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Predicting in-hospital mortality for MIMIC-III patients

A nomogram combined with SOFA score

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Abstract

Predicting the mortality of patients provides a reference for doctors to judge their physical condition. This study aimed to construct a nomogram to improve the prediction accuracy of patients' mortality. Patients with severe diseases were screened from the Medical Information Mart for Intensive Care (MIMIC) III database; 70% of patients were randomly selected as the training set for the model establishment, while 30% were used as the test set. The least absolute shrinkage and selection operator (LASSO) regression method was used to filter variables and select predictors. A multivariable logistic regression fit was used to determine the association between in-hospital mortality and risk factors and to construct a nomogram. A total of 9276 patients were included. The area under the curve (AUC) for the clinical nomogram based on risk factors selected by LASSO and multivariable logistic regressions were 0.849 (95% confidence interval [CI]: 0.835–0.863) and 0.821 (95% CI: 0.795–0.846) in the training and test sets, respectively. Therefore, this nomogram might help predict the in-hospital mortality of patients admitted to the intensive care unit (ICU).

Abbreviations: AUCs = area under curves, BMI = body mass index, CI = confidence interval, ICU = intensive care unit, IQRs = interquartile ranges, LASSO = least absolute shrinkage and selection operator, MIMIC-III = medical information mart for intensive care III, OR = odds ratio, SOFA = the sequential organ failure assessment.

Keywords: in-hospital mortality, intensive care unit, nomogram, prediction tool

1. Introduction

The intensive care unit (ICU) provides a continuous monitoring system for critically ill patients with potential for rehabilitation or life-threatening diseases and is committed to providing targeted monitoring and best care.[1] Due to the high fatality rate and expensive medical resources, the ICU has attracted extensive attention in the medical community.[2] To facilitate continuous monitoring of all patients and ensure that any deterioration of their condition is detected and corrected before it becomes a fatal disease, the ICU staff to patients ratio is often very high, which has been proven to improve results.[3] Therefore, the ICU is a data-rich environment crucial for quantifying patients' health and predicting future results. One of the most directly relevant results for ICU is patient mortality.[4] Mortality prediction based on patient characteristics provides a reference for doctors to judge their physical condition and determine survival rates and plays an important role in health care and resource allocation. Since 1991, various studies have developed models for mortality prediction, especially the Apache-III scoring system proposed by Knaus et al,[5] which is still one of the criteria for predicting the severity of patients in ICUs. Other scoring systems have also been developed, including the Acute Physiology Score III,[6] Simplified Acute Physiology Score,[7] Simplified Acute Physiology Score II,[8] the Sequential Organ Failure Assessment (SOFA) score,[9] the Logistic Organ Dysfunction Score,[10] and the Oxford Acute Severity of Illness Score.[11] However, some previous studies[12–14] have indicated that traditional scoring systems are weighted according to the severity, vital signs, and other parameters of ICU patients to predict whether they will experience life-threatening events such as sepsis, cardiac arrest, and respiratory arrest, presenting unsatisfactory prediction sensitivity and specificity. Although Yun et al used 43 demographic, laboratory, hemodynamic, surgical, and disease-specific variables to construct a machine learning model to improve the

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Since this study is a retrospective study, it only collects the clinical data of patients with no treatment plans and will not bring risks to the patient's physiology. Therefore, the need for informed consent was waived in our study.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

The database was approved by the institutional review boards (IRB) of the Massachusetts Institute of Technology (MIT) and BIDMC.

Supplemental Digital Content is available for this article.

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predictive accuracy of mortality, it contains multiple cumbersome metrics to calculate.[4] Therefore, more precise, and easy-to-use prediction models are needed to improve mortality prediction of ICU patients.

Nomograms are recommended for predicting the prognosis of various cancers.[12,15,16] They are easier to calculate and transform into a normalized individual mortality probability, facilitating the comprehension of individual mortality risk for patients without professional medical knowledge. Therefore, this study aimed to develop and validate a nomogram for predicting the in-hospital mortality of ICU patients.

2. Material and Methods

2.1. Data source

This study used the Medical Information Mart for Intensive Care (MIMIC) III database, a publicly available clinical database developed through a collaboration among the Massachusetts Institute of Technology, Philips Healthcare, and Beth Israel Deaconess Medical Center. This database includes information on patients admitted to various ICUs of Beth Israel Deaconess Medical Center in Boston, Massachusetts, from 2001 to 2012.[17,18] To access this database, we needed to complete the National Institutes of Health's web-based course: Protecting Human Research Participants (certification number 37796456).

2.2. Study population and potential predictive variables

Referring to clinical experience, published literature, and the MIMIC-III database, we selected potential predictive variables, including the following patient characteristics at hospital admission: sex; age; BMI; SOFA; serum levels of Na^+, K^+, and Ca^+; blood glucose; mean creatinine; mean osmotic pressure; mean albumin; and complications: cardiac arrhythmia, chronic pulmonary disease, peripheral vascular disease, liver disease, diabetes, cancer, and fluid and electrolyte disorders. Additionally, the Elixhauser comorbidity score is a composite scoring system commonly used to evaluate the prognosis of inpatients for the underlying disease and is often used in studies to reflect disease severity and as an important confounding factor requiring adjustment.[19–21] Herein, the Elixhauser comorbidity score was directly extracted to visualize the MIMIC III database (Supplemental Digital Content 1, http://links.lww.com/MD/H674).

