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ORIGINAL RESEARCH

Construction and Validation of a Risk Prediction Model for Sepsis-Induced Myocardial Injury

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Background: Sepsis patients face a high risk of myocardial injury, which increases the risk of death. Therefore, the rapid and accurate assessment of myocardial injury risk is crucial for improving prognosis.

Objective: To construct and validate a risk prediction model for sepsis-induced myocardial injury (SMCI).

Methods: Patients were randomly assigned to a training cohort and an internal validation cohort in a 7:3 ratio. Least Absolute Shrinkage and Selection Operator (LASSO) regression and multivariate logistic regression were used to identify independent predictors for the construction of a nomogram. The model's discrimination, calibration, and clinical applicability were evaluated using area under curve (AUC), Hosmer-Lemeshow tests, decision curve analysis (DCA) and clinical impact curve (CIC). Meanwhile, internal validation was conducted.

Results: The study included 370 patients, with 262 in the training cohort and 108 in the validation cohort. 3 independent risk factors were identified, including Log myoglobin (Myo), Log B-type natriuretic peptide (BNP), and Log interleukin-6 (IL-6) and a nomogram incorporating these factors was constructed. The AUC in the training and validation cohorts was 0.856 and 0.853, respectively. The Hosmer-Lemeshow test indicated good calibration in both cohorts, while DCA and CIC demonstrated strong clinical applicability.

Conclusion: The nomogram based on Log Myo, Log BNP, and Log IL-6 may serve as a practical tool for the early identification of high-risk patients by facilitating the rapid calculation of SMCI risk.

Keywords: myocardial injury, sepsis, prediction model, IL-6

Introduction

Sepsis, as a major challenge in global emergency and critical care medicine, is a life-threatening organ dysfunction caused by a dysregulated host immune response to infection.[1] Its incidence and mortality rates remain consistently high, and it has become one of the leading causes of death among emergency and critically ill patients.[2,3] According to statistics, annual global sepsis cases exceed 48.9 million, with related deaths reaching 11 million, accounting for 19.7% of global total deaths.[4] It is estimated that from 2017 to 2019, there were 4.8 million to 6.1 million hospitalized cases of sepsis in China each year.[5] In the multiple organ dysfunction caused by sepsis, myocardial injury is a common and severe complication, referred to as SMCI, with an incidence as high as 13.8% to 79%.[6–8] The occurrence of SMCI not only significantly increases the difficulty of treatment but also is closely associated with poor prognosis. Studies have shown that, as an independent risk factor for mortality in sepsis, patients with SMCI have a mortality rate of 32.6% to 43.7%, which is significantly higher than that in patients without myocardial injury.[8–10] Although the clinical significance of SMCI has been widely recognized, its early identification still faces numerous challenges. Current diagnosis mainly relies on elevations in myocardial biomarkers (such as troponin T/I, brain natriuretic peptide) or the evidence of cardiac dysfunction demonstrated by echocardiography.[8,11] However, elevated troponin levels in sepsis may be influenced by multiple factors such as inflammation and renal injury, leading to insufficient specificity.[11] Although echocardiography can assess ventricular systolic and diastolic function, it is affected by factors such as equipment conditions, operator

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experience, and patients' hemodynamic status, making it difficult to be applied in real-time and dynamically in emergency departments.[12] More importantly, the condition of sepsis patients progresses rapidly. When typical clinical symptoms or definite biomarker abnormalities manifest, myocardial injury has often entered the moderate to advanced stage, missing the optimal timing for intervention. Therefore, the early identification of high-risk patients for SMCI and the timely implementation of targeted interventions have become a key link in improving the prognosis of sepsis patients.

As a quantitative tool that integrates multiple factors, the risk prediction model can provide clinicians with individualized risk assessments and assist in early decision-making by screening independent risk factors and developing visual prediction models (eg, nomograms). It has shown significant value in risk stratification and prognostic evaluation for various diseases.[13,14] Currently, existing studies have explored the risk factors for SMCI and found that lactate levels, septic shock, age, hemoglobin levels, etc. are independent risk factors.[7,15,16] However, Risk factor analysis fails to intuitively, visually, and conveniently calculate the risk of SMCI occurrence, thus having limited guiding value for clinical practice. Nomograms, as visual tools of the model, intuitively demonstrate the relationship between various clinical variables and the probability of SMCI. By developing a nomogram, rapid risk assessment of myocardial injury can be performed via user-friendly digital interfaces, which facilitates rapid prediction of the probability of myocardial injury in sepsis patients, thereby enabling timely implementation of interventions to reduce morbidity and mortality.[17,18] Although Jiangquan Yu et al[19] constructed a risk prediction model for SMCI, their study had two limitations: First, the indicators included in model development were dichotomous variables, converting continuous variables into dichotomous variables is not conducive to the accurate calculation of the probability of SMCI occurrence. Second, it lacked model validation and evaluation of clinical applicability. Other studies have addressed these limitations.[17,20] However, they included sepsis patients admitted to the intensive care unit (ICU); patients admitted to the ICU generally have a longer disease course, which may result in a certain delay in prediction. In addition, the mechanism of SMCI involve immune dysregulation, cytokine storm, and oxidative stress induced by infection and insufficient tissue perfusion.[21] However, their studies incorporated relatively few inflammatory indicators, only routinely including white blood cell count (WBC) and procalcitonin (PCT), but not C-reactive protein (CRP), IL-6, or serum amyloid A (SAA) etc. Thus, this study systematically collected the initial clinical data of sepsis patients at the time of their presentation to the emergency department, including indicators reflecting immunity and cytokine storm, indicators reflecting tissue perfusion, and other commonly used clinical indicators. Using these indicators, an SMCI risk prediction model was constructed. The model's discrimination, calibration, and clinical applicability were evaluated and internally validated, aiming to provide clinical evidence for the early identification of SMCI. This may facilitate the early detection, early diagnosis, and early treatment of SMCI, thereby improving patient prognosis.

