

ORIGINAL RESEARCH



Nomogram for predicting in-hospital mortality of patients with respiratory failure caused by severe community-acquired pneumonia

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Abstract

Background: To identify clinical factors associated with in-hospital mortality in patients suffering from respiratory failure due to severe community-acquired pneumonia and develop a predictive nomogram for clinical outcomes. **Methods:** A retrospective analysis was conducted on the clinical data of individuals who experienced respiratory failure due to severe community-acquired pneumonia. Univariate analysis investigated the correlation between clinical variables. Multivariate stepwise logistic regression analysis identified independent risk factors for mortality. Based on these factors, a nomogram was established to predict in-hospital mortality. **Results:** Out of the total 527 patients, 225 (42.6%) survived while 302 (57.4%) eventually passed away. There was a positive correlation between age, sepsis, heart rate, and blood lactate levels and in-hospital mortality. On the other hand, there was a negative correlation between systolic and diastolic blood pressure, hemoglobin oxygen saturation, platelets, blood sodium, C reactive protein (CRP), and bicarbonate ion levels. The multivariate analysis revealed that age, heart rate, systolic blood pressure, platelets, blood sodium, CRP, blood lactate, and bicarbonate ion were independent risk factors. The developed nomogram, incorporating eight factors, demonstrated high predictive accuracy, as indicated by the area under the receiver operating characteristic curve (ROC) of 0.813. Both calibration plots and decision curve analysis supported the nomogram's predictive accuracy and clinical utilization. **Conclusions:** The study successfully created a nomogram that includes eight independent risk factors for predicting in-hospital mortality in patients with respiratory failure caused by severe community-acquired pneumonia. This tool can assist clinicians in evaluating patient prognosis and making well-informed decisions about patient care.

Keywords

Community-acquired pneumonia; Nomogram; Severe pneumonia; Respiratory failure; Intensive care unit

1. Introduction

Community-acquired pneumonia (CAP) is a common disorder associated with significant morbidity and mortality [1, 2]. The overall prevalence of community-acquired pneumonia varies from 1 to 25 occurrences per 1000 individuals annually [3]. Severe CAP (sCAP) is the most life-threatening form of CAP, characterized by high morbidity and mortality [4]. *Streptococcus pneumoniae* is the primary pathogen of sCAP [5].

Acute hypoxemic respiratory failure, primarily due to pulmonary infection, is one of the leading causes of intensive care unit (ICU) admission in adults, often requiring endotracheal intubation and invasive mechanical ventilation [6]. A considerable percentage of individuals experiencing acute hypoxemic respiratory failure satisfy the diagnostic criteria for acute respiratory distress syndrome (ARDS) [7]. Tracheal

intubation often requires invasive mechanical ventilation to save lives and ensure proper gas exchange. However, it is important to note that this intervention can also increase the overall morbidity and mortality of ARDS [8]. Prompt evaluation and suitable therapeutic approaches for individuals experiencing respiratory failure and pulmonary infection can significantly reduce mortality rates.

However, the lack of an effective metric or tool for evaluating the prognosis and condition of patients with hypoxic respiratory failure and or severe pneumonia frequently results in delays in administering accurate treatment for patients. In addition, the existing tools used to predict mortality of pneumonia such as Confusion, urea, respiratory rate blood pressure, age65 (CURB-65), Pneumonia Severity Index (PSI), Sequential Organ Failure Assessment (SOFA) and Acute Physiology

and Chronic Health Evaluation (APACHE) scores often lack accuracy and precision [9–12]. Nomograms are gradually being acknowledged as valuable instruments for personalized risk prediction and have been employed in several medical domains, particularly for evaluating clinical prognosis [13–15].

This retrospective study aimed to identify prognostic factors and develop a prognostic nomogram model for predicting hospital mortality in ICU patients with acute hypoxemic respiratory failure and severe pneumonia. The study was conducted due to the high mortality and poor prognosis associated with these conditions.

2. Materials and methods

2.1 Study design

This study is a retrospective cohort study undertaken at a single center, specifically our hospital. The study included patients who had developed respiratory failure as a result of severe community-acquired pneumonia and were hospitalized to the intensive care unit (ICU) between January 2021 and December 2023.

2.2 Patients selection

Patients were eligible for inclusion provided they satisfied the criteria for severe pneumonia as outlined by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) [16], of which the guideline was recently updated [17]. Severe CAP is characterized by the presence

of the presence of either one major criterion or a minimum of three minor criteria. The primary indicators for severe pneumonia are the presence of acute respiratory failure necessitating mechanical ventilation, or the occurrence of severe shock requiring the use of vasopressors. The minor criteria for this condition are as follows: (1) Blood urea nitrogen (BUN) >20 mg/dL (7.14 mmol/L); (2) Confusion or disorientation; (3) Hypotension requiring aggressive fluid resuscitation; (4) Hypothermia with a core temperature $<96.8^{\circ}\text{F}$ (36°C); (5) Leukopenia with white blood cell count $<4000/\mu\text{L}$ ($4.00 \times 10^9/\text{L}$) due to infection alone (*i.e.*, not chemotherapy induced); (6) Multilobe infiltrates; (7) PaO_2 to FiO_2 ratio ≤ 250 ; (8) Respiratory rate >30 breaths/minute; (9) Thrombocytopenia with a platelet count $<100,000/\mu\text{L}$ ($100 \times 10^9/\text{L}$) [18]. Respiratory failure was defined as either hypoxemic respiratory failure ($\text{PaO}_2 < 60$ mmHg with a normal/low arterial carbon dioxide tension (PaCO_2)) or hypercapnic respiratory failure ($\text{PaCO}_2 > 50$ mmHg) requiring mechanical ventilation [19]. The whole process of patient selection was shown in Fig. 1.