2.3. Primary study outcome

The outcome of our study was in-hospital death, defined as mortality status at hospital discharge. Only the first ICU stay was considered for patients with more than one stay. The beginning of follow-up was considered the date of the patient's admission. The date of death was obtained from the US government's Social Security Death Index records and should not exceed the discharge date from the hospital.

2.4. Statistical analysis

Due to the ICU particularities, it is impossible to guarantee that each patient's data will be fully recorded. Hence, some patients may lack some data or present some errors. In our dataset, we characterized the missing data as "Missing Completely at Random (MCAR)" and "Missing at Random (MAR)," assuming that the staff in the hospital would not delete the values on purpose or that patients would not refuse to do the tests. Thus, we could use some imputation methods to process the

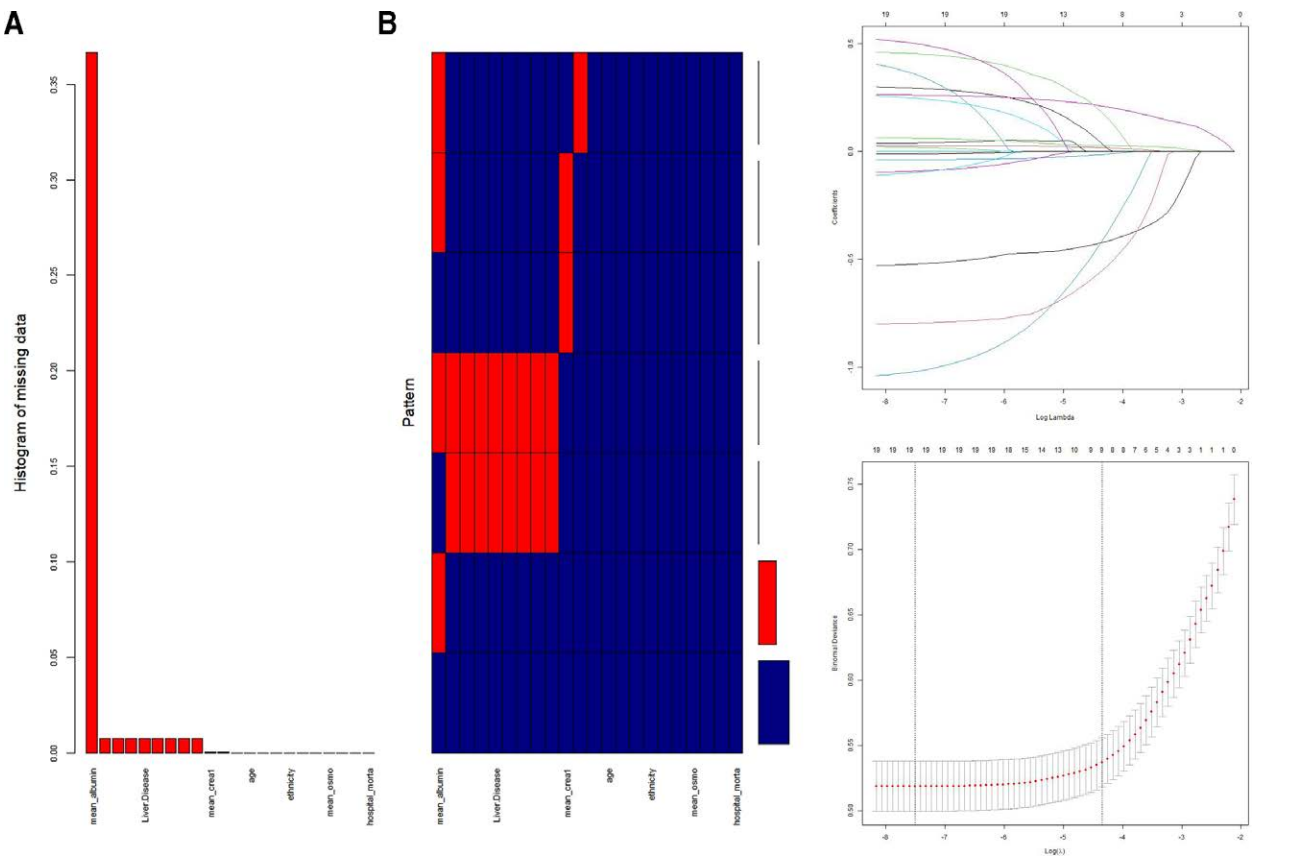

Figure 1. The pattern of missing values in the dataset (A) and the LASSO regression method was applied to filter variables and select predictors (B). LASSO = least absolute shrinkage and selection operator.

Table 1

Baseline characteristics of participants.