Methods

Patients

A retrospective analysis was performed on the clinical data of 370 sepsis patients admitted to the Emergency Resuscitation Area of the First Affiliated Hospital of Xinjiang Medical University from September 2022 to December 2024. The study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments, and was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University (K202505-32). Because this study was retrospective, informed consent was waived by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University. To protect patient privacy, all personally identifiable information (eg, names, hospital identification numbers, national ID numbers) was de-identified during data collection and analysis, thus ensuring that the data were utilized exclusively by the research team in an anonymous format.

Inclusion criteria: 1) Age ≥ 18 years; 2) Diagnosis of sepsis, based on the Sepsis-3 diagnostic criteria:[1] patients with infection or suspected infection, combined with an increase of ≥ 2 points in the Sequential Organ Failure Assessment (SOFA) score from baseline at admission; 3) Hospitalization duration >24 hours. Exclusion criteria were as follows: 1) Malignant tumor; 2) History of myocardial infarction, chronic heart failure, chronic renal failure, and chronic hepatic failure; 3) Decompensated liver cirrhosis; 4) Incomplete data. We included 520 patients with sepsis. A total of 150 patients were excluded according to the exclusion criteria. Finally, 370 patients were included in the statistical analysis.

The diagnosis of SMCI was based on the following criterion: two consecutive cardiac troponin I (cTnI) levels > 0.04 μg/L in sepsis patients.[22] Based on this criterion, patients were divided into the SMCI group (n = 170) and Non-SMCI group (n = 200). The cTnI levels in the two groups were 0.151 (0.074, 0.684) μg/L and 0.012 (0.012, 0.021) μg/L. These patients were randomly assigned to the training cohort or internal validation cohort. A stratified sampling method was adopted, with "serial_number" as the stratification variable, and the dataset was divided into a training set and a validation set at a 7:3 ratio. Specifically, the create Data Partition function in the caret package was used for data splitting, and the random seed was set to 123 to ensure reproducibility. A flowchart of patient enrollment is shown in Figure 1.

Data Collection

Comprehensive clinical data were obtained on the first day of admission to emergency resuscitation area, which included: age, gender, SOFA score, Acute Physiology and Chronic Health Evaluation II (APACHE-II), Glasgow Coma Scale (GCS), comorbidities, infection site, temperature, mean arterial pressure (MAP), heart rate, respiratory rate, pH, $PaCO_2$, PaO_2, HCO_3^-, oxygenation index, standard base excess (SBE), K+, Na+, Ca^2+, glucose, lactic acid, WBC, absolute neutrophil count (ANC), absolute lymphocyte count (ALC), absolute monocyte count (AMC), hemoglobin, platelet count, fibrinogen, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), thrombin time (TT), D-dimer, cTnI, creatine kinase isoenzyme MB (CK-MB), Myo, BNP, CRP, IL-6, PCT, SAA. Since the levels of D-dimer, Myo, BNP, and IL-6 vary by thousands of folds among patients, we performed log transformation on these indicators to reduce the impact of extreme values and improve the applicability of subsequent statistical analyses and the reliability of the results. First, LASSO regression was used to screen for predictive variables. Then, univariate and multivariate logistic regression analyses were performed to identify the independent risk factors for SMCI. Subsequently, a nomogram was constructed using these independent risk factors. The AUC was used to evaluate the discriminative ability of the model, the Hosmer-Lemeshow tests and calibration curve were used to assess calibration, and DCA and CIC were used to evaluate clinical applicability. Meanwhile, internal validation was performed.

Statistical Analyses

Data analyses were performed using R software (version 4.5.1). Quantitative data were expressed as mean ± standard deviation or median (interquartile range [IQR], 25th–75th percentiles). For normally distributed quantitative data, comparisons between two groups were performed using the *t*-test; for non-normally distributed data, intergroup comparisons were performed using the Mann–Whitney *U*-test. Categorical data were presented as n (%), and intergroup comparisons were made using the χ^2-test. $P<0.05$ is considered statistically significant, and Benjamini-Hochberg procedure was applied the to control the false discovery rate (FDR) at 5% for multiple comparisons across all clinical variables. Based on multiple linear regression, variance inflation factor (VIF) was calculated to assess the multi-collinearity of the variables. To prevent overfitting, LASSO regression was employed to select optimal features. LASSO feature selection was performed using the "glmnet" package. Univariate and multivariate logistic regression analyses were performed using the "glm" package. Model stability was assessed using the events-per-variable (EPV) ratio. Nomograms were plotted using the "regplot" package. ROC curve plotting and AUC calculation were performed using the "pROC" package. Hosmer-Lemeshow tests and calibration plots were generated using the "rms" package. DCAs were performed using the "rmda" package. CICs were plotted using the "ggplot2" package.

Results

Clinical Characteristics

Of the 370 sepsis, 226 were men and 144 were women; 170 had myocardial injury and 200 did not. The numerous statistical tests increase the risk of type I error. Therefore, we use the Benjamini-Hochberg method to calculate the FDR to reduce the risk of type I error in multiple testing. The clinical characteristics of patients in the two groups are presented in Table 1. These patients were randomly assigned to the training cohort or validation cohort at a ratio of 7:3, resulting in 262 patients in the training cohort and 108 in the validation cohort. No significant differences were observed in age,