2.3 Data collection

Clinical data, including medical history, demographic information, symptoms, vital signs, comorbidities, laboratory findings at ICU admission, clinical management, and outcomes, were extracted from electronic medical records. Demographic data included age and sex. Comorbidities encompassed hypertension, diabetes, chronic obstructive pulmonary disease (COPD), and chronic renal disease. Vital signs included heart rate, respiratory rate, blood pressure, and hemoglobin oxygen

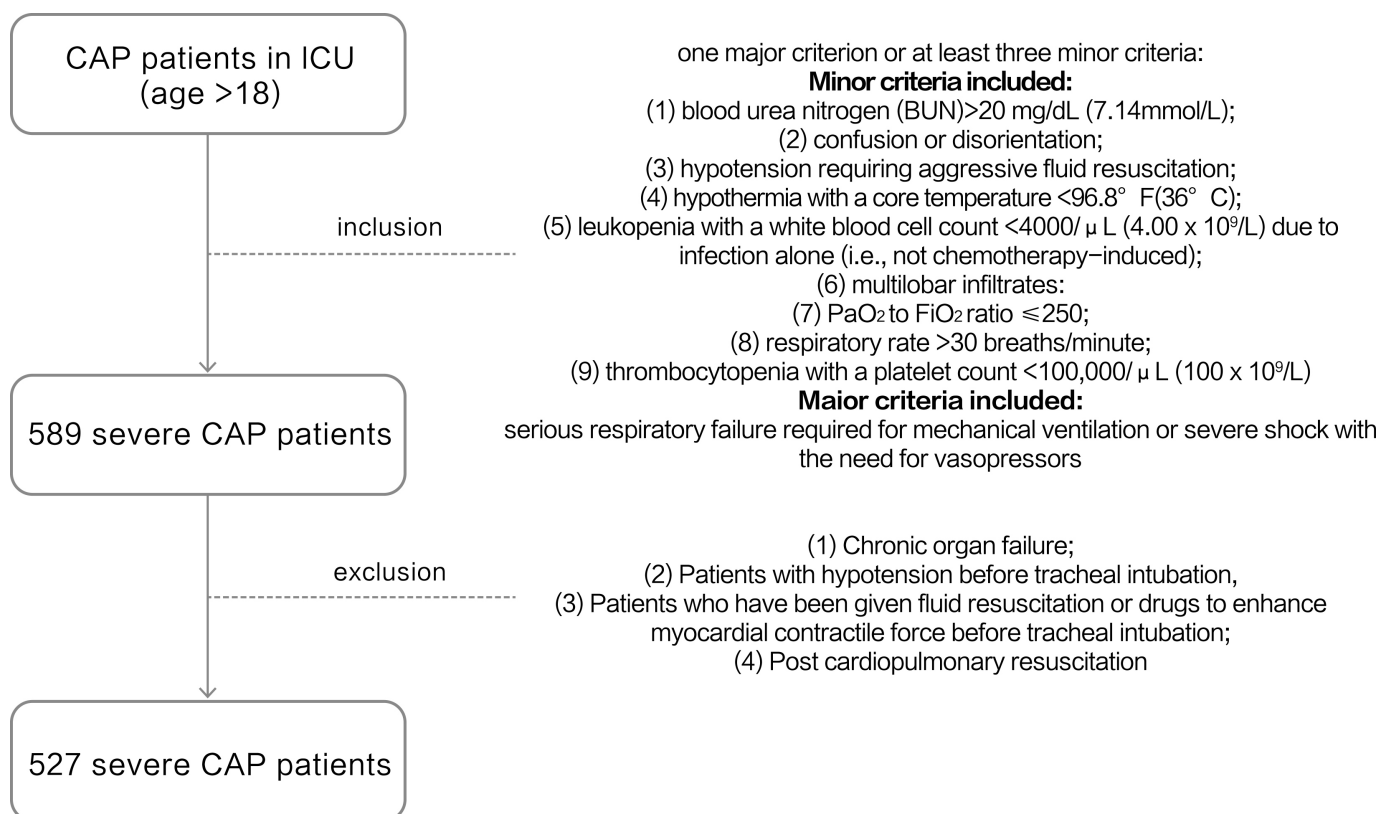


FIGURE 1. Flow Chart of the whole patient selection process. CAP, community-acquired pneumonia; ICU, intensive care unit.

