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Construction and Validation of a Predictive Model for Long-Term Major Adverse Cardiovascular Events in Patients with Acute Myocardial Infarction

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Purpose: Current scoring systems used to predict major adverse cardiovascular events (MACE) in patients with acute myocardial infarction (AMI) lack some key components and their predictive ability needs improvement. This study aimed to develop a more effective scoring system for predicting 3-year MACE in patients with AMI.

Patients and Methods: Our statistical analyses included data for 461 patients with AMI. Eighty percent of patients (n=369) were randomly assigned to the training set and the remaining patients (n=92) to the validation set. Independent risk factors for MACE were identified in univariate and multifactorial logistic regression analyses. A nomogram was used to create the scoring system, the predictive ability of which was assessed using calibration curve, decision curve analysis, receiver-operating characteristic curve, and survival analysis.

Results: The nomogram model included the following seven variables: age, diabetes, prior myocardial infarction, Killip class, chronic kidney disease, lipoprotein(a), and percutaneous coronary intervention during hospitalization. The predicted and observed values for the nomogram model were in good agreement based on the calibration curves. Decision curve analysis showed that the clinical nomogram model had good predictive ability. The area under the curve (AUC) for the scoring system was 0.775 (95% confidence interval [CI] 0.728–0.823) in the training set and 0.789 (95% CI 0.693–0.886) in the validation set. Risk stratification based on the scoring system found that the risk of MACE was 4.51-fold higher (95% CI 3.24–6.28) in the high-risk group than in the low-risk group. Notably, this scoring system demonstrated better predictive ability than the GRACE risk score (AUC 0.776 vs 0.731; P=0.007).

Conclusion: The scoring system developed from the nomogram in this study showed favorable performance in prediction of MACE and risk stratification of patients with AMI.

Keywords: acute myocardial infarction, long-term outcome, MACE, nomogram, risk prediction model

Introduction

Acute myocardial infarction (AMI) is the most serious type of coronary artery disease (CAD) with high rates of death and disability. Even among survivors, the probability of major adverse cardiovascular events (MACE) is substantially higher after AMI than before this event.[1,2] Furthermore, the prognosis of AMI patients varies widely depending on their clinical presentation, age, cardiovascular risk factors, and comorbidities.[3] Therefore, there is a need for a validated tool that can predict the long-term prognosis of these patients.

The guidelines suggest that patients with AMI should be risk-stratified using the GRACE (Global Registry of Acute Coronary Events) and TIMI (Thrombolysis In Myocardial Infarction) risk scores.[4] However, these scores were developed

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to assist clinicians in formulating rapid medical strategies and predicting the short-term risks of reinfarction and death based on the clinical information obtained in the emergency room.[5–7] Therefore, in terms of predicting the longer-term prognosis, these scoring systems overlook several significant factors. The management of patients with AMI has significantly improved over the past 20 years. As a result, the risk factors for MACE have evolved, along with changes in the strength of their associations with these outcomes.[1,8] Therefore, there is a pressing need to update the variables included in the scoring systems that are used to predict out-of-hospital MACE in patients with AMI. Furthermore, the long-term prognosis of these patients goes beyond the risks of reinfarction and death, given that the risks of stroke and heart failure are also substantially elevated in this population[3] and impose a serious burden that should not be ignored in lifelong out-of-hospital management after AMI. Overall, the issue of insufficient predictive performance of widely used classical models is becoming increasingly apparent in clinical practice.

In this study, we conducted a comprehensive retrospective analysis of 3-year adverse outcomes in patients with acute myocardial infarction. Our goal was to develop a novel scoring system that enhances the prediction of long-term adverse events, providing more accurate risk stratification for this patient population.

Material and Methods

Population and Study Design

The study included patients with AMI who were selected based on the "Fourth Universal Definition of Myocardial Infarction (2018)", which requires detection of elevated cardiac troponin values, with at least one value being above the 99th percentile upper reference limit, and at least one of the following: symptoms of acute myocardial ischemia; new ischemic electrocardiographic changes; development of pathological Q waves; imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology; and identification of coronary thrombus by angiography, including intracoronary imaging.[3]

The following exclusion criteria were applied: age younger than 18 years; presence of another cardiac condition, such as congenital heart disease, valvular heart disease, cardiomyopathy, arrhythmia, or cardiopulmonary disease; cerebral hemorrhage, gastrointestinal hemorrhage, or major surgery within the previous 6 months; no secondary prevention medications for coronary heart disease; pregnancy and lactation; incomplete medical history or examination results; death during hospitalization; and refusal to participate or loss to follow-up.

Acute kidney injury was defined as acute prerenal kidney injury as a result of changes in circulatory hemodynamics during AMI and characterized by an increase in serum creatinine of more than 1.5-fold from baseline within 7 days of enrollment, an absolute increase of 26.5 μmol/L within 48 hours, or initiation of renal replacement therapy for the first time. Chronic kidney disease (CKD) was defined as a baseline estimated glomerular filtration rate of <60 mL/min/1.73 m^2 after exclusion of acute kidney injury. Previous percutaneous coronary intervention (PCI) was classified as invasive treatment during the course of CAD (prior PCI for CAD) or during a previous MI (prior PCI for MI). Timely PCI was defined as interventional therapy received within 12 hours of onset of AMI during the current hospitalization or if AMI had persisted for over 12 hours, showing signs of progressive myocardial ischemia, hemodynamic instability, fatal arrhythmia, or successful resuscitation from cardiac arrest. Procedures performed after the acute phase were defined as delayed PCI. Acceptance of at least one current invasive strategy was defined as PCI during hospitalization. The detailed definition of rapidly changing variables is provided in the Supplementary Instruction.

