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A nomogram risk prediction model for ischemic mitral regurgitation after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction

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Abstract

Aim This study developed a nomogram to predict the risk of ischemic mitral regurgitation (IMR) after percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) patients and evaluate their long-term prognosis.

Methods Data from 342 STEMI patients were collected. Logistic regression identified independent risk factors for IMR during hospitalization, while Cox regression assessed risk factors during follow-up. The nomogram was developed based on these factors. ROC evaluated its predictive value, and decision curve analysis/clinical impact curves assessed clinical utility. Kaplan–Meier analysis evaluated the model's prognostic value.

Results The independent risk factors for hospitalized IMR after PCI in STEMI patients included Gensini score (OR 1.009; $P=0.047$), left ventricular ejection fraction (LVEF) (OR 0.941; $P=0.007$), albumin (OR 0.941; $P=0.046$), and systemic immune-inflammatory index (SII) (OR 1.096; $P<0.001$). During follow-up, diabetes mellitus (HR: 1.154; $P=0.019$), hemoglobin (HR: 0.991; $P=0.028$), Gensini score (HR: 1.007; $P=0.022$), LVEF (HR: 0.972; $P=0.015$), and SII/100 (HR: 1.034; $P<0.001$) were identified as independent predictors of IMR. The nomogram showed strong clinical benefit, good calibration, and predictive value. Patients with lower scores had better long-term outcomes.

Conclusion This nomogram effectively predicts the occurrence of IMR after PCI in STEMI patients, providing valuable prognostic insights.

Keywords ST-segment elevation myocardial infarction, Mitral regurgitation, Major adverse cardiovascular events, Nomogram, Prognosis

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Introduction

Ischemic mitral regurgitation (IMR) typically results from an imbalance between mitral valve closure and the forces exerted by myocardial cord rupture or left ventricular remodeling following ST-segment elevation myocardial infarction (STEMI) [1]. Compared to patients without IMR, those with IMR have higher mortality rates and worse overall event-free survival [2]. IMR occurs due to severe blockage of at least one major coronary artery, with a higher probability when the affected artery is on the right side rather than the systolic branch. IMR can lead to hemodynamic compromise and, in severe cases, refractory pulmonary edema or cardiogenic shock, significantly increasing the risk of symptomatic heart failure and mortality [3]. Patients with IMR are typically managed with noninvasive treatments, including intravenous diuretics, vasodilators, and positive inotropic agents. In cases of severe mitral regurgitation (MR), surgical intervention such as mitral valve replacement or repair is required, although the perioperative mortality risk is as high as 25% [1].

Several factors, including a patient's preexisting health conditions, the management of coronary revascularization during emergency percutaneous coronary intervention (PCI), and postoperative rehabilitation strategies, can influence the development of IMR in STEMI patients. However, it remains unclear whether specific pathophysiological factors contribute to IMR in STEMI patients following PCI. Numerous studies have demonstrated that the inflammatory immune response significantly affects patient prognosis and plays a crucial role in cardiovascular diseases [4, 5]. The systemic immune-inflammatory index (SII), a recently developed metric for assessing inflammation, reflects the balance between inflammation and immune response. SII has been associated with the incidence of acute coronary syndromes and the severity of coronary artery disease [6]. The Gensini score, a reliable indicator of coronary artery severity, is also linked to IMR development. A higher Gensini score indicates more severe coronary artery disease, and in cases of complete coronary occlusion, the body experiences a heightened inflammatory immune response, leading to structural and functional abnormalities in the heart. Additionally, other clinical markers may be associated with IMR development following PCI in STEMI patients.

To improve the prognosis of this patient population, this study investigates the relationship between common clinical indicators and the incidence of IMR in STEMI patients undergoing emergency PCI. Furthermore, we developed a nomogram risk prediction model to estimate the likelihood of IMR in STEMI patients at an early stage, allowing for timely intervention.

Materials and methods

General information of patients

This study included patients diagnosed with STEMI who underwent PCI at the 904th Hospital of Joint Logistic Support Force of PLA between January 2019 and December 2022. A long-term physical examination was conducted for all enrolled patients at our hospital, and the results were linked to the cardiac ultrasound examinations performed prior to the illness. The diagnostic criteria for the patients were based on the fourth general rule (2018) for STEMI [7], which includes three main components: (1) typical chest pain lasting more than 10 min, (2) common electrocardiographic (ECG) changes upon emergency admission, and (3) elevated markers of myocardial injury. Patients with the following conditions were excluded from the study: (1) a history of organic heart valve disease or mitral valve surgery, (2) severe inflammatory diseases, hematologic disorders, malignant tumors, hepatic or renal insufficiency, or incomplete clinical data, (3) patients lost to follow-up or discharged early, and (4) those who had previously undergone coronary stenting for unstable angina or coronary artery bypass grafting (CABG) (Fig. 1).

Before PCI, all STEMI patients received loading doses of aspirin and Tegretol. Two cardiovascular interventionalists performed the PCI and coronary angiography procedures. They assessed the coronary lesions, noting the condition and quantity of lesions, reviewed angiographic results, and used the Gensini score to determine the severity of coronary artery disease [8].

Data collection

General clinical data were collected for all patients, including their age, gender, Killip classification, history of hypertension, diabetes mellitus, smoking, and occurrence of major adverse cardiovascular events (MACEs) during hospitalization and long-term follow-up after discharge. MACEs included cardiac death, nonfatal myocardial infarction, acute heart failure, malignant arrhythmias (ventricular tachycardia), and others. Enteric-coated aspirin and Tegretol antiplatelet treatment were given to all patients upon discharge, unless contraindications were present.

Before the emergency PCI procedure, blood samples were collected from each patient for laboratory analysis. The tests included albumin, C-reactive protein, uric acid, cystatin C, serum creatinine, urea, glucose, β2-microglobulin, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), lipoprotein(a) [Lp(a)], triglycerides, total cholesterol, apolipoprotein A1, apolipoprotein B, and