saturation. Laboratory findings involved white blood cell count, neutrophils, lymphocytes, hemoglobin, platelets, albumin, creatinine, blood glucose, blood sodium, blood potassium, pH, procalcitonin, CRP, lactic acid, and bicarbonate (bicarbonate ion). Clinical management details included direct ICU admission, invasive mechanical ventilation requirement, and vasopressor requirement. Sepsis was assessed using the Sequential Organ Failure Assessment (SOFA) score and APACHE (Acute Physiology and Chronic Health Evaluation)-II score. The primary outcome was hospital mortality. Data were independently cross-checked by two clinicians. Clinical characteristics at ICU admission were compared between the survival and non-survival groups, and a nomogram was developed to predict hospital mortality in ICU patients with severe pneumonia.

2.4 Univariate and multivariate analysis

In order to investigate the between basic clinical characteristics such as demographic data, vital signs, laboratory results and patient outcomes a univariate and multivariate analysis was done. Variables with more than 20% missing data were excluded. For variables with less than 20% missing data, multiple imputations were performed using the “mice” R package. The total patients were randomly divided into a 70% training set to develop the prediction model and a 30% testing set for independent internal validation using the “caret” R package. The training set was used to develop the prediction model, while the testing set was used to validate its performance. The least absolute shrinkage and selection operator (LASSO) method was used to select candidate predictive features, and a 10-fold cross-validation method was applied to determine the regularization parameter lambda, which yielded the minimum mean cross-validated concordance index. Variables selected by the LASSO method were included in the multivariate logistic regression analysis to identify independent risk factors.

2.5 Nomogram construction

The prediction model was developed using the “rms” R package based on the results of the multivariate logistic regression analysis. Finally, a nomogram for predicting hospital mortality was constructed based on the prediction model. The prediction nomogram was validated in both the training and testing sets. Calibration, discrimination, and clinical usefulness of the nomogram were assessed to evaluate its performance. Prediction accuracy was evaluated using Harrell’s concordance index (C-index) and its 95% Confidence Interval (CI), as well as the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. Calibration curves were used to compare predicted and actual values, while decision curve analysis (DCA) was performed to assess the clinical utility of the prognostic nomogram.

2.6 Statistical analysis

The sample size ($n = 527$) was determined based on available data, with a mortality rate of 302, exceeding the recommended event per variable value of ten. Baseline characteristics were compared between survivors and patients who ultimately died.

Categorical variables were presented as frequencies and percentages (%) and compared using χ^2 tests. The Kolmogorov-Smirnov test was used to assess the normality of continuous data. Continuous data normally distributed were expressed as the mean and standard deviation and compared using the Student’s t test. Non-normally distributed data were expressed as median (IQR) and compared using the Mann Whitney U test. A two-tailed p -value < 0.05 was considered statistically significant. Unless stated otherwise, all other statistical analyses were conducted using R Studio, version 4.0.5.

3. Results

3.1 Patients characteristics

The study included a cohort of 527 patients who experienced respiratory failure as a result of severe community-acquired pneumonia. Out of the total, 225 individuals (42.6%) were classified as survivors, whereas 302 individuals (57.4%) were categorized as patients who eventually passed away. Out of the total of 527 patients, the male population constituted the majority, making up 64.7% (341 individuals), while the female population accounted for 35.3% (186 individuals). Univariate analysis identified correlations between several clinical variables and patient outcomes. Age, heart rate, and blood lactate levels were positively associated with in-hospital mortality. In contrast, systolic and diastolic blood pressure, hemoglobin oxygen saturation, platelet count, blood sodium levels, CRP levels, and bicarbonate ion levels were negatively associated with mortality (Table 1).

3.2 Multivariate logistic regression variable screening

Multivariate logistic regression analysis was conducted using a stepwise method with the previously mentioned factors. The analysis identified age, heart rate, systolic blood pressure, platelet count, blood sodium levels, CRP levels, blood lactate levels, and bicarbonate ion levels as independent risk factors for mortality in patients with sCAP and respiratory failure (Table 2).

3.3 Nomogram development

A nomogram was developed to predict the in-hospital outcomes of patients with the eight identified independent risk factors (Fig. 2). Each predictive factor was assigned a single score, displayed on the top line of the nomogram. The total score for each patient was calculated as the sum of these individual scores. The nomogram provided the predicted probability of hospital mortality based on the total scores. As shown in the nomogram, patients with higher age, lower systolic blood pressure, higher heart rate, lower blood sodium, higher blood lactate, lower bicarbonate ion, lower platelet count, and lower CRP levels received higher total points, indicating a more unfavorable prognosis.

3.4 Performance of the nomogram model

The ROC curve demonstrated the predictive accuracy of the nomogram (Fig. 3). The AUC in the testing set was 0.813

TABLE 1. Characteristics of the patients.