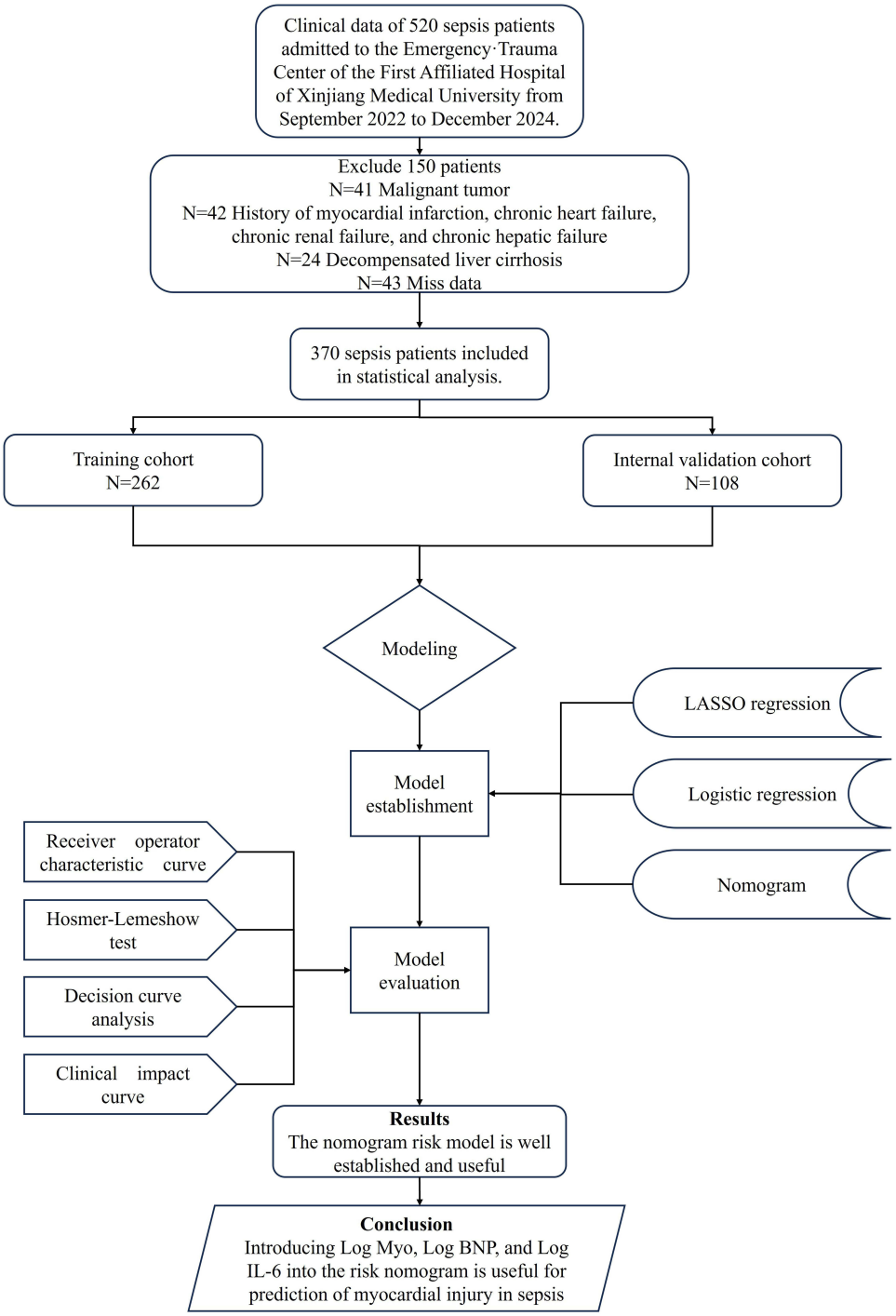

Figure 1 Flow diagram of study design.
Abbreviations: LASSO, least absolute shrinkage and selection operator; Myo, myoglobin; BNP, B-type natriuretic peptide; IL-6, interleukin-6.

SOFA score, APACHE II score, GCS score, comorbidities, or infection site between the training and validation cohorts, indicating that the two cohorts were comparable (stable 1).

Independent Risk Factors in the Training Cohort

As shown in Table 1, there were many variables with statistically significant differences between the SMCI and Non-SMCI groups. Prior to LASSO regression, we calculated the VIF of the variables; since the VIF values of multiple variables