Variables	Survival (n = 8183)	Death (n = 1093)	*P* value
Age, median (IQR)	65.0 (52.0, 77.0)	75.0 (61.0, 84.0)	<.001
BMI, median (IQR)	24.0 (22.2, 27.1)	22.5 (21.7, 25.5)	<.001
Na^+, median (IQR)	138.8 (136.9, 140.6)	139.5 (136.2, 142.4)	<.001
K^+, median (IQR)	4.1 (3.9, 4.3)	4.1 (3.9, 4.5)	.001
Blood glucose, median (IQR)	7.1 (5.8, 9.1)	7.6 (5.9, 9.8)	<.001
Mean osmotic pressure, median (IQR)	299.8 (295.4, 305.5)	308.0 (299.8, 316.9)	<.001
Ca^+, median (IQR)	2.1 (2.0, 2.2)	2.1 (2.0, 2.2)	<.001
Mean creatinine, median (IQR)	79.6 (61.9, 106.8)	109.0 (70.7, 180.1)	<.001
SOFA, median (IQR)	6.0 (3.0, 9.0)	10.0 (7.0, 14.0)	<.001
Mean albumin, median (IQR)	3.3 (2.9, 3.7)	2.8 (2.4, 3.2)	<.001
Elixhauser comorbidity score, median (IQR)	4.0 (0.0, 5.0)	0.0 (0.0, 5.0)	<.001
Fluid and electrolyte disorders, n (%)			.006
No	8102 (88.31)	1072 (11.69)	
Yes	81 (79.41)	21 (20.59)	
Cancer, n (%)			.309
No	294 (86.47)	46 (13.53)	
Yes	7889 (88.28)	1047 (11.72)	
Sex, n (%)			<.001
Male	4673 (89.56)	545 (10.44)	
Female	3510 (86.50)	548 (13.50)	
Cardiac arrhythmia, n (%)			<.001
No	5119 (85.37)	877 (14.63)	
Yes	3064 (93.41)	216 (6.59)	
Chronic pulmonary disease, n (%)			<.001
No	7351 (89.33)	878 (10.67)	
Yes	832 (79.47)	215 (20.53)	
Peripheral vascular disease, n (%)			<.001
No	7010 (86.90)	1057 (13.10)	
Yes	1173 (97.02)	36 (2.98)	
Liver disease, n (%)			<.001
No	8055 (88.49)	1048 (11.51)	
Yes	128 (73.99)	45 (26.01)	
Diabetes, n (%)			
No	8075 (88.13)	1088 (11.87)	.015
Yes	108 (95.58)	5 (4.42)	

BMI = body mass index, IQR = interquartile range, SOFA = sequential organ failure assessment.

missing data. Multiple imputations are preferable rather than entirely removing data in some areas,[22] used in some studies for preprocessing missing values. Predictive mean matching usually presents the best performance when <50% of cases have missing values.[23–25] Thus, we used multiple imputations with predictive mean matching for missing data.[26]

Participant characteristics are represented using descriptive statistics. Categorical variables are presented as numbers and percentages, such as sex, fluid and electrolyte disorders, cancer, cardiac arrhythmia, chronic pulmonary disease, peripheral vascular disease, liver disease, and diabetes. Continuous variables, including age, BMI, Na^+, K^+, initial glucose, mean osmotic pressure, Ca^+, mean creatinine, SOFA, mean albumin, and the Elixhauser comorbidity score were analyzed by the Kolmogorov-Smirnov test, and none of them satisfied the normality hypothesis. Thus, these non-normal variables are presented as medians and interquartile ranges (IQRs). Differences in categorical variables between the death and survival groups were compared using the χ^2 test for large samples, whereas numerical variables were compared using the Mann–Whitney *U* test.

Least absolute shrinkage and selection operator (LASSO) was applied to these potential variables for feature selection using the "Glmnet" R package. Then, we used logistic regression for multivariable analysis of the selected features. A nomogram was formulated based on the results of the multivariable analysis using the "regplot" R package (v. 3.6.0; http://www.r-project.org/). The "pROC" R package was used to draw the receiver operating characteristic curve and evaluate the model effects by calculating the area under the curve (AUC). The performance of the nomogram was assessed by comparing nomogram-predicted versus observed probability. Bootstraps with 1000 resamples were used for these activities. Finally, the calibration curve was derived from the regression analysis. All statistical tests were 2-sided, with the significance level set at 0.05. We used the STROBE checklist when writing our report.

3. Results

The database contains records for 58,976 admissions. Here, 12,509 were excluded due to duplications. Of the remaining

Table 2

Results of multivariable analysis.

	Training set		Test set	
Variables	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Sex	1.444 (1.211–1.722)	<.001	1.378 (1.049–1.812)	.021
Age	1.023 (1.017–1.029)	<.001	1.021 (1.012–1.030)	<.001
BMI	0.946 (0.930–0.963)	<.001	0.944 (0.917–0.971)	<.001
Mean osmotic pressure	1.039 (1.031–1.047)	<.001	1.046 (1.033–1.060)	<.001
SOFA	1.266 (1.239–1.294)	<.001	1.235 (1.192–1.279)	<.001
Mean albumin	0.468 (0.404–0.542)	<.001	0.526 (0.420–0.659)	<.001

BMI = body mass index, CI = confidence interval, SOFA = sequential organ failure assessment.

