving as a reliable marker for risk stratification.[21] In a study involving 4337 patients, LIU J et al reported that SHR in STEMI patients was independently associated with one-year and long-term all-cause mortality.[22] NLR, a novel inflammatory marker closely associated with inflammation, is easy to calculate and more stable than conventional blood cell parameters. The study by LI Q et al confirmed that an NLR≥2.83 significantly increases the risk of adverse cardiac events in patients with acute coronary syndrome.[23] Early recruitment of

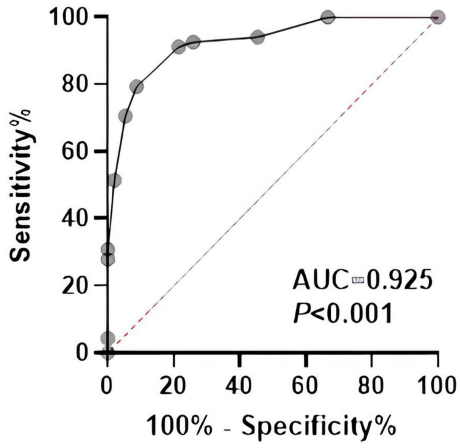

Figure 3 The ROC curve of the new rating scale predicts MACE.

neutrophils in the infarcted area leads to further myocardial damage, while a low lymphocyte count is directly related to poorer cardiac outcomes. A study on 1,550 elderly AMI patients showed that NLR could predict in-hospital mortality risk in elderly AMI patients better than PLR. This study confirms the predictive value of NLR but found no statistical difference in PLR between the MACE and non-MACE groups, (Table 2) likely due to the limited effective sample size.[24] The Systemic Immune-Inflammation Index (SII), including neutrophil, platelet, and lymphocyte counts, is another novel inflammatory marker. This study has shown that SII is closely associated with the risk of MACE in patients with ACS.[25] However, after adjusting for multiple confounding factors in this study, the correlation of SII with adverse cardiac events no longer held statistical significance, (Table 3) indicating that SII's role in differentiating cardiovascular disease risk might not be stable enough.

Cardiogenic shock is one of the common adverse cardiac outcomes in AMI patients, with studies showing that serum lactate is an independent predictor of short-term mortality in AMI patients with CS.[26] An increase in serum lactate concentration indicates insufficient tissue perfusion, promoting metabolic acidosis, decreasing myocardial contractility, altering systemic vascular resistance, promoting cellular hypoxia, and poor tissue perfusion.[27] Secondary hyperkalemia caused by acidosis can also increase the probability of arrhythmias. The study found that the L/A ratio (lactate to albumin ratio) is positively correlated with 30-day all-cause mortality in AMI patients.[28] In our experiment, elevated serum lactate levels were positively correlated with adverse cardiac events, maintaining a stable prognostic value after adjusting for multiple confounding factors (Table 4).

As the exploration and development of frailty assessments in cardiovascular diseases progress, over 30 frailty assessment tools have been widely used in AMI patients. Frailty is usually used in elderly patients,[29] but recent studies show that frailty is significantly related to the one-year mortality rate in AMI patients under 65,[30] In this study, both frailty phenotype and frailty scale showed significant differences between the MACE and non-MACE groups, (Table 2) with the frailty scale scoring performing well in risk prediction (Figure 2).

By filtering through a series of potential risk factors, we have identified indicators capable of assessing both the physiological and pathological progression in patients with acute myocardial infarction. The AUC result (0.925) demonstrates that this novel integrated assessment system possesses excellent sensitivity and specificity (Figure 3). For short-term prognosis evaluation in AMI patients, the scoring system encompassing these five indicators also offers simplicity and ease of operation.

Limitations

As a retrospective study, its non-interventional nature may lead to incomplete data collection and loss of sample size. Whether the new scoring system has a positive effect on the risk prediction of MACE needs to be confirmed by further prospective cohort studies. Additionally, the population data collected from specific hospitals may not fully represent the entire acute myocardial infarction population. Some medical histories, such as hyperlipidemia and diabetes mellitus, are mainly self-reported by patients, and there may be reporting bias and limited inclusion of covariates, and there may be confounding factors. In addition, there may be incomplete confounding factors such as troponin, BNP, and echocardiographic parameters, and these factors should be further considered.[31] Lastly, only two frailty assessment tools were used in this study, and the impact of different assessment methods on the predictive value of this scoring system has not been considered.

Conclusion

This novel evaluation system, which combines laboratory indicators, biomarkers, and a frailty scoring scale, can be used for the short-term prognosis assessment of patients with acute myocardial infarction. It allows healthcare professionals to objectively, quickly, and effectively differentiate patient risk, thus facilitating better medical decision-making.

Abbreviations

MI, Myocardial Infarction; AMI, Acute Myocardial Infarction; ACS, Acute Coronary Syndrome; MACE, Major Adverse Cardiovascular Events; BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; SBP, Systolic Blood

Pressure; DBP, Diastolic Blood Pressure; CaB, Calcium Blocker; ARB, Angiotensin II Receptor Blocker; ACEI, Angiotensin-Converting Enzyme Inhibitor; PLT, Platelet Count; Hb, Hemoglobin; NLR, Neutrophil to Lymphocyte Ratio; PLR, Platelet to Lymphocyte Ratio; SII, Systemic Immune-Inflammation Index; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; LDL-C, Low-Density Lipoprotein Cholesterol; HDL-C, High-Density Lipoprotein Cholesterol; SHR, Stress Hyperglycemia Ratio; BNP, B-Type Natriuretic Peptide.

Disclosure

Tianqing Cao and Fei Liu are co-first authors for this study. The authors report no conflicts of interest in this work.

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