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Development and validation of a nomogram to predict survival in septic patients with heart failure in the intensive care unit

Tong Tong[1,2,5], Yikun Guo[2,3,5], Qingqing Wang[1], Xiaoning Sun[1], Ziyi Sun[1], Yuhan Yang[1,2], Xiaoxiao Zhang[1] & Kuiwu Yao[4]✉

Heart failure is a common complication in patients with sepsis, and individuals who experience both sepsis and heart failure are at a heightened risk for adverse outcomes. This study aims to develop an effective nomogram model to predict the 7-day, 15-day, and 30-day survival probabilities of septic patients with heart failure in the intensive care unit (ICU). This study extracted the pertinent clinical data of septic patients with heart failure from the Critical Medical Information Mart for Intensive Care (MIMIC-IV) database. Patients were then randomly allocated into a training set and a test set at a ratio of 7:3. Cox proportional hazards regression analysis was used to determine independent risk factors influencing patient prognosis and to develop a nomogram model. The model's efficacy and clinical significance were assessed through metrics such as the concordance index (C-index), time-dependent receiver operating characteristic (ROC), calibration curve, and decision curve analysis (DCA). A total of 5,490 septic patients with heart failure were included in the study. A nomogram model was developed to predict short-term survival probabilities, using 13 variables: age, pneumonia, endotracheal intubation, mechanical ventilation, potassium (K), anion gap (AG), lactate (Lac), activated partial thromboplastin time (APTT), white blood cell count (WBC), red cell distribution width (RDW), hemoglobin-to-red cell distribution width ratio (HRR), Sequential Organ Failure Assessment (SOFA) score, and Charlson Comorbidity Index (CCI). The C-index was 0.730 (95% CI 0.719–0.742) for the training set and 0.761 (95% CI 0.745–0.776) for the test set, indicating strong model accuracy, indicating good model accuracy. Evaluations via the ROC curve, calibration curve, and decision curve analyses further confirmed the model's reliability and utility. This study effectively developed a straightforward and efficient nomogram model to predict the 7-day, 15-day, and 30-day survival probabilities of septic patients with heart failure in the ICU. The implementation of treatment strategies that address the risk factors identified in the model can enhance patient outcomes and increase survival rates.

Keywords Nomogram model, Sepsis, Heart failure, Retrospective analysis, MIMIC-IV database

Sepsis is an exaggerated immune response by the host to infection, often resulting in multiple organ dysfunction and mortality[1,2]. Despite significant advancements in early recognition, etiological treatment, fluid resuscitation, vasopressor administration, and supportive care for critically ill patients in recent years, the mortality rate associated with sepsis remains alarmingly high[3]. Current data indicate that the mortality rates for sepsis in intensive care units (ICU) and hospitals are 25.8% and 35.3%, respectively[4]. This has led to annual healthcare costs exceeding $24 billion[5]. Consequently, developing more precise clinical management strategies for sepsis patients with various comorbidities has become a focal point of research.

Heart failure (HF) is a complex clinical syndrome resulting from structural or functional abnormalities of the heart and is characterized by impaired cardiac contractility or relaxation that fails to meet the metabolic needs of tissues[6]. More than 40 million individuals worldwide are affected by HF[7], with approximately 17–45% of these patients dying within the first year of diagnosis and a five-year mortality rate approaching 50%[8] The mortality

[1]Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China. [2]Beijing University of Chinese Medicine, Chao Yang District, Beijing 100029, China. [3]Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing, China. [4]China Academy of Chinese Medical Sciences, Beijing, China. [5]Tong Tong and Yikun Guo have contributed equally to this work and share first authorship. ✉email: yaokuiwu@126.com

rate associated with septic shock is approximately 40%[9], and sepsis accounts for one-quarter of all deaths among HF patients[10]. The pathophysiological processes of HF are often associated with compromised intestinal barrier function and subsequent bacterial translocation, which can lead to secondary organ damage[11]. This makes HF patients more susceptible to infections, including sepsis. In this population, circulatory dysfunction and reduced cardiac reserve further exacerbate the pathological cycle, with many deaths in HF patients attributed to septic complications. Research indicates that patients with HF are at an increased risk of developing sepsis, and those with concurrent HF and sepsis experience significantly poorer clinical outcomes during hospitalization[12,13]. Therefore, early identification and risk stratification are critical for guiding the treatment of septic patients with HF, ultimately aiming to improve their prognosis.

Clinical prediction models serve as vital tools for risk assessment, enabling the estimation of current and future patient outcomes based on specific algorithms. These models provide timely and accurate information that can significantly enhance clinical decision-making. Various models have been developed to assess the prognostic risk associated with sepsis and its related complications. For example, a 30-day mortality prediction model for septic patients utilizing the XGBoost algorithm[14] and a model for sepsis-associated acute kidney injury developed by Fan, both demonstrate robust predictive performance[15]. However, research specifically focusing on clinical prediction models for septic patients with HF remains relatively limited. Given the complexity and rapid progression of these conditions, there is a pressing need for further investigations in this area to increase predictive accuracy and improve clinical outcomes.

Early warning scoring systems, such as the Sequential Organ Failure Assessment (SOFA) and the Simplified Acute Physiology Score II (SAPS II), are widely utilized for prognostic evaluation in critically ill patients. However, due to the complex pathophysiology associated with sepsis combined with HF, these singular scoring systems often lack sufficient specificity and sensitivity. Consequently, there is a growing trend in research towards integrating existing biomarkers and scoring systems to develop more precise clinical risk prediction models. Among these models, nomograms have garnered significant attention for their interpretability and broad applicability. They can quantitatively integrate multiple independent prognostic factors and present this information in a visual format, enabling clinicians to swiftly identify high-risk patients and implement tailored treatment strategies[16,17]. Consequently, this study conducted a retrospective cohort analysis based on the Medical Information Mart for Intensive Care IV (MIMIC-IV version 2.2) database. This study aimed to develop a nomogram model that effectively predicts short-term survival probabilities for septic patients with HF. By enhancing the accuracy of clinical decision-making, this model will aid clinicians in risk stratification and the formulation of tailored treatment strategies.

Materials and methods

Data sources and ethical approval

The MIMIC-IV database, provided by the Massachusetts Institute of Technology (MIT), offers detailed medical information on patients who underwent ICU treatment at Beth Israel Deaconess Medical Center (BIDMC) from 2008 to 2019. It includes demographics, vital signs, interventions, lab results, imaging, nursing notes, and discharge summaries. Ethical approval for this study was obtained from the Institutional Review Boards of MIT and BIDMC. As all personal data in the database were deidentified before analysis, the requirement for institutional review board approval was waived, and patient consent was not needed. The author (Yikun Guo) has successfully completed the requisite training for utilizing the database and is certified to use it for research purposes (certification number: 62099487). The reporting of this study followed the Transparent Reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines[18].