Variables	Overall (n = 527)	Survival (n = 225)	Death (n = 302)	<i>p</i>
Demographic data				
Age, yr	63.64 ± 17.62	60.50 ± 17.73	65.98 ± 17.19	<0.001
Male gender (%)	341 (64.7%)	140 (62.2%)	201 (66.6%)	0.383
Comorbidities (%)				
Hypertension	170 (32.3%)	74 (32.8%)	96 (31.7%)	0.567
Diabetes	112 (21.3%)	50 (22.2%)	62 (20.5%)	0.639
Chronic obstructive pulmonary disease	152 (28.8%)	63 (28.0%)	89 (29.6%)	0.712
Chronic renal disease	123 (23.3%)	46 (20.4%)	77 (25.5%)	0.175
Vital signs				
Heart rate, times/min	120.70 ± 26.77	117.36 ± 27.24	123.19 ± 26.17	0.013
Respiratory rate, times/min	33.50 ± 9.79	33.51 ± 9.68	33.49 ± 11.85	0.982
Systolic blood pressure, mmHg	127.49 ± 27.32	133.86 ± 26.85	122.74 ± 26.73	<0.001
Diastolic blood pressure, mmHg	74.88 ± 18.28	77.86 ± 18.38	72.66 ± 17.92	0.001
Hemoglobin oxygen saturation	84.57 ± 11.86	85.99 ± 11.75	83.52 ± 11.85	0.018
Laboratory results				
White blood cells, 10 ⁹ /L	13.79 ± 20.55	13.61 ± 14.99	13.92 ± 23.89	0.864
Neutrophils, 10 ⁹ /L	10.70 ± 8.57	11.07 ± 7.48	10.42 ± 9.30	0.391
Lymphocytes, 10 ⁹ /L	0.88 ± 3.06	1.07 ± 3.94	0.73 ± 2.17	0.209
Hemoglobin, g/L	107.51 ± 29.93	108.94 ± 30.51	106.44 ± 29.49	0.344
Platelets, 10 ⁹ /L	129.99 ± 107.43	151.69 ± 103.72	113.80 ± 107.47	<0.001
Albumin, g/L	30.71 ± 11.66	31.37 ± 9.22	30.22 ± 13.18	0.264
Creatinine, μmol/L	133.30 ± 163.34	129.00 ± 182.35	136.50 ± 147.82	0.602
Blood glucose, mmol/L	9.97 ± 9.03	10.46 ± 11.09	9.60 ± 7.12	0.284
Blood sodium, mmol/L	135.55 ± 9.27	136.47 ± 7.26	134.86 ± 10.47	0.049
Blood potassium, mmol/L	4.25 ± 4.34	3.88 ± 0.82	4.52 ± 5.68	0.093
PH*	5.56 ± 3.15	5.56 ± 3.17	5.56 ± 3.14	0.997
Procalcitonin, ng/mL	13.27 ± 38.58	11.74 ± 29.35	14.42 ± 44.24	0.430
CRP, mg/L	91.05 ± 125.30	107.60 ± 132.59	78.72 ± 118.30	0.009
Blood lactate	2.87 ± 3.75	2.15 ± 2.79	3.41 ± 4.25	<0.001
bicarbonate ion	16.68 ± 12.55	18.45 ± 13.20	15.35 ± 11.90	0.005

*PH, *pondus hydrogeni*.

TABLE 2. Logistic analysis.

Variables	OR ¹	95% CI ²	<i>p</i>
Age, yr	1.032	1.019–1.044	<0.001
Heart rate, times/min	1.012	1.004–1.020	0.002
Systolic blood pressure, mmHg	0.983	0.973–0.993	0.001
Platelets, 10 ⁹ /L	0.998	0.996–0.999	0.019
Blood sodium, mmol/L	0.965	0.940–0.991	0.009
CRP, mg/L	0.998	0.997–0.999	0.018
Blood lactate	1.105	1.036–1.178	0.003
bicarbonate ion	0.984	0.969–0.999	0.048

¹OR, odds ratio; ²CI, confidence interval.

