ORIGINAL RESEARCH

# Predicting In-Hospital Mortality in Myocardial Infarction: A Nomogram-Based Retrospective Analysis of the MIMIC-IV Database

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**Background:** Despite significant advancements in early reperfusion therapy and pharmacological treatment, which have reduced mortality rates after myocardial infarction in recent decades, the in-hospital mortality rate remains high due to factors such as rapid disease progression, comorbid conditions, and potential complications. We aimed to develop and validate a predictive model for inhospital mortality in myocardial infarction patients.

Methods: LASSO regression analysis, univariate analysis, and multivariate logistic analysis were used to construct the nomogram in the training set, followed by model comparison, internal validation, and sensitivity analysis.

**Results:** The analysis comprised 4688 patients in total. The population of patients was randomly assigned to the training set (n = 3512) and validation set (n = 1176). According to the results of LASSO regression analysis and other results, our nomogram contained a total of 10 independent variables related to patient death, including age, respiratory rate, blood glucose, lactate, PTT, BUN, cerebrovascular disease, chronic lung disease, mild liver disease, and metastatic solid cancer. Moreover, the web calculator and nomogram performed exceptionally well at predicting in-hospital death in myocardial infarction patients. The AUC for the training and validation sets' respective prediction models was 0.869 (95% CI: 0.849–0.889) and 0.846 (95% CI: 0.807–0.875) (p<0.01). Compared to the Sequential Organ Failure Assessment (SOFA), the nomogram showed greater discrimination in the training and validation sets, and the calibration plots demonstrated an adequate fit for the nomogram in predicting the risk of in-hospital mortality in both groups. The decision curve analysis (DCA) of the nomogram demonstrated a higher net benefit in the training and validation sets and in terms of clinical usefulness than the SOFA.

**Conclusion:** We developed a useful nomogram model and developed a nomogram-based web calculator to predict in-hospital mortality in myocardial infarction patients, which will support doctors in patient counseling and logical diagnosis and therapy. Keywords: myocardial infarction, nomogram, predictive models, web calculator, in-hospital mortality

#### Introduction

Cardiovascular disease is a major worldwide health issue. About one-third of people worldwide pass away from cardiovascular disease, with 80% of cardiovascular deaths occurring in developing countries.<sup>1,2</sup> The in-hospital mortality rate after myocardial infarction (MI), despite advancements in treatment and early reperfusion therapy, remains higher than 4%.3-5 This is primarily because MI progresses quickly, which increases the risk of developing serious complications like heart failure and cardiogenic shock.<sup>6</sup> Patients also frequently have a number of comorbid conditions, including

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diabetes mellitus and hypertension, which can make their condition worse.<sup>7</sup> In addition, potential complications during hospitalization, like infections and arrhythmias, as well as delays in or inadequate treatment for some patients, also greatly raise the risk of death.<sup>8,9</sup> This emphasizes the urgent need for effective predictive models to assess the risk of inhospital mortality in MI patients.

Myocardial infarction, a severe form of coronary artery disease, is the leading cause of heart-related deaths. Its incidence has been steadily increasing due to socioeconomic development and improved living standards.<sup>10</sup> Early detection of infarct-related arteries using ECG plays a crucial role in predicting the extent of myocardium at risk and improving patient outcomes.<sup>11</sup> While significant progress has been made in diagnosing and treating acute myocardial infarction, predicting prognosis, especially in resource-limited settings, remains challenging.<sup>12</sup>

Predictive models have been developed for assessing the risk of death in patients with chronic and acute heart failure.<sup>13,14</sup> However, there is a paucity of predictive models specifically addressing the risk of in-hospital mortality in myocardial infarction patients in the ICU.<sup>15</sup> Nomograms, which provide visual representations of predictive model outcomes, are valuable tools for medical decision-making.<sup>16</sup> These user-friendly tools calculate the probability of specific outcomes based on individual predictors, aiding in risk assessment. Nomograms have proven beneficial in various diseases, including prostate cancer, COVID-19, and chronic heart failure.<sup>17–19</sup> In this study, we propose a nomogram to predict the overall in-hospital mortality risk for patients with myocardial infarction, utilizing clinical records from public databases.

Patients with myocardial infarction in the ICU face a significantly high in-hospital mortality rate, often succumbing to the disease before discharge due to various reasons. Unlike other conditions in the ICU, myocardial infarction progresses rapidly and presents a substantial risk of in-hospital mortality. The alarming 14.4% incidence of in-hospital mortality among these patients highlights the importance of developing a predictive model specifically for ICU patients with myocardial infarction. This model will not only assist healthcare professionals in determining prognosis but also provide valuable survival information to the families of affected individuals.

By studying the variables that influence mortality after myocardial infarction, clinicians can make informed management decisions and provide reliable prognostic information to patients and their families. In this study, we utilize the Medical Information Mart for Intensive Care IV (MIMIC-IV) database to explore factors affecting mortality in ICU patients with cardiac infarction. Our aim is to construct a nomogram that predicts in-hospital death in myocardial infarction patients, thereby adding further evidence to support the feasibility and significance of our predictive model.

## **Participants and Methods**

### Data Source

The information was obtained from the Medical Information Mart for Intensive Care (MIMIC-IV) for this study. The MIMIC-IV is a sizable critical care database that is open and freely accessible. For data extraction, we used PostgreSQL (version 13.0, PostgreSQL Global Development Group). A structured query language was used to collect patient data. The MIMIC-IV database contains information on patient comorbidities, vital signs, biochemical indicators, demographics, laboratory tests, fluid balance, and vital status.<sup>20,21</sup> The MIMIC-IV database was searched for patients with myocardial infarction using ICD-9 and ICD-10 codes. If a patient was admitted more than once, data from the initial admission were included in the study. We used the data from the initial measurement if the patient's data was collected more than once. We collected data from MIMIC-IV after passing the Protecting Human Research Participants test and the National Institutes of Health (NIH) web-based training course. The database is accessible by authors who have passed the Collaborative Institutional Training Initiative exam.

