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Prognostic Value of Blood Urea Nitrogen-to-Albumin Ratio (BAR) in Patients with Cirrhosis and Sepsis and Development and Validation of a 28-Day Mortality Risk Prediction Model

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Prognostic Value of Blood Urea Nitrogen-to-Albumin Ratio (BAR) in Patients with Cirrhosis and Sepsis and Development and Validation of a 28-Day Mortality Risk Prediction Model

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Abstract

Background: Patients with cirrhosis are at high risk of bacterial infection and sepsis because of immune dysfunction, impaired intestinal barrier function, and bacterial translocation. Early and accurate risk stratification remains challenging. The blood urea nitrogen-to-albumin ratio (BAR) is a composite marker reflecting renal perfusion, catabolic stress, hepatic synthetic function, and systemic inflammation. This study aimed to develop and validate a BAR-based prediction model for 28-day mortality in patients with cirrhosis and sepsis.

Methods: We retrospectively extracted 1,269 eligible patients from the MIMIC-IV 3.1 database and randomly divided them into a training set (n = 889) and a test set (n = 380) at a 7:3 ratio. LASSO-Cox regression was used for predictor selection, followed by multivariable Cox regression and a nomogram. Model performance was evaluated using the C-index, ROC curves, calibration curves, and Kaplan-Meier (KM) risk stratification. An independent cohort of 177 patients from the Third Affiliated Hospital of Sun Yat-sen University was used for external validation. Time-dependent ROC curves, calibration curves, and KM survival analysis were used to assess generalizability. Decision curve analysis (DCA) and clinical impact curve (CIC) were used to evaluate clinical utility. Internal validation included 10-fold cross-validation, Bootstrap validation (1,000 resamples), and sensitivity analyses with time interaction terms.

Results: LASSO-Cox regression identified SOFA score, lactate, and BAR as independent predictors. The C-index was 0.766 in the training set and 0.745 in the test set. The 28-day AUC was 0.681 and 0.630, respectively, with consistent calibration trends. KM curves significantly distinguished low-, intermediate-, and high-risk groups (log-rank $P < 0.0001$). In the external validation set, the 28-day AUC was 0.772, and KM curves showed significant survival differences among risk groups (log-rank $P < 0.001$). Calibration curves showed consistent trends, and DCA/CIC indicated positive net benefit. Adding BAR to the SOFA + lactate model did not significantly improve overall discrimination (C-index: 0.7657 vs. 0.766; IDI not significant, $P = 0.786$), but significantly improved continuous NRI (NRI = 0.368, 95% CI: 0.177–0.557, $P < 0.001$) and model fit (LRT $P = 0.0017$, delta AIC = 7.83). Sensitivity analysis showed that the effect of

lactate on mortality risk attenuated over time (time interaction P = 0.001), and adding the interaction term significantly improved AIC (delta AIC = 9.81).
Conclusions: The nomogram incorporating SOFA, lactate, and BAR showed good discrimination, calibration, and clinical utility in internal and external validation. BAR was an independent risk factor for 28-day mortality. Although it did not significantly improve overall discrimination, it improved individual risk reclassification and model fit, supporting its clinical incremental value.
Keywords: cirrhosis; sepsis; 28-day mortality; MIMIC-IV; nomogram

1 Introduction

Patients with cirrhosis are at extremely high risk of bacterial infection and sepsis due to immune dysfunction, impaired intestinal barrier function, and gut microbiota translocation[1,2]. Approximately 25%–46% of hospitalized patients with cirrhosis develop bacterial infections, and infection-related sepsis occurs in approximately 5%–20% of hospitalized patients with cirrhosis[2]. A large study of more than 5 million hospitalized patients with cirrhosis showed that 30% developed infection during hospitalization, and infection was significantly associated with higher mortality, sepsis, and ICU admission [1]. Compared with patients without liver disease, patients with cirrhosis and infection have more than a fourfold higher short-term mortality risk[2]. Han et al.[3] reported a 30-day mortality of 25.0% in 84 patients with cirrhosis and sepsis. Liu et al.[4] found that the 28-day mortality of 236 patients with cirrhosis and sepsis was as high as 39.8%. Liu et al.[5] reported an overall mortality of 25.78% in 426 patients with cirrhosis and sepsis syndrome. These data indicate that cirrhosis complicated by sepsis remains a major clinical challenge.

Early and precise risk assessment and stratified management are essential. The Sequential Organ Failure Assessment (SOFA) score is widely used. Multiple studies have confirmed the value of SOFA in patients with cirrhosis and sepsis syndrome, but its predictive performance and contextual specificity are limited[5]. Patients with cirrhosis often have baseline hyperbilirubinemia and coagulopathy, which can chronically elevate some SOFA components, such as bilirubin and INR, making it difficult to accurately reflect acute sepsis-induced organ injury.

The blood urea nitrogen-to-albumin ratio (BAR) is a novel composite index. BAR is calculated from blood urea nitrogen (BUN) and serum albumin (ALB)[6]. Elevated BUN reflects renal hypoperfusion and enhanced catabolism, which are common in sepsis, whereas decreased albumin reflects impaired hepatic synthesis and increased consumption under systemic inflammation. The combination may reflect the imbalance of the liver-kidney-inflammation axis in patients with cirrhosis. Several studies have found that BAR differs significantly between survivors and non-survivors with hepatitis B-related cirrhosis, and BAR is an independent prognostic indicator of mortality[7,8]. In sepsis, BAR has been shown to be a reliable biomarker for mortality prediction. In addition, BAR has been identified as the strongest predictor of in-hospital mortality in patients with spontaneous bacterial peritonitis (SBP), outperforming the red cell distribution width-to-albumin ratio (RAR) and neutrophil-to-lymphocyte ratio (NLR).

This study aimed to integrate BAR with SOFA, mean lactate, and other key clinical indicators to develop a 28-day mortality risk prediction model for patients with cirrhosis and sepsis based on the MIMIC-IV database, and to develop a visual nomogram. We also included patients from our hospital as an external validation cohort to verify the generalizability and robustness of the model in different clinical settings.

2 Methods

2.1 Data Source and Study Population

This study retrospectively analyzed clinical data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, version 3.1. MIMIC-IV contains de-identified data from critically ill patients and has been approved by the institutional review board with waiver of informed consent. Inclusion criteria were: (1) age >=18 and <=80 years; (2) confirmed diagnosis of cirrhosis based on ICD-9/10 codes; (3) meeting Sepsis-3.0 criteria; and (4) ICU admission. Exclusion criteria were: (1) ICU stay <24 h; (2) missing key variables, such as SOFA, lactate, BAR, or 28-day outcome; and (3) history of liver transplantation, concomitant hepatocellular carcinoma or other malignancy, or end-stage renal disease requiring dialysis. The order of exclusion criteria was consistent with the flow diagram (Figure 1). A total of 1,269 patients were included and randomly divided into a training set (n = 889) and an internal test set (n = 380) at a 7:3 ratio. We also retrospectively collected data from 177 patients with cirrhosis and sepsis admitted to the Third Affiliated Hospital of Sun Yat-sen University between 2020 and 2025. The inclusion and exclusion criteria were identical to those of the MIMIC-IV cohort. BUN and albumin in the external data were used in mg/dL and g/dL, respectively, to calculate BAR.