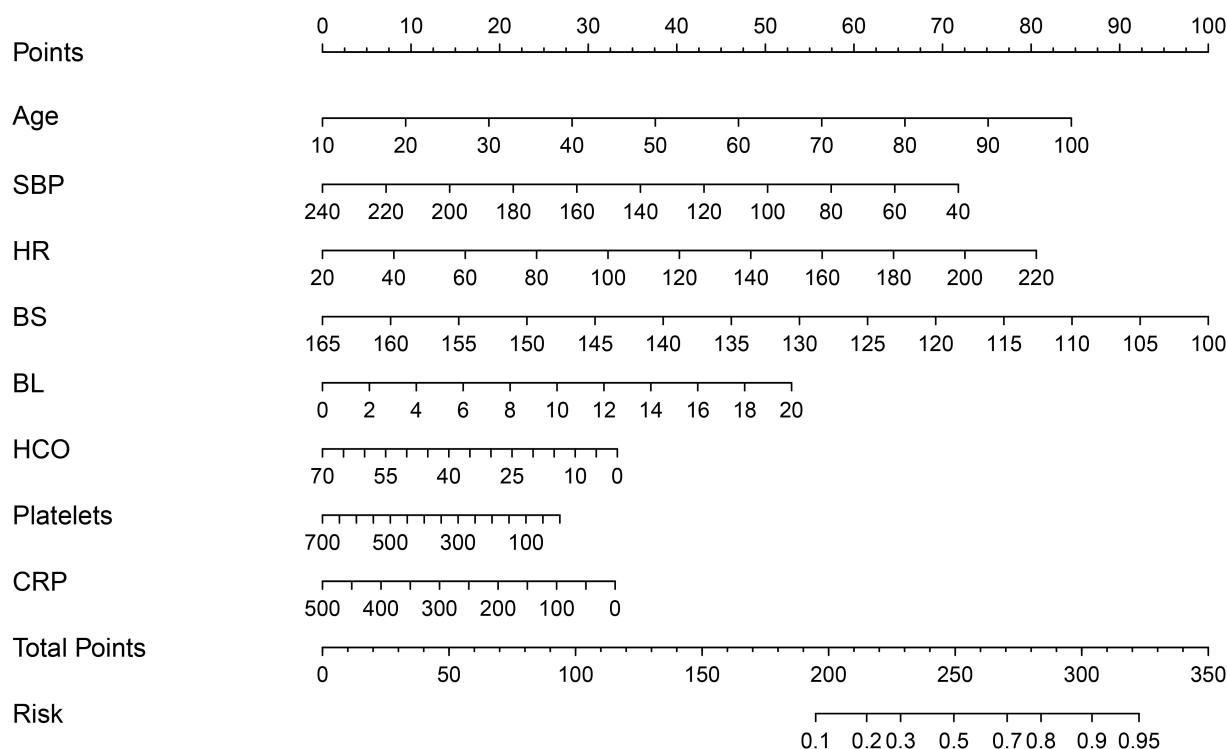


FIGURE 2. Nomogram to predict hospital mortality of patients with sCAP experiencing respiratory failure in the ICU. SBP, systolic blood pressure; HR, heart rate; BS, blood sodium; BL, blood lactate; HCO, bicarbonate ion; CRP, C reactive protein; sCAP, severe community-acquired pneumonia; ICU, intensive care unit.