## Study Design

Between 2008 and 2019, our retrospective cohort research included 4688 myocardial infarction patients. This study set out to discover predictors of in-hospital mortality in myocardial infarction patients and construct a nomogram based on a multivariate logistic regression model in the training set. In order to confirm the precision and utility of the nomogram, the performance and medical benefit of a nomogram were evaluated in a validation set. A total of 4688 myocardial

## Study Population

Our study population consisted of myocardial infarction patients. The criteria for inclusion were: (1) patient's age >18 years old; and (2) patients who are listed in the accessible MIMIC-IV database (more than 300,000 patients).

We excluded (1) patients under the age of 18; (2) patients with no demographic data; (3) patients with 20% of variables missing; (4) pregnant women; and (5) patients with old myocardial infarction (Figure 1).

## Data Extraction

The PostgreSQL tool's structured query language was used to extract clinical information for each patient, including demographic data, co-morbidities, vital signs, scoring systems, laboratory test results, and interventions. To ensure data quality, we conducted preliminary data cleaning and validation steps, including checking for inconsistencies and outliers.

Demographic parameters refer primarily to age, gender, and race, while vital signs include temperature, diastolic blood pressure, systolic blood pressure, respiratory rate, heart rate, and transcutaneous oxygen saturation. Age is fixed at 300 years for patients over 89 years to protect their privacy. Co-morbidities include cardiogenic shock, valvular heart disease, cardiac arrest, pulmonary circulatory disease, and congestive heart failure. The Simplified Acute Physiology Score II (SAPS II) and the Sepsis-related Organ Failure (SOFA) Score are used to assess disease severity. Laboratory tests include the calculation of haemoglobin, anion gap, chloride, white blood cells (WBC), platelets, blood urea nitrogen (BUN), activated partial thromboplastin time (APTT), potassium, sodium, creatinine, bicarbonate, partial thromboplastin time (PTT), prothrombin time (PT), and lactate. However, the severity and stage of myocardial infarction were not explicitly recorded in the MIMIC-IV database, which may limit the granularity of our analysis. Additionally, our study focused on in-hospital mortality, and the lack of long-term follow-up data may introduce bias, particularly for patients with multiple admissions.



Figure I (A) Flowchart of patient selection (N=4688); (B) Model development flowchart.

Abbreviations: ICU, intensive care unit; LASSO, least absolute shrinkage and selection operator; MIMIC-IV, Medical Information Mart for Intensive Care IV.

## Missing Data

We removed variables that had significant missing data (more than 20% of total data missing). For variables with less than 20% of the total data missing, we then chose to use MissForest to interpolate the missing data. Imputation of missing data was carried out using the missForest method. For the imputation, all the variables that were accessible were used.<sup>22</sup>

## Statistical Analysis

While categorical variables expressed as frequencies and proportions were tested using the chi-square test or Fisher's exact probability test, continuous variables were reported as mean standard deviation or median (IQR) and compared using the *t*-test or Mann–Whitney *U*-test. To reduce the number of unnecessary variables entering the prediction model and to address the problem of multicollinearity, we used LASSO regression analysis for variable selection. LASSO regression analysis is well suited to minimizing high-dimensional data for screening available clinical predictors of inhospital mortality risk characteristics in patients with myocardial infarction in intensive care units.<sup>23,24</sup> LASSO regression analysis compresses otherwise small coefficients to zero, which correspond to variables that are considered non-significant, and we then choose to exclude such variables to avoid overfitting the data.<sup>25</sup> Clinical prediction models were developed by conducting univariate regression analyses, multiple regression analyses (*p*<0.05), and combining the non-zero coefficient characteristics screened by LASSO regression analysis. The probability of in-hospital mortality for patients with myocardial infarction in the ICU was further calculated using these factors by creating a nomogram and online calculator. The data from the validation set was then used to verify the nomogram.

Using the survivor ROC package in R, the area under the curves (AUC) of our model and the current Oasis were compared in order to evaluate the model's discriminative capability. To evaluate the model's predictive accuracy, Harrell's consistency index (C-index) was selected to measure it. Greater AUC values suggest a more precise stratification of predictions.<sup>26</sup> Additionally, we utilized DCA to confirm the clinical validity of our model.

The statistical tools R (<u>http://www.r-project.org</u>, The R Foundation) and EmpowerStats (<u>http://www.empowerstats.com</u>, X&Y Solutions, Inc., Boston, MA) were used to conduct the statistical tests. Significant values were defined as p<0.05.<sup>27</sup>

## Results

## **Baseline Characteristics of Subjects**

The study included a total of 4688 patients with myocardial infarction after the inclusion and exclusion criteria were applied. Of these, the training set consisted of 3512 patients, whereas the validation set included 1176 patients who were selected at random. In our study, in-hospital deaths occurred in 675 patients (14.4%) with myocardial infarction.

The median age of the participants was 71.05 years, and most of the patients (2976, 63.48%) were male. Table 1 (A) contains specific demographic and clinical information about the myocardial infarction patients in the intensive care unit. Table 1 (A) also shows comparisons between the training and validation sets and between demographics and variables for patients who died during hospitalisation versus those who survived. In addition, the baseline clinical data did not significantly differ, except for SBP, DBP, MBP, platelet, Abs basophils, and ALP between the training set and validation set (P-value for the training set vs validation set <0.05).