Data Collection and Patient Follow-Up

Consecutive patients who attended the First Affiliated Hospital of Zhengzhou University between January 1, 2018 and December 31, 2019 with AMI were recruited. We collected baseline data, examination and test results, and information on use of medications and on surgical and device applications, among other relevant information. Enrollment and clinical data were recorded for each patient by experienced cardiologists.

After discharge, all patients were actively followed up for 36 months, with the following endpoint events defined as MACE: nonfatal myocardial reinfarction, hospitalization for heart failure, cardiac death, nonfatal stroke, and all-cause

mortality (except for accidents).[9–12] Patients were assessed by trained physicians and nurses who were blinded to the purpose of the study based on outpatient follow-up, rehospitalization, or telephone follow-up data.

Participant Grouping

Participants were randomly grouped in a ratio of 4:1, with 80% assigned to the training set for exploration of independent long-term prognostic factors in patients with AMI and for development of the novel scoring system. The remaining 20% were assigned to the validation set to confirm the prediction performance of the scoring system.

Statistical Analysis

Baseline patient characteristics were compared between the training and validation sets using the chi-squared test for categorical variables, independent *t*-test for continuous variables, and Mann–Whitney *U*-test for nonparametric distributions. Between-group differences were examined using SPSS for Windows software (version 27.0; IBM Corp., Armonk, NY, USA).

The scoring system was constructed and validated using R version 4.3.1 (The R Foundation for Statistical Computing, Vienna, Austria). Continuous numerical variables were dichotomized based on expert opinion or optimal cut-off values identified by receiver-operating characteristic (ROC) analyses. Univariate logistic regression analyses were performed in the training set, and candidate variables were selected from statistically significant results, guided by published models[6,13–16] and clinical expert opinion.[4,17,18] All candidate variables were initially included in the multivariable logistic regression model, and the model was iteratively refined using the backward elimination method, progressively removing non-significant variables until only significant predictors remained. The regression coefficients of the final model were used as weights for the corresponding variables. A nomogram was constructed using the "rms" package in R to develop a clinically feasible scoring system. The prediction performance of the model was evaluated by calibration curves, decision curve analysis, and ROC curve analysis. Survival analysis was used to assess the ability of the scoring system to risk-stratify patients with AMI. Finally, ROC curve analysis was performed to compare the prediction performance of the novel scoring system with that of the GRACE score. Statistical significance was defined as an α value of 0.05, with a *P*-value of < 0.05 considered statistically significant.

Results

Study Populations

The study included 461 patients with AMI from the First Affiliated Hospital of Zhengzhou University. Eighty percent of these patients (n=369) were randomly assigned to the training set and the remaining patients (n=92) to the validation set. A flow diagram showing the patient selection process is shown in Figure 1. The baseline characteristics of patients in the training and validation sets are summarized in Table 1.

Exploration of Prognostic Predictors in the Training Set

In the training set, 22 factors were identified to show significant differences between patients with and without MACE (Supplementary Table 1). Twenty of these parameters remained statistically significant following univariate logistic regression analyses (Supplementary Table 2). To construct a clinically feasible prediction model, we selected candidate variables from those that were identified to be statistically significant in the univariate logistic regression analyses, guided by previously published models. The results of the univariate logistic regression analyses of the candidate variables are shown as a forest plot in Figure 2. Analysis of these candidate variables in a multivariate logistic regression model identified the following seven factors as being significant: age, diabetes, prior MI, Killip class, CKD, lipoprotein(a) [Lp(a)] level, and PCI during hospitalization (Table 2).

Construction of the Nomogram and Novel Scoring System in the Training Set

A nomogram was developed based on the factors identified in the multivariate logistic regression model (Figure 3a). The nomogram demonstrated robust discriminative ability, with an area under the curve (AUC) of 0.775 (95% CI 0.728–0.823) (Supplementary Figure 1). The *P*-value was 0.295 (Hosmer–Lemeshow test), indicating that the nomogram was well