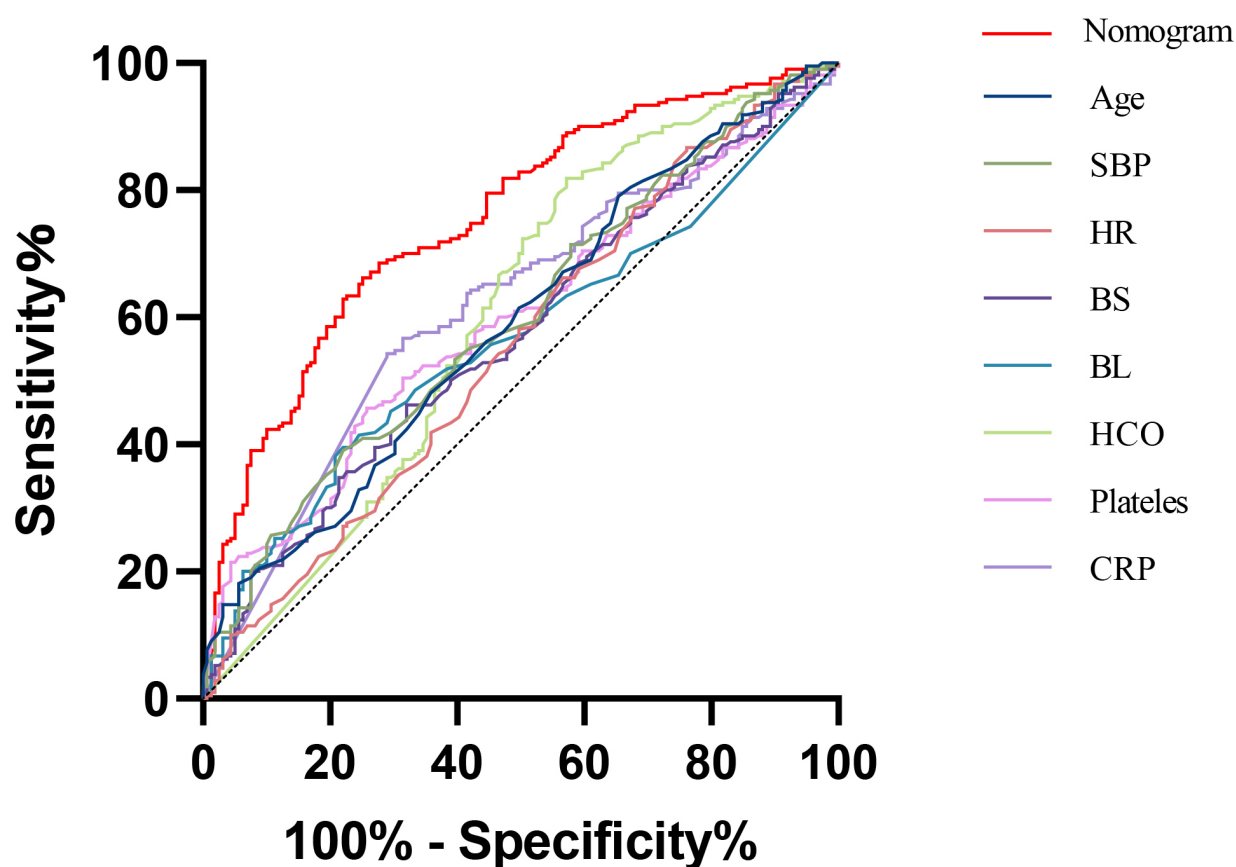


FIGURE 3. ROC (receiver operating characteristic) analysis. SBP, systolic blood pressure; HR, heart rate; BS, blood sodium; BL, blood lactate; HCO, bicarbonate ion; CRP, C reactive protein.

(95% CI: 0.803–0.694), indicating good predictive performance. Calibration plots showed that the nomogram had good predictive accuracy for hospital mortality compared to the 45-degree ideal model (Fig. 4), which indicated that the nomogram curve perfectly accorded with the trend of reference ideal curve. Decision curve analysis demonstrated the net benefits obtained from the application of our nomogram in both the training and testing sets (Fig. 5), from which we could discover that the Model Predicted Risk Probability was greater than the Threshold Probability all the time. Therefore, the model nomogram showed the ideal predictive accuracy under the complete and comprehensive estimation.

4. Discussion

The present study offers a thorough analysis of factors influencing in-hospital mortality among patients with sCAP experiencing respiratory failure. Our findings highlight the importance of several clinical parameters as independent predictors of mortality, which have been incorporated into a novel nomogram designed to aid clinicians in assessing patient prognosis. Moreover, the clinical factors we adopted in this study were more comprehensive and complete than the APACHE II or SOFA scores, which were divided into three parts demographic data, vital signs and laboratory results.

Our examination of 527 patients revealed a mortality rate of 57.4%, which is consistent with the high morbidity and mortality rates associated with CAP in previous studies, particularly in those with severe presentations [20–26]. The predominance of male patients in our study (64.7%) aligns with existing literature that suggests men are more susceptible to severe CAP [27, 28]. This could be attributed to differences in lifestyle, comorbidities, or inherent biological factors between genders [29]. The strong correlation between conventional clinical parameters such as age, sepsis, heart rate, and blood lactate with in-hospital mortality found in our univariate analysis aligns with the established understanding of CAP severity markers.

The multivariate logistic regression analysis identified eight independent risk factors for mortality in patients with sCAP and respiratory failure. These factors include both physiological parameters: age, heart rate, systolic blood pressure, and blood sodium, and laboratory markers: platelet count, CRP, blood lactate, and bicarbonate ion. These findings are in line with previous research that has highlighted the prognostic value of these factors in patients with CAP [30–32]. The inclusion of both types of markers in the analysis underscores the complexity of CAP and the multifactorial nature of its impact on patient outcomes.