Variable	Total	Patients		P-value	Patients		P-value
		Training set (%)	Validation set (%)		Alive (%)	Died (%)	
Number, n	4688	3512	1176		4013	675	
Age (years)	71.05 ± 13.06	71.10 ± 13.03	70.93 ± 13.18	0.702	70.39 ± 12.97	75.00 ± 12.95	<0.001
Gender, n (%)				0.598			<0.001
Male	2976 (63.48%)	2237 (63.70%)	739 (62.84%)		2602 (64.84%)	374 (55.41%)	
Female	1712 (36.52%)	1275 (36.30%)	437 (37.16%)		1411 (35.16%)	301 (44.59%)	

Table I Participant's Baseline Characteristics (N =4688)

(Continued)

#### Table I (Continued).

Variable	Total	Patients		P-value	Patients		P-value
		Training set (%)	Validation set (%)		Alive (%)	Died (%)	
Insurance, n (%)				0.475			0.004
Medicare	2427 (51.77%)	1835 (52.25%)	592 (50.34%)		2040 (50.83%)	387 (57.33%)	
Medicaid	2073 (44.22%)	1535 (43.71%)	538 (45.75%)		1814 (45.20%)	259 (38.37%)	
Other	188 (4.01%)	142 (4.04%)	46 (3.91%)		159 (3.96%)	29 (4.30%)	
Vital signs							
Heart rate (bpm)	81.99 ± 14.45	81.97 ± 14.46	82.07 ± 14.41	0.831	80.94 ± 13.53	88.29 ± 17.77	<0.001
SBP (mmHg)	4.8  ±  4.66	114.44 ± 14.53	115.93 ± 14.97	0.003	115.87 ± 13.93	108.47 ± 17.13	<0.001
DBP (mmHg)	61.45 ± 10.76	61.15 ± 10.72	62.36 ± 10.84	<0.001	61.84 ± 10.62	59.14 ± 11.33	<0.001
MBP (mmHg)	76.80 ± 10.18	76.51 ± 10.17	77.67 ± 10.13	<0.001	77.39 ± 9.83	73.30 ± 11.41	<0.001
Respiratory rate (bpm)	19.38 ± 3.54	19.36 ± 3.49	19.46 ± 3.68	0.386	18.99 ± 3.21	21.69 ± 4.40	<0.001
Temperature (°C)	36.74 ± 0.60	36.74 ± 0.59	36.73 ± 0.63	0.593	36.77 ± 0.47	36.54 ± 1.09	<0.001
SPO2 (%)	96.79 ± 2.59	96.79 ± 2.64	96.80 ± 2.44	0.928	96.99 ± 1.73	95.62 ± 5.26	<0.001
Laboratory parameters							
Hematocrit (%)	32.64 ± 5.86	32.64 ± 5.84	32.65 ± 5.94	0.985	32.75 ± 5.81	32.02 ± 6.15	0.001
Hemoglobin (g/dL)	10.82 ± 2.06	10.82 ± 2.04	10.83 ± 2.09	0.879	10.90 ± 2.05	10.37 ± 2.01	<0.001
Platelet (K/uL)	209.08 ± 88.57	203.64 ± 84.58	213.64 ± 92.53	<0.001	209.94 ± 85.97	203.98 ± 102.65	0.106
WBC (K/uL)	13.02 ± 8.34	12.89 ± 7.11	3.4  ±   .23	0.064	12.63 ± 8.23	15.39 ± 8.61	<0.001
RDW (%)	14.59 ± 1.89	14.58 ± 1.90	14.62 ± 1.88	0.507	14.41 ± 1.75	15.65 ± 2.30	<0.001
RBC (m/uL)	3.63 ± 0.69	3.63 ± 0.69	3.63 ± 0.70	0.961	3.65 ± 0.68	3.51 ± 0.73	<0.001
Anion gap (mEq/L)	14.93 ± 4.09	14.95 ± 4.09	14.88 ± 4.08	0.647	14.30 ± 3.67	18.18 ± 5.74	<0.001
Albumin (g/dL)	3.26 ± 0.63	3.26 ± 0.63	3.27 ± 0.64	0.836	3.35 ± 0.59	2.96 ± 0.69	<0.001
Phosphate (IU/L)	3.84 ± 1.29	3.84 ± 1.27	3.83 ± 1.32	0.872	3.67 ± 1.09	4.74 ± 1.82	<0.001
Lactate (mmol/L)	2.45 ± 2.03	2.47 ± 2.02	2.38 ± 2.06	0.319	2.01 ± 1.07	4.36 ± 3.57	<0.001
Magnesium (mg/dL)	2.15 ± 0.38	2.15 ± 0.39	2.16 ± 0.37	0.590	2.15 ± 0.39	2.15 ± 0.36	0.179
Bicarbonate (mEq/L)	22.78 ± 3.88	22.75 ± 3.90	22.88 ± 3.80	0.314	23.24 ± 3.44	20.01 ± 5.05	<0.001
BUN (mg/dL)	28.46 ± 20.94	28.56 ± 21.25	28.17 ± 19.99	0.575	26.12 ± 19.00	42.61 ± 25.99	<0.001
Calcium (mg/dL)	8.47 ± 0.80	8.46 ± 0.74	8.50 ± 0.93	0.202	8.50 ± 0.68	8.30 ± 1.23	<0.001
Chloride (mEq/L)	103.76 ± 5.18	103.82 ± 5.15	103.56 ± 5.26	0.140	103.86 ± 4.79	103.14 ± 7.04	<0.001
Creatinine (mg/dL)	1.56 ± 1.47	1.57 ± 1.50	1.51 ± 1.38	0.274	1.44 ± 1.39	2.24 ± 1.73	<0.001
Glucose (mEq/L)	154.99 ± 60.54	155.59 ± 61.46	153.20 ± 57.68	0.242	149.34 ± 51.03	188.97 ± 93.31	<0.001
Sodium (mEq/L)	137.54 ± 4.08	137.57 ± 4.05	137.44 ± 4.18	0.326	137.42 ± 3.67	138.27 ± 5.96	<0.001
Potassium (mEq/L)	4.29 ± 0.53	4.30 ± 0.52	4.27 ± 0.54	0.059	4.27 ± 0.48	4.42 ± 0.72	<0.001
PTT (seconds)	47.30 ± 24.79	47.22 ± 24.83	47.56 ± 24.70	0.691	45.36 ± 23.02	58.80 ± 31.05	<0.001
PT (seconds)	15.38 ± 6.31	15.43 ± 6.35	15.25 ± 6.21	0.422	14.77 ± 5.34	18.99 ± 9.61	<0.001
INR	1.40 ± 0.61	1.41 ± 0.61	1.39 ± 0.58	0.373	1.34 ± 0.51	1.75 ± 0.94	<0.001
Bilirubin (mg/dL)	0.60 (0.40-1.00)	0.60 (0.40-1.00)	0.65 (0.40-1.00)	0.986	0.60 (0.40-0.90)	0.77 (0.50-1.40)	<0.001
CKMB (U/L)	21.50 (7.50-71.00)	21.50 (7.50-73.50)	21.50 (7.50-68.50)	0.640	20.50 (7.00-72.38)	24.00 (9.00-68.25)	<0.001
ALT (U/L)	35.00 (20.50–77.50)	36.00 (21.00-81.00)	33.00 (20.00-70.00)	0.653	32.00 (20.00-62.00)	62.00 (26.00-207.75)	<0.001
ALP (U/L)	77.00 (58.50–102.50)	76.00 (58.00-101.50)	79.00 (60.00–105.50)	0.026	74.00 (57.00–96.50)	90.50 (67.00–132.50)	<0.001
AST (U/L)	66.50 (33.00-178.50)	67.00 (34.00-182.00)	64.00 (31.00-158.88)	0.627	56.50 (31.00-142.50)	121.25 (54.00-418.75)	<0.001
Abs basophils (%)	0.03 (0.02-0.05)	0.03 (0.02-0.05)	0.03 (0.02-0.06)	0.008	0.03 (0.02-0.05)	0.03 (0.02-0.06)	0.390
Abs eosinophils (%)	0.09 (0.03-0.17)	0.08 (0.03-0.16)	0.10 (0.04-0.18)	0.081	0.10 (0.04–0.17)	0.05 (0.02-0.11)	<0.001
Abs monocytes (%)	0.55 (0.36-0.83)	0.55 (0.36-0.82)	0.55 (0.37-0.87)	0.197	0.54 (0.36-0.80)	0.62 (0.38-1.06)	<0.001
Abs neutrophils (%)	9.80 (6.73-13.52)	9.75 (6.71–13.43)	10.05 (6.79–13.95)	0.386	9.47 (6.57–12.84)	11.83 (8.07-16.60)	<0.001
LOS (days)	1.06 (0.42-2.62)	1.06 (0.42-2.58)	1.08 (0.42-2.76)	0.069	1.00 (0.39–2.38)	1.81 (0.58-4.36)	<0.001
DMV (days)	2.14 (1.22-4.05)	2.13 (1.22-4.00)	2.20 (1.21-4.20)	0.138	2.09 (1.22-3.84)	2.96 (1.20-6.46)	<0.001
Mechanical ventilation (%)	4017 (85.69%)	3001 (85.45%)	1016 (86.39%)	0.423	3405 (84.85%)	612 (90.67%)	<0.001
Scorning systems							
APSIII	48.26 ± 24.80	48.18 ± 24.62	48.50 ± 25.34	0.696	43.32 ± 20.45	77.61 ± 27.93	<0.001
OASIS	32.27 ± 9.56	32.19 ± 9.55	32.52 ± 9.60	0.306	30.80 ± 8.63	41.06 ± 10.10	<0.001
SOFA	5.39 ± 3.92	5.40 ± 3.90	5.36 ± 3.97	0.770	4.71 ± 3.42	9.44 ± 4.24	<0.001