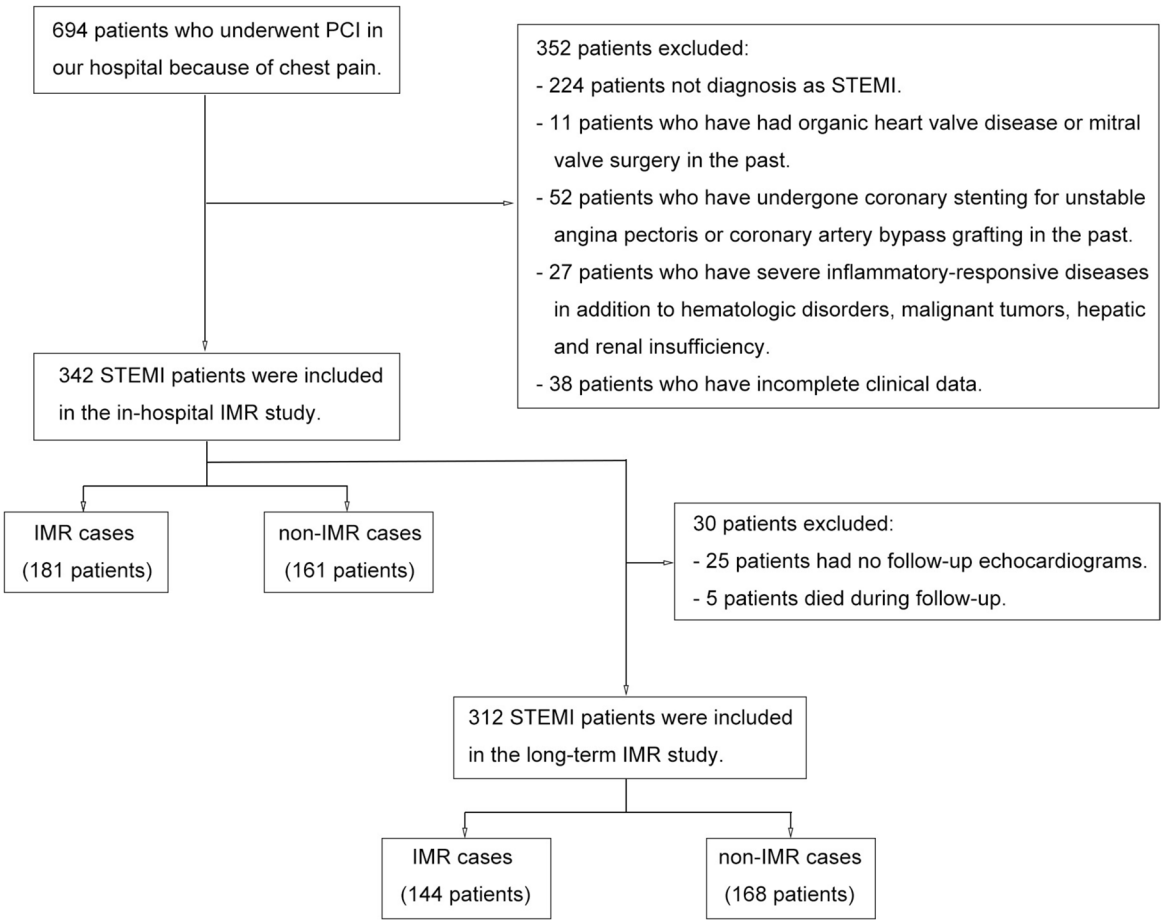

Fig. 1 Flowchart of patient inclusion. PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction; IMR: ischemic mitral regurgitation

other biochemical tests; myoglobin, troponin I, and other markers of myocardial injury; and coagulation markers like D-dimer and fibrinogen. Routine blood tests included leukocytes, neutrophils, lymphocytes, hemoglobin, monocytes, and platelets. To investigate the association between SII and the patient's phenotype, the SII/100 was calculated: SII/100 = (neutrophil count × platelet count)/lymphocyte count/100.

During each patient's hospital stay, bedside echocardiography was performed to assess left ventricular ejection fraction (LVEF) and detect any valve regurgitation or other valvular diseases. Patients were monitored for a substantial amount of time after discharge, and one cardiovascular physician collected follow-up data by reviewing inpatient or outpatient medical records and periodically checking echocardiograms to monitor changes in the severity of heart valve disease and related markers.

Statistical analysis

R software (version 4.4.0) and SPSS version 26.0 were used for statistical analysis. The Kolmogorov–Smirnov test was applied to verify the normality of continuous data. Continuous variables with a normal distribution are presented as mean ± standard deviation, and comparisons between two groups were performed using the *t*-test. For continuous variables with skewed distributions, the median (interquartile range [IQR], 25–75th percentile) is reported, and the Mann–Whitney *U* test was used to compare differences between groups. The chi-square test was used for categorical variables, which are presented as frequencies (percentages). The variance inflation factor (VIF) was calculated to examine multicollinearity among variables. Univariate and multivariate logistic regression models were used to identify independent risk factors for IMR during hospitalization. Univariate

and multivariate Cox regression analyses were conducted to identify independent risk factors for IMR during long-term follow-up after discharge. Receiver operating characteristic (ROC) curves were used to evaluate the predictive value and optimal cut-off value of the nomogram risk prediction model, and the DeLong test compared the predictive value of the model with various metrics. Decision curve analysis (DCA) and clinical impact curve (CIC) were used to evaluate the model's net clinical benefit and utility. Internal bootstrap validation and repeated sampling (1000 replications) were used to assess the consistency of the prediction model with real-world scenarios. The Kaplan–Meier technique and the log-rank test were used to predict the long-term MACEs risk in the high-score group (> 95.67) and low-score group (≤ 95.67), and survival curves were plotted. $P < 0.05$ was considered statistically significant for all two-tailed statistical analyses.

Results

General information of patients

Based on whether IMR occurred during hospitalization, 342 STEMI patients were divided into the IMR group ($n = 181$) and the non-IMR group ($n = 161$) according to the inclusion and exclusion criteria (Table 1). Compared to the non-IMR group, a statistically significant proportion of patients in the IMR group had a Killip classification ≥ II ($P = 0.027$) and experienced MACEs during hospitalization ($P = 0.002$). Additionally, the IMR group had significantly higher levels of age ($P = 0.046$), hemoglobin ($P = 0.001$), neutrophil counts ($P < 0.001$), SII/100 ($P < 0.001$), C-reactive protein ($P < 0.001$), myoglobin ($P = 0.028$), D-dimer ($P = 0.001$), fibrinogen ($P = 0.029$), and Gensini score ($P = 0.001$). The non-IMR group had significantly lower levels of lymphocyte count ($P = 0.011$), albumin ($P = 0.003$), and LVEF ($P = 0.003$). All differences were statistically significant.

Compared with the non-IMR group, the IMR group had a higher percentage of patients with Killip classification ≥ II ($P = 0.027$), MACEs during hospitalization ($P = 0.001$), and a lower percentage of patients with a history of smoking ($P = 0.039$), which was statistically significant. In the IMR group, the levels of age ($P = 0.012$), neutrophil count ($P < 0.001$), SII/100 ($P < 0.001$), C-reactive protein ($P < 0.001$), myoglobin ($P = 0.006$), D-dimer ($P = 0.001$), fibrinogen ($P = 0.008$), and Gensini score ($P = 0.001$) were significantly higher compared to the non-IMR group, while the levels of hemoglobin ($P < 0.001$), lymphocyte count ($P = 0.002$), albumin ($P = 0.002$), and hospitalized LVEF ($P = 0.003$) were significantly lower.

Based on echocardiographic results during follow-up, patients were categorized into the IMR group ($n = 144$) and the non-IMR group ($n = 168$) (Table 2). A statistically significant difference was found in the percentage of patients with diabetes mellitus ($P = 0.006$), Killip classification ≥ II ($P = 0.002$), and the occurrence of MACEs during hospitalization ($P < 0.001$) between the IMR and non-IMR groups. The IMR group had significantly higher levels of age ($P = 0.023$), neutrophil count ($P < 0.001$), SII/100 ($P < 0.001$), C-reactive protein ($P = 0.005$), urea ($P = 0.004$), myoglobin ($P = 0.045$), D-dimer ($P = 0.012$), fibrinogen ($P = 0.006$), and Gensini score ($P = 0.011$) compared to the non-IMR group. Conversely, the non-IMR group had significantly lower levels of hemoglobin ($P < 0.001$), lymphocyte count ($P < 0.001$), albumin ($P = 0.014$), and LVEF ($P = 0.003$).