Currently, the prognosis of CAP or hospital-acquired pneu-

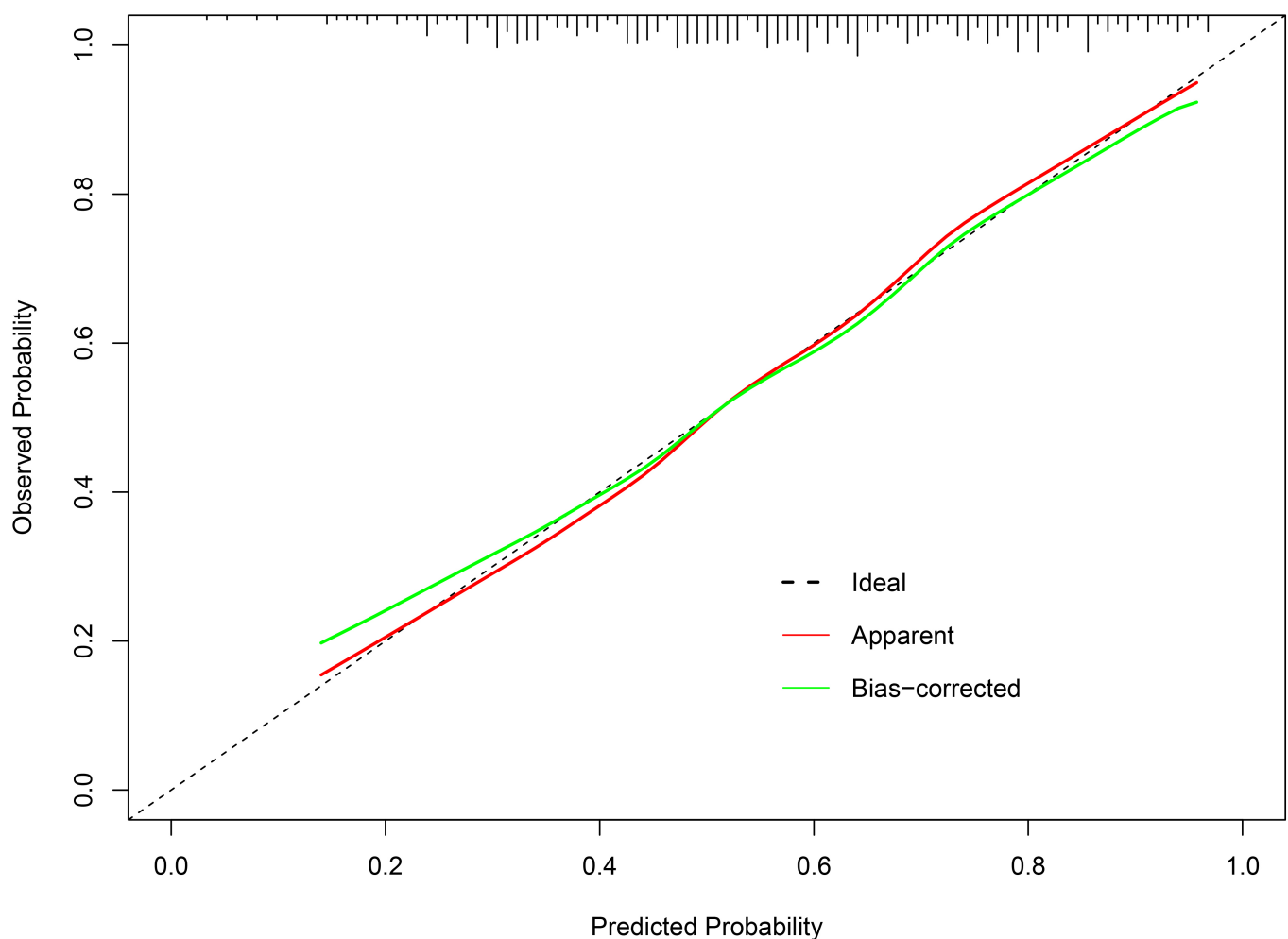


FIGURE 4. Calibration curve analysis.