(Continued)

#### Table I (Continued).

Variable	Total	Patients		P-value	Patients		P-value
		Training set (%)	Validation set (%)		Alive (%)	Died (%)	
Comorbidities, n (%)							
Congestive heart failure	2300 (49.06%)	1714 (48.80%)	586 (49.83%)	0.542	1913 (47.67%)	387 (57.33%)	<0.001
Peripheral vascular	733 (15.64%)	542 (15.43%)	191 (16.24%)	0.509	611 (15.23%)	122 (18.07%)	0.059
Cerebrovascular disease	637 (13.59%)	483 (13.75%)	154 (13.10%)	0.569	504 (12.56%)	133 (19.70%)	<0.001
Dementia	157 (3.35%)	120 (3.42%)	37 (3.15%)	0.655	118 (2.94%)	39 (5.78%)	<0.001
Chronic pulmonary disease	1154 (24.62%)	849 (24.17%)	305 (25.94%)	0.225	949 (23.65%)	205 (30.37%)	<0.001
Rheumatic disease	175 (3.73%)	121 (3.45%)	54 (4.59%)	0.073	143 (3.56%)	32 (4.74%)	0.135
Peptic ulcer disease	107 (2.28%)	73 (2.08%)	34 (2.89%)	0.106	87 (2.17%)	20 (2.96%)	0.201
Mild liver disease	307 (6.55%)	224 (6.38%)	83 (7.06%)	0.415	196 (4.88%)	(16.44%)	<0.001
Diabetes uncomplicated	1420 (30.29%)	1056 (30.07%)	364 (30.95%)	0.568	1204 (30.00%)	216 (32.00%)	0.296
Diabetes complicated	675 (14.40%)	511 (14.55%)	164 (13.95%)	0.609	578 (14.40%)	97 (14.37%)	0.982
Paraplegia	132 (2.82%)	100 (2.85%)	32 (2.72%)	0.821	105 (2.62%)	27 (4.00%)	0.044
Renal disease	1306 (27.86%)	985 (28.05%)	321 (27.30%)	0.619	1047 (26.09%)	259 (38.37%)	<0.001
Malignant cancer	320 (6.83%)	242 (6.89%)	78 (6.63%)	0.761	231 (5.76%)	89 (13.19%)	<0.001
Severe liver disease	77 (1.64%)	58 (1.65%)	19 (1.62%)	0.933	41 (1.02%)	36 (5.33%)	<0.001
Metastatic solid tumor	115 (2.45%)	87 (2.48%)	28 (2.38%)	0.853	79 (1.97%)	36 (5.33%)	<0.001
In-hospital mortality	675 (14.40%)	506 (14.41%)	169 (14.37%)	0.975	-	-	-

Abbreviations: SBP, Systolic blood pressure; RBC, red blood cell; SPO2, percutaneous oxygen saturation; PTT, partial thromboplastin time; BUN, blood urea nitrogen; WBC, white blood cell; PT, prothrombin time; DBP, Diastolic blood pressure; SAPSII, simplified acute physiology score II; LOS, the length of ICU stay; DMV, the duration of mechanical ventilation.