Population selection criteria

This study identified septic patients with HF via the International Classification of Diseases (ICD) codes from the MIMIC-IV database. The relevant ICD-9 codes included 99,591–99,592, 4280, 42,820–42,823, 42,830–42,833, and 42,841–42,843, and the relevant ICD-10 codes included A419, R6520-R6521, I5021-I5023, and I5030-I5033. According to the Sepsis-3 guidelines[19], patients with suspected infection and a Sequential Organ Failure Assessment (SOFA) score of ≥ 2 were also classified as having sepsis. HF is defined as a syndrome characterized by inadequate cardiac output due to structural or functional abnormalities of the heart, resulting in congestion in the systemic or pulmonary circulation, encompassing all types of HF with varying ejection fractions[11]. The exclusion criteria included age < 18 years or > 100 years, an ICU stay duration < 24 h, and only the first admission was considered for patients with multiple ICU admissions. Patients meeting the inclusion criteria were randomly divided into training and test sets at a ratio of 7:3.

Data collection

We utilized structured query language (SQL) within PostgreSQL software (version 13.7.2) to extract common clinical parameters from MIMIC-IV, focusing on six key areas: (1) Demographic information: age, sex, and weight. (2) Vital signs: Heart rate (HR), mean blood pressure (MBP), systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate (RR), temperature, and blood oxygen saturation (SpO2). (3) Laboratory indicators: White blood cell count (WBC), red blood cell count (RBC), platelet count (PLT), hemoglobin (HGB), red cell distribution width (RDW), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), chloride (Cl), potassium (K), sodium (Na), calcium (Ca), magnesium (Mg), glucose (Glu), anion gap (AG), pH, partial pressure of oxygen (PO2), partial pressure of carbon dioxide (PCO2), lactate (Lac), activated partial thromboplastin time (APTT), international normalized ratio (INR), creatinine (Cr), and blood urea nitrogen (BUN). (4) Complications: Hypertension, diabetes, myocardial infarction, malignancy, pneumonia, stroke, chronic obstructive pulmonary disease (COPD), atrial fibrillation, acute kidney injury (AKI), liver disease, and coronary heart disease (CHD).

(5) Scoring systems: Sequential Organ Failure Assessment (SOFA) score, Charlson Comorbidity Index (CCI).
(6) Outcome indicators: ICU length of stay, and ICU survival status.

The variables included in the nomogram model comprised only clinical data from the first day of ICU admission. Only the first measurement was used if multiple measurements were taken within the first 24 h of ICU admission. During the data preprocessing stage, we computed certain indicators, such as the hemoglobin-to-red cell distribution width ratio (HRR), which is derived from hemoglobin (Hb) levels and the red cell distribution width (RDW). Since missing data are a common issue in the MIMIC-IV database, directly excluding patients with missing values or analyzing variables with missing data could introduce bias. To ensure the reliability and completeness of our analysis, we employed multiple imputation techniques via the missForest R package to address missing data[20,21], particularly for variables with over 20% missing data.

Statistical analysis

Continuous variables with nonnormal distributions were reported as medians (interquartile ranges, 25th to 75th percentiles) and were compared between groups via the nonparametric Mann-Whitney U test. Continuous variables with normal distributions were presented as the mean ± SD, and group differences were assessed via t-test. Qualitative variables were expressed as n (%) and analyzed via Fisher's exact or chi-square tests.

We employed the Cox proportional hazards model to analyze and identify independent prognostic factors for patients with sepsis complicated by HF. Variance inflation factor (VIF) calculations were conducted to detect multicollinearity among the variables. Based on the selected variables, we constructed a nomogram model for short-term prognosis in septic patients with HF. The model's performance was further evaluated via a testing dataset, in which the concordance index (C-index) and time-dependent receiver operating characteristic (ROC) curve analysis were used to assess the predictive ability of the nomogram. We also utilized calibration curves to examine the model's accuracy and conducted decision curve analysis (DCA) to evaluate its clinical utility. All the statistical tests were performed via a two-tailed approach, and the analyses were conducted via R software (version 4.2.1, http://www.Rproject.org) and EmpowerStats software (version 4.0, http://www.empowerstats.com), with a p-value of ≤ 0.05 considered statistically significant.

Results

We enrolled a total of 5,490 patients with sepsis and HF from the MIMIC-IV database. The patients were randomly assigned to a training set (3,842 patients) or a test set (1,648 patients) at a ratio of 7:3(Fig. 1).

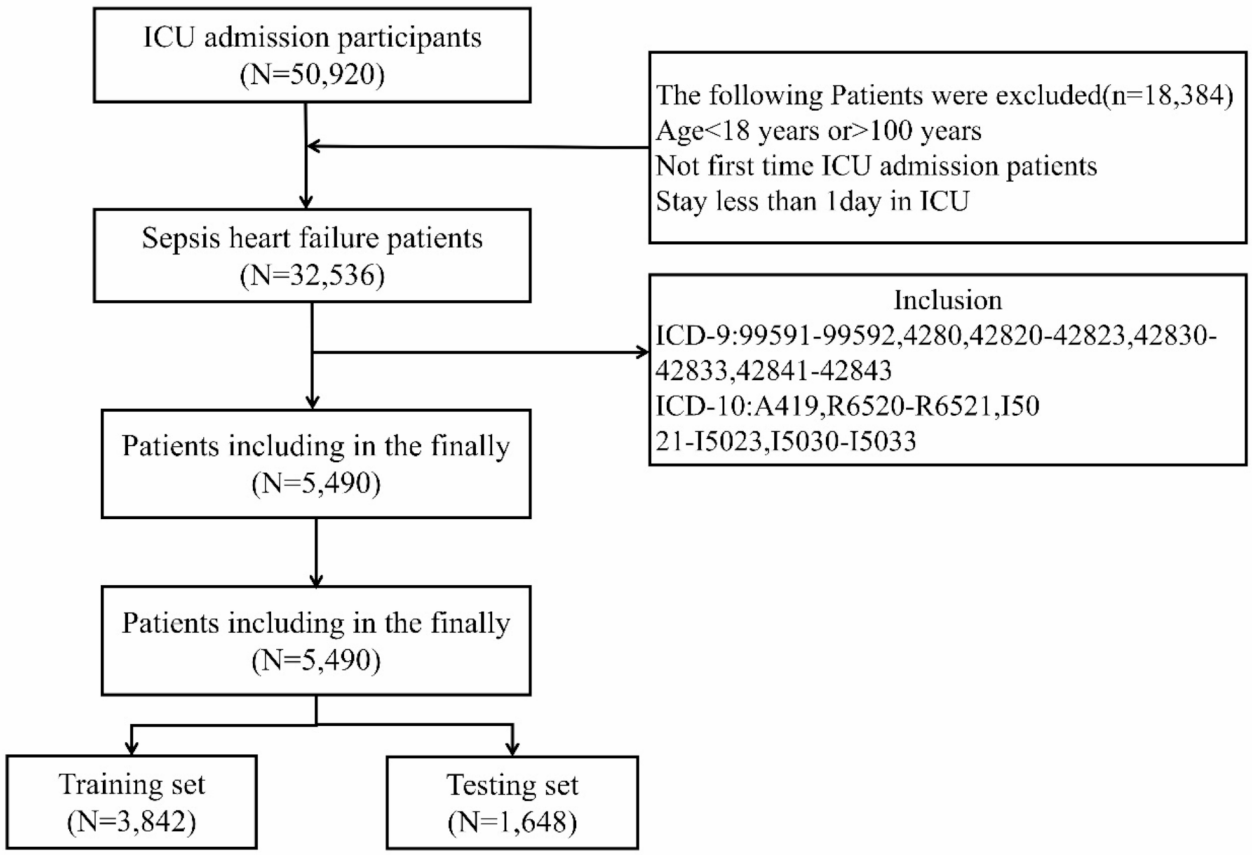


Fig. 1. Selecting Flowchart.