2.2 Data Collection and Predictors

The following candidate variables were extracted: age, sex, SOFA score, MELD score, lactate, white blood cell (WBC) count, platelet count, blood urea nitrogen (BUN), and albumin. BAR was calculated as BUN/albumin. All laboratory indicators were averaged within the first 24 h after ICU admission if multiple measurements were available. The primary outcome was all-cause mortality within 28 days after admission.

2.3 Model Development and Variable Selection

Least absolute shrinkage and selection operator (LASSO)-Cox regression was used for variable selection in the training set. The optimal penalty coefficient lambda (lambda.min) was determined by 10-fold cross-validation. Selected variables were included in a multivariable Cox proportional hazards model to construct the final prediction model. Multicollinearity was assessed using the variance inflation factor (VIF). Based on the final Cox model, a nomogram was drawn to visualize the regression equation, assigning scores to each predictor and mapping the total score directly to the 28-day mortality probability.

2.4 Statistical Analysis

All statistical analyses were performed using R software (version 4.5.2). Two-sided $P < 0.05$ was considered statistically significant. Reporting followed the TRIPOD statement. Discrimination was assessed using the C-index and time-dependent area under the ROC curve (AUC) in the training, test, and external validation sets. For external validation, the linear predictor (LP) of external patients was calculated directly using the final Cox model built from the MIMIC-IV training set without refitting. Because of the special outcome coding in the external dataset, discrimination was mainly evaluated by 28-day time-dependent AUC. Bootstrap resampling (1,000 times) was used for internal validation to calculate the corrected C-index, and calibration curves were plotted. Patients were divided into low-, intermediate-, and high-risk groups according to the tertiles of LP in the training set. Kaplan-Meier survival curves were plotted and log-rank tests were performed. DCA was used to evaluate net clinical benefit across threshold probabilities, and CIC was used to evaluate the number of high-risk patients and the proportion of true positives at specific thresholds. Continuous NRI and IDI were used to evaluate

the incremental predictive value of adding BAR to the base model (SOFA + lactate). Nested model likelihood ratio tests (LRT) and Akaike information criterion (AIC) were used to assess improvement in model fit. Ten-fold cross-validation was used to evaluate model stability. Schoenfeld residual tests were used to assess the proportional hazards (PH) assumption. If violated, a time interaction term was introduced, and AIC before and after correction was compared. Sensitivity analyses evaluated model performance at 14 and 60 days and recalculated the C-index after excluding extremely early deaths with hospital stay <2 days.

3 Results

3.1 Baseline Characteristics

A total of 1,269 patients with cirrhosis and sepsis were included. They were randomly divided into a training set (n = 889; 236 deaths, 26.5%) and a test set (n = 380; 123 deaths, 32.4%) at a 7:3 ratio. In addition, 177 patients were included in the external validation set (80 deaths). Baseline characteristics were similar among the three groups for age, sex, and WBC, but MELD score, lactate, BUN, and platelet count differed significantly between the external validation set and the MIMIC-IV cohort ($P < 0.05$), suggesting that the external cohort had more severe disease. These baseline differences were addressed by directly applying the Cox model fitted in the MIMIC-IV training set for external validation (Table 1).

Table 1. Baseline characteristics of the training, test, and external validation cohorts.

Variable	Overall (n=1269)	Train (n=889)	Test (n=380)	External(n=177)	P_value
Age (years)	58.29 (49.86, 65.77)	58.34 (50.01, 65.22)	58.21 (49.59, 67)	58 (49, 66.75)	0.883
SOFA score	11 (8, 14)	11 (8, 14)	11 (8, 15)	10 (7, 13)	0.107
MELD score	26.93 (19, 34.16)	26.64 (19, 34.2)	27.17 (19, 34)	19.35 (13.04, 28.9)	<0.001
BAR	10 (6.11, 16.46)	10.4 (6.24, 16.72)	9.47 (5.73, 16.08)	12.25 (7.63, 19.84)	0.001
Lactate (mmol/L)	2.33 (1.7, 3.63)	2.4 (1.7, 3.65)	2.26 (1.67, 3.57)	3.95 (2.32, 8.35)	<0.001
WBC (×10⁹/L)	10.75 (6.88, 16.03)	10.82 (6.92, 16.25)	10.6 (6.84, 15.45)	11.86 (6.58, 16.27)	0.678
Platelet (×10⁹/L)	93.14 (61, 142.5)	94 (62, 141.5)	88.05 (59.96, 142.91)	72 (39, 126.75)	<0.001
BUN (mg/dL)	28.67 (17.17, 49)	29 (17.75, 49.25)	26.9 (16.5, 46.56)	36.32 (22.34, 53.05)	0.001
Albumin (g/dL)	2.9 (2.5, 3.3)	2.9 (2.5, 3.3)	2.94 (2.5, 3.39)	2.88 (2.62, 3.34)	0.853
Follow-up time (days)	12.3 (6.7, 23.2)	12.7 (6.7, 24)	11.8 (6.68, 20.8)	13.5 (7, 25)	0.317
Male, n (%)	782 (61.6%)	553 (62.2%)	229 (60.3%)	144 (80.9%)	<0.001
28-day mortality, n (%)	359 (28.3%)	236 (26.5%)	123 (32.4%)	80 (45.2%)	<0.001

3.2 Variable Selection and Multivariable Cox Regression

LASSO-Cox regression was used for variable selection in the training set (Figure 2A). Ten-fold cross-validation showed that when the optimal penalty parameter was lambda.min = 0.0016, eight candidate variables were selected: SOFA, MELD, lactate, WBC, platelet, BUN, albumin, and BAR. To construct a parsimonious and clinically applicable model, and considering previous literature and clinical significance, the final model retained SOFA score (HR = 1.150, 95% CI: 1.114-1.188, $P < 0.001$), lactate (HR = 1.164, 95% CI: 1.130-1.200, $P < 0.001$), and BAR (HR = 1.018, 95% CI: 1.007-1.029, $P = 0.0011$) (Supplementary Table 1, Figure 3). After adjustment for SOFA and lactate, each 1-unit increase in BAR was associated with an 1.8% increase in 28-day mortality risk (HR = 1.018, 95% CI: 1.007-1.029, $P = 0.0011$). The overall C-index of the model was 0.766 (SE = 0.016), and the likelihood ratio test = 222.8 (df = 3, $P < 2e-16$).

3.3 Construction of the Nomogram

Based on the three independent predictors above, a nomogram was constructed to predict the

28-day mortality risk of patients with decompensated cirrhosis and sepsis (Figure 4). The total score was obtained by summing the scores corresponding to each variable, and the 28-day mortality probability was then read directly. A higher total score indicated a higher 28-day mortality risk.