Table 1 A Comparison of the Clinical Characteristics of SMCI and Non-SMCI Groups

Clinical Characteristics	SMCI (N=170)	Non-SMCI (N=200)	χ2/t/Z	*P*-value	FDR
Age (years old)	65.0(53.0, 78.0)	64.0(52.0, 76.8)	−0.343	0.732	0.752
Male (n, %)	100 (58.8)	126 (63.0)	0.674	0.412	0.824
Disease severity score					
SOFA (score)	8.0(4.0, 14.0)	4.5(2.0, 9.0)	−5.168	<0.001	<0.001
APACHE-II (score)	13.0(10.0, 19.0)	11.0(8.0, 14.8)	−5.057	<0.001	<0.001
GCS (score)	15.0(13.0, 15.0)	15.0(15.0, 15.0)	−3.273	0.001	0.003
Comorbidity (n, %)					
Hypertension	91 (53.5)	93 (46.5)	1.816	0.178	0.890
Diabetes	55 (32.4)	58 (29.0)	0.487	0.485	0.808
Coronary heart disease	23 (13.5)	24 (12.0)	0.194	0.660	0.733
Chronicpulmonary disease	13 (7.6)	23 (11.5)	1.533	0.213	0.533
Autoimmune diseases	4 (2.4)	7 (3.5)	0.419	0.517	0.739
Infection site (n, %)					
Respiratory tract	126 (74.1)	132 (66.0)	2.869	0.090	0.900
Abdominal cavity	32 (18.8)	49 (24.5)	1.732	0.188	0.627
Urinary tract	11 (6.5)	10 (5.0)	0.371	0.542	0.678
Others	7(4.1)	8(4.0)	0.003	0.954	0.954
Vital signs					
Temperature (°C)	38.7(38.3, 39.0)	38.5(38.0, 38.9)	−2.949	0.003	0.007
MAP (mmHg)	76.5(61.0, 83.0)	80.5(68.0, 89.0)	−3.901	<0.001	<0.001
Heart rate (times/min)	113.0(98.0, 132.0)	109.0(91.0, 123.0)	−2.229	0.026	0.043
Respiratory rate (times/min)	27.0(25.0, 29.0)	26.0(25.0, 28.0)	−1.666	0.096	0.140
Blood gas analysis					
pH	7.43(7.35, 7.47)	7.45(7.41, 7.48)	−2.979	0.003	0.007
$PaCO_2$ (mmHg)	25.5(21.0, 30.0)	28.5(24.0, 33.0)	−3.329	<0.001	<0.001
PaO_2 (mmHg)	88.5(72.8, 129.3)	86.0(73.0, 111.8)	−0.761	0.447	0.500
HCO_3^- (mmol/L)	17.7(13.3, 21.7)	19.9(16.5, 23.3)	−3.569	<0.001	<0.001
Oxygenation Index	318.0(242.0, 436.3)	343.5(243.1, 433.0)	−0.843	0.399	0.459
SBE	−5.4(−10.8, −2.2)	−2.8(−7.2, −0.40)	−3.783	<0.001	<0.001
K^+ (mmol/L)	3.9(3.4, 4.5)	3.7(3.3, 4.1)	−2.549	0.011	0.021
Na^+ (mmol/L)	134.1(130.8, 138.6)	133.7(130.4, 137.4)	−1.059	0.290	0.367
Ca^{2+} (mmol/L)	2.0(1.9, 2.2)	2.1 (2.0, 2.2)	−2.242	0.025	0.043
Glucose (mmol/L)	7.6(6.1, 11.4)	7.8(6.2, 10.8)	−0.057	0.954	0.954
Lactic acid (mmol/L)	2.6(1.8, 4.1)	2.1(1.4, 2.9)	−4.185	<0.001	<0.001
Complete blood count					
WBC ($10^3/mm^3$)	12.6(8.7, 18.5)	10.2(7.6, 13.9)	−3.012	0.003	0.006
ANC ($10^3/mm^3$)	10.3(7.1, 16.0)	8.7(5.9, 12.4)	−3.229	0.001	0.003
ALC ($10^3/mm^3$)	0.7(0.4, 1.2)	0.8(0.5, 1.2)	−1.305	0.192	0.261
AMC ($10^3/mm^3$)	0.7(0.3, 1.1)	0.6(0.3, 1.0)	−1.042	0.298	0.365
Hemoglobin (g/L)	116.0(92.8, 133.0)	122.0(97.3, 138.0)	−1.929	0.054	0.082
Platelet ($10^3/mm^3$)	157.5(82.8, 221.3)	181.5(124.5, 241.8)	−2.411	0.016	0.029
Coagulation parameters					
Fibrinogen (ug/mL)	4.4±1.8	4.5±1.7	−0.564	0.573	0.573
PT (s)	13.9(12.3, 16.3)	13.5(12.2, 15.2)	−1.433	0.152	0.214
INR	1.2(1.1, 1.4)	1.2(1.1, 1.3)	−1.061	0.289	0.379
APTT (s)	31.3(28.0, 35.0)	31.1(28.6, 35.2)	−0.357	0.721	0.761
TT(s)	20.1(18.1, 22.0)	19.0(17.7, 20.8)	−2.744	0.006	0.012
Log D-dimer	3.3(2.9, 3.7)	3.0(2.6, 3.3)	−4.976	<0.001	<0.001

(*Continued*)

Table 1 (Continued).

Clinical Characteristics	SMCI (N=170)	Non-SMCI (N=200)	χ2/t/Z	*P*-value	FDR
Myocardial injury markers					
CK-MB (ng/mL)	2.9(1.4, 6.2)	0.9(0.4, 1.6)	−10.008	<0.001	<0.001
Log Myo	2.5(2.1, 3.0)	1.9(1.6, 2.2)	−9.195	<0.001	<0.001
Log BNP	3.6(3.3, 4.2)	2.8(2.4, 3.3)	−9.344	<0.001	<0.001
Inflammatory markers					
CRP (mg/L)	86.0(51.1, 90.0)	86.5(44.8, 90.0)	−0.584	0.559	0.607
Log IL-6	2.6(2.3, 3.3)	2.2(1.6, 2.7)	−6.795	<0.001	<0.001
Procalcitonin (ng/mL)	9.1(1.5, 41.5)	2.3(0.3, 12.7)	−4.873	<0.001	<0.001
SAA (mg/L)	239.6(113.8, 271.4)	226.8(66.9, 257.4)	−2.187	0.029	0.046

Abbreviations: SMCI, sepsis-induced myocardial injury; FDR, false discovery rate; SOFA, sequential organ Failure assessment; APACHE-II, acute physiology and chronic health evaluation II; GCS, Glasgow Coma Scale; MAP, mean arterial pressure; SBE, standard base excess; WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; AMC=absolute monocyte count; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; TT, thrombin time; cTnI, cardiac troponin I; CK-MB, creatine kinase isoenzyme MB; Myo, myoglobin; BNP, B-type natriuretic peptide; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A.

exceeded 10, there was a problem of severe multicollinearity. Therefore, we used LASSO regression to eliminate redundant variables and reduce the risks of collinearity and overfitting. In the training cohort, LASSO regression analysis was performed with cross-validation, and 4 variables with non-zero coefficients (Log D-dimer, Log Myo, Log BNP, Log IL-6) were selected based on optimal λ and 1 standard error (Figures 2A and 2B). The VIF values of Log D-dimer, Log Myo, Log BNP, and Log IL-6 were 1.05, 1.03, 1.09, and 1.11, respectively, indicating no substantial multicollinearity in our final model. In our training cohort (n=262), the number of patients with the outcome event (SMCI) was 121, and the number of predictor parameters retained in the final LASSO model was 4. This yields an EPV of 30.3 (121÷4), which substantially exceeds the widely accepted minimum threshold of 10–20 events per variable. This high EPV provides strong evidence for the stability of our prediction model and indicates a very low risk of overfitting. Through univariate and multivariate logistic regression analysis, we determined that Log Myo, Log BNP, and Log IL-6 were independent risk factors for SMCI (Table 2).