Baseline demographic and clinical characteristics

Table 1 outlines the clinical characteristics and baseline data of septic patients with HF. The average age of the patients was 73.6 years; 3,080 (56.1%) were males and 2,410 (43.9%) were females. Among these patients, 689 individuals passed away during their ICU stay, resulting in an ICU mortality rate of 12.6%, with an average ICU length of stay of 5.8 days. Common comorbidities observed at admission included pneumonia (43.2%), diabetes (39.5%), and renal insufficiency (38.6%), whereas fewer patients presented with liver disease (0.3%) or COPD (9.6%). Only 0.4% of patients lacked systemic inflammatory response syndrome (SIRS), and inflammatory markers and disease scores generally exceeded the normal clinical range. Importantly, there were no significant differences in the baseline characteristics between the training set and the test set ($P > 0.05$), suggesting the comparability of the two groups.

Cox regression analysis

Univariate and multivariate Cox regression analyses revealed 13 independent predictors of survival in septic patients with HF (Fig. 2). These predictors included age (HR = 1.03, 95% CI: 1.02–1.04, $p < 0.001$)、pneumonia (HR = 1.25, 95% CI: 1.06–1.46, $p = 0.006$)、endotracheal intubation (HR = 1.57, 95% CI: 1.32–1.87, $p < 0.001$)、mechanical ventilation (HR = 0.67, 95% CI: 0.50–0.89, $p = 0.007$)、K (HR = 1.18, 95% CI: 1.02–1.36, $p = 0.026$)、AG (HR = 1.01, 95% CI: 1.01–1.06, $p = 0.016$)、Lac (HR = 1.05, 95% CI: 1.00–1.11, $p = 0.049$)、APTT (HR = 1.01, 95% CI: 1.00–1.01, $p = 0.001$)、WBC (HR = 1.01, 95% CI: 1.00–1.02, $p = 0.001$)、SOFA (HR = 1.04, 95% CI: 1.01–1.07, $p = 0.015$)、CCI (HR = 1.04, 95% CI: 1.01–1.08, $p = 0.039$)、RDW (HR = 1.07, 95% CI: 1.03–1.12, $p = 0.001$)、HRR (HR = 2.59, 95% CI: 1.35–4.97, $p = 0.004$).The variance inflation factor (VIF) values for these variables were all less than 4, indicating the absence of multicollinearity (Table 2).

Constructing and validating nomogram models

Based on the Cox proportional hazards model, we constructed a nomogram incorporating 13 risk factors to predict the 7-day, 15-day, and 30-day survival probabilities of septic patients with HF (Fig. 3). The nomogram calculates each patient's total points by summing the scores assigned to each feature (points). The total points correspond vertically to the respective survival probability scale (7-day, 15-day, and 30-day survival rates), indicating the predicted survival rate for each patient.

The training set and test set had C-indexes of 0.730 (95% CI 0.719–0.742) and 0.761 (95% CI 0.745–0.776), respectively, indicating good model accuracy. ROC curve analysis (Fig. 4), calibration curve analysis (Fig. 5), and decision curve analysis (Fig. 6) were performed to validate the model's accuracy. The AUCs for the nomogram model predicting 7-day, 15-day, and 30-day survival probabilities were 0.739, 0.699, and 0.684 in the training set, and 0.777, 0.771, and 0.730 respectively in the test set, demonstrating good predictive accuracy. Calibration curve analysis showed good consistency between the predicted and actual values. Additionally, decision curve analysis indicated a substantial net benefit of our model in both the training set and test set.

Discussion

Using the large publicly available MIMIC-IV database, our study developed a straightforward nomogram model to predict the short-term mortality risk of septic patients with HF in the Intensive Care Unit (ICU). Our nomogram incorporates 13 easily accessible and assessable predictive variables, including age, pneumonia, endotracheal intubation, mechanical ventilation, potassium (K), anion gap (AG), lactate (Lac), activated partial thromboplastin time (APTT), white blood cell count (WBC), red cell distribution width (RDW), hemoglobin-to-red cell distribution width ratio (HRR), Sequential Organ Failure Assessment (SOFA) score, and Charlson Comorbidity Index (CCI).

The model exhibited strong discriminatory and calibration performance in training and testing cohorts, confirming its reliability and clinical applicability without necessitating complex tests, advanced imaging, or invasive procedures. This nomogram may be a valuable tool for clinicians and researchers in predicting and assessing the severity of illness in septic patients with HF, facilitating advanced management strategies. In the future, this model could be integrated into the hospital's clinical decision support system, leveraging routinely collected clinical data for automated monitoring and real-time assessment of mortality risk in septic patients with HF, ultimately optimizing the allocation of medical resources.

In our analysis, age emerged as a critical independent risk factor influencing short-term survival probabilities in septic patients with HF. The prevalence and mortality rates associated with both sepsis and HF increase significantly with increasing age[22]. Data indicate that approximately 60% of sepsis cases occur in patients aged 65 and older, which is closely linked to age-related immunodeficiency, neurohormonal dysregulation, and the coexistence of multiple chronic conditions[23]. Furthermore, the increasing age of patients with HF is often accompanied by a decline in cardiovascular structure and function, further exacerbating the risk of adverse outcomes[24]. Additionally, age-related metabolic remodeling, persistent chronic inflammation, and excessive oxidative stress contribute to a reduced cardiovascular reserve, negatively impacting patient survival prognosis[25].

Our study identified that pneumonia, endotracheal intubation, and mechanical ventilation are associated with survival probabilities in septic patients with HF. The lungs are among the most vulnerable organs in patients suffering from sepsis and heart failure. Pulmonary complications, such as pneumonia, acute lung injury, and respiratory failure, are among the most common complications in ICU patients and are significantly linked to poor prognoses and increased mortality rates in those with sepsis and HF. Epidemiological studies indicate that approximately 40–60% of sepsis cases originate from respiratory tract infections, with pneumonia being the primary cause[26]. Infections trigger a systemic inflammatory response, leading to an inflammatory storm that exacerbates cardiac burden and can precipitate or worsen HF[27]. Furthermore, the use of certain antibiotics during the treatment of sepsis can introduce cardiotoxic effects, complicating the management of HF patients and increasing the risk of adverse events in those with sepsis and HF[27].