3.4 Model Performance Evaluation

The C-index was 0.766 in the training set and 0.745 in the test set. The mean C-index from 10-fold cross-validation was 0.767 (95% CI: 0.639-0.894). Bootstrap internal validation (1,000 resamples) showed that the corrected C-index was 0.765 (95% CI: 0.735-0.795). Time-dependent ROC showed that the 28-day AUC was 0.681 in the training set and 0.630 in the test set (Figure 5). The calibration curve in the training set closely approximated the ideal diagonal; the calibration curve in the test set showed slight overestimation, but the overall trend was consistent (Figure 6).

3.5 Risk Stratification and Survival Analysis

Patients were divided into low-, intermediate-, and high-risk groups according to the tertiles of LP in the training set. Kaplan-Meier survival curves showed significant differences in 28-day survival among the three groups in both the training and test sets (log-rank $P < 0.0001$, Figure 7). The 28-day survival rate of the high-risk group was significantly lower than that of the intermediate- and low-risk groups.

3.6 Clinical Utility Assessment

DCA in the training and test sets showed that within the threshold probability range of 10%-50%, the net benefit of the model was higher than that of treat all and treat none strategies (Figure 8A, B). CIC at the 20% threshold showed that the model identified a reasonable number of high-risk patients in both the training and test sets (Figure 8C, D).

3.7 Incremental Value Analysis

The C-index of the base model (SOFA + lactate) was 0.7657, and it was 0.766 after adding BAR. Continuous NRI analysis showed that adding BAR significantly improved risk reclassification (NRI = 0.3684, 95% CI: 0.1768-0.5572, $P < 0.001$). However, IDI was not statistically significant (IDI = 0.0222, 95% CI: -0.1319 to 0.1746, $P = 0.786$). Nested model likelihood ratio test showed that adding BAR significantly improved model fit (LRT chi-square = 9.83, df = 1, $P = 0.0017$), and AIC decreased from 3063.81 to 3055.98 (delta AIC = 7.83).

3.8 Sensitivity Analysis and Proportional Hazards Correction

Schoenfeld residual tests showed that the overall model slightly violated the PH assumption (global chi-square = 15.43, $P = 0.0015$), with lactate violating the PH assumption ($P = 0.0012$), while SOFA and BAR satisfied the PH assumption (Figure 9E-G). Therefore, an interaction term between lactate and log(time) was introduced. After correction, AIC decreased from 3055.98 to 3046.17 (delta AIC = 9.81). The time-varying HR of lactate gradually attenuated from 1.213 on day 1 to 1.075 on day 28 (Figure 10). The model predicted 14-day mortality with AUCs of 0.748 (training set) and 0.701 (test set), and 60-day mortality with AUCs of 0.646 (training set) and 0.601 (test set) (Figure 11A-D). After excluding patients with extremely early death (ICU stay <2 days), the C-index only slightly decreased to 0.757.

3.9 External Validation Results

The external validation set included 177 patients, of whom 80 (45.2%) died within 28 days. The 28-day time-dependent AUC in the external validation set was 0.772 (Figure 12A). Calibration curves showed that predicted probabilities and observed probabilities generally followed the same trend, but there was some underestimation (Figure 12B). Based on LP tertiles,

external patients were divided into low-, intermediate-, and high-risk groups. Kaplan-Meier survival curves showed significant differences in 28-day survival among the three groups (log-rank $P < 0.001$) (Figure 12C). DCA showed a certain clinical net benefit within a certain range (Figure 12D). CIC showed that at the 20% threshold, the number of high-risk patients identified by the model was consistent with the trend of actual deaths among them (Figure 12E).

4 Discussion

This study constructed a model based on SOFA score, mean lactate, and BAR to predict the 28-day mortality risk of patients with cirrhosis and sepsis. The model showed good discrimination in the training set (C-index 0.766), and the Bootstrap-corrected AUC was 0.765 (95% CI: 0.735-0.795). In the external validation set, the AUC was 0.772, and Kaplan-Meier risk stratification analysis showed significant differences in survival among low-, intermediate-, and high-risk groups (log-rank $P < 0.001$).

In this study, BAR was independently associated with 28-day mortality risk, consistent with recent research on BAR in critical illness prognosis[9,10]. The prognostic value of BAR can be explained by its two components: BUN reflects glomerular filtration, effective circulating volume, neurohormonal activation, and catabolic stress; albumin reflects hepatic synthetic function and inflammatory consumption. In patients with cirrhosis and sepsis, sepsis-induced vasodilation and capillary leakage lead to insufficient effective circulating volume, activating RAAS and the sympathetic nervous system, causing decreased renal perfusion and increased urea reabsorption; portal hypertension and splanchnic vasodilation further aggravate this hemodynamic disturbance[11]. Inflammatory mediators such as TNF-alpha can promote albumin catabolism and urea production[12]. Albumin participates in maintaining colloid osmotic pressure, drug binding and transport, free radical scavenging, antioxidant defense, and microvascular integrity[13]. Therefore, BAR simultaneously captures renal dysfunction and hepatic synthetic failure.

Previous studies have shown that the MELD score has good predictive value for cirrhosis prognosis. However, in this study, MELD score showed no significant difference in Cox analysis in the training set, possibly because the discriminatory ability of MELD is limited in the context of sepsis. The advantage of BAR is that it is simple to calculate, requiring only BUN and albumin, and can simultaneously reflect renal perfusion status, hepatic synthetic reserve, and systemic inflammation severity.

After adding BAR to the SOFA + lactate base model, the C-index only increased from 0.7657 to 0.766, and IDI was not significant ($P = 0.786$). However, the nested model likelihood ratio test showed that adding BAR significantly improved model fit (LRT $P = 0.0017$, delta AIC = 7.83). Continuous NRI suggested possible improvement in individual risk reclassification (NRI = 0.3684, 95% CI: 0.1768-0.5572, $P < 0.001$). The fact that NRI was significant while IDI was not may indicate a risk that reclassification improvement is overestimated; it may also be due to information overlap between lactate and BAR in tissue perfusion and metabolic disturbance. This pattern has also been observed in other cirrhosis studies. Duan et al.[11] reported that after adding BAR to SOFA, the continuous NRI for 30-day mortality was 0.135 ($P = 0.006$) and IDI was 0.007 ($P = 0.014$); the increment was more significant when added to OASIS. This suggests that the incremental value of BAR depends on the composition of the base model.

This study ultimately retained only SOFA, lactate, and BAR to construct the model. The three-variable simplified model and the full model containing all Cox-significant variables showed similar 28-day time-dependent AUCs: training set 0.698 vs. 0.681, test set 0.665 vs. 0.630, and

external validation set 0.762 vs. 0.772. The differences were less than 0.04 across all three datasets. From the perspective of clinical practicality, the three-variable model requires only routine bedside indicators and does not require additional testing or proprietary software.