46,467 admissions, 37,191 were excluded because the patients were neonates (7870) or had incomplete data (29321). Finally, 9276 ICU patients were included, 1093 non-survivors and 8183 survivors, comprehending a mortality rate of 11.78% (Supplemental Digital Content 2, http://links.lww.com/MD/H675). Some missing values in the dataset and the amount of missing data in the variables are shown in Supplemental Digital Content 3, http://links.lww.com/MD/H676. We used the VIM package to evaluate the pattern of missing values (Fig. 1A). The red line separates part of the area, and most missing values are on mean albumin. Using the "MICE" R package, we set the number of iterations to 50 to reduce the impact of random factors. Nineteen baseline and clinical features were selected based on medical expertise and practical clinical experience (Table 1). These results showed that, apart from 3 cancer complications, all variables were significantly different between the deceased and survived groups ($P < .05$). The median age of patients in the deceased group was 75 years (IQR: 61.0–84.0), significantly higher than the survival group (median age: 65 years, IQR: 52.0–77.0). The mean BMI ranged from 21.7 to 25.5 kg/m^2 in the death group and from 22.2 to 27.1 kg/m^2 in the survival group. The initial glucose level of the death group (median: 7.556 mg/dL) was higher than the survival group (median: 7.056 mg/dL); the mean osmotic pressure of the death group (median: 308.028 mmol/L) was significantly higher than that of the survival group (299.844 mmol/L). However, both were within the normal osmotic pressure range specified by MIMIC (290–309 mmol/L). The SOFA score of the death group (median: 10, IQR: 7–14) was significantly higher than the survival group (median: 6, IQR: 3–9). We also observed appreciable differences by sex ($P < .05$). The complications with significant differences included fluid and electrolyte disorders, cancer, cardiac arrhythmia, chronic pulmonary disease, peripheral vascular disease, liver disease, and diabetes.

Furthermore, all characteristic variables were included in the LASSO regression to evaluate their impact on in-hospital mortality (Fig. 1B). After feature selection, 6 variables remained significant predictors of in-hospital mortality: age, BMI, mean osmotic pressure, SOFA, mean albumin, and sex. Including 19 variables in a LASSO-logistic regression model resulted in 6 variables that were independently statistically significant predictors of in-hospital mortality (Table 2). The multivariable analysis in training test demonstrated that sex (odds ratio [OR], 1.444; 95% confidence interval [CI]: 1.211–1.722), age (OR, 1.023; 95% CI: 1.017–1.029), mean osmotic pressure (OR, 1.039; 95% CI: 1.031–1.047), and SOFA (OR, 1.266; 95% CI: 1.239–1.294) were independent protectors for in-hospital mortality of ICU patients (all $P < .05$); BMI (OR, 0.946; 95% CI: 0.930–0.963) and mean albumin (OR, 0.468; 95% CI: 0.404–0.542) were independent risk factors (all $P < .05$). A similar result was observed in the test set. The nomogram incorporating all significant independent factors from the multivariable analysis for predicting in-hospital mortality is presented in Figure 2. The calibration curve for the training and test sets are shown in Figure 3A and B, respectively, and illustrate the good agreement between predictions and observations. In the training set, the AUC was 0.849 (95% CI: 0.835–0.863) (Fig. 3C), close to the observed in the test set (AUC: 0.821, 95% CI: 0.795–0.846) (Fig. 3D). These AUCs were higher than the SOFA alone (AUC: 0.746; 95% CI: 0.717–0.776) (Fig. 4). Therefore, the nomogram performed well in predicting the mortality of ICU patients.