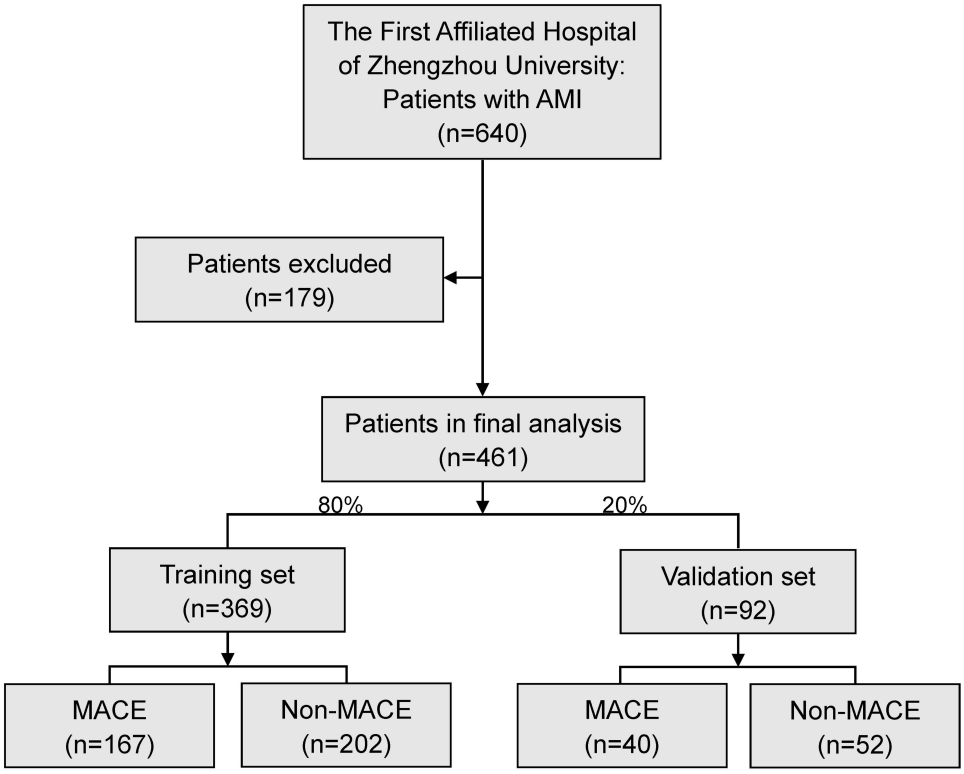

Figure 1 Flowchart of patient selection.
Abbreviations: AMI, acute myocardial infarction; MACE, major adverse cardiovascular events.

calibrated. The calibration curve demonstrated satisfactory consistency between the observed and predicted values in the nomogram (Figure 3b). The clinical value of the nomogram was also evaluated by decision curve analysis (Figure 3c), which revealed that the net benefit of the model significantly exceeded that of the two extreme cases in the training set.

Table 1 Baseline Characteristics of the Training Set and Validation Set

Variables	Total (n=461)	Training Set (n=369)	Validation Set (n=92)	*P*
Clinical characteristics				
Age, years	63.51±12.69	63.85±12.58	62.14±13.20	0.248
Male, n (%)	337 (73.1)	269 (72.9)	68 (73.9)	0.896
Heart rate, bpm	79±16	79±16	78±15	0.859
Systolic blood pressure, mmHg	131±23	131±22	133±27	0.619
Diastolic blood pressure, mmHg	78±15	77±14	79±16	0.237
Body mass index, kg/m^2	24.33±2.98	24.38±2.93	24.13±3.21	0.514
CVD risk factors				
Current smoker, n (%)	167 (36.2)	137 (37.1)	30 (32.6)	0.468
Family history of CAD, n (%)	63 (13.7)	52 (14.1)	11 (12.0)	0.735
Hypertension, n (%)	280 (60.7)	226 (61.2)	54 (58.7)	0.721
Diabetes, n (%)	186 (40.3)	147 (39.8)	39 (42.2)	0.722
Prior MI, n (%)	81 (17.6)	68 (18.4)	13 (14.1)	0.363
MACE, n (%)	207 (44.9)	167 (45.3)	40 (43.5)	0.815
Nonfatal MI, n (%)	46 (10.0)	34 (9.2)	12 (13.0)	0.329
Recurrent heart failure, n (%)	94 (20.4)	79 (21.4)	15 (16.3)	0.314
Nonfatal stroke, n (%)	15 (3.3)	11 (3.0)	4 (4.3)	0.513
Cardiac death, n (%)	35 (7.6)	31 (8.4)	4 (4.3)	0.270
All-cause mortality, n (%)	52 (11.3)	43 (11.7)	9 (9.8)	0.715

(*Continued*)

Table 1 (Continued).