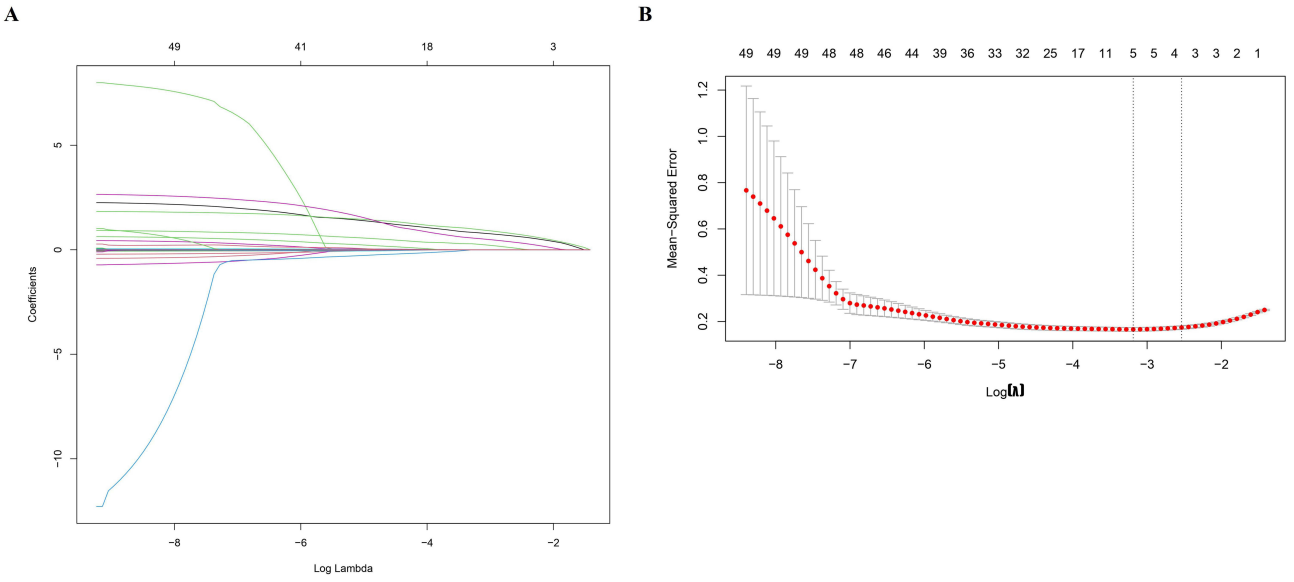

Figure 2 Variable selection for the LASSO regression model. (**A**) coefficient profile plot was constructed based on the log(λ) sequence. (**B**) By deriving the optimal lambda, 4 variables with non-zero coefficients were selected. After validating the optimal λ in the LASSO model, we plotted the partial likelihood deviance (binomial deviance) curve against log(lambda), with dashed vertical lines drawn according to the 1-standard error criterion.
Abbreviation: LASSO, least absolute shrinkage and selection operator.

Table 2 Results of the Univariate and Multivariate Logistic Regression Analysis Using the Training Cohort

	Univariate Logistic Regression Analysis			Multivariate Logistic Regression Analysis		
	OR	*95% CI*	*P*-value	*OR*	*95% CI*	*P*-value
Log D-dimer	3.700	2.175, 6.294	<0.001	1.810	0.952, 3.440	0.070
Log Myo	6.169	3.623, 10.506	<0.001	3.096	1.704, 5.627	<0.001
Log BNP	4.683	3.054, 7.179	<0.001	4.068	2.498, 6.624	<0.001
Log IL-6	3.164	2.141, 4.677	<0.001	2.461	1.505, 4.024	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval; Myo, myoglobin; BNP, B-type natriuretic peptide; IL-6, interleukin-6.

Development of SMCI-Predicting Nomogram

Based on the results of multivariable Logistic regression analysis: Score = −11.354 + 1.130×Log Myo + 1.403×Log BNP + 0.901×Log IL-6, a nomogram was constructed to predict the risk of SMCI (Figure 3).

Evaluation and Validation of Nomogram

Discrimination Ability

The AUC of the nomogram was 0.856 in the training cohort (Figure 4A) and 0.853 in the internal validation cohort (Figure 4B), indicating moderately good performance.

Calibration Ability

A calibration curve and Hosmer–Lemeshow test were used to assess the calibration of the predictive model. From the calibration curves, the model showed a good fit in both the training and validation cohorts. As shown by the Hosmer–Lemeshow test, the predicted and actual probabilities were highly consistent (training cohort, P = 0.6229, Figure 5A; validation cohort, P = 0.3553, Figure 5B).