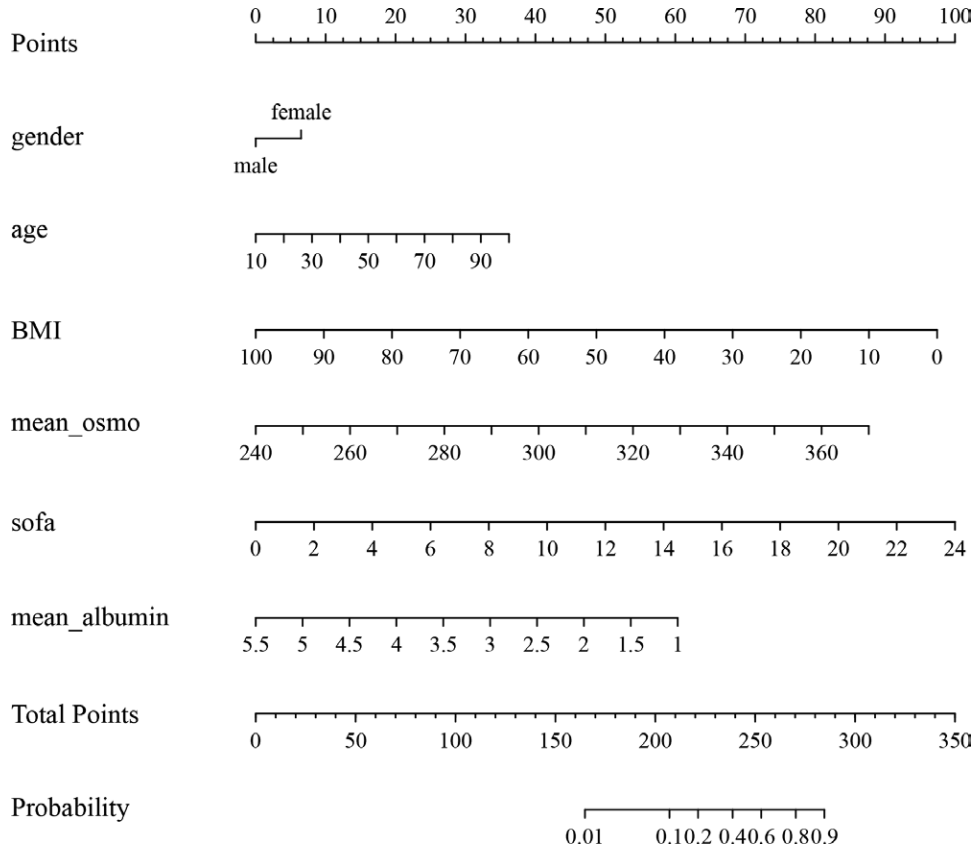

Figure 2. Nomogram for predicting in-hospital mortality. To use the nomogram, an individual patient's value is located on each variable axis, and a line is drawn upward to determine the number of points received for each variable value. The sum of these numbers is located on the Total Points axis, and a line is drawn downward to the risk of in-hospital mortality. BMI = body mass index, SOFA = sequential organ failure assessment.