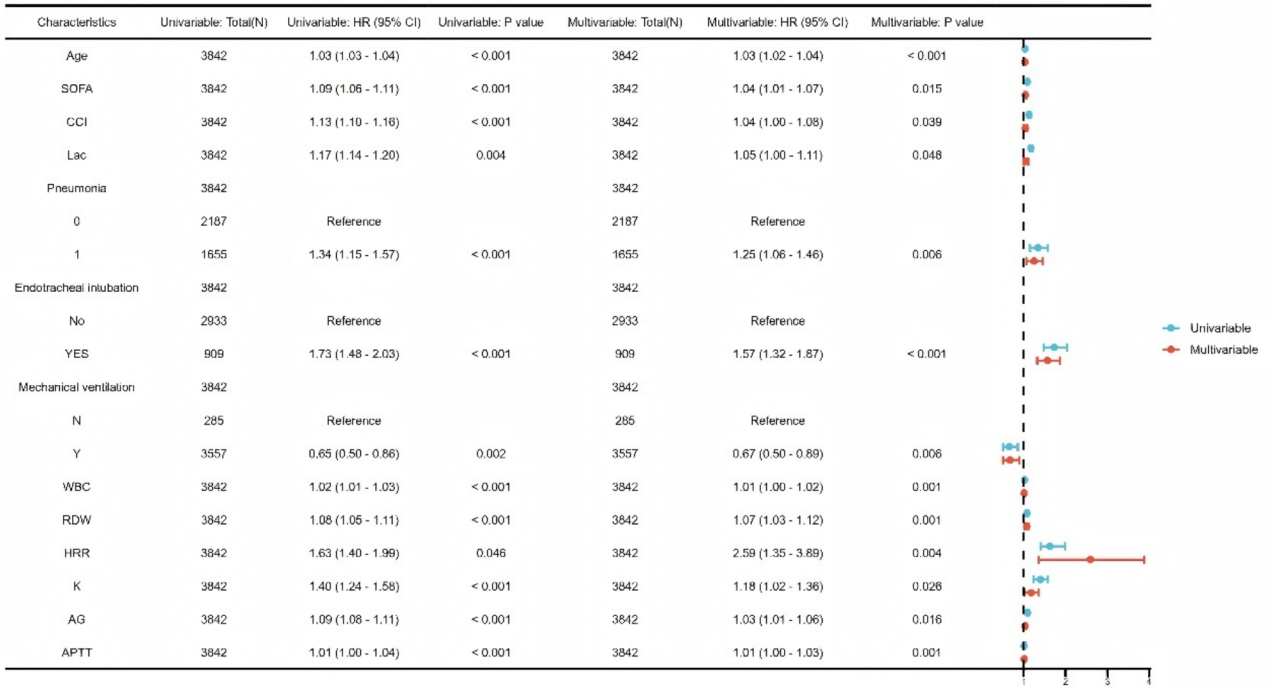
Variable			Training set ($N=3,842$)	Testing set ($N=1,648$)	Total($N=5,490$)	*P*-value
Demographic						
	Gender, N(%)					0.632
		Male	2,164 (56.3%)	916 (55.6%)	3,080 (56.1%)	
		Female	1,678 (43.7%)	732 (44.4%)	2,410 (43.9%)	
	Age, (year)		73.8(60.6,87)	73.4(59.9,86.9)	73.6 (60.3,86.9)	0.283
	weight(kg)		84.5(58.4,110.6)	83.6 (58.9,108.3)	84.3 (58.6,109.7)	0.187
Vital signs						
	HR, (times/min)		89.0(68.3,109.7)	89.0(69.1,108.9)	89.0(68.5, 109.5)	0.964
	RR, (times/min)		19.7(13.2,26.2)	19.7(13.4, 26.0)	19.7(13.3, 26.1)	0.729
	Temperature, (℃)		36.6(34.3,38.9)	36.7(34.9, 38.5)	36.7(34.6, 38.8)	0.502
	DBP, (mmHg)		65.4(46.9,84.3)	69.6(50.9, 88.3)	66.7(48.7, 84.7)	0.308
	SBP, (mmHg)		118.8(94.4,143.2)	118.8(94.2,143.4)	118.8(94.3, 143.3)	0.973
	MBP, (mmHg)		78.6(55.6,101.6)	78.5(60.0, 97.1)	78.6(56.8, 100.4)	0.895
	Spo2,(%)		96.7(82.0,111.4)	96.4(91.7, 101.1)	96.6(84.0, 109.2)	0.166
Scoring systems						
	SOFA		6.4(3.1, 9.7)	6.3(2.9, 9.7)	6.4(3.0, 9.8)	0.463
	CCI		7.0(4.5, 9.5)	6.9(4.3, 9.5)	7.0(4.4, 9.6)	0.664
Laboratory results						
	WBC, (K/UL)		13.4(5.3, 21.5)	13.5(5.7, 21.3)	13.4(5.3, 21.5)	0.885
	RBC, (m/UL)		3.5(2.8, 4.2)	3.5(2.8, 4.2)	3.5(2.8, 4.2)	0.143
	Platelet, (K/UL)		201.2(101.7,300.7)	203.5(97.8,311.2)	201.9(100.4, 303.4)	0.458
	Hemoglobin, (g/dL)		10.4(8.5, 12.3)	10.3(8.4, 12.2)	10.3(8.4, 12.2)	0.094
	RDW, (%)		15.5(13.3, 17.7)	15.6(13.2, 17.8)	15.5(13.2,17.8)	0.213
	HCT, (%)		31.9(25.3, 38.5)	31.6(25.1, 38.2)	31.8(25.2, 38.4)	0.081
	HRR		0.7(0.5, 0.9)	0.7(0.5, 0.9)	0.7(0.5, 0.9)	0.101
	RPR		0.1(0.0, 0.2)	0.1(0.0, 0.2)	0.1(0.0, 0.2)	0.535
	MCH, (pg)		32.5(30.8, 34.2)	32.5(30.8, 34.2)	32.5(30.8, 34.2)	0.248
	MCHC, (g/L)		29.9(27.2, 32.6)	29.8(27.0, 32.6)	29.8(27.1, 32.5)	0.748
	MCV, (fL)		91.9(84.7, 99.1)	91.9(84.4, 99.4)	91.9(84.6, 99.2)	0.741
	Na, (mmol/L)		138.4(133.5, 143.3)	138.4(133.6, 143.2)	138.4(133.6, 143.2)	0.737
	K, (mmol/L)		4.3(3.7, 4.9)	4.3(3.7, 4.9)	4.3(3.7, 4.9)	0.644
	Ca, (mmol/L)		8.3(7.6, 9.0)	8.3(7.6, 9.0)	8.3(7.6, 9.0)	0.468
	Cl, (mmol/L)		103.3(97.0, 109.6)	103.2(96.7, 109.7)	103.3(96.9, 109.7)	0.433
	Mg, (mmol/L)		2.1(1.6, 2.6)	2.1(1.3, 2.9)	2.1(1.5, 2.7)	0.562
	Glu, (mmol/L)		8.2(5.0, 11.4)	8.3(5.0, 11.6)	8.2(5.0, 11.4)	0.641
	APTT, (s)		42.0(21.8, 62.2)	42.4(21.7, 63.1)	42.1(21.7, 62.5)	0.496
	INR		1.7(0.8, 2.6)	1.6(0.6, 2.6)	1.7(0.7, 2.7)	0.817
	Cr, (mg/dL)		1.8(0.2, 3.4)	1.9(0.2, 3.6)	1.8(0.2, 3.4)	0.527
	BUN, (mg/dL)		36.1(11.4, 60.8)	36.0(11.6, 60.4)	36.1(11.5, 60.7)	0.956
	AG		15.2(11.3, 19.1)	15.2(11.4, 19.0)	15.2(11.3, 19.1)	0.846
Blood gas analysis						
	PH, (%)		7.4(7.3, 7.5)	7.4(7.3, 7.5)	7.4(7.3, 7.5)	0.603
	CO2,(mmHg)		42.8(33.4, 52.2)	43.0(33.1, 52.9)	42.8(33.2, 52.4)	0.409
	PO2,(mmHg)		154.0(37.6, 270.4)	154.6(40.4, 268.8)	154.2(38.4, 270.0)	0.765
	Lac, (mmol/L)		2.2(0.8,3.6)	2.2(0.8, 3.6)	2.2(0.8, 3.6)	0.519
Comorbidities						
	SIRS	0	13 (0.3%)	9 (0.5%)	22 (0.4%)	0.783
		1	332 (8.6%)	135 (8.2%)	467 (8.5%)	
		2	1,094 (28.5%)	465 (28.2%)	1,559 (28.4%)	
		3	1,672 (43.5%)	716 (43.4%)	2,388 (43.5%)	
		4	731 (19%)	323 (19.6%)	1054 (19.2%)	
	Hypertension					0.228
		No	2,655 (69.1%)	1,111 (67.4%)	3,766 (68.6%)	
		Yes	1,187 (30.9%)	537 (32.6%)	1,724 (31.4%)	
	Diabetes					0.952