Variables	Total (n=461)	Training Set (n=369)	Validation Set (n=92)	*P*
GRACE risk score	173 (147–203)	174 (149–203)	170 (143–198)	0.254
Cardiac-related indicators				
Peak cTNI, pg/mL	3.35 (1.21–13.63)	3.32 (1.18–13.36)	3.77 (1.30–13.90)	0.281
Peak pro-BNP, pg/mL	2498 (903–7634)	2456 (855–8547)	2700 (1072–5862)	0.929
LVEF, %	54 (45–60)	54 (45–60)	53 (46–60)	0.696
Killip class ≥ II	369 (80.0)	293 (79.4)	76 (82.6)	0.561
HFrEF, n (%)	69/369 (18.7)	56/293 (19.1)	13/76 (17.1)	0.654
HFmrEF, n (%)	92/369 (24.9)	70/293 (23.9)	22/76 (28.9)	
HFpEF, n (%)	208/369 (56.4)	167/293 (57.0)	41/76 (53.9)	
Renal function				
eGFR, mL/min/1.73m^2	84.0 (55.3–97.0)	84.5 (54.0–96.9)	84.5 (64.3–99.2)	0.324
Creatinine, μmol/L	80 (65–104)	80 (64–106)	79 (67–99)	0.830
Changes of renal function during hospitalization				
IRF, n (%)	58/363 (16.0)	41/289 (14.2)	17/74 (23.0)	0.160
SRF, n (%)	238/363 (65.6)	192/289 (66.4)	46/74 (62.2)	
WRF, n (%)	67/363 (18.5)	56/289 (19.4)	11/74 (14.6)	
Lipids				
Lp(a), mg/dL	17.2 (8.7–33.4)	15.5 (8.4–33.0)	21.1 (9.2–40.5)	0.162
TC, mmol/L	3.57 (2.97–4.46)	3.57 (2.98–4.52)	3.52 (2.87–4.26)	0.616
TG, mmol/L	1.29 (0.92–1.82)	1.29 (0.93–1.80)	1.38 (0.90–2.01)	0.856
LDL, mmol/L	2.07 (1.54–2.79)	2.06 (1.55–2.85)	2.14 (1.53–2.73)	0.730
HDL, mmol/L	0.99 (0.82–1.19)	0.99 (0.82–1.19)	0.96 (0.77–1.18)	0.498
Inflammation				
CRP, mg/L	8.88 (2.19–31.73)	7.93 (2.12–34.95)	10.65 (2.47–29.65)	0.735
NLR, ratio	4.61 (2.86–8.21)	4.58 (2.85–8.32)	4.68 (2.88–7.11)	0.823
PLR, ratio	151.8 (104.45–220.55)	152.9 (105.54–231.58)	142.8 (103.20–211.63)	0.293
Coagulation function				
PT, s	11.54±5.17	11.58±5.62	11.38±2.77	0.745
APTT, s	30.98±10.81	31.19±11.84	30.17±4.95	0.425
Fibrinogen, g/L	3.60±1.38	3.55±1.29	3.78±1.70	0.156
D-Dimer, mg/L	0.19 (0.09–039)	0.19 (0.09–0.40)	0.18 (0.07–0.34)	0.173
Other laboratory findings				
HbA1c, %	6.87±1.68	6.88±1.71	6.84±1.57	0.872
WBC, 10^9/L	9.22±1.09	9.16±4.16	9.47±3.86	0.507
Hb, g/L	125.79±24.60	125.21±24.91	128.13±23.43	0.312
PLT, 10^9/L	210.00±77.32	209.72±78.74	211.14±72.16	0.875
ALT, μ/L	27 (17–43)	27 (17–44)	26 (18–41)	0.990
AST, μ/L	36 (22–85)	36 (22–82)	37 (22–83)	0.778
Total bilirubin, mmol/L	10.3 (7.0–15.0)	10.3 (7.1–14.9)	11.0 (6.7–15.2)	0.923
ALB, g/L	39.3 (35.8–42.2)	39.4 (35.8–42.1)	39.3 (35.7–42.4)	0.881
Percutaneous coronary intervention				
Prior PCI for CAD, n (%)	58 (12.6)	45 (12.2)	13 (14.1)	0.601
Prior PCI for MI, n (%)	53/81 (65.4)	48/73 (65.8)	5/8 (62.5)	1.000
Timely PCI, n (%)	159 (34.5)	124 (33.6)	35 (38.0)	0.462
Delayed PCI, n (%)	299 (64.9)	236 (64.0)	63 (68.5)	0.465
PCI during hospitalization, n (%)	384 (83.3)	306 (82.9)	78 (84.8)	0.765

Note: Data are presented as mean±SD, median (25th-75th), or count (%).

Abbreviations: CAD, coronary artery disease; MI, myocardial infarction; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; eGFR, estimated glomerular filtration rate; IRF, improvement in renal function; SRF, stable renal function; WRF, worsening renal function; Lp(a), lipoprotein(a); TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PT, prothrombin time; APTT, activated partial thromboplastin time; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate transaminase; ALB, albumin.