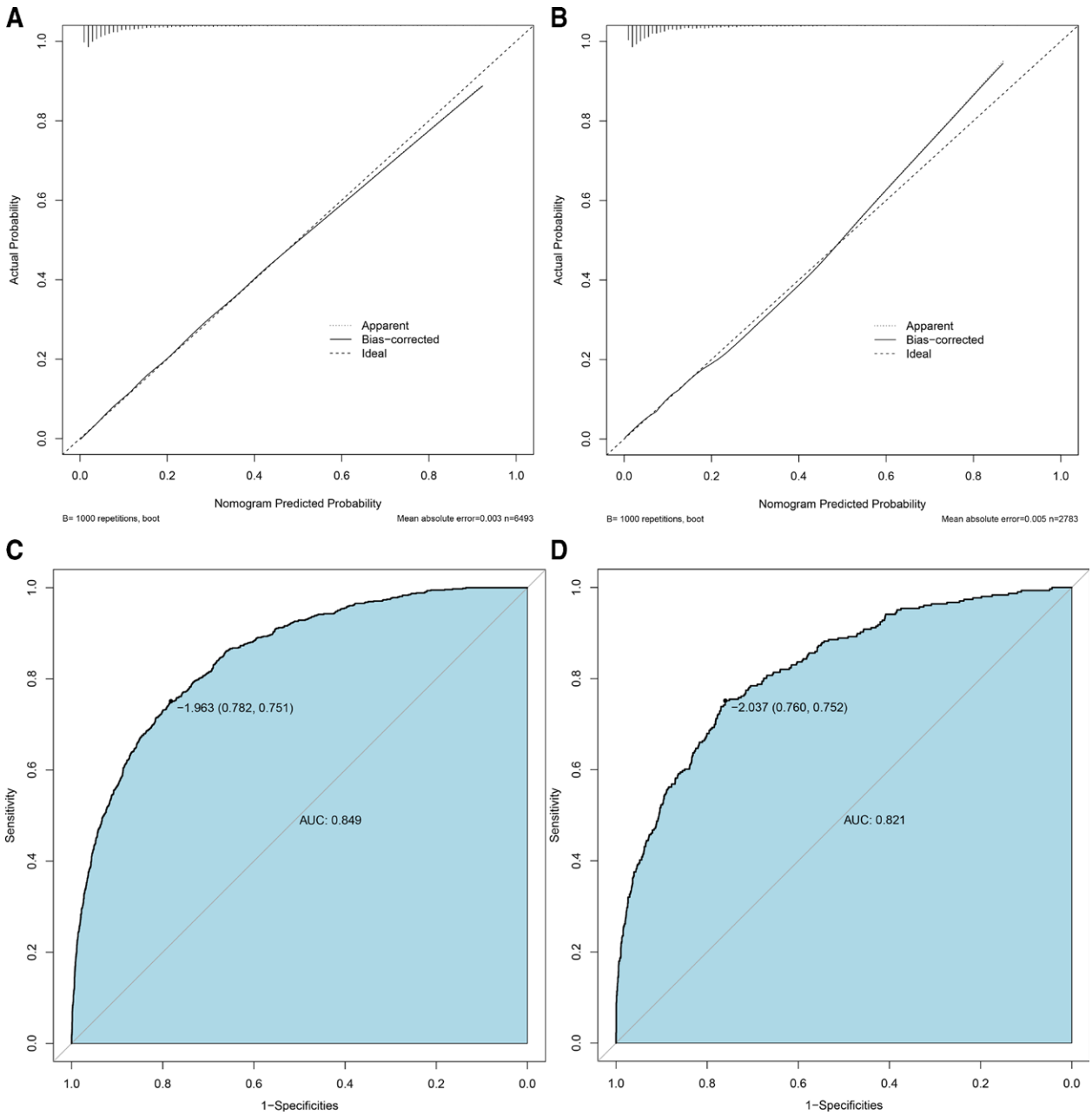

Figure 3. The calibration curves indicate the goodness-of-fit of the nomogram and ROC curves identifying the optimal cutoff value for predicting in-hospital mortality. (A) Calibration curve for the training set. (B) Calibration curve for the test set. The dotted line 45 degrees represents the ideal prediction, and the other dotted line represents the predictive performance of the nomogram. The closer the dotted line approaches the ideal prediction line, the better the predictive efficacy of the nomogram is. The solid line represents the internal validation curve based on Bootstrap sampling. (C) ROC curves for the training set. (D) ROC curves for the test set. AUC = the area under curve, ROC curve = receiver operating characteristic curve.

4. Discussion

Herein, we combined the SOFA score to construct an improved model to predict the development of critical illness among hospitalized patients. We evaluated the effectiveness of the newly developed prediction model, and the results were similar to an existing scoring system (the SOFA score). Accurate prediction of mortality risk for patients admitted to an ICU can help assess the severity of a patient's disease to a certain extent, as well as their prognoses, so that medical resources can be reasonably allocated. Although most previous models based on scoring systems for outcome prediction have been developed for a long time, and some have been widely used, they can be considered suboptimal since any score dependent on clinical criteria and laboratory variables can be subject to variation during assessments. These variations might be related to differences in laboratory assays, changes in personnel performing the examinations and confounders not measured within the score.[27] For example, Yun et al used 43 variables to build a machine learning model to improve the accuracy of mortality prediction. However, a small number of variables were beneficial to help clinicians make quick decisions because they do not require additional laboratory testing.[4]

Nomograms are 2-dimensional graphic calculators that can conveniently diagnose diseases and rapidly evaluate prognosis.[28,29] Many studies[15,29] have shown their potential value in clinical practice. In the present study, we first determined the main potential risk factors affecting the mortality of critically ill patients based on MIMIC-III data and relevant literature. The univariate analysis showed that all variables might be related to

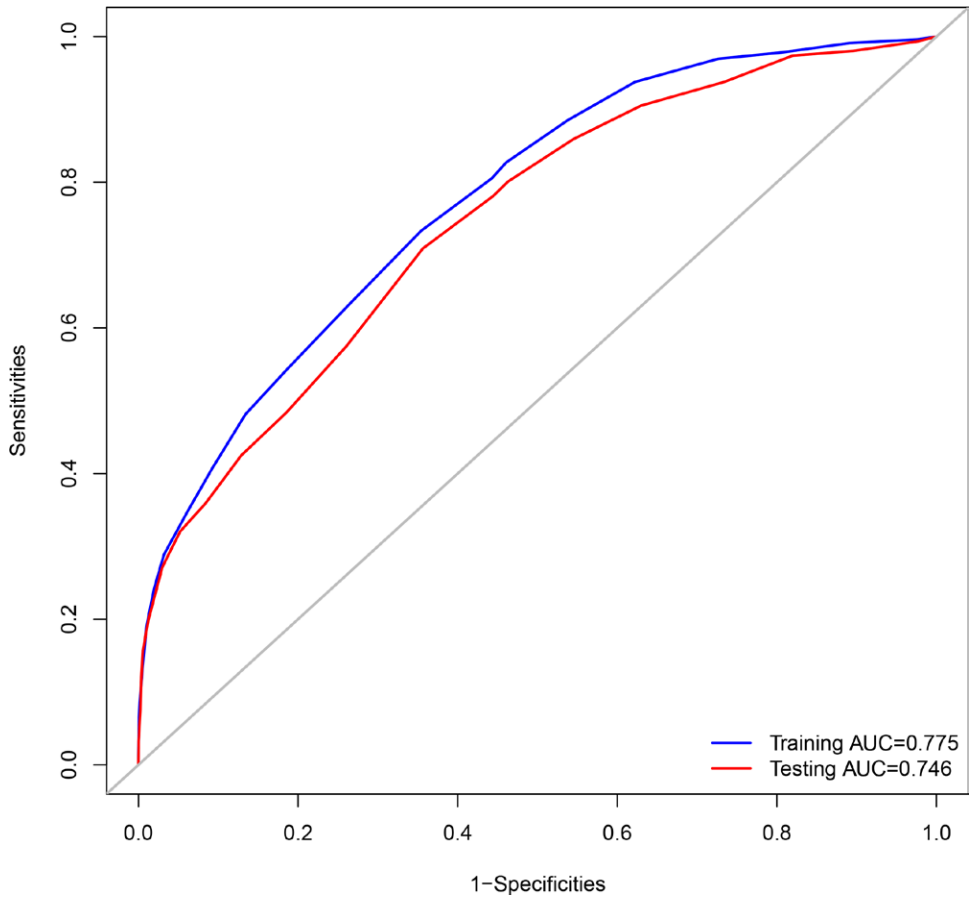

Figure 4. The ROC curve of SOFA score for the training set and the test set. ROC curve = receiver operating characteristic curve, SOFA = sequential organ failure assessment.