ICU myocardial infarction patients had in-hospital death rates of 14.41% and 14.37% in the training set and validation set, respectively. Our study found a higher in-hospital mortality rate in the intensive care unit than previously reported for other myocardial infarction patients. Consistent with previous reports: older patients had high in-hospital mortality. A large number of myocardial infarction patients who died during hospitalisation had congestive heart failure, chronic lung disease, diabetes, and renal disease. Compared to patients who survived hospitalisation, laboratory indicators such as Age, Heart rate, Respiratory rate, WBC, RDW, Anion gap, Phosphate, Lactate, BUN, Creatinine, Glucose, Abs neutrophils, PTT, PT, ALT, ALP, AST, Bilirubin, and CKMB etc. were higher in patients who died in the hospital. The three scoring systems (SOFA, APSIII, and OASIS) were significantly higher in patients with myocardial infarction who experienced in-hospital death than in those who did not. In addition, SPO2, bicarbonate, and blood pressure levels etc. were reduced in patients who died during their hospitalisation.

### Variables Analysis and Selection

Figure 1B shows the methodology and process we used to develop the model and select the variables.

Based on a training set of 3512 patients with myocardial infarction, LASSO regression screened 18 potential predictors of Age, Heart rate, SBP, Respiratory rate, Temperature, ALP, Anion gap, Glucose, Lactate, PTT, BUN. Phosphate, Cerebrovascular disease, Chronic pulmonary disease, Mild liver disease, Diabetes complicated, Malignant cancer, Metastatic solid cancer (Figure 2A and B). Table 1 shows the characteristics of patients with myocardial infarction in the ICU and participants in the training and validation groups at baseline and at ICU admission. The results show that there was little statistical difference between the two groups in all variables.

### Model Development

The following are some major risk variables for in-hospital mortality in myocardial infarction patients that were identified by the final multivariate analysis: Age (OR=1.03, 95% CI 1.02 to 1.04), Respiratory rate (OR=1.08, 95% CI 1.03 to 1.12), Lactate (OR=1.47, 95% CI 1.32 to 1.64), BUN (OR=1.02, 95% CI 1.01 to 1.02), PTT (OR=1.01, 95% CI 1.00 to 1.01), Cerebrovascular disease (OR=1.64, 95% CI 1.06 to 2.53), Chronic pulmonary disease (OR=1.51, 95% CI 1.06 to 2.15), Mild liver disease (OR=1.93, 95% CI 1.20 to 3.11), Metastatic solid tumor (OR=2.84, 95% CI 1.21 to 6.68), (Table 2).



Figure 2 LASSO regression: selection of significant parameters in variables in the training set. (A) Ten-fold cross-validation for tuning parameter selection in the LASSO model; (B) LASSO coefficient profiles. Predictor variables selected by LASSO. The LASSO was used for regression of high dimensional predictors. The advantage of the LASSO regression method that we adopted is that by penalizing regression on all variable coefficients, the relatively minor independent coefficients are reduced to zero and are thus disregarded in the modeling. Using 10-fold cross-validation, the vertical line was drawn at the value chosen, where the optimal results was 18 features with non-zero coefficients. Abbreviations: LASSO, least absolute shrinkage and selection operator.

Based on LASSO regression analysis, univariate analysis, and multiple logistic regression analysis, the predictive variables for in-hospital mortality in patients with myocardial infarction were as follows: logit(P)=-9.05941 +0.02501\*AGE+0.09918\*RESPIRATORYRATE+0.00395\*GLUCOSE+0.01290\*PTT+0.48817\*LACTATE +0.02280\*BUN+0.36930\*CEREBROVASCULARDISEASE+0.32606\*CHRONICPULMONARYDIS +0.80434\*MILDLIVERDISEASE +1.14367\*METASTATICSOLIDTUMO.

Variables	Univariate an	alysis	Multivariate analysis		
	OR (95% CI)	P-value	OR (95% CI)	P-value	
Age	1.03 (1.02, 1.04)	<0.0001	1.03 (1.02, 1.04)	<0.0001	
Heart rate	1.04 (1.03, 1.04)	<0.0001	NA	NA	
Respiratory rate	1.23 (1.20, 1.26)	<0.0001	1.08 (1.03, 1.12)	0.0014	
SBP	0.96 (0.95, 0.96)	<0.0001	NA	NA	
Temperature	0.55 (0.48, 0.64)	<0.0001	NA	NA	
ALP	1.00 (1.00, 1.01)	<0.0001	NA	NA	
Lactate	1.87 (1.73, 2.02)	<0.0001	1.47 (1.32, 1.64)	<0.0001	
BUN	1.03 (1.03, 1.03)	<0.0001	1.02 (1.01, 1.02)	0.0001	
Phosphate	1.74 (1.62, 1.87)	<0.0001	NA	NA	
Glucose	1.01 (1.01, 1.01)	<0.0001	1.01 (1.00, 1.01)	0.0004	
Anion gap	1.30 (1.26, 1.33)	<0.0001	NA	NA	
PTT	1.02 (1.01, 1.02)	<0.0001	1.01 (1.00, 1.01)	0.0494	
Cerebrovascular disease	1.74 (1.37, 2.22)	<0.0001	1.64 (1.06, 2.53)	0.0267	
Chronic pulmonary disease	1.42 (1.16, 1.75)	0.0009	1.51 (1.06, 2.15)	0.0222	