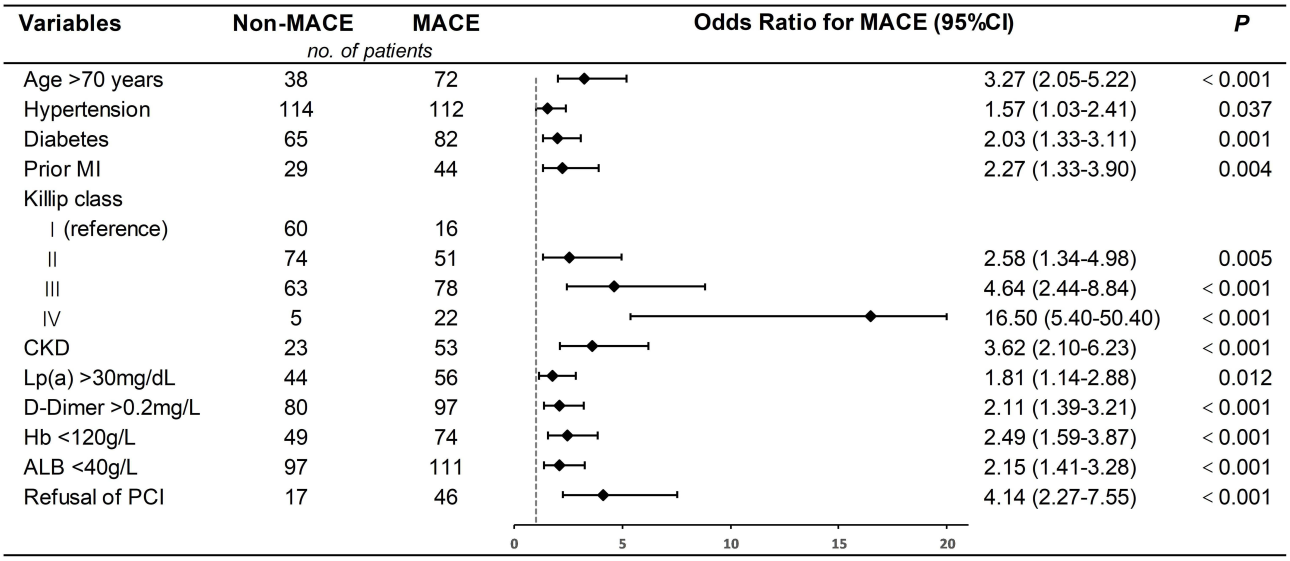

Figure 2 Forest plot of the significant parameters in the univariate logistic regression analyses (candidate variables).
Abbreviations: DBP, diastolic blood pressure; Prior MI, prior myocardial infarction; CKD, chronic kidney disease; Lp(a), lipoprotein(a); Hb, hemoglobin; ALB, albumin; Refusal of PCI, refusal of percutaneous coronary intervention: patients refused to receive PCI treatment during hospitalization.

To facilitate application of this prediction nomogram in clinical practice, we transformed the model into a scoring system with the following integer points: aged (40 points), diabetes (32 points), prior MI (38 points), Killip class (per level) (33 points), CKD (51 points), elevated Lp(a) (36 points), and refusal of PCI (43 points) (Table 3).

Prediction Performance of the Scoring System in the Training and Validation Sets

In the training set, the calibration curves demonstrated a high degree of consistency and fit with the scoring system (P=0.293, Hosmer–Lemeshow test) (Figure 4a), with an AUC of 0.775 (95% CI 0.728–0.823) (Figure 4c).

In the validation set, the calibration curve confirmed the robust predictive ability of the scoring system (P=0.355, Hosmer–Lemeshow test) (Figure 4b), with an AUC of 0.789 (95% CI 0.693–0.886) (Figure 4d).

For all patients, the optimal cut-off point derived from ROC analysis was 100 points (sensitivity 0.783; specificity 0.661). Patients with scores of <100 were classified as a low-risk group and those with scores of ≥100 as a high-risk group. Kaplan–Meier analysis revealed that cumulative event-free survival rates were significantly lower in patients in the high-risk group than in those in the low-risk group (P<0.001, Log rank test) (Figure 5a). Cox regression analysis indicated that the risk of MACE was 4.51-fold higher (95% CI 3.24–6.28) in the high-risk group.

Table 2 Results of Multivariate Logistic Regression Analysis in the Training Set

Variables	Odds Ratio for MACE (95% CI)	P
Aged	2.06 (1.22–3.49)	0.007
Diabetes	1.77 (1.10–2.86)	0.019
Prior MI	1.98 (1.08–3.64)	0.028
Killip class	1.82 (1.37–2.42)	<0.001
CKD	2.49 (1.36–4.56)	0.003
Elevated Lp(a)	1.93 (1.15–3.23)	0.013
Refusal of PCI	2.18 (1.09–4.34)	0.027

Abbreviations: Aged: age >70 years; MI, myocardial infarction; CKD, chronic kidney disease; Elevated Lp(a): serum lipoprotein(a) >30mg/dL; Refusal of PCI, refusal of percutaneous coronary intervention: patients refused to receive PCI treatment during hospitalization.