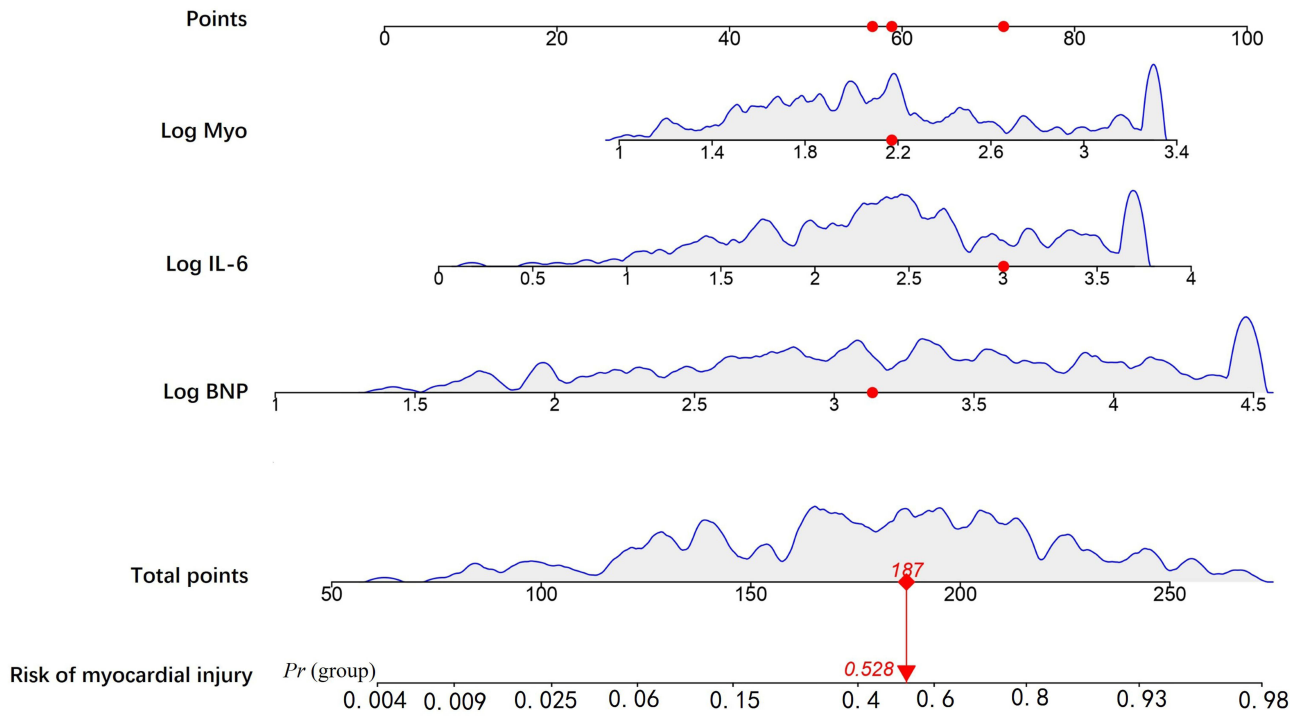

Figure 3 Independent risk factors of Log Myo, Log BNP, and Log IL-6 for nomogram prediction model. The significance of the asterisks beside each variable in part represent importance of all the risk factors.
Abbreviations: Myo, myoglobin; BNP, B-type natriuretic peptide; IL-6, interleukin-6.

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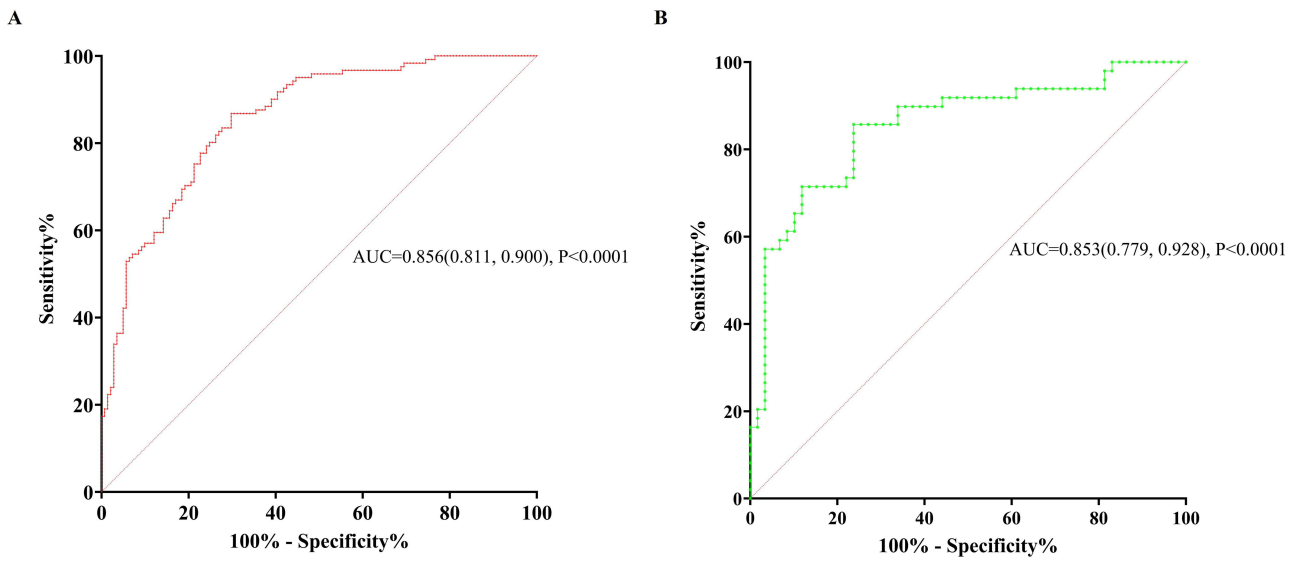

Figure 4 ROC validation of the SMCI risk nomogram prediction. (**A**) The performance of the nomogram in the training cohort. (**B**) The performance of the nomogram in the internal validation cohort.
Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

Clinical Usefulness

DCA showed that in the training cohort, if the threshold probability was within the range of 4%–98%, using this nomogram to predict the risk of SMCI could yield a net benefit (Figure 6A); in the validation cohort, the threshold probability range for net benefit was 13%–86% (Figure 6B). As indicated by the CIC, in the training cohort, when the threshold probability was 58.8% (Figure 6C), the number of high-risk individuals predicted by this nomogram was equal to the number of actual cases; in the validation cohort, this threshold probability was 40.5% (Figure 6D). Taken together, the DCA and CIC results indicate that this model has good clinical applicability.

Discussion

Sepsis patients are at high risk of developing myocardial injury, and those with myocardial injury exhibit an increased risk of mortality.[6,9] Developing a risk prediction model for myocardial injury in sepsis patients can help clinicians quickly and accurately assess such risk, thereby enabling them to formulate individualized, targeted intervention strategies to reduce the incidence of myocardial injury and improve patient survival. In this study, four predictive variables (Log D-dimer, Log Myo, Log BNP, and Log IL-6) were screened using LASSO regression. Through univariate