Continued

Variable			Training set ($N=3,842$)	Testing set ($N=1,648$)	Total($N=5,490$)	*P*-value
		No	2,324 (60.5%)	999 (60.6%)	3,323 (60.5%)	
		Yes	1,518 (39.5%)	649 (39.4%)	2,167 (39.5%)	
	Myocardial infarction					0.396
		No	3,331 (86.7%)	1,414 (85.8%)	4,745 (86.4%)	
		Yes	511 (13.3%)	234 (14.2%)	745 (13.6%)	
	Cancer					0.456
		No	3,213 (83.6%)	1,364 (82.8%)	4,577 (83.4%)	
		Yes	629 (16.4%)	284 (17.2%)	913 (16.6%)	
	Pneumonia					0.823
		No	2,187 (56.9%)	932 (56.6%)	3,119 (56.8%)	
		Yes	1,655 (43.1%)	716 (43.4%)	2,371 (43.2%)	
	Stroke					0.383
		No	3,406 (88.7%)	1,475 (89.5%)	4,881 (88.9%)	
		Yes	436 (11.3%)	173 (10.5%)	609 (11.1%)	
	COPD					0.757
		No	3,471 (90.3%)	1,494 (90.7%)	4,965 (90.4%)	
		Yes	371 (9.7%)	154 (9.3%)	525 (9.6%)	
	Atrial fibrillation					10
		No	1,843 (48%)	790 (47.9%)	2,633 (48%)	
		Yes	1,999 (52%)	858 (52.1%)	2,857 (52%)	
	AKI					0.966
		No	2,361 (61.5%)	1,011 (61.3%)	3,372 (61.4%)	
		Yes	1,481 (38.5%)	637 (38.7%)	2,118 (38.6%)	
	Hepatopathy					10
		No	3,832 (99.7%)	1,643 (99.7%)	5,475 (99.7%)	
		Yes	10 (0.3%)	5 (0.3%)	15 (0.3%)	
	Coronary heart disease					0.157
		No	3,146 (81.9%)	1,322 (80.2%)	4,468 (81.4%)	
		Yes	696 (18.1%)	326 (19.8%)	1,022 (18.6%)	
Treatment						
	Mechanical ventilation					0.435
		No	285 (7.4%)	133 (8.1%)	418 (7.6%)	
		Yes	3,557 (92.6%)	1,515 (91.9%)	5,072 (92.4%)	
	Endotracheal intubation					0.685
		No	2,933 (76.3%)	1,249 (75.8%)	4,182 (76.2%)	
		Yes	909 (23.7%)	399 (24.2%)	1,308 (23.8%)	
Outcome						
	Los of ICU, (days)		5.8(1.3, 10.3)	5.7(1.1, 10.5)	5.8(1.2, 10.4)	0.798
	ICU mortality, n (%)					
		Alive	3,349 (87.2%)	1,452 (88.1%)	4,801 (87.4%)	0.359
		Dead	493 (12.8%)	196 (11.9%)	689 (12.6%)	

Table 1. Descriptions of the characteristics of sepsis patients with heart failure. HR: Heart rate; RR: Respiratory rate; SBP: Systolic blood pressure; SpO2: Blood oxygen saturation; SOFA: Sequential Organ Failure Assessment; CCI: Charlson comorbidity index; WBC: white blood cel; RDW: Red cell distribution width; HRR: hemoglobin-to-red cell distribution width ratio; COPD: chronic obstructive pulmonary disease; AKI: acute kidney injury; Na: sodium; K: potassi um; Cl: chlorine; Mg: magnesium; AG: anion gap; Lac: lactic acid; Glu: glucose; BUN: blood urea nitrogen; Cr: creatinine; APTT: activated partial thromboplastin time INR: international normalized ratio.