Independent variables affecting the incidence of IMR in STEMI patients hospitalized following PCI

Univariate logistic regression was used to analyze the variables compared in the general information table of STEMI patients in the IMR and non-IMR groups during hospitalization ($P < 0.05$). Correlation analysis revealed that SII/100 was positively associated with both neutrophil ($r = 0.772$, $P < 0.001$) and lymphocyte counts ($r = -0.608$, $P < 0.001$), with no multicollinearity observed with the other variables (VIF < 10). Based on the results of univariate logistic regression and after adjusting for confounders, age, smoking, Killip classification ≥ II, hospitalized MACEs, hemoglobin, albumin, C-reactive protein, Gensini score, hospitalized LVEF, and SII/100 were included in multivariate logistic regression analyses. The results, shown in Table 3, identified Gensini score (OR 1.009; 95% CI 1.000–1.017; $P = 0.047$), hospitalized LVEF (OR 0.941; 95% CI 0.900–0.983; $P = 0.007$), albumin (OR 0.941; 95% CI 0.886–0.999; $P = 0.046$), and SII/100 (OR 1.096; 95% CI 1.054–1.139; $P < 0.001$) as independent factors influencing hospitalized MR after PCI in STEMI patients.

Independent influences on the occurrence of IMR in STEMI patients at long-term follow-up after PCI

Univariate Cox regression was used to include variables with $P < 0.05$ from the general information table of STEMI patients in the IMR and non-IMR groups during long-term follow-up after discharge. Age, diabetes mellitus, Killip classification ≥ II, hospitalized MACEs, hemoglobin, urea, D-dimer, fibrinogen, Gensini score, LVEF, and SII/100 were included in the multivariate Cox regression analyses. The findings revealed the independent factors influencing IMR in STEMI patients discharged from the hospital and followed up long-term after PCI (Table 4). These included diabetes mellitus (HR

Table 1 Comparison of clinical data between ischemic mitral regurgitation (IMR) group and non-IMR group in hospital

Baseline characteristics	IMR group, $n=181$	non-IMR group, $n=161$	*P* value
Demographics			
Age (years)*	63 (52,73)	59 (48,69)	0.012
Gender: male, *n* (%)	126 (69.6)	113 (70.2)	0.908
Smoking, *n* (%)	115 (63.5)	119 (73.9)	0.039
Hypertension, *n* (%)	118 (65.2)	110 (68.3)	0.540
Diabetes mellitus, *n* (%)	58 (32.0)	37 (23.0)	0.062
Killip classification ≥ II, *n* (%)	51 (28.2)	29 (18.0)	0.027
MACEs in hospital, *n* (%)	65 (35.9)	32 (19.9)	0.001
Laboratory parameters			
Hemoglobin (g/L)*	139 (130,154)	148 (140,158)	< 0.001
Neutrophil count (10^9/L)*	7.31 (5.44,10.74)	6.03 (4.17,8.20)	< 0.001
Lymphocyte count (10^9/L)*	1.70 (1.13,2.44)	1.94 (1.42,2.86)	0.002
Monocyte count(10^9/L)	0.66 (0.47,0.91)	0.62 (0.49,0.82)	0.484
Platelet (10^9/L)*	210 (170,242)	207 (161,250)	0.498
SII/100*	8.47 (5.13,15.90)	6.46 (2.72,9.65)	< 0.001
Albumin (g/L)*	37.30 (34.85,40.30)	38.70 (36.05,41.05)	0.002
C-reactive protein (mg/L)*	9.84 (4.40,33.60)	6.50 (1.99,14.31)	< 0.001
Uric acid (μmol/L)*	377 (306,444)	371 (308,446)	0.952
Cystatin C (mg/L)*	0.92(0.76,1.13)	0.89 (0.76,1.07)	0.298
Serum creatinine (μmol/L)*	73.00 (63.00,85.00)	72.00 (61.00,83.00)	0.375
Urea (μmol/L)*	5.25 (4.38,6.70)	5.27 (4.41,6.37)	0.455
Glucose (mmol/L)*	6.16 (5.23,8.18)	6.18 (5.36,7.69)	0.671
β_2-microglobulin (mg/L)*	1.78 (1.41,2.37)	1.86 (1.29,2.45)	0.912
LDL cholesterol (mmol/L)*	2.62 (2.16,3.14)	2.60 (2.07,3.10)	0.520
HDL cholesterol (mmol/L)*	1.02 (0.89,1.17)	1.02 (0.84,1.14)	0.274
Lp(a) (mg/L)*	143.00 (55.00,267.00)	111.00 (59.00,248.00)	0.324
Triglyceride (mmol/L)*	1.54 (0.98,2.02)	1.55 (1.14,2.28)	0.061
Total cholesterol (mmol/L)*	4.40 (3.76,4.90)	4.38 (3.67,5.11)	0.801
Apolipoprotein A1 (g/L)*	0.96 (0.83,1.04)	0.97 (0.82,1.06)	0.984
Apolipoprotein B (g/L)*	2.09 ± 1.24	2.05 ± 1.07	0.511
Myoglobin (ng/mL)*	63.00 (22.83,218.03)	37.90 (15.89,124.85)	0.006
Troponin I (ng/mL)*	9.30 (1.26,26.22)	5.09 (0.56,22.88)	0.076
D-dimer (mg/L)*	0.38 (0.22,0.75)	0.28 (0.17,0.49)	0.001
Fibrinogen (g/L)*	3.28 (2.67,3.89)	2.91 (2.41,3.66)	0.008
Angiographic characteristics			
Gensini score*	63.00 (39.00,82.50)	48.00 (32.00,72.50)	0.001
LVEF on admission (%)	58 (57,61)	60 (58,62)	< 0.001
Number of diseased arteries ≥ 2, *n* (%)	138 (76.2)	112 (69.6)	0.165

MACEs: Major adverse cardiac events; LDL cholesterol: Low-density lipoprotein cholesterol; HDL cholesterol: High-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index

* Mean and standard deviation or median and interquartile range

1.154; 95% CI 1.072–2.141; $P=0.019$), hemoglobin (HR 0.991; 95% CI 0.984–0.999; $P=0.028$), Gensini score (HR 1.007; 95% CI 1.001–1.012; $P=0.022$), LVEF (HR 0.972; 95% CI 0.949–0.994; $P=0.015$), and SII/100 (HR 1.034; 95% CI 1.018–1.049; $P<0.001$).

Development and verification of the nomogram risk prediction model for IMR in STEMI patients during post-PCI hospitalization

The four significant risk factors—Gensini score, LVEF, albumin, and SII/100—were combined to create a nomogram risk prediction model based on the findings of multivariate logistic regression analysis.