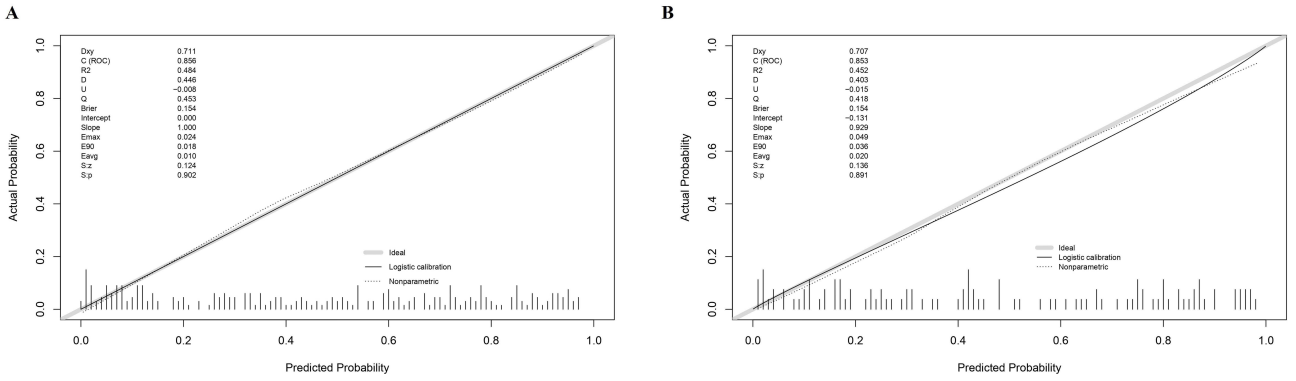

Figure 5 Calibration curve of risk of SMCI. The y-axis represents actual diagnosed cases of SMCI, the x-axis represents the predicted risk of SMCI. (**A**) training cohort; (**B**) validation cohort.
Abbreviations: SMCI, sepsis-induced myocardial injury; ROC, receiver operating characteristic.

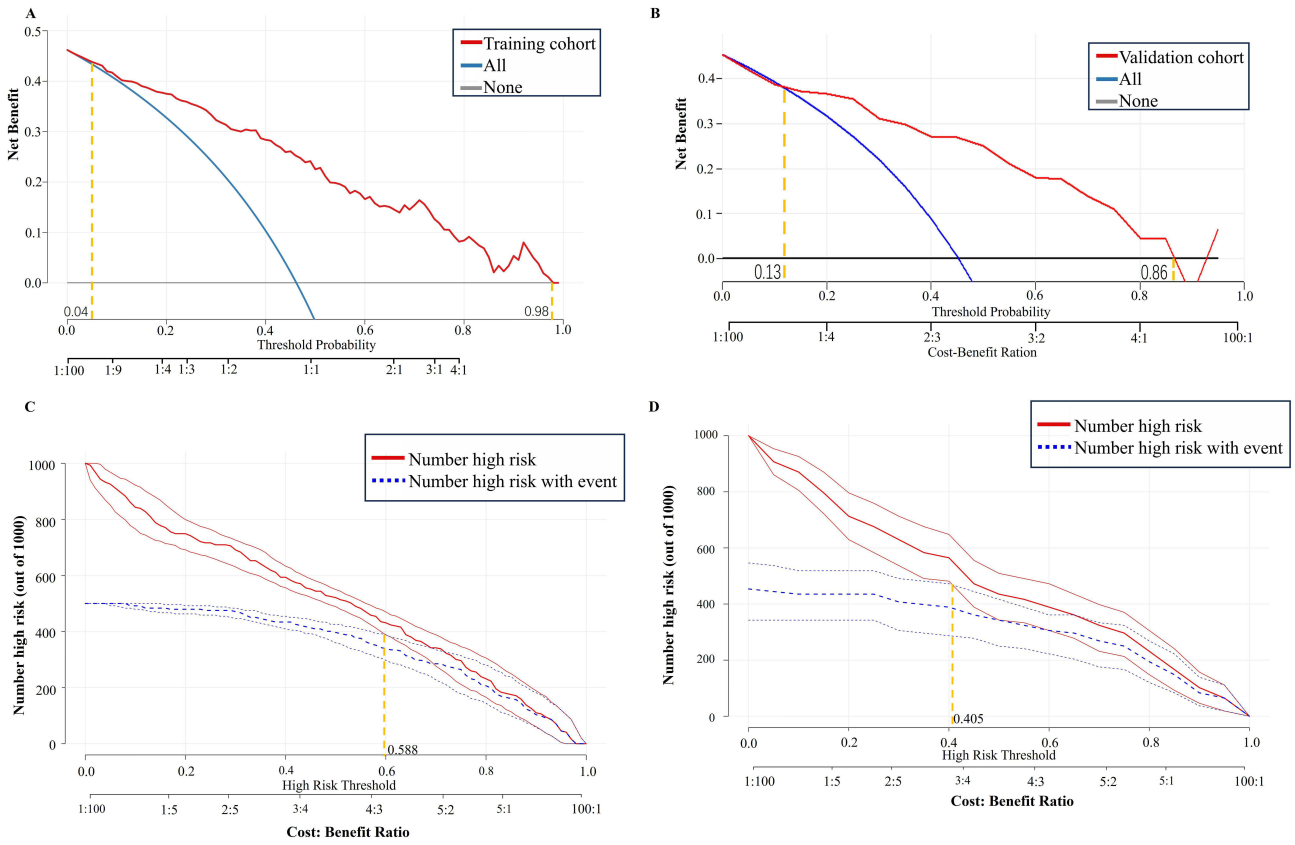

Figure 6 DCA and CIC of the nomogram prediction model for the risk of cardiac dysfunction in patients with sepsis. (**A**) DCA for training cohort; (**B**) DCA for validation cohort; (**C**) CIC for training cohort; (**D**) CIC for validation cohort.
Abbreviations: DCA, decision curve analysis; CIC, clinical impact curve.

and multivariate logistic regression, Log Myo, Log BNP, and Log IL-6 were identified as independent predictors. A nomogram for SMCI risk prediction was developed based on these three factors. For patients, scores of relevant predictive variables are obtained by drawing vertical lines from their variable values to the top score line; the sum of scores of all variables is the total score, and the corresponding predicted probability indicates the patient's risk of developing SMCI. The AUC of the prediction model was 0.856 in the training cohort and 0.853 in the internal validation cohort, indicating that the model has good discriminative ability. Hosmer-Lemeshow tests and calibration curves revealed that the prediction model also has good calibration. Additionally, the DCAs and CICs further demonstrated that the model has good clinical applicability.