 
 Table 2 Univariate and Multivariate Logistic Analyse Variables Screened by LASSO in the Training Set

(Continued)

Variables	Univariate analysis		Multivariate analysis		
	OR (95% CI)	P-value	OR (95% CI)	P-value	
Mild liver disease	3.99 (2.98, 5.33)	<0.0001	1.93 (1.20, 3.11)	0.0066	
Diabetes complicated	0.93 (0.71, 1.23)	0.6215	NA	NA	
Malignant cancer	2.25 (1.66, 3.04)	<0.0001	NA	NA	
Metastatic solid tumor	2.47 (1.54, 3.97)	0.0002	2.84 (1.21, 6.68)	0.0163	



Abbreviations: WBC, white blood cell; PTT, Partial Thromboplastin Time; SPO2, percutaneous oxygen saturation; DBP, Diastolic blood pressure; SAPSII, simplified acute physiology score II.

By scaling each variable's value upward on a small scale, the score for each parameter is calculated (point). The total points are calculated by adding the points given to the corresponding factors. The mortality rate increases as the total score rises (Figure 3).

Nomogram creation and validation in accordance with the results of LASSO regression analysis, univariate analysis, and multiple logistic regression analysis (Figure 3). A novel nomogram containing 10 independent variables associated with patient death was developed (Table 2) to predict the risk of in-hospital death in the training set. Age, Respiratory rate, Glucose, Lactate, PTT, BUN, Cerebrovascular disease, Chronic pulmonary disease, Mild liver disease, and Metastatic solid cancer were all significant predictors.



Figure 3 The nomogram for predicting in-hospital mortality in patients with myocardial infarction. The nomogram included 10 variables, including Age, Respiratory rate, Glucose, PTT, Lactate, Cerebrovascular disease, Chronic pulmonary disease, Mild liver disease, and Metastatic solid tumor. In order to calculate the score when utilizing the nomogram, a vertical line should be drawn from each variable to the "Points" line. The values should then be totaled to determine the final score. Finally, to determine the in-hospital mortality of the myocardial infarction patients, a vertical line is drawn downward from the "Total Points.".

Abbreviations: RR Respiratory rate; PTT Partial Thromboplastin Time; CD Cerebrovascular disease; CPD Chronic pulmonary disease; MLD Mild liver disease; MST Metastatic solid tumor.

#### Model Validation

The operating characteristic (ROC) curves for the participants (training set) of our nomogram were compared to the validation cohort (Figure 4). Using the calibration curve results and C-index, the nomogram's prediction abilities were further validated. The AUC for the training and validation sets' respective prediction models was 0.869 (95% CI: 0.849–0.889) and 0.846 (95% CI: 0.807–0.875) (Figure 4A and B).

Figure 5 shows the findings of our comparison of the nomogram and SOFA in predicting the probability of in-hospital death in myocardial infarction patients. The findings reveal that in both the training and validation sets, the AUC of our nomogram is much higher than that of SOFA, demonstrating that the present prediction model has superior discriminative capacity over SOFA in predicting the risk of in-hospital death from myocardial infarction.

We built bias-corrected lines using bootstrap methods and showed calibration curves for the training and validation sets. The predicted values in both sets were higher than those of SOFA, demonstrating that the nomogram has better predictive calibration than SOFA, even though the apparent curve and bias-corrected curve in both sets slightly deviated from the reference line while still keeping strong agreement between observation and prediction (Figure 6A and B). The results show that the nomogram has a high discriminative ability in estimating the probability of in-hospital mortality in myocardial infarction patients. The calibration plots further demonstrated significant agreement between projected and actual in-hospital mortality. The calibration plotted standard curves were all extremely near the typical 45-degree diagonal, showing excellent agreement between expected and observed results (Figure 6).

Eventually, the DCA curve for the net benefit shows that the model has significant clinical validity for predicting death (Figure 7). By incorporating several evaluation criteria, our model effectively predicts in-hospital mortality in myocardial infarction patients.

#### Development of Webserver for Easy Access of Our New Model

For the benefit of academics and clinicians, a visual illustration of our nomogram online (Figure 8) is available at <u>http://</u><u>www.empowerstats.net/pmodel/?m=20358\_inhospitalmortality</u>. It is simple to calculate the predicted survival probability over time by entering clinical features and examining the figures and tables that the website outputs.



Figure 4 The ROC curve for predictive model. (A)Training set. (B)Validation set. Receiver Operating Characteristic (ROC) curve and area under the ROC curve (AUC). (A) The ROC in the training set; (B) The ROC in the internal validation set.



Figure 5 The ROC curve for predictive model. (A) Training set. (B) Validation set. The ROC curve combined model, the prediction model (Model I) and SOFA (Model 2) in the Training set (A) and Validation set (B). The combined model is incorporated by all the independent risk variables. The prediction nomogram includes Age, Respiratory rate, Glucose, PTT, Lactate, Cerebrovascular disease, Chronic pulmonary disease, Mild liver disease, and Metastatic solid tumor.



Figure 6 Calibration plots. (A) Training set. (B) Validation set. Bootstrap-based calibration curves in the training set (A) and validation set (B) Calibration plots. Show the consistency of the predicted potentiality and actual values of the training set and validation set. A excellent conformity between observation and prediction is seen in both sets, even though the apparent curve and bias-corrected curve both somewhat diverged from the reference line.

# Discussion

Myocardial infarction, caused by acute and prolonged ischemia in the coronary arteries, is a type of heart muscle death that can be fatal. It is often exacerbated by arrhythmias, shock, or heart failure and is a major cause of death and disability, especially as the population ages.<sup>6</sup> During periods of vessel wall inflammation, it can lead to sudden, severe events or go unnoticed in chronic conditions.<sup>8,28</sup>



Figure 7 Decision Curve Analysis. (A) Training set. (B) Validation set. The DCA curve of the prediction model (Model 1) and SOFA (Model 2) in the training set (A) and validation set (B). Show the net benefit, represented by a backslash with a negative slope, in the training set and validation set.