In this study, lactate violated the proportional hazards assumption. After introducing a time interaction term, model fit improved significantly (AIC 3055.98 to 3046.17, delta AIC = 9.81), and the time-varying HR of lactate attenuated from 1.213 on day 1 to 1.075 on day 28. Patients with cirrhosis have impaired lactate clearance, which is more obvious in sepsis[15]. Early high lactate mainly represents acute hemodynamic disturbance, while persistent or recurrent high lactate later may indicate hepatic clearance failure, secondary infection, or decompensation of liver function. Wei et al.[16] confirmed that patients with high-risk lactate trajectories had significantly increased 30-day mortality risk (HR 2.73-3.44, P < 0.001). Shabbir et al.[17] showed that lactate clearance >=35% within 24 h was associated with improved 30-day survival (OR 0.41, 95% CI 0.31-0.53). The time-varying effect in this study is consistent with these findings.

The C-index of this model was 0.766 in the training set, and the 28-day time-dependent AUC in the external validation set was 0.772. The nomogram model constructed by Hu et al.[18] based on MIMIC-IV and eICU-CRD had AUCs of 0.783, 0.763, and 0.745 in the training, internal validation, and external validation sets, respectively. Another nomogram model incorporating INR and lactate had an external validation AUC of 0.784 (95% CI 0.732-0.846) and a C-index of 0.77[19]. The XGBoost machine learning model constructed by Cao et al.[20] achieved AUCs of 0.946, 0.878, and 0.819 in the training, test, and temporal validation sets, respectively. However, machine learning models are less interpretable and clinically accessible than traditional regression models.

The external validation set and the MIMIC-IV development cohort differed significantly in baseline characteristics: lactate, BUN, and platelet were lower in the external cohort, and 28-day mortality was higher (45.2% vs. 26.5%). However, the MELD score was lower (19.35 vs. 26.64, P < 0.001). Despite these differences, the model maintained a 28-day AUC of 0.772 and significant risk stratification ability in external validation (log-rank P < 0.001). However, the external calibration curve showed underestimation in the high predicted probability range (intercept -0.588, slope 0.630), suggesting that absolute risk estimates need recalibration before use in individualized decision-making.

5 Limitations

First, this was a retrospective study. The external validation sample size was small, and mortality was significantly higher than in the modeling population (45.2% vs. 26.5%). The low 28-day AUC in the test set also suggests that model stability needs to be verified in larger prospective cohorts. Second, the model did not include treatment-related variables such as infection site, pathogen, timing of antibiotics, albumin infusion, and organ support. Third, SOFA score has known limitations in patients with cirrhosis. Fourth, BAR is affected by renal function, diuretics, gastrointestinal bleeding, and exogenous albumin. Using the 24-h average lactate may mask dynamic trajectories. Finally, the study excluded patients aged >80 years, those on dialysis, and those after liver transplantation.

6 Conclusions

The Cox model based on SOFA score, lactate, and BAR showed good discrimination in the internal training set (C-index 0.766) and stable risk stratification in external validation (28-day AUC 0.772, log-rank P < 0.001). BAR was an independent risk factor for 28-day mortality.

Although it did not improve overall discrimination, it improved model fit (LRT P = 0.0017, delta AIC = 7.83), and DCA/CIC showed positive clinical net benefit. The time-dependent effect of lactate suggests that the early admission period is a key intervention window. The nomogram can conveniently achieve individualized 28-day risk prediction. Future multicenter prospective cohorts are needed to validate and recalibrate the model.

Declarations

Abbreviations: BAR, blood urea nitrogen-to-albumin ratio; BUN, blood urea nitrogen; ALB, albumin; SOFA, Sequential Organ Failure Assessment; MELD, Model for End-Stage Liver Disease; AUC, area under the curve; ROC, receiver operating characteristic; KM, Kaplan-Meier; DCA, decision curve analysis; CIC, clinical impact curve; NRI, net reclassification improvement; IDI, integrated discrimination improvement; LRT, likelihood ratio test; AIC, Akaike information criterion; PH, proportional hazards; ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV; SBP, spontaneous bacterial peritonitis; RAR, red cell distribution width-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; WBC, white blood cell; CI, confidence interval; HR, hazard ratio; LP, linear predictor; TRIPOD, Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis.

Ethics approval and consent to participate: The MIMIC-IV database contains de-identified data and has been approved by the institutional review board of the Beth Israel Deaconess Medical Center with a waiver of informed consent. The external validation cohort from the Third Affiliated Hospital of Sun Yat-sen University was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University [approval number: SL-II2026-183-02]. Because of the retrospective nature of the study, the requirement for informed consent was waived.

Consent for publication: Not applicable.

Availability of data and materials: The MIMIC-IV data are publicly available from PhysioNet. The external validation dataset is not publicly available because of patient privacy and institutional restrictions, but can be obtained from the corresponding author upon reasonable request.

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Authors' contributions: Dai Chunwei and Cui Fan designed the study. Yang Yang and Fu Zijie collected and analyzed the data. Zhang Yongbiao and Yang Xiaoyan drafted the manuscript. Zheng Changlong critically revised the manuscript. All authors read and approved the final manuscript.

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in-hospital mortality in patients with liver cirrhosis and sepsis. Sci Rep. 2026 Apr 2;16(1):15885.
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Figure Legends

Figure 1. Flowchart of patient selection in the MIMIC-IV development cohort.

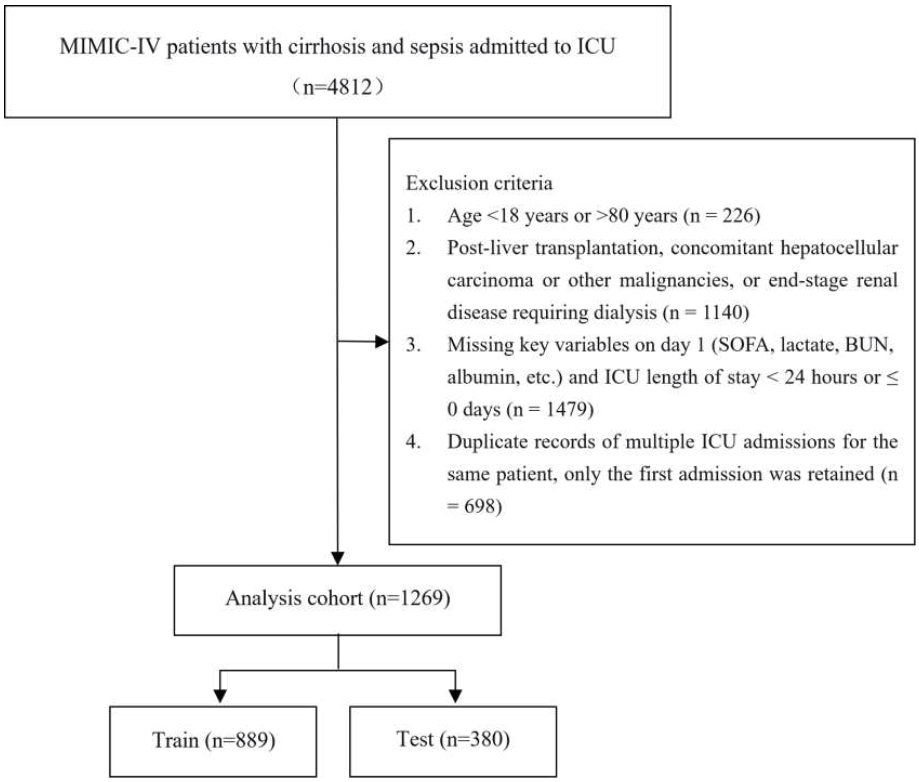
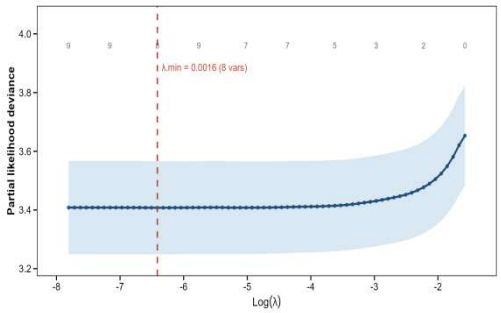