Table 2 Comparison of clinical data between long-term ischemic mitral regurgitation (IMR) group and non-IMR group

Baseline characteristics	IMR group, $n=144$	non-IMR group, $n=168$	*P* value
Demographics			
Age (years)*	63 (54,74)	61 (48,69)	0.023
Gender: male, *n* (%)	92 (64.8)	123 (72.4)	0.155
Smoking, *n* (%)	89 (62.7)	123 (72.4)	0.068
Hypertension, *n* (%)	97 (68.3)	108 (63.5)	0.376
Diabetes mellitus, *n* (%)	50 (35.2)	37 (21.8)	0.008
Killip classification ≥ II, *n* (%)	46 (32.4)	29 (17.1)	0.002
MACEs in hospital, *n* (%)	54 (38.0)	34 (20.0)	< 0.001
Laboratory parameters			
Hemoglobin (g/L)*	138.47 ± 19.99	146.57 ± 15.37	< 0.001
Neutrophil count (10^9/L)*	7.55 (5.57,10.26)	5.94 (4.14,8.60)	< 0.001
Lymphocyte count (10^9/L)*	1.57 (1.12,2.28)	1.99 (1.53,3.02)	< 0.001
Monocyte count(10^9/L)	0.66 (0.47,0.92)	0.62 (0.48,0.84)	0.805
Platelet (10^9/L)*	215 (171,250)	205 (164,242)	0.136
SII/100*	8.86 (6.15,18.24)	6.18 (2.95,9.39)	< 0.001
Albumin (g/L)*	37.46 ± 4.15	38.59 ± 3.86	0.014
C-reactive protein (mg/L)*	10.27 (4.85,32.63)	6.83 (2.30,18.15)	0.005
Uric acid (μmol/L)*	371 (306,471)	381 (305,440)	0.841
Cystatin C (mg/L)*	0.92 (0.80,1.16)	0.89 (0.76,1.06)	0.151
Serum creatinine (μmol/L)*	74.00 (63.00,87.00)	73.00 (63.00,84.00)	0.387
Urea (μmol/L)*	5.71 (4.65,7.23)	5.11 (4.25,6.31)	0.004
Glucose (mmol/L)*	6.28 (6.40,8.42)	5.90 (5.16,7.65)	0.051
β_2-microglobulin (mg/L)*	1.86 (1.40,2.61)	1.78 (1.41,2.36)	0.364
LDL cholesterol (mmol/L)*	2.64 (2.21,3.13)	2.60 (2.09,3.06)	0.594
HDL cholesterol (mmol/L)*	1.05 (0.92,1.17)	1.01 (0.87,1.14)	0.076
Lp(a) (mg/L)*	135.90 (60.78,242.60)	115.00 (50.50,285.50)	0.604
Triglyceride (mmol/L)	1.44(0.98,2.11)	1.53 (1.06,2.10)	0.450
Total cholesterol (mmol/L)*	4.42 (3.72,4.96)	4.37 (3.70,5.08)	0.750
Apolipoprotein A1 (g/L)*	1.00 (0.85,1.06)	0.95 (0.81,1.04)	0.179
Apolipoprotein B (g/L)*	0.87 (0.70,1.03)	0.86 (0.68,1.05)	0.961
Myoglobin (ng/mL)*	62.10 (23.05,216.36)	41.30 (15.60,148.32)	0.045
Troponin I (ng/mL)*	8.60 (0.77,26.22)	7.38 (1.20,26.22)	0.856
D-dimer (mg/L)*	0.37 (0.23,0.80)	0.31 (0.18,0.52)	0.012
Fibrinogen (g/L)*	3.28 (2.80,4.00)	2.99 (2.39,3.65)	0.006
Angiographic characteristics			
Gensini score*	63.00 (40.75,80.25)	50.00 (34.00,77.38)	0.011
LVEF on admission (%)	58 (57,60)	60 (58,62)	0.003
Number of diseased arteries ≥ 2, *n* (%)	110 (77.5)	119 (70.0)	0.137

MACEs: Major adverse cardiac events; LDL cholesterol: Low-density lipoprotein cholesterol; HDL cholesterol: High-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index

* Mean and standard deviation or median and interquartile range

The corresponding total score for each patient was determined (Fig. 2A). The Hosmer–Lemeshow goodness-of-fit test showed no statistically significant departure between the predicted and observed risk values ($\chi^2=4.858$, df = 8, $P=0.773$), indicating good agreement. The nomogram model was validated using internal bootstrap validation and repeated sampling (1000 repetitions). The calibration curve demonstrated a mean absolute error of 0.026 (Fig. 2B), indicating a strong agreement between the model and the actual data. When the high-risk threshold was set at > 0.4, decision curve analysis (DCA) showed (Fig. 2C) that the model had a high clinical prediction efficiency with strong agreement between model predictions and actual events.

Table 3 Univariate and multivariable logistic regression analysis of ischemic mitral regurgitation (IMR) occurrence in hospital

	IMR in hospital							
	Univariate analysis				Multivariable analysis			
	P-value	OR	95% CI		*P*-value	OR	95% CI	
Age	0.019	1.020	1.003	1.037				
Smoking	0.040	0.615	0.387	0.978				
Killip classification ≥ II	0.028	1.786	1.066	2.992				
MACEs in hospital	0.001	2.259	1.381	3.695				
Hemoglobin	0.003	0.980	0.967	0.993				
Neutrophil count	< 0.001	1.189	1.108	1.276				
Lymphocyte count	0.002	0.735	0.606	0.892				
Albumin	0.011	0.931	0.881	0.984	0.046	0.941	0.886	0.999
C-reactive protein	0.003	1.013	1.004	1.022				
Gemini score	< 0.001	1.015	1.007	1.022	0.047	1.009	1.000	1.017
LVEF on admission	0.001	0.929	0.890	0.970	0.007	0.941	0.900	0.983
SII/100	< 0.001	1.102	1.063	1.144	< 0.001	1.096	1.054	1.139

MACEs: Major adverse cardiac events; LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index; OR: Odds ratio; CI: Confidence interval

Table 4 Univariate and multivariable Cox proportional hazard regression analysis of occurrence of long-term ischemic mitral regurgitation (IMR)

	long-term IMR							
	Univariate analysis				Multivariable analysis			
	P-value	HR	95% CI		*P*-value	HR	95% CI	
Age	0.006	1.019	1.005	1.032				
Diabetes mellitus	0.009	1.589	1.125	2.245	0.019	1.514	1.072	2.141
Killip classification ≥ II	< 0.001	2.243	1.568	3.208				
MACEs in hospital	< 0.001	2.014	1.433	2.831				
Hemoglobin	0.001	0.989	0.983	0.996	0.028	0.991	0.984	0.999
Neutrophil count	< 0.001	1.088	1.041	1.137				
Lymphocyte count	< 0.001	0.651	0.537	0.788				
Urea	0.002	1.036	1.013	1.059				
D-dimer	0.029	1.043	1.004	1.083				
Fibrinogen	0.035	1.139	1.009	1.286				
Gemini score	0.001	1.009	1.004	1.015	0.022	1.007	1.001	1.012
LVEF on admission	< 0.001	0.957	0.937	0.979	0.015	0.972	0.949	0.994
SII/100	< 0.001	1.042	1.027	1.057	< 0.001	1.034	1.018	1.049

MACEs: Major adverse cardiac events; LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index; HR: Hazard ratio; CI: Confidence interval

DCA revealed (Fig. 2D) that the model produced a greater net benefit when the expected risk of IMR during hospitalization following PCI in STEMI patients was between 0.15 and 0.95.