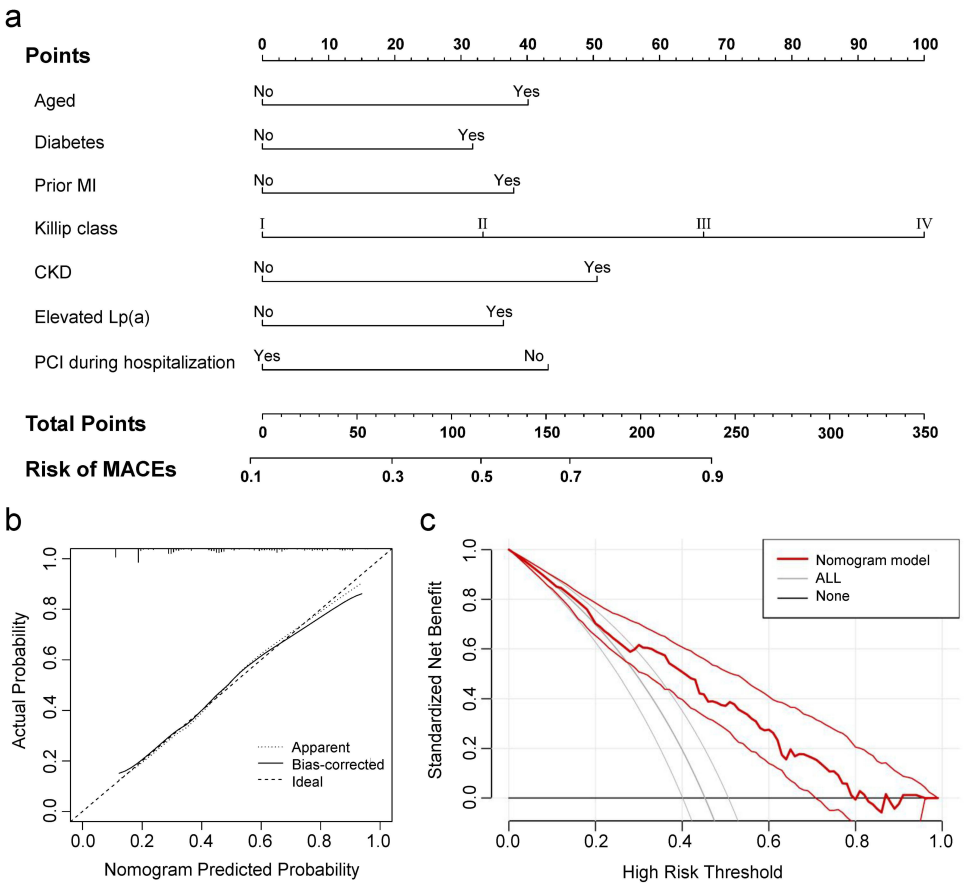

Figure 3 Calibration and clinical use of a predictive nomogram for the prediction of 3-year MACE: nomogram (**a**) for predicting 3-year MACE in AMI patients, calibration curve (**b**) and decision curve analysis (**c**) of the nomogram.

Abbreviations: Aged: age >70 years; MI, myocardial infarction; CKD, chronic kidney disease; Elevated Lp(a): serum lipoprotein(a)>30mg/dL; PCI, percutaneous coronary intervention.

Comparison of the Novel Scoring System with the GRACE Risk Score

A statistically significant difference between the AUCs was observed for the two scoring systems in terms of ability to predict 3-year MACE (P=0.007, Delong's test) (Figure 5b). The AUC for the GRACE risk score was 0.731 (95% CI 0.686–0.777) and that for our scoring system was 0.776 (95% CI 0.733–0.819).

Table 3 A Novel Scoring System Developed from the Nomogram

Parameters	Score Generated from Nomogram (points)	Score modified from Nomogram (points)
Aged (>70 years)	40.1	40
Diabetes	31.8	32
Prior MI	38.0	38
Killip class (per level)	33.3	33
CKD	50.6	51
Elevated Lp(a) (>30mg/dL)	36.4	36
Refusal of PCI	43.2	43

Abbreviations: MI, myocardial infarction; CKD, chronic kidney disease; Lp(a), lipoprotein(a); PCI, percutaneous coronary intervention.