Figure 2. LASSO-Cox regression for variable selection. (A) Ten-fold cross-validation curve. (B) LASSO-Cox coefficient path plot.

A



B

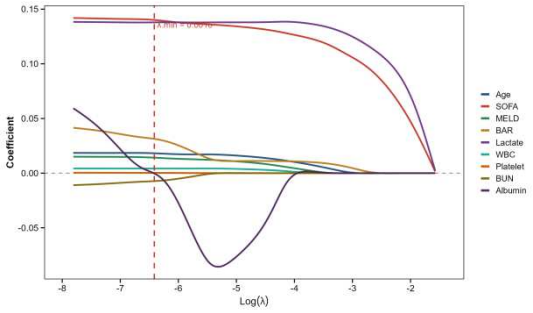


Figure 3. Forest plot of multivariable Cox regression analysis for 28-day mortality risk.

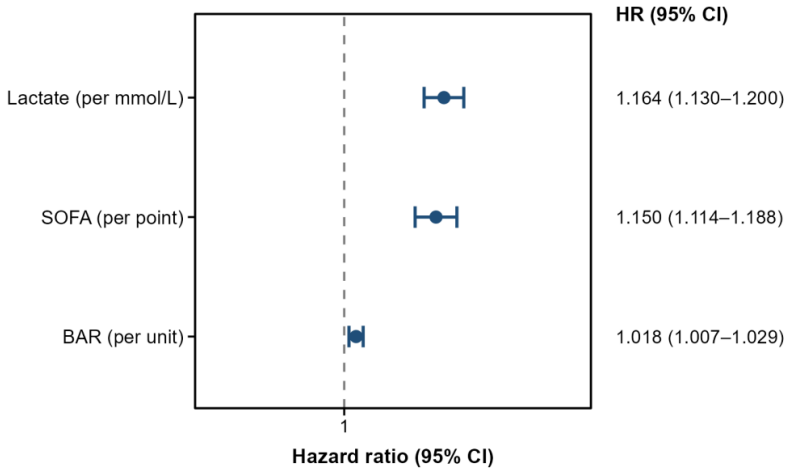


Figure 4. Nomogram for predicting 28-day mortality risk in patients with decompensated cirrhosis and sepsis.

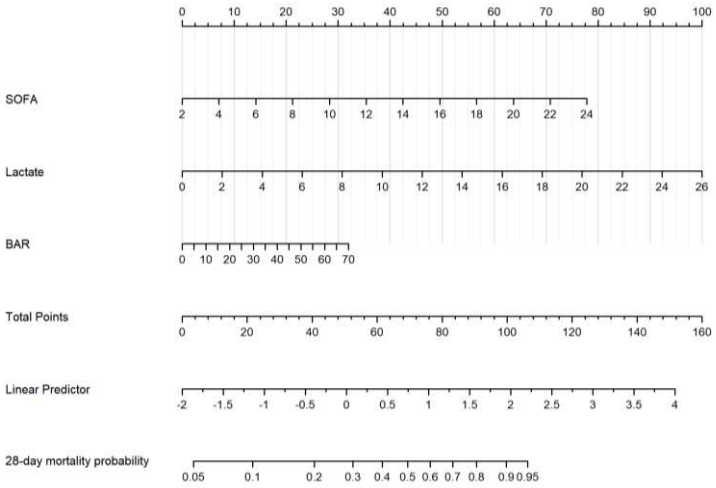
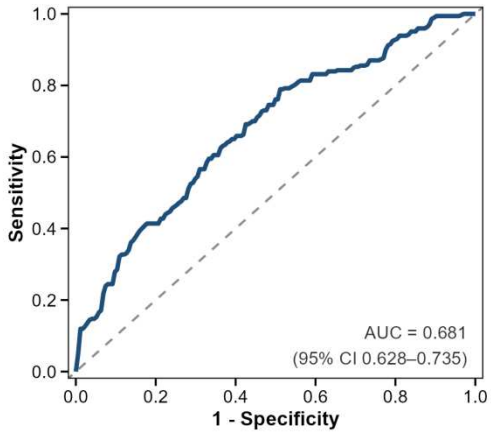


Figure 5. ROC curves for predicting 28-day mortality. A. Training set; B. Test set.

A



B

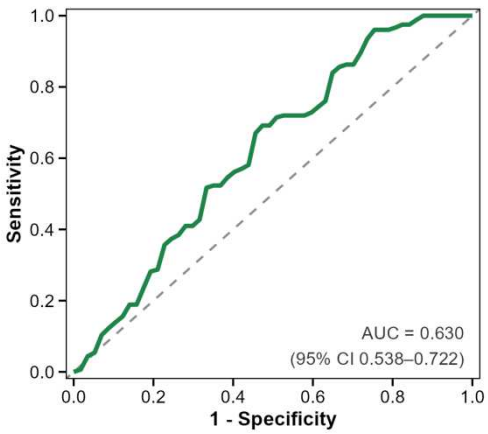
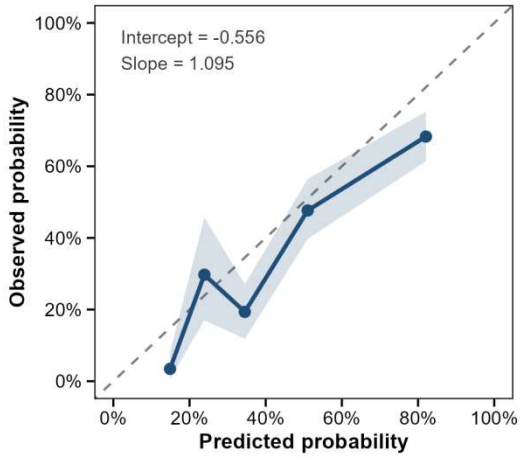


Figure 6. Calibration curves for 28-day mortality. A. Training set; B. Test set.