The area under the curve (AUC) was calculated via ROC curve analysis for the predictive model and each of the three independent risk factors. The diagnostic performance of the nomogram risk prediction model was compared with that of the Gensini score, LVEF, and SII/100 using the DeLong test. The results showed (Fig. 2E, F) that the nomogram performed better than SII/100 [0.714 (95% CI 0.663–0.762) vs. AUC 0.659 (95% CI 0.606–0.709), $P=0.012$], LVEF [AUC 0.714 (95% CI 0.663–0.762) vs. AUC 0.618 (95% CI 0.564–0.670), $P=0.002$], Gensini score [AUC 0.695 (95% CI 0.640–0.745) vs. AUC 0.607 (95% CI 0.550–0.661), $P=0.005$], and albumin [AUC 0.714 (95% CI 0.663–0.762) vs. AUC 0.598 (95% CI 0.544–0.650), $P=0.001$].

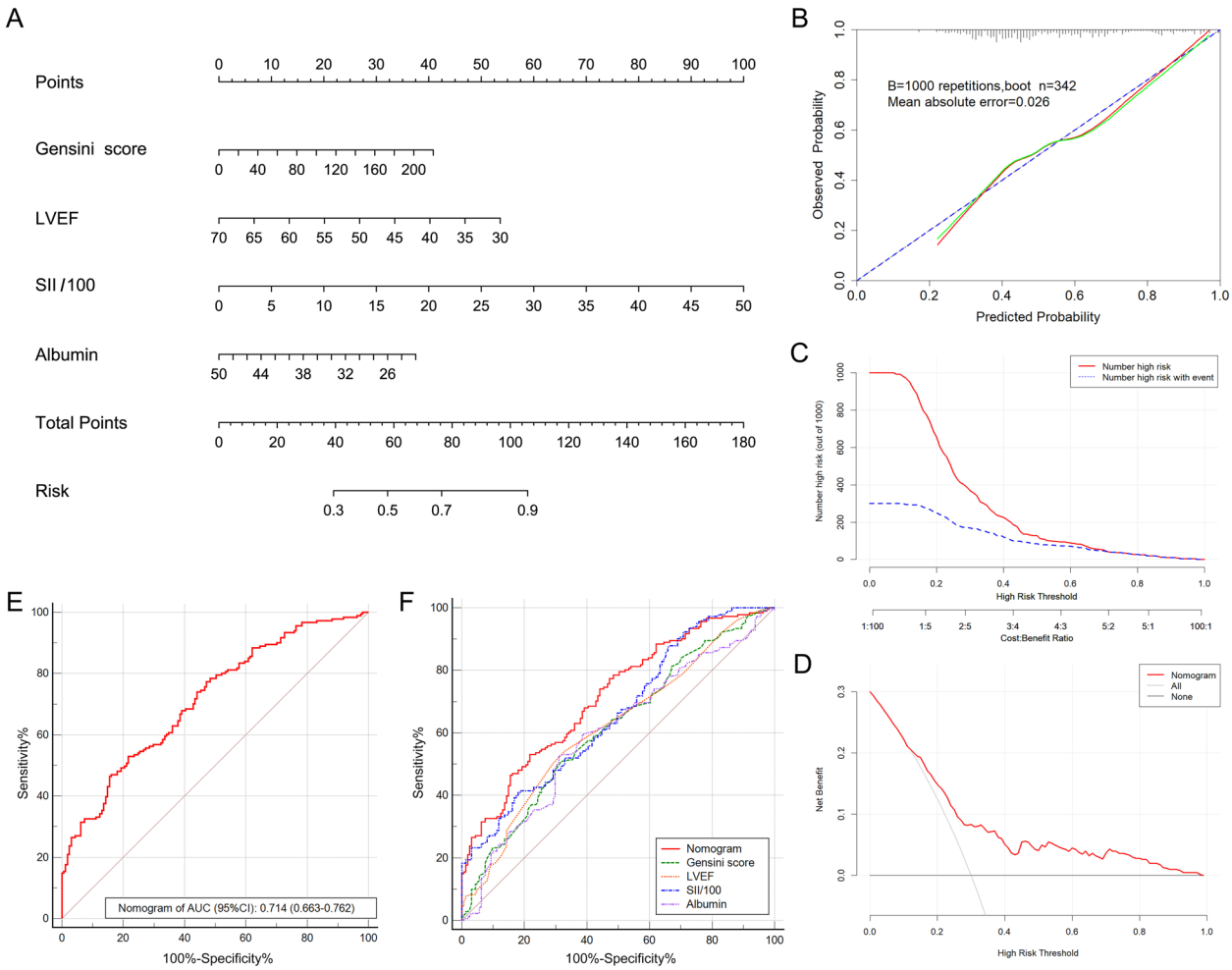

Fig. 2 Development and verification of a nomogram risk prediction model for the incidence of IMR in STEMI patients hospitalized following PCI. **A** Nomogram predicting the risk of IMR during hospitalization in STEMI patients following PCI; (**B**) Model calibration curves predicting the risk of IMR during hospitalization; (**C**) Clinical impact curves of the model; (**D**) Model decision curve analysis; (**E**) ROC curves to evaluate the diagnostic performance of the model; (**F**) Comparison of the SII/100, LVEF, Gensini score, albumin and ROC curves of the nomogram risk prediction model. LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index

Development and verification of a nomogram risk prediction model for predicting the incidence of IMR in STEMI patients following PCI follow-up

A nomogram risk prediction model was developed to predict the risk of IMR in STEMI patients undergoing follow-up care after PCI. This model was based on the results of multifactorial Cox regression analysis and included five significant risk factors: diabetes mellitus, hemoglobin, Gensini score, LVEF, and SII/100. The total score for each patient was calculated by summing the values of these indices, which predicted the likelihood of IMR at 12, 24, and 36 months of follow-up. The corresponding points for each patient's indices were plotted (Fig. 3).

The ROC curves of the nomogram model revealed the following AUC values for predicting IMR: 0.779 (95% CI 0.708–0.849) at 12 months, 0.699 (95% CI 0.625–0.772) at 24 months, and 0.740 (95% CI 0.664–0.817) at 36 months (Fig. 4). These values demonstrate the strong diagnostic efficacy of the model.

Furthermore, the calibration curves for the nomogram model at 12, 24, and 36 months (Fig. 5A–C) showed no significant difference between the predicted and actual outcomes, indicating good agreement. Decision curve analysis (DCA) (Fig. 5D–F) demonstrated that the model provided significant net clinical benefits, highlighting its clinical utility.