the in-hospital mortality of ICU patients, except cancer complications. Then, we used multivariable logistic regression analysis to find independent risk factors for in-hospital mortality. We noticed that if all variables were included in the model, it would be detrimental to parameter estimation due to the large number of variables. Additionally, we expect to use the fewest and clinically significant variables to construct the nomogram model for clinical applications. Therefore, we used the LASSO regression model for variable screening. The principle of this method is to add a penalty term based on least squares to compress the estimated parameters. When the parameter is compressed to a threshold, it becomes 0.[30] Thus, the independent variables with relatively greater influence can be screened, and the corresponding regression coefficients can be calculated. Besides, LASSO regression is often used to deal with the problem of multicollinearity between independent variables. The univariate analysis indicated that age, BMI, sex, Ca^+, Na^+, K^+, blood glucose, mean creatinine, mean osmotic pressure, mean albumin, Elixhauser comorbidity score, fluid and electrolyte disorders, cancer, cardiac arrhythmia, chronic pulmonary disease, peripheral vascular disease, liver disease, and diabetes were associated with in-hospital death. Incorporating them into the LASSO-logistic regression model showed that sex, age, BMI, mean osmotic pressure, SOFA score, and mean albumin were independent risk factors for in-hospital death of ICU patients. Next, we constructed nomograms based on logistic regression and evaluated them via the AUCs and the calibration curve. Finally, we compared it with the traditional SOFA scoring system, demonstrating that our model performed well.

Several factors have been reported regarding the ICU mortality risk, such as SOFA, BMI, age, and mean osmotic pressure. The SOFA score was proposed by the European Association of Critical Care Medicine in 1994 to assess organ failure in critically ill patients.[9,31] Many studies have shown that the SOFA score is closely related to the prognosis of ICU patients,[32] becoming a necessary tool for sepsis diagnosis according to the new definition of sepsis.[33] However, the conclusions on the prognostic value of the SOFA score at different time points are inconsistent.[27] For example, Vincent et al[31] followed up 40 intensive care patients in multiple countries and found that the SOFA score during hospitalization was related to hospital death. Ferreira et al[32] followed up 352 hospitalized patients in a single-center ICU and found that, compared to the SOFA score at admission, the average and maximum SOFA score during hospitalization had a higher prognostic predictive ability, consistent with our current findings. We also observed that older patients presented a higher mortality risk. Regarding the BMI, some studies[34] have shown that obese or overweight ICU patients had markedly lower 30-day and 1-year mortality risks, besides higher incidences of many comorbidities and similar admission acuity compared to normal-weight counterparts. Another study has also indicated that being overweight is a risk factor leading to a poor prognosis.[35] Furthermore, osmotic pressure disorders are common in ICU patients and are related to intracellular dehydration or edema, leading to undesirable consequences. Holtfreter et al[36] evaluated the ability of the mean osmotic pressure to predict the mortality of ICU patients (AUC: 0.732) and found an "S"-shaped relationship between the mean osmotic pressure and mortality. These results might be related to the heterogeneity of patients admitted to the ICU, which was ignored.

Our current study also has some limitations. First, its post hoc nature should be considered when evaluating the findings. Although

we attempted to eliminate the confounding factors through several adjustments and models, residual confounders might remain. Second, we used data source which may not fully capture all of the clinical factors associated with discharge bias, meaning that the differences in discharge bias that we observed may be partially attributable to unmeasured clinical variables, which might lead to detection or misclassification biases. Third, MIMIC-III is a single-center database. Thus, future research should use data from multiple centers or hospitals to increase the generalization performance and obtain a more widely usable model. Finally, for internal validation, the calibration plot demonstrated that the predicted probability derived from the nomogram corresponded well with the observed probability. However, further external validation is required to validate the recommended nomogram.

5. Conclusion

We demonstrated that our nomogram outperformed conventional and widely used SOFA scoring systems. This model might be clinically valuable and assist clinicians in tailoring precise management and therapy for ICU patients. Nevertheless, additional studies are required to increase the generalization performance.

Author contributions

Conceptualization: Ran Liu, Haiwang Liu.
Methodology: Haiwang Liu.
Supervision: Zhixue Wang, Yan Li.
Writing – original draft: Ran Liu, Haiwang Liu, Ling Li.
Writing – review & editing: Zhixue Wang, Yan Li.