Mechanical ventilation and endotracheal intubation influence patient prognosis, often indicating a severe clinical condition and a reduced likelihood of survival. Sepsis frequently leads to acute respiratory distress syndrome (ARDS), resulting in impaired oxygenation and ventilation, which further exacerbates respiratory failure[28]. While the necessity for intubation and mechanical ventilation suggests a critical state for patients, these interventions can also improve their prognosis by alleviating pulmonary strain and promoting the recovery of lung function[29]. Consequently, optimizing lung-protective ventilation strategies, such as using low tidal volumes and positive end-expiratory pressure (PEEP), is essential for delivering effective respiratory support[30]. However,



Characteristics	Univariable: Total(N)	Univariable: HR (95% CI)	Univariable: P value	Multivariable: Total(N)	Multivariable: HR (95% CI)	Multivariable: P value
Age	3842	1.03 (1.03 - 1.04)	< 0.001	3842	1.03 (1.02 - 1.04)	< 0.001
SOFA	3842	1.09 (1.06 - 1.11)	< 0.001	3842	1.04 (1.01 - 1.07)	0.015
CCI	3842	1.13 (1.10 - 1.16)	< 0.001	3842	1.04 (1.00 - 1.08)	0.039
Lac	3842	1.17 (1.14 - 1.20)	0.004	3842	1.05 (1.00 - 1.11)	0.048
Pneumonia	3842			3842		
0	2187	Reference		2187	Reference	
1	1655	1.34 (1.15 - 1.57)	< 0.001	1655	1.25 (1.06 - 1.46)	0.006
Endotracheal intubation	3842			3842		
No	2933	Reference		2933	Reference	
YES	909	1.73 (1.48 - 2.03)	< 0.001	909	1.57 (1.32 - 1.87)	< 0.001
Mechanical ventilation	3842			3842		
N	285	Reference		285	Reference	
Y	3557	0.65 (0.50 - 0.86)	0.002	3557	0.67 (0.50 - 0.89)	0.006
WBC	3842	1.02 (1.01 - 1.03)	< 0.001	3842	1.01 (1.00 - 1.02)	0.001
RDW	3842	1.08 (1.05 - 1.11)	< 0.001	3842	1.07 (1.03 - 1.12)	0.001
HRR	3842	1.63 (1.40 - 1.99)	0.046	3842	2.59 (1.35 - 3.89)	0.004
K	3842	1.40 (1.24 - 1.58)	< 0.001	3842	1.18 (1.02 - 1.36)	0.026
AG	3842	1.09 (1.08 - 1.11)	< 0.001	3842	1.03 (1.01 - 1.06)	0.016
APTT	3842	1.01 (1.00 - 1.04)	< 0.001	3842	1.01 (1.00 - 1.03)	0.001

Fig. 2. COX regression analysis. SOFA: Sequential Organ Failure Assessment; CCI: Charlson comorbidity Index; WBC: white blood cell; RDW: red blood cell distribution width; HRR: hemoglobin-red cell distribution width ratio; K: potassium; Lac: lactic acid; AG: anion gap; APTT: activated partial thromboplastin time.

postintubation hypotension (PIH) is a common complication that may increase hospital mortality and the length of stay for patients with septic HF[31,32]. Therefore, it is imperative to actively address and correct hypotension in patients suspected of having hypovolemia to improve outcomes.

Other biomarkers also influence the prognosis of patients with septic and HF. An elevated WBC count reflects immune system activation, suggesting a potential excessive inflammatory response, and is associated with an increased risk of mortality, which is commonly used in relevant studies for predicting sepsis and sepsis-related damage[33–35]. APTT is associated with poor prognosis in septic patients with HF, possibly related to disseminated intravascular coagulation (DIC) caused by inflammation[36], endothelial cell damage induced by inflammation, microvascular thrombosis formation, and microcirculatory deterioration[37]. RDW is a routine parameter reflecting red blood cell size heterogeneity and distinguishing anemia types, is significantly correlated with the systemic inflammatory response[38]and has been linked in multiple studies to the prognosis of HF[39], sepsis[40], coronary artery disease[41], pulmonary hypertension[42], acute pulmonary embolism[43], stroke[44], and other diseases, demonstrating its unique clinical value in critically ill patients. Furthermore, the HRR is considered to be associated with poor prognosis in septic patients with HF, and increasing evidence suggests that the HRR can serve as a new prognostic indicator for critically ill patients. For example, Rahamim et al.. reported that the HRR effectively predicts mortality in HF patients[45]; Wang et al..'s study indicated that the HRR performs well in predicting adverse outcomes in septic atrial fibrillation patients[46]; Chi et al. found that a low HRR is associated with dual risks of disease progression or cancer recurrence and used them to predict adverse outcomes in cancer patients[47]. Our study also found that HRR can be utilized as a predictor of survival rates in patients with sepsis-induced heart failure.

Potassium ion (K+) are crucial cations for maintaining the cell membrane potential and transmitting nerve impulses, with elevated baseline levels possibly indicating compromised heart function, renal insufficiency, or more severe diseases[48], and HF patients are more sensitive to fluctuations in potassium ion levels[49]. Therefore, K + can be a predictive indicator for survival rates in septic patients with HF.

The anion gap (AG), a biochemical parameter, is widely used to evaluate acid-base balance, electrolyte imbalances, and metabolic disorders. Studies have shown that elevated AG levels are linked to the severity and mortality of conditions such as chronic kidney disease[50],stroke[51], cardiac arrest[52], and aortic aneurysm[53]. In sepsis management, serum lactate (Lac) is a critical marker for early identification and risk stratification, reflecting inadequate tissue perfusion in sepsis patients and correlating closely with increased mortality rates. However, the use of lactate measurement may be limited in settings outside of intensive care or in resource-constrained environments. Consequently, some scholars have proposed that the anion gap could be used as a substitute for lactate measurement in these circumstances[54]. While the AG does not accurately predict lactate level changes, it can still effectively identify the mortality risk in septic patients when resources are limited, thus guiding subsequent treatment decisions[55]. This study also revealed that the AG can be used to predict and identify adverse outcomes in septic patients with HF. However, the specific mechanisms and therapeutic efficacy require further investigation.

Variable	VIF
Age	1.2173
Pneumonia	
NO	Reference
YES	1.0391
Endotracheal intubation	
NO	Reference
YES	1.1048
Mechanical ventilation	
NO	Reference
YES	1.0457
WBC	1.0294
RDW	2.0944
HRR	2.1055
K	1.1544
Lac	1.9609
AG	2.1305
APTT	1.0227
SOFA	1.2706
CCI	1.2728

Table 2. VIF results for variables. SOFA: Sequential Organ Failure Assessment; CCI: Charlson comorbidity Index; WBC: white blood cell; RDW: red blood cell distribution width; HRR: hemoglobin-red cell distribution width ratio; K: potassium; Lac: lactic acid; AG: anion gap; APTT: activated partial thromboplastin time.