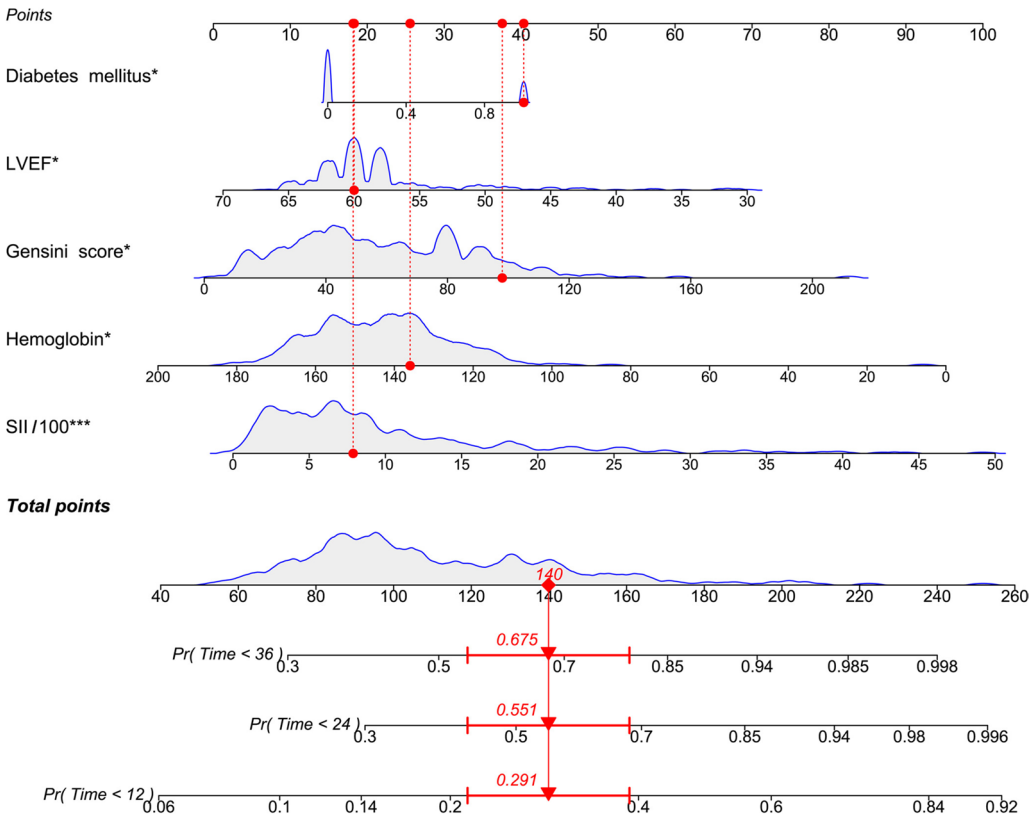

Fig. 3 Nomogram showing the incidence of IMR in STEMI patients 12, 24, and 36 months following PCI. LVEF: Left ventricular ejection fraction; SII: Systemic immune-inflammation index

Relationship between IMR and MACEs in STEMI patients following PCI

STEMI patients may experience MACEs after PCI, which can negatively impact their prognosis. In this study, we found that the incidence of in-hospital events was significantly lower in the non-IMR group [($n=65$, 35.9%) vs. ($n=32$, 19.9%), $P=0.001$] compared to those who developed IMR during hospitalization following PCI. Furthermore, long-term follow-up showed that the incidence of MACEs was higher in the IMR group compared to the non-IMR group 3 years after hospital discharge [($n=65$, 54.9%) vs. ($n=64$, 38.2%), $P=0.006$] (Fig. 6).

ROC curves were used to determine the optimal cut-off value for the total score of the nomogram risk prediction model based on the results of Cox regression analysis. The optimal cut-off value was 95.67, and patients were categorized into two groups: ≤ 95.67 and > 95.67. Kaplan–Meier analysis was used to compare event-free survival rates for MACEs between the two groups. The results (Fig. 7) showed that patients with a total score > 95.67 had a significantly lower event-free survival rate compared to those with a score ≤ 95.67 (Log-rank $P=0.0004$). This suggests that the nomogram risk prediction model provides good long-term prognostic value for predicting the development of MACEs in STEMI patients after PCI.

Discussion

In this study, we examined the factors associated with the occurrence of IMR during hospitalization and long-term follow-up by reviewing medical records, clinical laboratory tests, echocardiographic results, and coronary angiography findings of STEMI patients post-PCI. We also developed a nomogram risk prediction model based on the independent risk factors for IMR to provide personalized survival predictions for patients and clinicians. Previous research has shown that IMR is a significant independent predictor of cardiovascular mortality and is associated with worse prognosis in early-stage STEMI patients [9]. The nomogram developed in this study combines the results of multiple cardiovascular examinations to provide a more accurate assessment of long-term prognosis.

In this study, separate nomogram models for admission IMR and follow-up IMR were created, incorporating independent risk factors such as SII, Gensini score, and LVEF. These models synthesized cardiovascular data to provide a reliable prognosis of long-term outcomes for

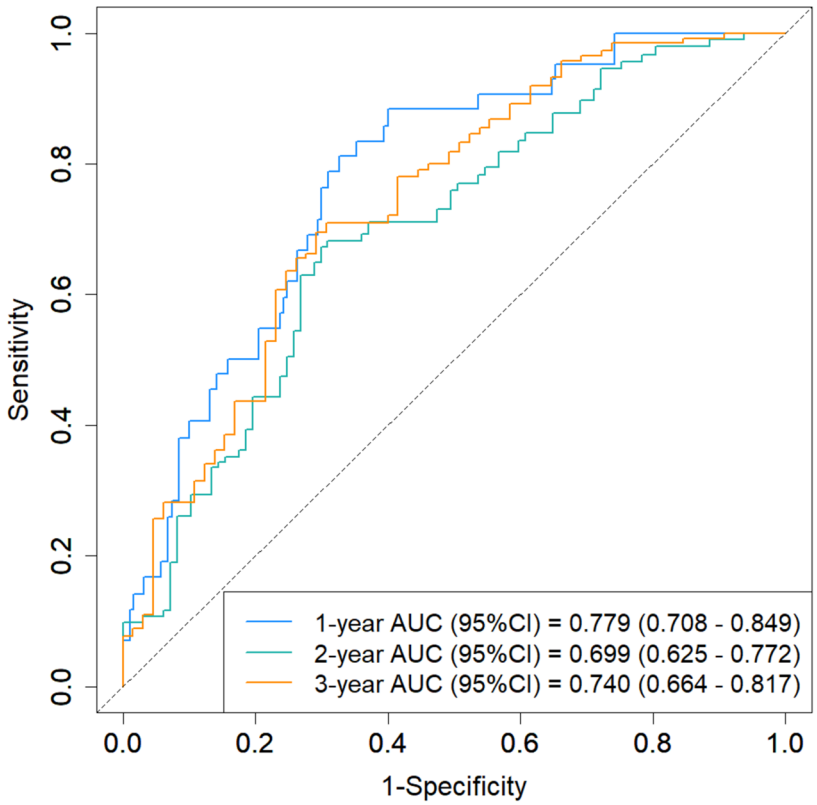

Fig. 4 ROC curves of the nomogram risk prediction model indicating the likelihood of IMR in STEMI patients following PCI at 12, 24, and 36 months of follow-up

patients. The ease of access and user-friendliness of the relevant indicators allows for straightforward evaluation of IMR severity in a clinical setting. Furthermore, it enables prompt, individualized interventions for STEMI patients following PCI, offering new perspectives on reducing the incidence of IMR and improving long-term prognosis.