References

[1] Soares Pinheiro FGM, Santana Santos E, Barreto IDC, et al. Mortality predictors and associated factors in patients in the intensive care unit: a cross-sectional study. Crit Care Res Pract. 2020;2020:1483827–1483827.
[2] Zhai Q, Lin Z, Ge H, et al. Using machine learning tools to predict outcomes for emergency department intensive care unit patients. Sci Rep. 2020;10:20919.
[3] Kane RL, Shamliyan TA, Mueller C, et al. The association of registered nurse staffing levels and patient outcomes—systematic review and meta-analysis. Med Care. 2007;45:1195–204.
[4] Yun K, Oh J, Hong TH, et al. Prediction of mortality in surgical intensive care unit patients using machine learning algorithms. Front Med. 2021;8:621861.
[5] Knaus WA, Zimmerman JE, Wagner DP, et al. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. Crit Care Med. 1981;9:591–7.
[6] Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest. 1991;100:1619–36.
[7] Le Gall JR, Loirat P, Nicolas F, et al. Use of a severity index in 8 multidisciplinary resuscitation centers. Presse Medicale (Paris, France: 1983). 1983;12:1757–61.
[8] Le Gall JR, Lemeshow S, Saulnier F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. JAMA. 1993;270:2957–63.
[9] Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European society of intensive care medicine. Intensive Care Med. 1996;22:707–10.
[10] Le Gall JR, Klar J, Lemeshow S, et al. The logistic organ dysfunction system. A new way to assess organ dysfunction in the intensive care unit. ICU scoring group. JAMA. 1996;276:802–10.
[11] Johnson AEW, Kramer AA, Clifford GD. A new severity of illness scale using a subset of acute physiology and chronic health evaluation data elements shows comparable predictive accuracy. Crit Care Med. 2013;41:1711–8.
[12] Guo C, Lu M, Chen J. An evaluation of time series summary statistics as features for clinical prediction tasks. BMC Med Inform Decis Mak. 2020;20:48.
[13] Keegan MT, Gajic O, Afessa B. Severity of illness scoring systems in the intensive care unit. Crit Care Med. 2011;39:163–9.
[14] Strand K, Flaatten H. Severity scoring in the ICU: a review. Acta Anaesthesiol Scand. 2008;52:467–78.
[15] Bozzetti F, Cotogni P, Lo Vullo S, et al. Development and validation of a nomogram to predict survival in incurable cachectic cancer patients on home parenteral nutrition. Ann Oncol. 2015;26:2335–40.
[16] Stephenson AJ, Di Blasio CJ, Eastham JA, et al. Predicting the 10-year probability of prostate cancer recurrence: an updated postoperative nomogram and a suite of nomograms for patients who are free of disease at one to five years after radical prostatectomy. J Urol. 2004;171:208–9.
[17] Goldberger AL, Amaral LAN, Glass L, et al. PhysioBank, PhysioToolkit, and PhysioNet–components of a new research resource for complex physiologic signals. Circulation. 2000;101:E215–20.
[18] Johnson AEW, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. Sci Data. 2016;3:160035.
[19] Elixhauser A, Steiner C, Harris DR, et al. Comorbidity measures for use with administrative data. Med Care. 1998;36:8–27.
[20] Kim LH, Chen YR. Risk adjustment instruments in administrative data studies: a primer for neurosurgeons. World Neurosurg. 2019;128:477–500.
[21] van Walraven C, Austin PC, Jennings A, et al. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care. 2009;47:626–33.
[22] Pester B, Lehmann T, Leistritz L, et al. Influence of imputation strategies on the identification of brain functional connectivity networks. J Neurosci Methods. 2018;309:199–207.
[23] Bhakta N, Liu Q, Ness KK, et al. The cumulative burden of surviving childhood cancer: an initial report from the St Jude Lifetime Cohort Study (SJLIFE). Lancet. 2017;390:2569–82.
[24] Wijnen BFM, Schat SL, de Kinderen RJA, et al. Burden of disease of people with epilepsy during an optimized diagnostic check for trajectory: costs and quality of life. Epilepsy Res. 2018;146:87–93.
[25] Marshall A, Altman DG, Holder RL. Comparison of imputation methods for handling missing covariate data when fitting a Cox proportional hazards model: a resampling study. BMC Med Res Methodol. 2010;10:112.
[26] Moriarity C, Scheuren F. A note on Rubin's statistical matching using file concatenation with adjusted weights and multiple imputations. J Bus Econ Stat. 2003;21:65–73.
[27] Lambden S, Laterre PF, Levy MM, et al. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. Crit Care. 2019;23:374.
[28] Balachandran VP, Gonen M, Smith JJ, et al. Nomograms in oncology: more than meets the eye. Lancet Oncol. 2015;16:E173–80.
[29] Zhou Z-R, Wang W-W, Li Y, et al. In-depth mining of clinical data: the construction of clinical prediction model with R. Ann Transl Med. 2019;7:796796.–796.
[30] Tibshirani R. The lasso method for variable selection in the Cox model. Stat Med. 1997;16:385–95.
[31] Vincent JL, de Mendonca A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European society of intensive care medicine. Crit Care Med. 1998;26:1793–800.
[32] Ferreira FL, Bota DP, Bross A, et al. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001;286:1754–8.
[33] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315:801–10.
[34] Abhyankar S, Leishear K, Callaghan FM, et al. Lower short- and long-term mortality associated with overweight and obesity in a large cohort study of adult intensive care unit patients. Crit Care. 2012;16:R235.
[35] Dube DS. Influence of overweight on ICU mortality - a prospective study. Chest. 2005;127:683–683.
[36] Holtfreter B, Bandt C, Kuhn SO, et al. Serum osmolality and outcome in intensive care unit patients. Acta Anaesthesiol Scand. 2006;50:970–7.