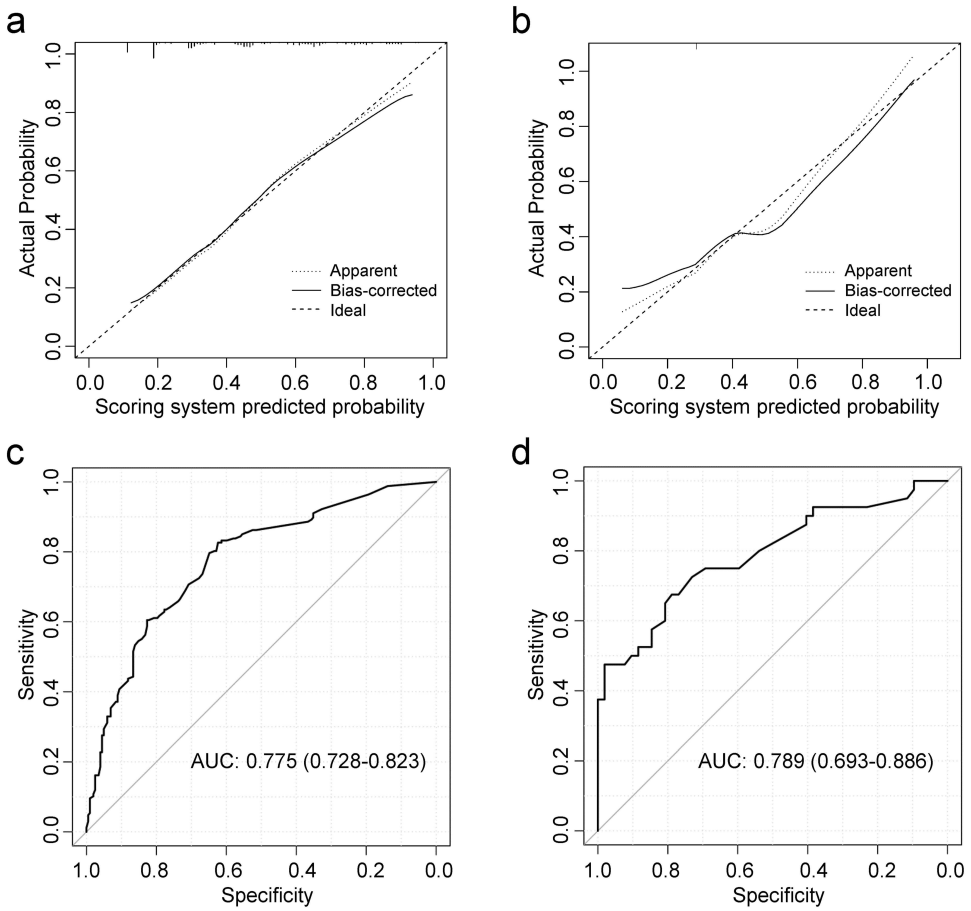

Figure 4 Predictive performance of the scoring system: calibration curves of the scoring system in the training set (**a**) and validation set (**b**), receiver operating characteristic curves of the scoring system in the training set (**c**) and the validation set (**d**).

Discussion

Effective long-term out-of-hospital management is a critical aspect of secondary prevention following AMI, and its implementation can considerably reduce the substantial personal and social healthcare burden associated with MACE.[19,20] Furthermore, the efficiency of out-of-hospital management may be improved by risk stratification.

The aim of this study was to develop a scoring system for risk stratification of the long-term prognosis in patients with AMI based on a nomogram. This scoring system was designed to provide clinicians with a tool to assess overall risk in these patients, thereby guiding effective secondary prevention and out-of-hospital management strategies. The key findings of the study were as follows: independent long-term prognostic factors in patients with AMI include age, diabetes, prior MI, Killip class, CKD, Lp(a), and PCI during hospitalization; our novel scoring system derived from the nomogram demonstrated robust prediction of long-term cardiovascular events and risk stratification for patients with AMI; and there is a clear need to optimize and update existing prediction models.

In this study, the ability of our scoring system to predict the long-term prognosis of patients with AMI was superior to that of the GRACE risk score (AUC 0.775 vs 0.731). The variation in predictive performance between the two scoring systems is primarily attributed to the differences in variable selection, which we explore in detail in the following discussion.

The GRACE risk score includes the following eight variables: Killip class, systolic blood pressure, ST-segment deviation, cardiac arrest at presentation, elevated cardiac enzymes, heart rate, age, and serum creatinine level.[21] The first six variables predominantly reflect the extent of cardiomyocyte injury and resulting hemodynamic changes.[16,19,22,23] The GRACE investigators leveraged these cardiac-related metrics to enhance the weighting of cardiac injury in their prediction model, aligning with its predictive objectives and underlying pathophysiological mechanisms.[20] In contrast, our scoring

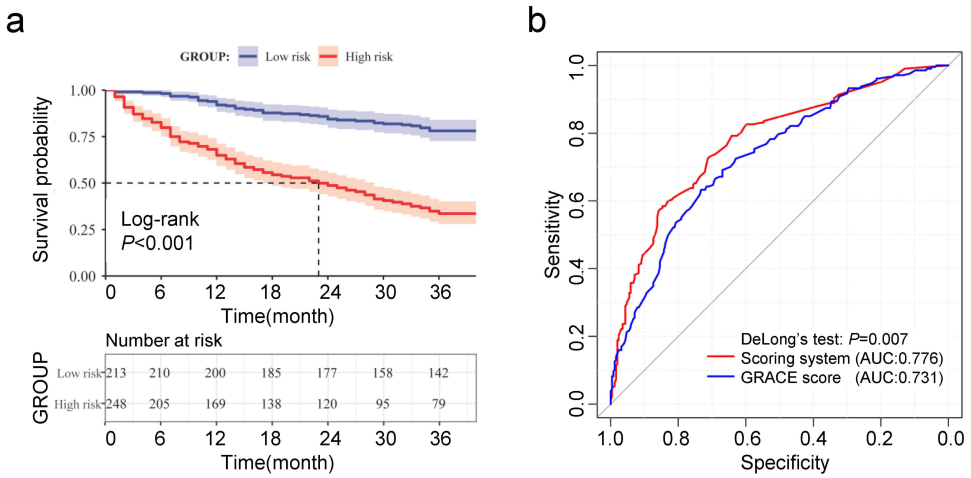

Figure 5 Kaplan–Meier curve for 3-year MACE according to risk levels (**a**). Receiver operating characteristic curves of the GRACE risk score and the scoring system (**b**).

system was specifically designed to predict the risk of long-term adverse outcomes. Therefore, we used only the Killip class to capture the acute phase of the disease while emphasizing independent risk factors pertinent to the long-term prognosis.

Both the GRACE risk score and the scoring system developed in our study recognize the significant role of renal function in the prognosis of patients with AMI. The prognosis tends to be worse in those with poor renal function, potentially because of the presence of additional cardiac risk factors, including secondary hypertension, chronic inflammation, and anemia of chronic renal disease.[24] Furthermore, such patients often show abnormal platelet activity and coagulation.[25] The GRACE score uses the serum creatinine level to evaluate renal function. However, several prediction models have integrated indicators reflecting renal insufficiency, including daily urine volume, blood urea nitrogen, serum creatinine, and glomerular filtration rate.[26–29] Interestingly, a large number of patients with AMI develop acute kidney injury as a result of hemodynamic alterations:[30–32] Hemodynamic changes during AMI are the result of a combination of weakened cardiac contractility, reduced compliance, and uncoordinated myocardial contraction. The combined effect of these changes is a lack of cardiac output and a drop in blood pressure, which exceeds the ability to autoregulate renal blood flow, leading to so-called acute ischemic kidney injury with acute changes in daily urine volume, blood urea nitrogen, serum creatinine, and glomerular filtration rate.[30,31,33] Overall, the renal status reflected by the serum creatinine level is disturbed by impaired cardiac function during AMI. In our study, CKD was chosen as a more suitable proxy for renal function, aligning better with long-term prognostic pathophysiology.