A



B

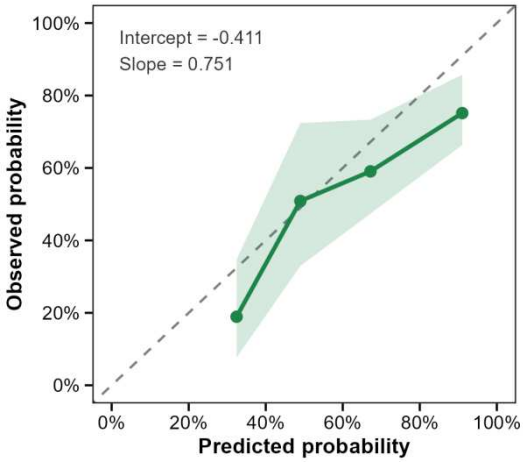
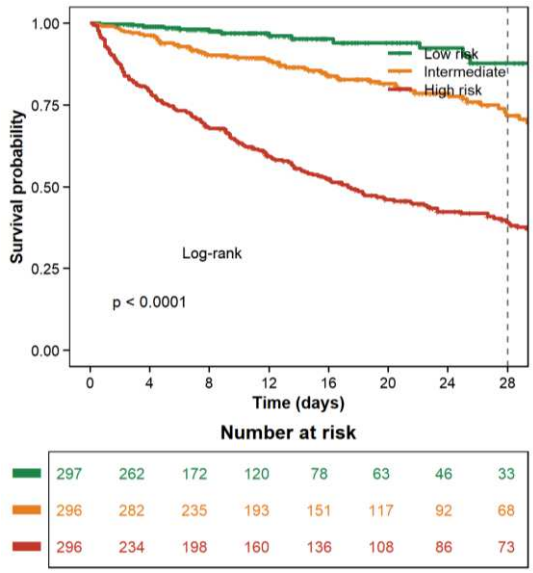


Figure 7. Kaplan-Meier survival curves based on risk stratification in the training and test sets. A. Training set; B. Test set.

A



B

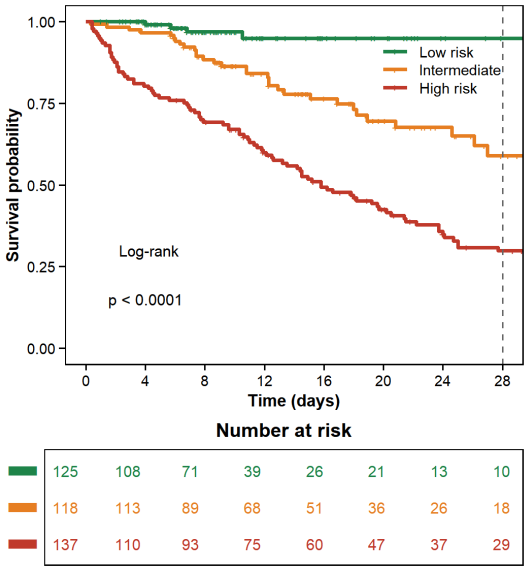


Figure 8. Decision curve analysis (DCA) and clinical impact curve (CIC) of the prediction model for 28-day mortality. (A) DCA in the training set; (B) DCA in the test set; (C) CIC in the training set; (D) CIC in the test set.

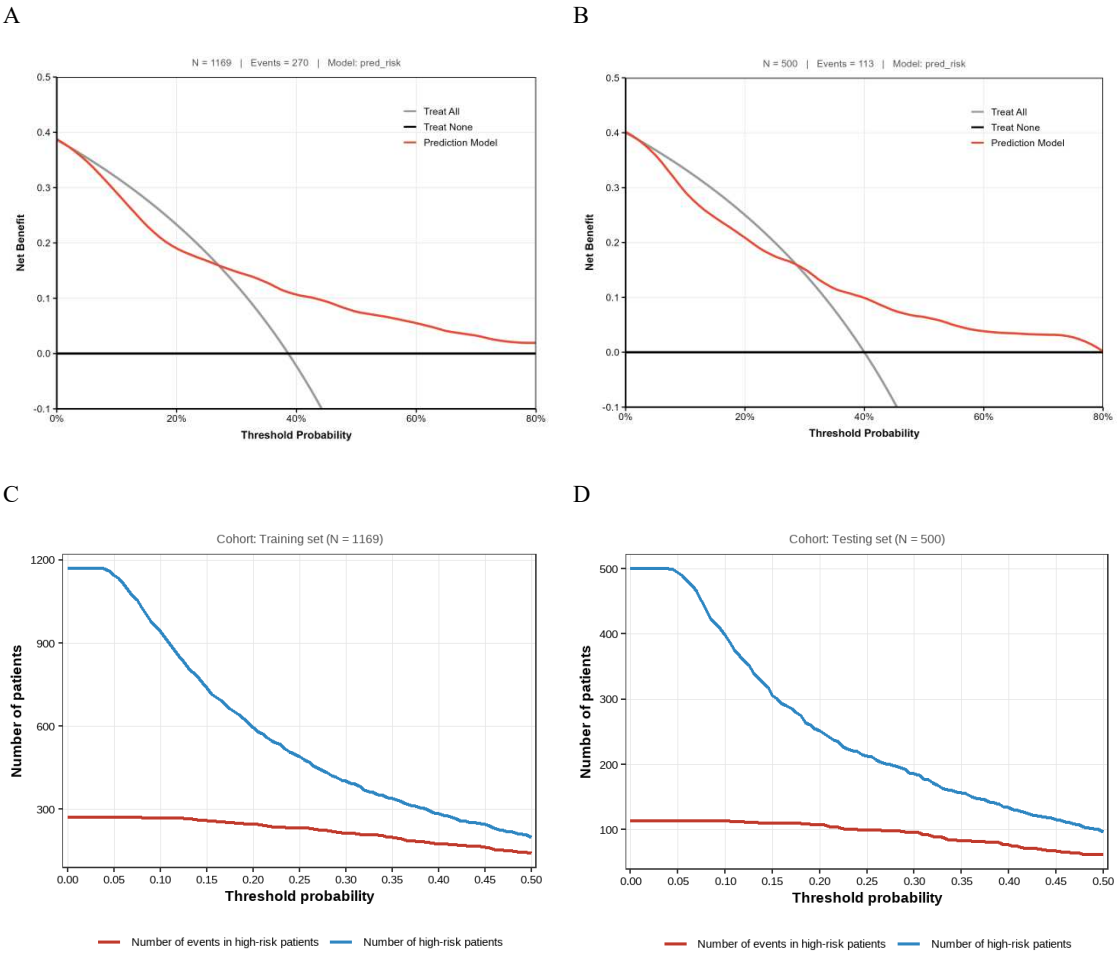


Figure 9. Diagnostic plots of the Cox proportional hazards model. (A) Deviance residuals; (B-D) Martingale residuals vs. SOFA, lactate, and BAR; (E-G) Schoenfeld residuals vs. time.