Myocardial infarction, common in Europe and the US with 1.5 million cases yearly, draws medical focus due to its high rates of illness, disability, and death, along with financial costs.<sup>8</sup> Despite limited patient-doctor collaboration, various scores (GRACE, TIMI, OASIS, Duke Treadmill Score) are used to predict outcomes for these patients.<sup>29–32</sup> These existing systems, while widely used, have limitations in accurately predicting mortality, particularly in patients with complex comorbidities or those who are elderly. For instance, the GRACE score, although useful, does not fully account for certain critical variables such as lactate levels and partial thromboplastin time (PTT), which are included in our nomogram.

However, there are no nomograms or online calculators for predicting in-hospital death for ICU patients with myocardial infarction. A practical, objective scoring model is needed to assess the risk of in-hospital death. Our model aims to help healthcare professionals estimate the presence of a condition (diagnostic) or the chance of a future event (prognostic), guiding their decision-making.<sup>33</sup>

Nomograms compute a total score depending on the values of their predictor variables, and from that total score, they determine the likelihood that an event will occur or the likelihood that a person will survive. They have been widely used in medicine in recent years. In practice, we often use clinical data and the various test results of patients to predict, for example, the risk of a patient developing an event or the probability of their survival that a person will survive. Our demand for an interconnected medical model is met by the capacity to construct individual probabilities of clinical outcomes by including various prognostic and deterministic data in a nomogram, and this allows us to further personalize therapy.<sup>34</sup>

We collected comprehensive patient data from the publicly accessible MIMIC-IV database, focusing on ICU patients in significant tertiary care institutions. Our nomogram, constructed using variables such as Age, Respiratory rate, Glucose, Lactate, PTT, BUN, Cerebrovascular disease, Chronic pulmonary disease, Mild liver disease, and Metastatic solid cancer, demonstrated superior predictive performance compared to existing scoring systems. Specifically, our nomogram achieved AUC scores of 0.869 in the training set and 0.846 in the validation set, indicating higher discriminative ability. Calibration plots confirmed a better fit for predicting in-hospital mortality risk. These AUC values are notably higher than those typically reported for existing scoring systems. For instance, the GRACE score, which is widely used for predicting mortality in acute coronary syndromes, generally reports AUC values around 0.75–0.80.<sup>35</sup> Similarly, the TIMI score and OASIS score also have lower discriminative ability compared to our nomogram. Additionally, DCA showed a higher net benefit across various threshold probabilities, underscoring its clinical utility.



Figure 8 Online version of the nomogram. http://www.empowerstats.net/pmodel/?m=20358\_inhospitalmortality.

Compared to traditional staging, we have also developed a web calculator to aid clinical decision-making through fast calculations performed through a user-friendly numerical interface, as well as a more accurate and easier-to-understand prognosis, combined with prognosis derived from the nomogram.

Although the MIMIC-IV database used in this study contains a variety of patient information from various hospitals, which to some extent reflects the characteristics of different populations, we acknowledge that the model's generalizability may be influenced by the characteristics of specific populations, healthcare resources in different regions, and differences in treatment options. Therefore, in order to more thoroughly evaluate the model's robustness and generalizability, future research could further validate it in various databases and clinical settings, even in light of the positive internal validation results in this study.

In general, the occurrence of heart attacks is inextricably linked to age. In addition, aging exacerbates myocardial damage after a heart attack. According to earlier research, age is an independent predictor.<sup>36</sup> The prognosis of elderly patients deteriorates with age because of diminished myocardial reserve capacity.<sup>37</sup> Myocardial infarction, hypertension, and atherosclerosis are only a few of the cardiovascular diseases (CVD) that are greatly increased by aging. An important contributing element to the advancement of illness, pathological arterial wall remodeling, and vascular aging is oxidative stress, which is brought on by excessive reactive oxygen species (ROS) generation and/or low expression of antioxidant enzymes.<sup>38</sup> Aging, the process through which cells cease multiplying and become dysfunctional, is a result of both inflammatory processes and oxidative stress.<sup>39</sup> In addition, in a recent study, the systemic immunoinflammatory index (SII) and systemic inflammatory response index (SIRI), as well as the combination of the patient's history at the time of admission to the hospital, were found to have good efficacy in predicting the risk of in-hospital mortality in elderly patients with AMI.<sup>40</sup>

In our study, laboratory indicators such as glucose, BUN, lactate, and PTT are important independent prognostic indicators.

Although age is a predictor of adverse events following the onset of coronary syndromes, including hospitalisation and posthospital mortality, older patients are not well represented in trials assessing myocardial infarction, and increased blood glucose values explain the poor outcome in older people. Increased mortality was linked to elevated blood glucose. Hyperglycemia is one of the acute glucose responses to stress in ST-segment elevation myocardial infarction (STEMI) in its early phases.<sup>7</sup> Researchers have discovered a strong correlation between increased short-term mortality in individuals with cardiogenic shock following acute myocardial infarction and an admission BUN >8.95 mmol/L.<sup>41</sup> At the time of admission, the level of circulating urea nitrogen was an independent predictor of cardiovascular death in patients with AMI. Urea nitrogen can be used to help identify patients who are at risk since it represents not just renal function but also acute haemodynamic and neurohumoral alterations during acute myocardial infarction.<sup>42</sup> Lactate concentration increases with poor tissue perfusion and has prognostic value in patients with cardiogenic shock. Martin Frydland et al recommend lactate measurement in patients with myocardial infarction, especially if there are signs of haemodynamic compromise.<sup>43</sup> Coagulation activation is a host response to pathogens during sepsis and is thought to be a cause of tissue damage and multi-organ failure. Alterations in coagulation markers are associated with inhospital mortality and sepsis.<sup>44</sup> A prospective study by Aihua Fei et al also demonstrated a link between coagulation abnormalities and mortality in ICU patients and had the ability to predict ICU mortality.<sup>45</sup>