Our research indicates that SII alone is a risk factor for the development of IMR. Compared to other inflammatory biomarkers, SII has demonstrated stronger predictive value for cardiovascular events. According to Candemir M et al. [10], SII has a higher predictive value than composite markers like neutrophil–lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and others, and correlates with the severity of stable coronary artery disease. It is also a known risk factor for atherosclerosis. SII is composed of neutrophil, platelet, and lymphocyte counts. The prognosis of cardiovascular disease can be predicted by combining these immune indices with complete blood count parameters, which reflect a wide range of immunological pathways and cellular processes [11–13]. There is evidence that mitral valve prolapse leads to platelet activation in the mitral valve, triggering a destructive inflammatory response. The degree of platelet activation is positively correlated with the severity of mitral regurgitation, potentially contributing to leukocyte recruitment and activation in ischemic mitral regurgitation. Although studies on the immune response and inflammatory cascade in IMR are still ongoing, there is evidence that platelet adhesion to the artery wall accelerates atherosclerosis progression and promotes leukocyte recruitment [14]. Lymphocytes may regulate the inflammatory response and prevent the progression of atherosclerosis [15]. After myocardial infarction, decreased peripheral lymphocyte counts are associated with severe reactions. Four weeks after STEMI, up-regulation of the genes CXCL9 and CLEC10A in mitral mesenchymal stromal cells suggests that dendritic cells may recruit lymphocytes into the mitral valve, reducing peripheral blood lymphocytes [16]. Neutrophils, known for their ability to release pro-inflammatory substances and enzymes, can produce matrix metalloproteinase (MMP)-9, which contributes to the breakdown of the basal lamina and plays a role in cardiovascular diseases [15].

Simultaneously, our hypothesis also suggests that the pathophysiological changes in IMR are linked to the development of MACEs, with SII and Gensini

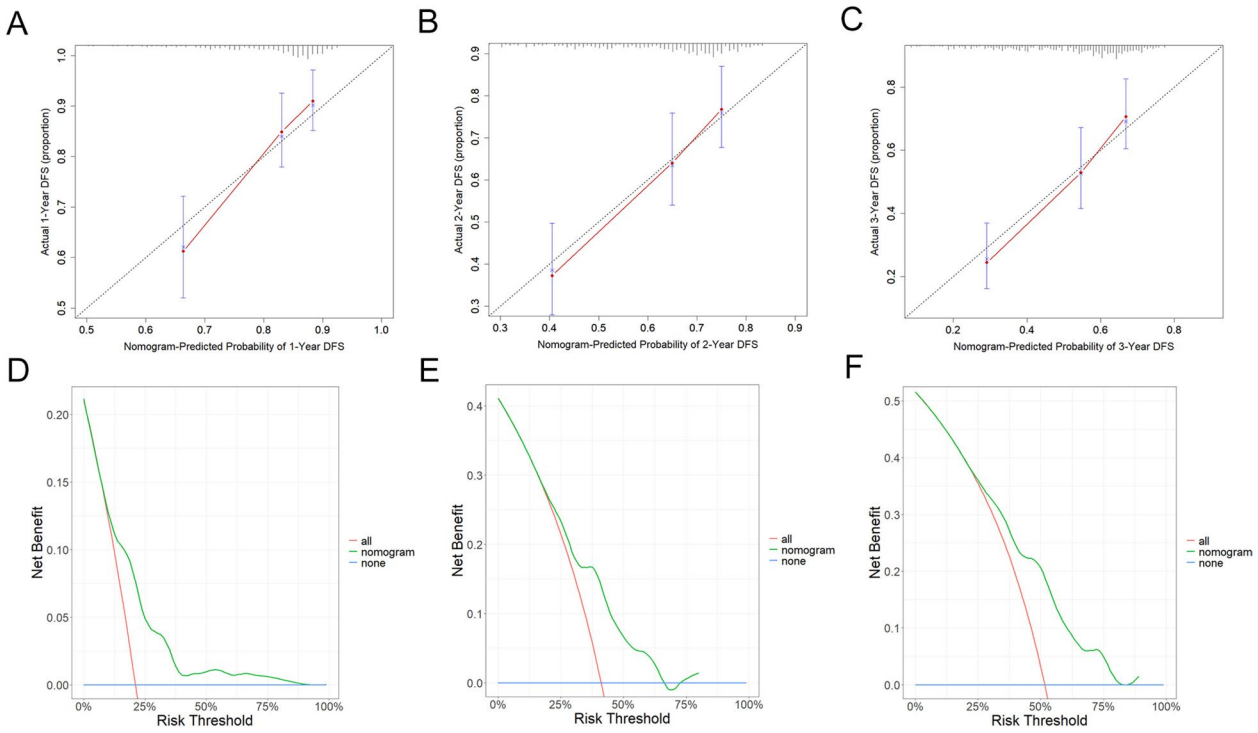

Fig. 5 The nomogram risk prediction model's calibration curves and decision curve analysis (DCA). The nomogram risk prediction model's calibration curves for the probability and proportion of actual IMR occurrence at 12 months (**A**), 24 months (**B**), and 36 months (**C**) are shown. Risk prediction model of DCA validation nomogram for IMR occurrence at 12 months (**D**), 24 months (**E**), and 36 months (**F**)

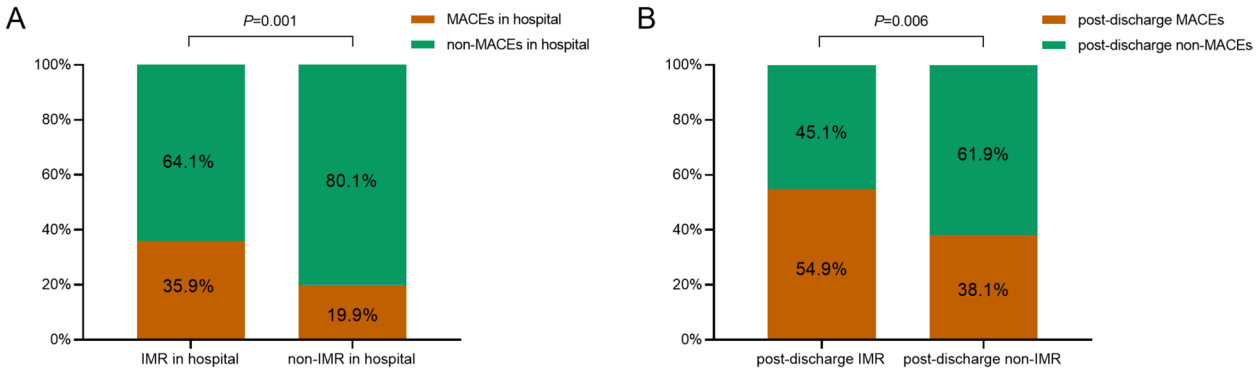

Fig. 6 MACEs in STEMI patients with IMR during hospitalization and during post-discharge follow-up following PCI. **A** Comparison of MACEs that patients in the IMR and non-IMR groups experienced during hospitalization. **B** Comparison of MACEs that occurred at discharge follow-up between patients in the IMR and non-IMR groups

score playing crucial roles in this process. SII has been shown to be associated with the incidence of MACEs and post-infarction risk factors in STEMI patients, including the Gensini score [17]. A higher Gensini score indicates more severe vascular disease and complicates the revascularization process, increasing the risk of IMR due to prolonged myocardial ischemia. Early revascularization is essential to prevent permanent IMR in STEMI patients and improve outcomes in those at risk of MACEs.