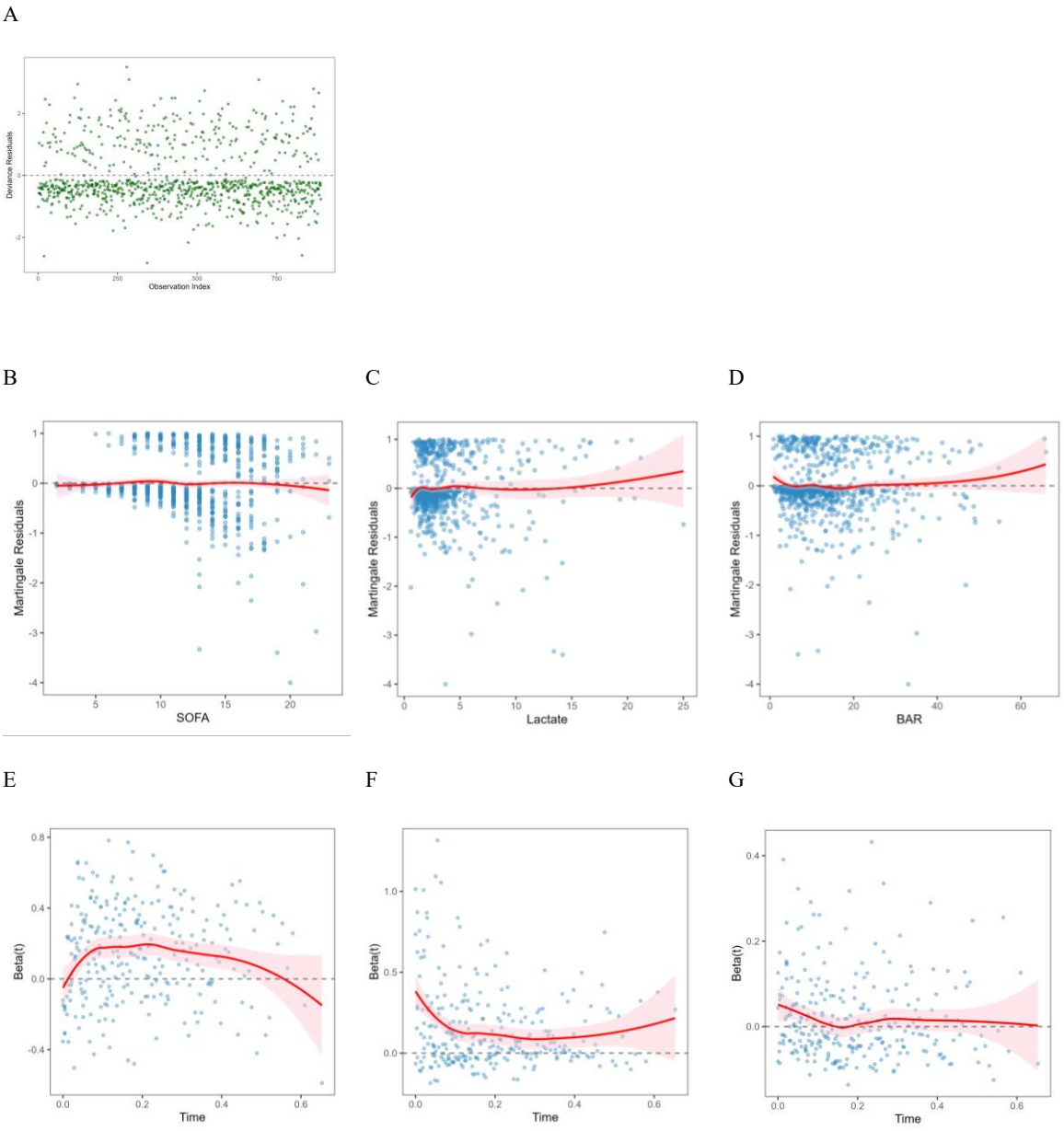


Figure 10. Time-varying effect of lactate on 28-day mortality risk.

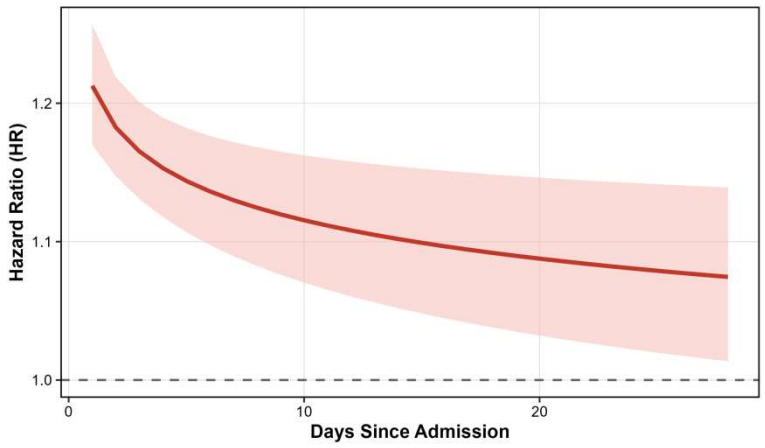
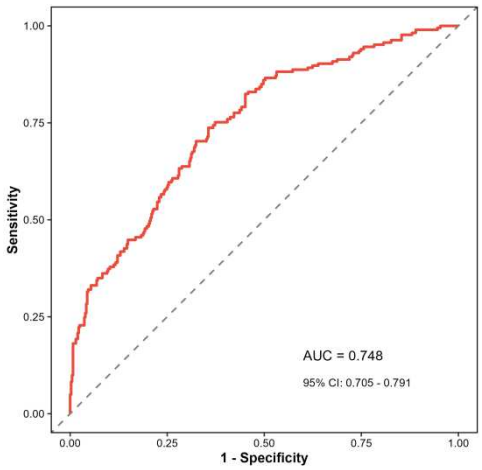
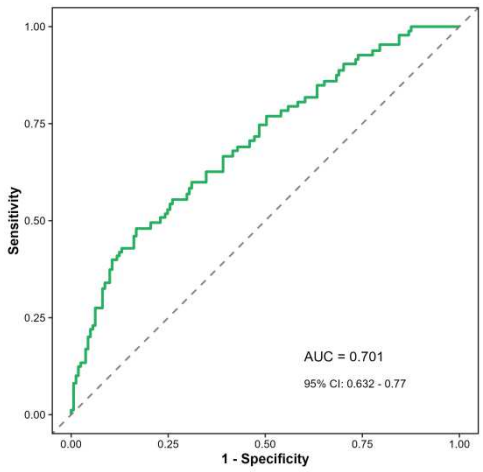


Figure 11. Time-dependent ROC curves for predicting 14-day and 60-day mortality. (A) Training set, 14-day mortality; (B) Test set, 14-day mortality; (C) Training set, 60-day mortality; (D) Test set, 60-day mortality.