Serum Lp(a), which is known to correlate with development of coronary atherosclerosis, aortic stenosis, and valvular heart disease, was also incorporated into our prognostic risk score.[34–36] A cohort study by Cao et al indicated that patients with elevated Lp(a) had a significantly increased risk of cardiovascular events and cardiac mortality.[37] Lp(a) serves as a "residual" lipid risk factor, contributing to the pathological process of coronary heart disease via its proatherogenic, prothrombotic, and proinflammatory properties.[38–40] Many guidelines, including those from China, Europe, and the USA, recommend incorporating Lp(a) when risk-stratifying patients with AMI.[40–43] Inclusion of Lp(a) in our study improved the overall prediction performance of the model.

Interestingly, in this study, low-density lipoprotein cholesterol (LDL-C), the primary lipid intervention target, did not have any prognostic relevance, which is consistent with a previous report.[44] This finding may be attributed to the widespread use of medications that target LDL-C in the management of patients with CAD, resulting in well-controlled LDL-C levels.

Moreover, PCI during hospitalization protects against long-term adverse outcomes.[45,46] As a primary reperfusion therapy for patients with MI, PCI has been performed at significantly high rates, substantially improving survival outcomes.[45] The guidelines endorse PCI as a category I recommendation for patients with ST-elevation myocardial infarction, despite certain situations necessitating comprehensive clinical judgment.[18,19] Our study confirmed this and

incorporated it into the scoring system. Notably, while the GRACE discharge score also included PCI during hospitalization, its prediction performance for 3-year MACE was even lower than that of the GRACE score.

Advanced age is a well-recognized poor prognostic factor in patients with cardiovascular disease. The GRACE score allows more detailed risk stratification based on age than was possible in our study and effectively capitalizes on its significance in risk stratification. Finally, we incorporated diabetes and prior MI, two recently recognized prognostic factors,[47,48] into our model, which possibly contributed to its overall prediction performance.

Our study confirms that traditional predictive models are insufficient for evaluating long-term prognostic risk (three years or longer). In contrast, our findings integrate commonly used clinical indicators with modern statistical modeling techniques, specifically logistic regression and nomograms, to provide a convenient and comprehensive risk assessment. While AI-based dynamic predictive models represent a promising direction for future development, our study continues to offer clinicians an intuitive visual risk prediction tool that can be effectively utilized for an extended period.

Future research strategies for long-term risk prediction in patients with AMI will evolve alongside innovations in medical technology and advancements in artificial intelligence. A primary focus should be on integrating multidimensional data, incorporating information from genomics, biomarkers, and lifestyle factors into predictive models to enhance the accuracy of personalized predictions.[49,50] Moreover, the use of wearable devices and telemedicine for dynamic monitoring and real-time predictions can enable clinicians to adjust treatment plans promptly.[51] Deep learning and AI techniques can effectively identify subtle lesions in imaging analyses, while explainable AI can enhance model transparency, thereby fostering greater clinical trust.[52] To ensure the generalizability of these models, validation across multicenter and large-scale populations is crucial. These strategies will facilitate the transition of acute myocardial infarction management toward precision medicine, ultimately improving survival rates and quality of life, while supporting more informed clinical decision-making.

Limitation

Our study is a single-center retrospective observational investigation with a limited sample size. Prior to clinical application, it is essential to conduct large-scale multicenter prospective studies to optimize and validate our predictive model.

Conclusion

The findings of this study underscore the need to update or reconstruct the existing models for prediction of the long-term prognosis of patients with AMI. Independent risk factors for long-term MACE in patients with AMI include age, diabetes, prior MI, Killip class, CKD, serum Lp(a), and PCI during hospitalization. Our scoring system, developed from a nomogram, performs favorably in terms of prediction of long-term MACE and risk stratification in patients with AMI.

Abbreviations

AMI, acute myocardial infarction; CAD, coronary artery disease; CKD, chronic kidney disease; GRACE, Global Registry of Acute Coronary Events; Lp(a), lipoprotein(a); MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction.

Patient and Public Involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Data Sharing Statement

Data are available on reasonable request from the corresponding author Professor Ying Wang.

Ethics Consent

The research was conducted in accordance with the Declaration of Helsinki, and the ethical review committee of the First Affiliated Hospital of Zhengzhou University reviewed and approved the study protocol (ethics number: 2023-KY-0150). Since this study was a retrospective analysis, the ethics review committee waived the requirement for written informed consent. All patients' private information was removed before data analysis.

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Author Contributions

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

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Disclosure

The authors report no conflicts of interest in this work.

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