Previous studies have found that the following indicators are independent risk factors for SMCI: elevated plasma histone H4,[23] elevated lactate levels,[7,16] hemoglobin level,[15] low systolic blood pressure,[24] and elevated BNP.[25] However, a simple risk factor analysis fails to calculate the probability of SMCI occurrence in a convenient, intuitive, and visually accessible manner. Although previous studies have developed risk prediction models for SMCI, their research exhibits the following limitations.[17–19] The study by Jiangquan Yu et al[19] neither validated the model nor evaluated its clinical applicability. Moreover, their study converted continuous variables into dichotomous categories, such as defining PCT > 40 ng/mL as an independent predictor. In clinical practice, there exists a considerable difference in the severity of infection and inflammatory response between PCT values of 0.1 ng/mL and 35 ng/mL, with PCT > 10 ng/mL generally considered a critical threshold. However, in their model, the risk of SMCI was assigned identically for PCT values of 0.1 ng/mL and 35 ng/mL, which may compromise the accurate assessment of SMCI probability. The studies by Yan Zhuang et al[20] and Peng-fei Sun et al[17] primarily utilized clinical data from sepsis patients admitted to the ICU. However, since sepsis patients typically first present to the emergency department, early identification of high-risk individuals and implementation of preventive measures in the emergency setting would be more effective in reducing

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incidence rates and improving clinical outcomes. Furthermore, the pathogenesis of SMCI involves excessive inflammatory response, cytokine storm, and coagulation dysregulation, while their study only incorporated routine parameters such as WBC and PCT, without including cytokine profiles or coagulation markers. Consequently, it failed to establish the crucial link between pathogenic mechanisms and clinical phenotypes.

This study collected comprehensive data from sepsis patients, including cytokines along with inflammatory, coagulation, hemodynamic, and tissue perfusion parameters etc. Ultimately three key indicators were incorporated into the final model: cytokine (IL-6), myocardial injury marker (Myo), and cardiac dysfunction marker (BNP). These collectively reflect the dynamic progression from infection-induced cytokine storm to myocardial cell injury and cardiac dysfunction in sepsis, thereby bridging pathogenic mechanisms with clinical phenotypes. Cytokines are small proteins secreted by immune cells and stromal cells, which mediate intercellular signaling.[21] Sepsis manifests as a dysregulated systemic inflammatory cascade, characterized predominantly by the overproduction of proinflammatory cytokines including tumor necrosis factor-α, IL-1, IL-6, IL-12, and interferons (IFN-α, IFN-β, IFN-γ).[26] These cytokines exacerbate inflammation, endoplasmic reticulum stress, mitochondrial dysfunction, and oxidative stress, ultimately leading to cardiomyocyte edema, myocardial injury, and even cardiac dysfunction.[21,27] This study has the following advantages: First, we employed LASSO regression to mitigate multicollinearity risks, and subsequent VIF confirmed the absence of multicollinearity among the four predictors. Additionally, we computed an EPV value of 30.3, which provides robust evidence for the stability of our prediction model and indicates a minimal risk of overfitting. Second, we collected commonly used laboratory indicators and disease severity scores within 24 hours of admission for sepsis patients in the emergency resuscitation area. Since sepsis patients primarily present in the emergency resuscitation room, using such commonly used clinical data from the emergency resuscitation room to predict the occurrence of myocardial injury offers advantages in clinical applicability and early prediction. Early identification of patients at high risk of myocardial injury in the emergency resuscitation room, coupled with timely prevention and intervention, can reduce the incidence and mortality of sepsis-induced myocardial injury.

This study has the following limitations. First, as a retrospective analysis, this model lacks real-time applicability and this study cannot prospectively control for biases. Second, although we included commonly used clinical laboratory indicators, disease severity scores, cytokines, coagulation parameters, hemodynamic parameters, and tissue perfusion parameters, factors such as fluid resuscitation, blood transfusion, antibiotic use, and oxygen therapy were not incorporated. Third, this study did not include traumatic sepsis, failing to explore the predictive value of these indicators in myocardial injury in traumatic sepsis. Fourth, although we performed internal validation and evaluated the model's discriminative ability, calibration, and clinical applicability, the model lacks external or multicenter validation to assess its generalizability. In the future, it is necessary to conduct prospective, multicenter, and longitudinal studies, integrate variables such as treatment-related, hemodynamic, novel inflammatory, and cytokine factors to establish and validate an SMCI risk prediction model.

Conclusion

The proposed nomogram based on Log Myo, Log BNP, and Log IL-6 may serve as a practical tool for early risk assessment of myocardial injury in sepsis, though external validation is required before clinical implementation.

Abbreviations

SMCI, sepsis-induced myocardial injury; LASSO, Least Absolute Shrinkage and Selection Operator; DCA, Decision Curve Analysis; CIC, Clinical Impact Curve; cTnI, cardiac troponin I; SOFA, Sequential Organ Failure Assessment; APACHE-II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale; MAP, mean arterial pressure; SBE, standard base excess; WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; AMC, absolute monocyte count; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; TT, thrombin time; CK-MB, creatine kinase isoenzyme; MB, Myo myoglobin; BNP, N-terminal pro-B-type natriuretic peptide; CRP, C-reactive protein; IL-6, interleukin-6; SAA, serum amyloid A; log, logarithmic; FDR, false discovery rate; VIF, variance inflation factor; EPV, events-per-variable; IFN, interferons.

Data Statement

Data are available upon request from Jian-Zhong Yang (yjz6542@126.com).

Ethics Statement

The study was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University (K202505-32). Because this study was retrospective, so informed consent was waived by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University. To protect patient privacy, all personally identifiable information (eg, names, hospital identification numbers, national ID numbers) was de-identified during data collection and analysis, thus ensuring that the data were utilized exclusively by the research team in an anonymous format.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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