In our study, we found that a low LVEF was a significant independent risk factor for the development of IMR post-PCI in STEMI patients. LVEF also affected the incidence of long-term MACEs in patients with IMR. Low LVEF, a marker of systolic left ventricular dysfunction, has been linked to high mortality rates after acute myocardial

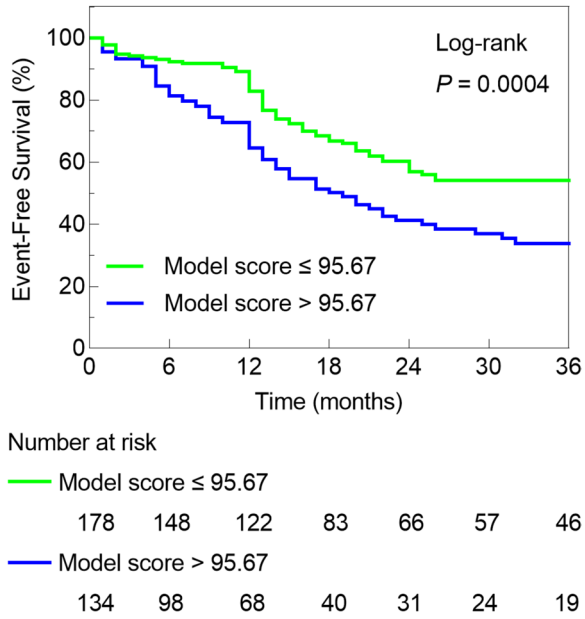

Fig. 7 Kaplan–Meier survival analysis of STEMI patients in the nomogram risk prediction model ≤ 95.67 and > 95.67 groups with follow-up MACEs

infarction [18, 19]. Consistent with our findings, Perl L et al. reported that lower LVEF is a risk factor for increased IMR severity [20]. Reduced LVEF, which reflects underlying cardiac disease, is also an independent risk factor for poor long-term prognosis in STEMI patients [21]. Pecini R et al. [22], found that heart failure patients with a significant drop in LVEF have a worse prognosis for MR. In patients with acute myocardial infarction who developed IMR, higher left ventricular end-diastolic and pulmonary artery pressures and lower LVEF were observed, complicating their treatment and increasing in-hospital mortality [23].

In our study, albumin was identified as an independent risk factor for in-hospital IMR occurrence, in addition to the Gensini score, LVEF, and SII. Feng KY et al. [24] found that low serum albumin levels are associated with fluid retention. We hypothesize that patients with in-hospital IMR often experience adverse conditions such as heart failure, leading to fluid retention and lower albumin levels. Moreover, unadjusted 4-year all-cause mortality was significantly higher in patients with low albumin levels, and low albumin levels were found to be an independent predictor of all-cause mortality after adjusting for confounding factors [24].

In addition to the Gensini score, LVEF, and SII, our study found that hemoglobin and a history of diabetes mellitus were independent risk factors for the development of IMR in STEMI patients after PCI. Anemia is known to be linked to poor outcomes in cardiovascular disease. Consistent with our findings, Simpson TF et al. [25] reported that hemoglobin levels were a primary cause of all-cause mortality in patients with moderate to severe MR. Lu Q et al. [26] also found that hemoglobin was independently associated with 2 year time-free survival in valvular heart disease patients. Anemia was also associated with increased mortality and rehospitalization rates in patients with secondary MR [27]. Diabetes, which causes numerous pathophysiological alterations such as oxidative stress and inflammation, is associated with worsened outcomes in MR patients [28]. About 28% of individuals with moderate-to-severe functional MR have a significant history of diabetes mellitus [29]. According to Ernande L et al. [30], diabetes mellitus is associated with more significant centrifugal remodeling, exacerbating adverse left ventricular remodeling in patients with chronic MR. Diabetes has been shown to be an independent predictor of 2 year adverse outcomes in MR patients [26]. Diabetes contributes to apoptosis and dysfunction, worsening the inflammatory response caused by ischemia in valvular endothelial cells and cardiomyocytes in STEMI patients, thereby affecting long-term prognosis [31, 32]. Sardu C et al. [33, 34] found that SGLT2 inhibitors improved the degree of myocardial ischemia, reduced the occurrence of MACEs and improved the prognosis of patients by improving glucose homeostasis, reducing the systemic burden of inflammation, and localizing the effects on inflammation in atherosclerotic plaques. This indirectly illustrates the impact of diabetes on patients' myocardial ischemia and prognosis, and the importance of intervening in diabetes and using drugs such as SGLT2 inhibitors as early as possible, thus improving patients' cardiovascular prognosis.

Limitations

Several limitations exist in this study. Potential selection bias is inherent due to the retrospective nature of this single-center study. Although the nomogram risk prediction model demonstrated good stability and clinical benefit after internal bootstrap validation, the limited sample size may introduce other unmeasured factors influencing IMR. To validate the accuracy of the results, larger sample sizes from multiple centers are needed. Lastly, since this study was a retrospective analysis, the clinical data used were primarily from the initial admission of STEMI patients. Further research is needed to investigate how the severity of IMR post-PCI and the dynamic fluctuations in inflammatory immune composite indices like SII evolve over time in STEMI patients.

Conclusion

Our study developed a nomogram risk prediction model based on independent risk factors associated with IMR, which can effectively predict the occurrence of IMR after PCI in patients with STEMI. Furthermore, the model demonstrated good predictive performance for the incidence of MACEs during a 3-year follow-up after PCI. These factors were found to have diagnostic significance and predictive value for IMR occurrence in STEMI patients post-PCI. Given that the markers included in the model are commonly observed in hospitalized STEMI patients, this nomogram risk prediction model could become a valuable tool for predicting the incidence of IMR in future clinical practice.

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Author contributions
JY performed the systematic literature searches. JY, RY, YL, WW, GW and GZ analyzed the data and were major contributors in writing the manuscript. DX and YL prepared figures. All authors read and approved the final manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The research was carried out in compliance with the Declaration of Helsinki and granted approval by the Joint Logistics Support Force of the Chinese People's Liberation Army, 904 Hospital Ethics Committee, Wuxi, China (Clinical trial number: 20240405). Written informed consent was obtained from all patients, allowing for the retrospective utilization of their de-identified data for health-related research purposes.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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