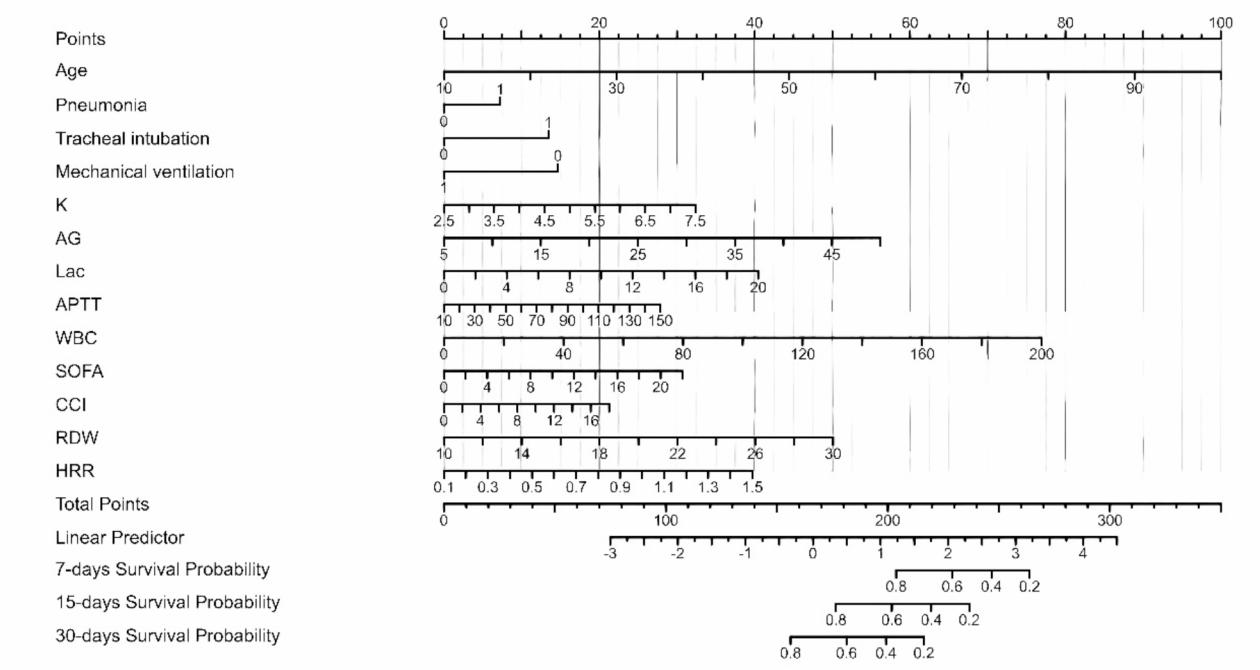


Fig. 3. Nomogram model for short-term survival probabilities in septic patients with HF. This model is utilized for estimating the 7, 15, and 30-day survival probabilities of patients with this condition. By assigning scores on a scale, the changes in each variable are represented through forest plots, followed by the calculation of a cumulative score to forecast the likelihood of an event occurrence. SOFA: Sequential Organ Failure Assessment; CCI: Charlson comorbidity Index; WBC: white blood cell; RDW: red blood cell distribution width; HRR: hemoglobin-red cell distribution width ratio; K: potassium; Lac: lactic acid; AG: anion gap; APTT: activated partial thromboplastin time.

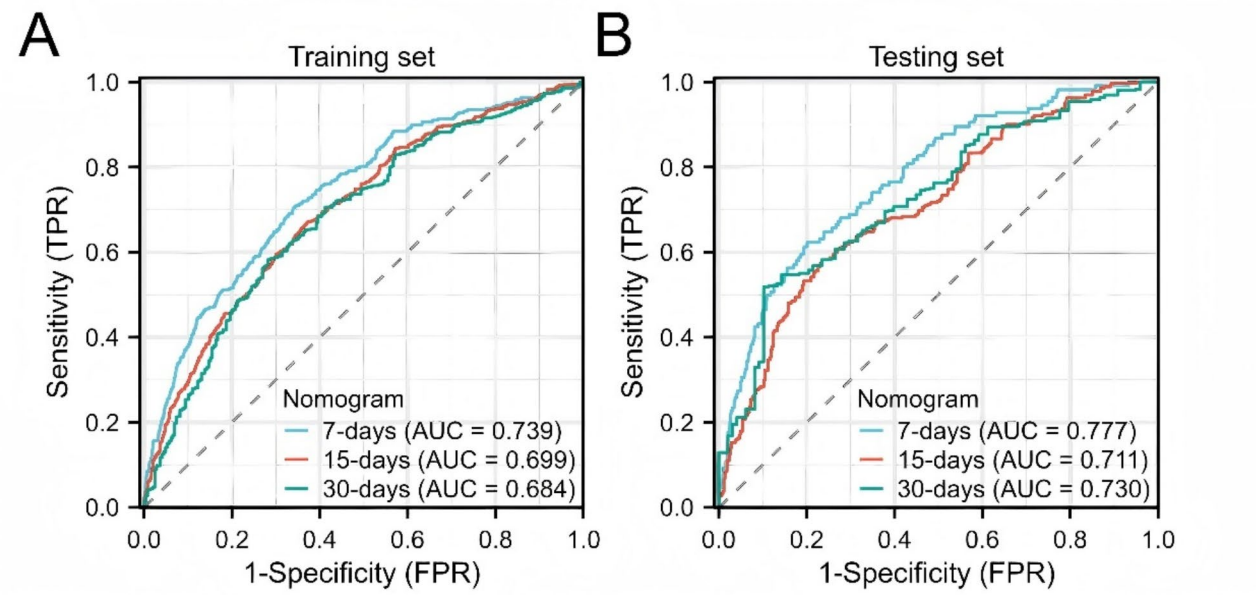


Fig. 4. The time-dependent ROC curve of the nomogram. (**A**) Training set; (**B**) testing set. To evaluate the accuracy of a model in predicting the 7-day, 15-day, and 30-day survival probabilities for septic patients with heart failure within both the training set (**A**) and the test set (**B**), the ROC curve was utilized. The model demonstrated robust predictive accuracy.

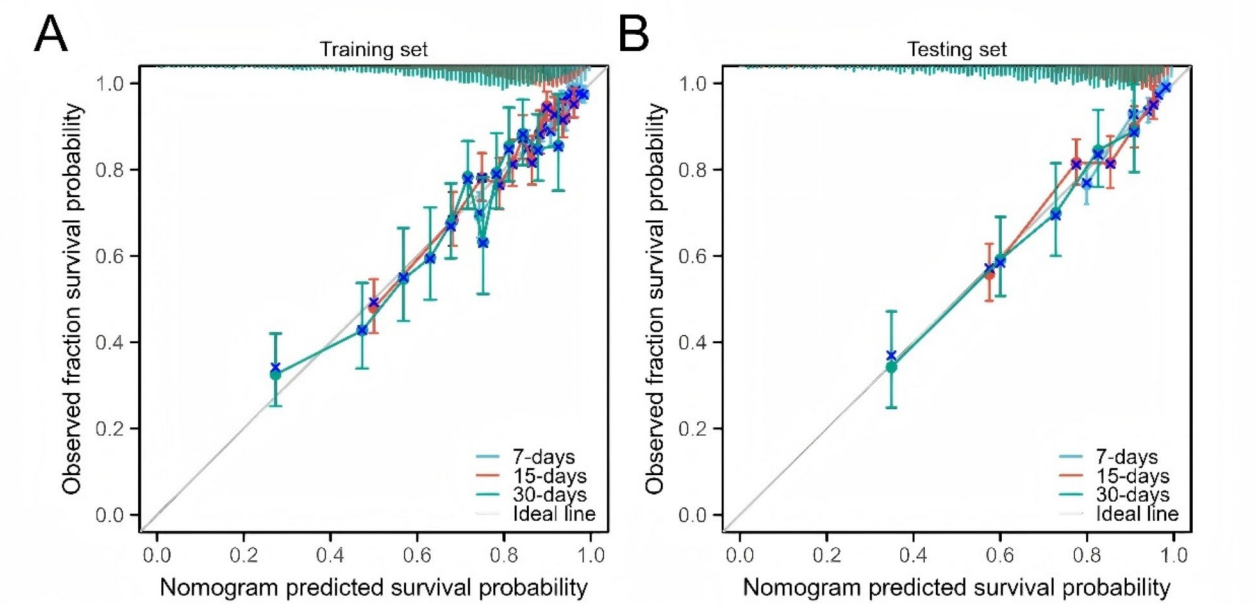


Fig. 5. Prognostic calibration curve plot. (**A**) Training set; (**B**) testing set. This figure displays the calibration curves for the established nomogram, indicating the agreement between predicted and observed survival probabilities in both the training set (**A**) and the test set (**B**).