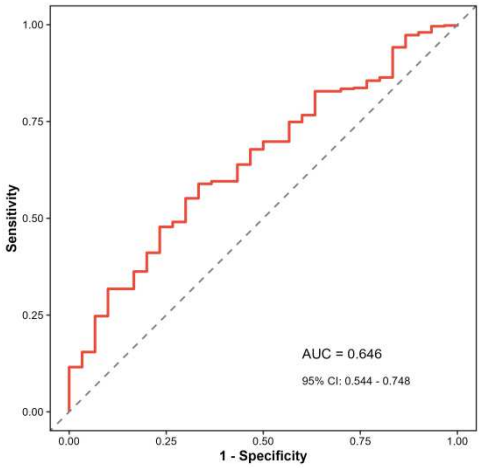
A



B



C



D

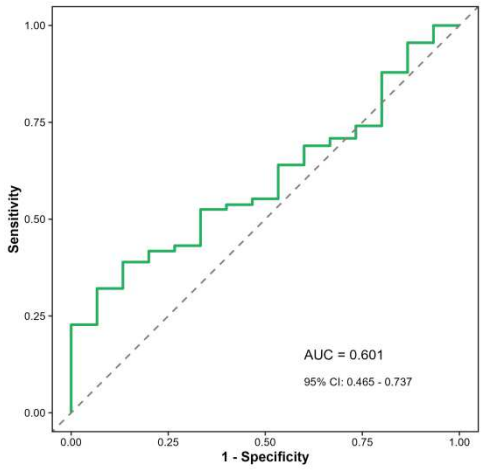
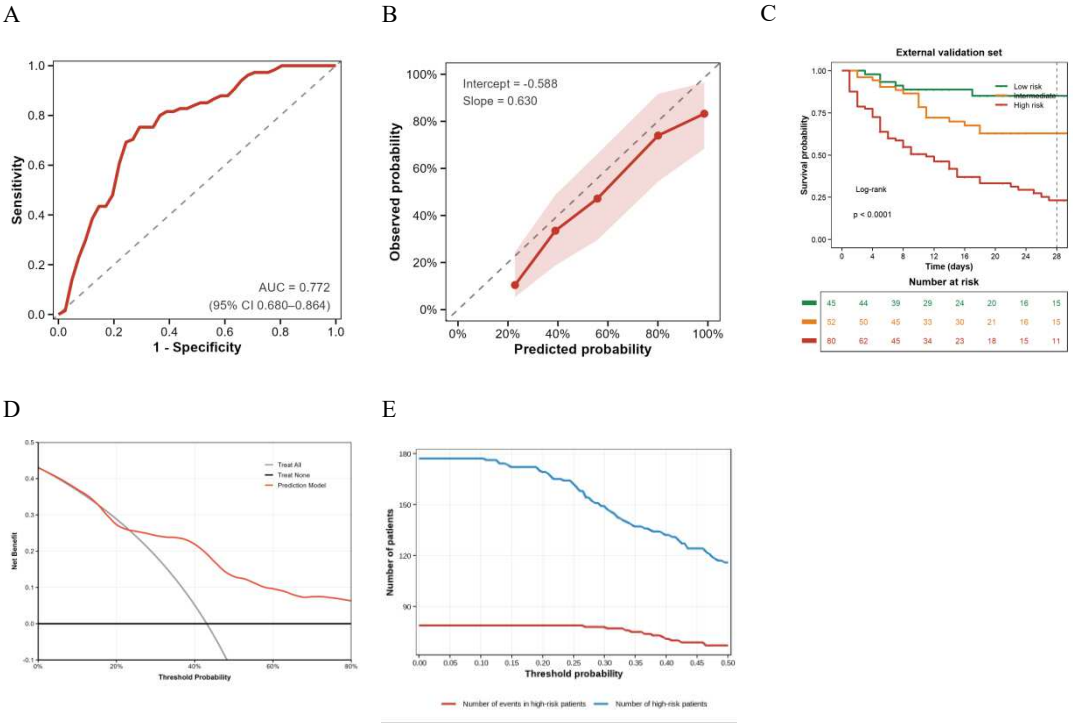


Figure 12. Comprehensive performance evaluation of the prediction model in the external validation set. (A) Time-dependent ROC curve for 28-day mortality; (B) Calibration curve for 28-day mortality; (C) Kaplan-Meier survival curves and risk table based on risk stratification; (D) Decision curve analysis; (E) Clinical impact curve.

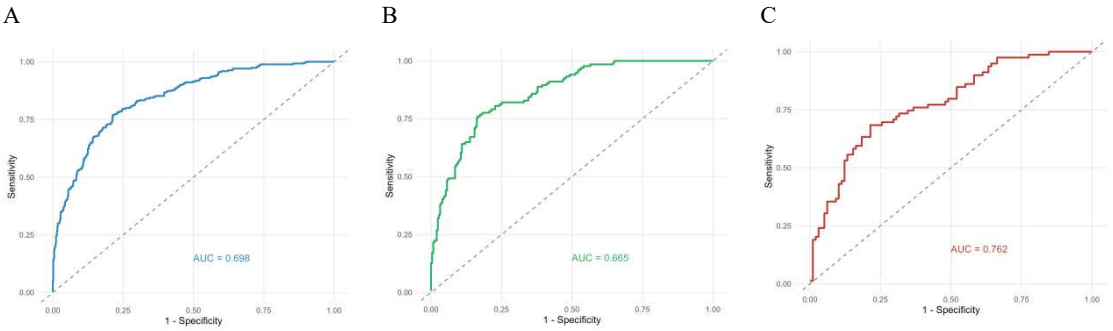


Supplementary Material

Supplementary Table 1. Multivariable Cox regression analysis for 28-day mortality.

Variable	HR (95% CI)	z	P value	Included in final model
Age (admission_age)	1.023 (1.011–1.035)	3.743	0.00018	No
SOFA	1.158 (1.116–1.202)	7.695	<0.001	Yes
MELD	1.020 (0.999–1.040)	1.895	0.058	No
BAR	1.039 (1.012–1.066)	2.89	0.0039	Yes
Lactate (lactate_avg)	1.147 (1.109–1.185)	8.073	<0.001	Yes
WBC (wbc_avg)	1.004 (0.993–1.016)	0.734	0.463	No
Platelet (platelet_avg)	1.001 (0.999–1.002)	0.587	0.557	No
BUN (bun_avg)	0.990 (0.981–0.999)	−2.109	0.035	No

Supplementary Table 2. Twenty-eight-day ROC curves of the significant-variable model in the training, test, and external validation sets. (A) Training set (AUC = 0.698); (B) Test set (AUC = 0.665); (C) External validation set (AUC = 0.762). The model included age, SOFA, BAR, lactate, and BUN.



Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.doc