Chronic pulmonary diseases, such as tuberculosis, lung abscess, silicosis, chronic obstructive pulmonary disease, lung cancer, bronchiectasis, and chronic respiratory failure, are prevalent extracardiac problems in patients in the ICU, may take place in cohorts of individuals with infarction, and are linked to increased mortality.<sup>46</sup> We also conclude that patients with myocardial infarction who have cancer have a higher probability of death, which is comparable to the view of Zheng R. and other research scholars.<sup>47,48</sup> If patients with heart disease have other complications, such as metastatic solid tumours or liver disease, then their mortality rate will be increased.<sup>49–52</sup>

The main advantages of our study: (1) We found new variables that could be used to build a nomogram to predict inhospital mortality in myocardial infarction patients. (2) The population of patients with myocardial infarction in our study was larger and more representative than in past studies. (3) To make the selection of variables more accurate, we used LASSO regression, univariate analysis, and multiple regression analysis. (4) Our study improves the AUC of the prediction model compared to other similar studies. (5) The validation of the prediction models in some previous studies has been mediocre, and although our study only did an internal validation, the validation was good. (6) We have developed a more convenient webpage calculator to replace the prediction formula.

Our study has several limitations: Firstly, due to the lack of relevant treatment information in the MIMIC-IV database, for example, we were unable to obtain treatment-related information such as thrombolysis risk scores for patients with myocardial infarction, and the important cardiovascular predictive data on patients' cardiac troponin were incomplete. These data, however, are critical for accurately assessing the severity and prognosis of myocardial infarction. Also, the severity and stage of myocardial infarction were not detailed in this study, which may further affect the predictive ability of the model. Future studies should consider incorporating more indicators about the severity of myocardial infarction, such as electrocardiogram data and echocardiogram data, to more comprehensively assess patients' conditions. In addition, we had no way to extract information about complications such as smoking, alcohol consumption, and hyperlipidemia in patients with myocardial infarction in the intensive care unit, which are very important factors for the construction of the model. Second, only internal validation was performed in this study using the MIMIC-IV database, and no external validation was performed. Despite the favorable results of the internal validation, the performance of the model in other datasets may be different. To further confirm the robustness and performance of the model, future studies need to perform external validation based on more independent datasets to verify the applicability of the model in different populations and healthcare settings. In addition, this study did not evaluate biomarkers that are not commonly used in laboratory testing, nor did it compare and analyse laboratory follow-up records. Finally, this study focused only on in-hospital mortality and did not address long-term follow-up after hospital discharge. Future studies need to consider longer-term follow-up data to fully assess the predictive power of the model and to better understand the long-term prognosis of patients with myocardial infarction.

## Conclusion

In order to predict in-hospital mortality in myocardial infarction patients based on objective demographics, laboratory results, and co-morbidities, we have built a practical nomogram model and developed a nomogram-based web calculator. Our model demonstrated superior discriminative ability compared to the Sequential Organ Failure Assessment (SOFA) score, with AUC values of 0.869 and 0.846 in the training and validation sets, respectively. This tool aids clinicians in risk stratification, treatment planning, and patient counseling by providing individualized mortality risk assessment. Key limitations of this study include the lack of detailed treatment data (eg, thrombolysis protocols) and cardiological parameters (eg, infarct location, echocardiographic findings), which may limit clinical applicability. Additionally, external validation across diverse populations and healthcare settings is necessary to confirm generalizability. Future studies should integrate long-term follow-up data, biomarkers beyond routine laboratory tests, and behavioral factors (eg, smoking, hyperlipidemia) to enhance predictive accuracy and utility.

## **Abbreviations**

MIMIC-IV, Medical Information Mart for Intensive Care IV; ICU, Intensive Care Unit; LASSO, Least Absolute Shrinkage and Selection Operator; AUC, Area Under the Curve; ROC, Receiver Operating Characteristic; SOFA, Sequential Organ Failure Assessment; C-index, Harrell's Consistency Index; DCA, Decision Curve Analysis; GRACE, Global Registry of Acute Coronary Events; TIMI, Thrombolysis in Myocardial Infarction; OASIS, Outcome Algorithm for Predicting In-Hospital Mortality in Acute Coronary Syndromes; ECG, Electrocardiogram; PTT, Partial Thromboplastin Time; BUN, Blood Urea Nitrogen; PT, Prothrombin Time; INR, International Normalized Ratio; CKMB, Creatine Kinase MB; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; AST, Aspartate Aminotransferase; CVD, cardiovascular diseases; ROS, reactive oxygen species; SII, Systemic Immune-Inflammatory Index; SIRI, Systemic Inflammatory Response Index; STEMI, ST-Segment Elevation Myocardial Infarction; AMI, Acute Myocardial Infarction.

## **Data Sharing Statement**

The datasets are available in the physionet (https://physionet.org/content/mimiciv/0.4/).

# **Consent to Participation and Ethical Approval**

This study utilized data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, which is a publicly available dataset that has been de-identified and is approved for research use under existing ethical guidelines. The MIMIC-IV database has already obtained the necessary ethical approvals and patient consents. According to the regulations of our institution and in compliance with national guidelines (eg, Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects, China, dated February 18, 2023), this study is exempt from additional Institutional Review Board (IRB) approval because it involves the use of publicly available, de-identified data. Therefore, no further IRB approval was required for this study.

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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. Shixuan Peng: Conceptualization, methodology, formal analysis, writing – original draft, project administration. Qisheng Chen: Formal analysis, data curation, validation. Weiqi Ke: Writing – review & editing, supervision.

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## Disclosure

The authors report no conflicts of interest in this work.

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