The mortality rate among septic patients with HF remains alarmingly high, undeniably increasing the complexity and challenges associated with their clinical management. Various scoring systems, such as SOFA, mSOFA, qSOFA, APACHE II, and SAPS II, are widely employed for the clinical assessment of sepsis patients[56,57]. However, these scoring systems exhibit varying degrees of sensitivity and specificity in the early identification and rapid evaluation of sepsis, each accompanied by certain limitations[58–60]. In light of the constraints of these singular assessment tools and the urgent need in clinical practice, numerous researchers are focused on integrating scoring systems with biomarkers to achieve early identification and precise risk stratification for patients with sepsis and its complications. This integrated evaluation approach demonstrates superior predictive

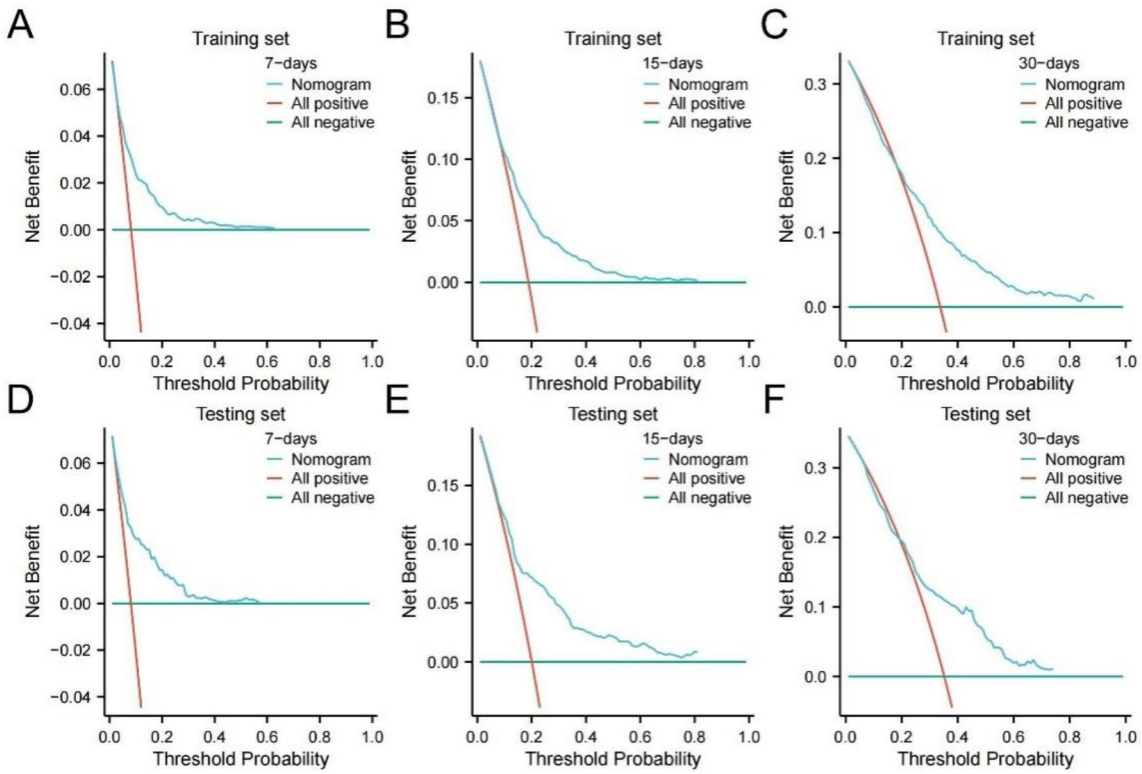


Fig. 6. Prognostic DCA plot. (**A**-**C**) Training set; (**D**-**F**) testing set. This figure presents the DCA for predicting survival probabilities in septic patients with heart failure within both the training set (**A**-**C**) and the test set (**D**-**F**). The curves evaluate the clinical utility of the model, demonstrating that our model yields substantial net clinical benefit in both the test set and the training set.

and identification capabilities compared to standalone scoring systems[33,61,62]. Our study further explores the combination of the SOFA score, CCI score, and biomarkers to predict the survival probability of septic patients with HF. The results indicate a promising level of accuracy, suggesting that this method could provide robust quantitative support for clinical decision-making, optimize treatment strategies, and ultimately improve patient outcomes.

This study utilized the MIMIC database to analyze the clinical data of septic patients with HF, developing a nomogram model to predict 7-day, 15-day, and 30-day survival probabilities. The risk factors included in this study are common clinical complications and widely used laboratory indicators, enhancing the clinical practicability of the model. Despite limitations, including bias in retrospective cohort studies and undefined causality, our large sample cohort mitigated these. While MIMIC-IV provided reliable data, single-center design limited generalizability. Future plans include multi-center validation to enhance generalization. Residual confounding and unmeasured variables remain challenges despite using multivariate Cox regression. Subsequent research should expand the sample size, incorporate more influencing factors, and consider adopting more advanced statistical methods and machine learning techniques, such as random forest, ensemble learning, etc., to further optimize the prediction model for the short-term mortality risk of septic patients with heart failure. However, it is worth noting that although advanced machine learning techniques are used to develop prediction models, they also need to be reasonably selected based on specific backgrounds and circumstances[63].

Conclusion

This retrospective study developed and validated a nomogram model to predict short-term survival probabilities in septic patients with HF. Our model exhibited strong predictive performance compared to traditional scoring systems, emphasizing its potential utility in clinical practice. The model aids clinicians in making rapid initial clinical decisions and can be utilized in managing septic patients with HF.

Data availability

The datasets used/analyzed in the current study are available from corresponding authors on reasonable request. The datasets presented in this study are accessible within the MIMIC repository at [https://mimic.physionet.org].

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Author contributions

The study was conceived and designed by T.T. and Y.G. K.Y. was responsible for supervision, funding acquisition, and project administration. Clinical data were collected by Y.G. and T.T. Data analysis and interpretation were performed by Y.G. T.T. and Y.G. wrote the main manuscript text, and Q.W., X.S., Z.S., Y.Y., X.Z., and K.Y. translated and revised it. All authors reviewed the manuscript and agreed to submit it.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to K.Y.