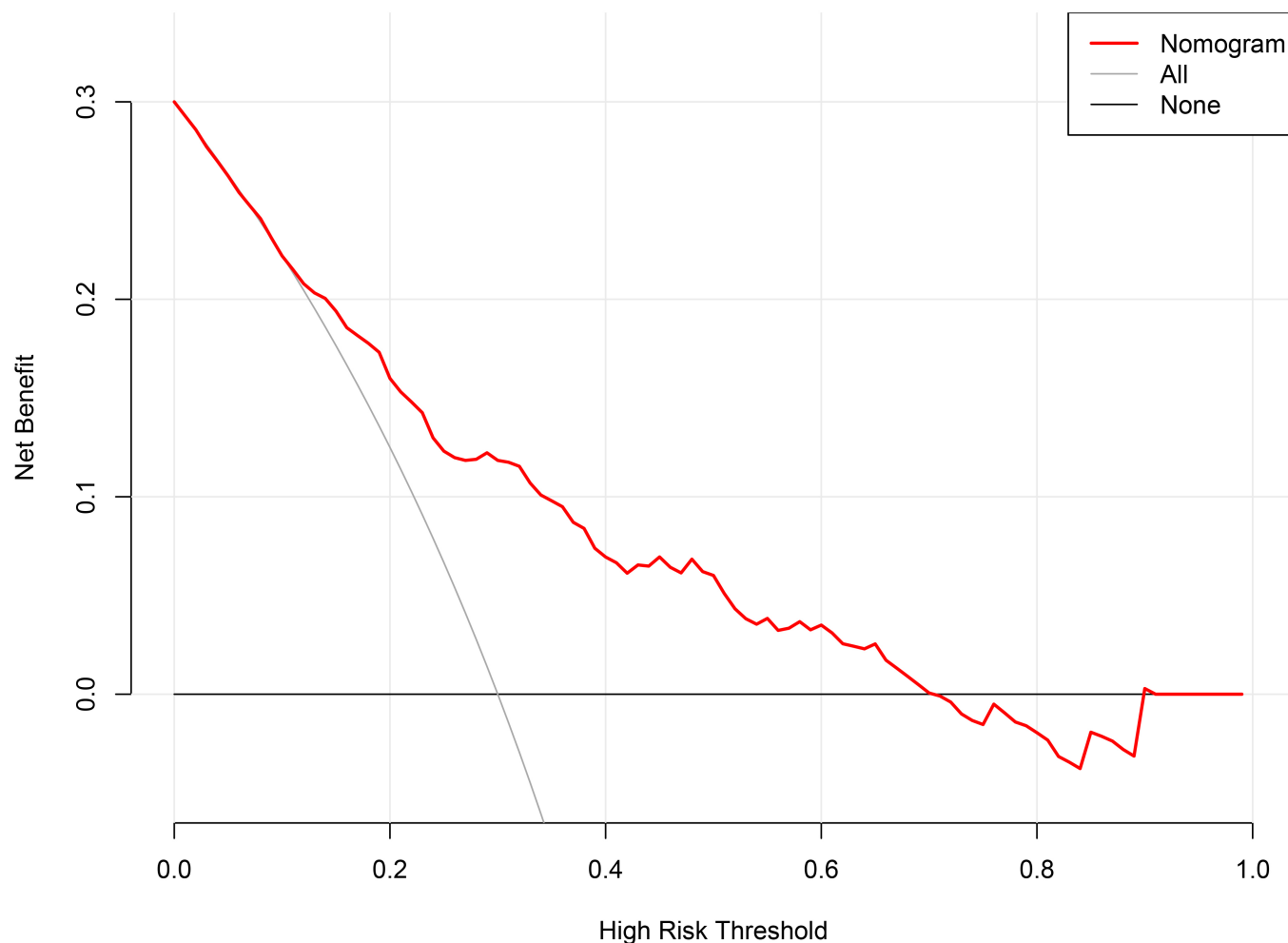


FIGURE 5. Decision curve analysis.

monia (HAP) is commonly assessed using pneumonia severity index (PSI), acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment (SOFA) [33, 34]. Typically, these scoring scales consist of three components: demographic data, vital signs and laboratory results. Although our nomogram only adopted eight clinical factors which were fewer in comparison to that present in the three scoring scales, it incorporates two crucial parameters for CRP and blood lactate that are not included in the three scales. CRP is an acute-phase protein primarily synthesized in the liver. Its production is swiftly triggered by cytokines, notably interleukin (IL)-6, in response to infection or tissue inflammation [35]. In patients with severe CAP, a reduction of CRP levels on the second day was found to be significantly associated with a higher risk of 30-day all-cause mortality [33].

Blood lactate is an essential indicator of insufficient tissue perfusion and cellular hypoxia [36]. Recent research has confirmed that blood lactate is a reliable predictive biomarker for developing adverse outcomes in patients with sepsis and blood lactate measured at admission in patients with CAP could forecast a poor prognosis independently of other indicators [37]. Besides, Zhang *et al.* [34] previously have conducted comparative study on the values of PSI, APACHE II and SOFA scores in prognosis of Chinese patients with hospital-acquired pneumonia. The study revealed that the AUC values of the

three scoring scales were 0.80, 0.73 and 0.66 respectively, all of which were lower than that of our nomogram (AUC = 0.813). Our nomogram seemed to be able to contribute to a better predictive accuracy for the prognosis of CAP.

Managing patients with CAP depends critically on currently in use severity assessment techniques such as CURB-65, PSI and National Early Warning Score (NEWS) [38–40]. However, their predictive accuracy for CAP patients with respiratory failure is somewhat limited. To address this shortcoming, we developed a nomogram designed to predict in-hospital outcomes specifically for very elderly patients with CAP. The nomogram incorporates eight independent variables as depicted in Fig. 1. These factors include age, systolic blood pressure, heart rate, blood sodium, blood lactate, bicarbonate (HCO_3^-), platelets, and CRP. Each factor was assigned a score presented on the top line of the nomogram.

Clinicians calculate a patient's total score by summing the individual scores from each of these predictors. The total score corresponds to the predicted probability of hospital mortality, which is displayed at the bottom of the nomogram. Higher total scores, indicating a worse prognosis, are typically associated with older age, lower systolic blood pressure, higher heart rate, lower blood sodium levels, higher blood lactate levels, lower bicarbonate levels, lower platelet counts, and lower CRP levels. This nomogram allows clinicians to quickly assess the

severity and mortality risk of a patient's condition, thereby aiding in crafting appropriate and targeted treatment strategies. Doctors can apply more intensive therapies to patients with higher risk scores by categorizing them into different risk groups.

The nomogram attained a satisfactory AUC value, indicating the model's robust discriminatory ability and practical usefulness. By using indicators commonly seen in typical healthcare settings, our nomogram provides a precise way to identify groups of CAP patients who are at high risk. This has important benefits for both clinical practice and society as a whole. In addition, this uncomplicated risk assessment tool is expected to be favorably embraced by healthcare practitioners.

The development of a nomogram incorporating these eight independent risk factors represents a contribution to the clinical management of CAP. And the capability to reasonably predict in-hospital mortality (AUC: 0.813) empowers clinicians to make informed decisions regarding the level of care and potential interventions. The calibration plot and decision curve analysis further validate the clinical utilization of our nomogram, demonstrating its strong performance in both the training and testing sets. Moreover, it gives clear advantages across various choice thresholds. The nomogram created in this research represents a significant advancement in the personalized evaluation of risk for patients with severe CAP. By incorporating both physiological and laboratory markers in the nomogram enables a thorough assessment of patient risk. This is particularly important given the complex nature of CAP, where a single parameter often does not provide sufficient prognostic information.

The nomogram's robust performance in both the training and testing sets indicates that it has the potential to be a significant supplement to current clinical guidelines for managing CAP. However, it is important to note that while the AUC of 0.813 indicates good predictive ability, there is still room for improvement. Future studies could explore the integration of additional variables, such as comorbid conditions, immune response markers, and genetic predispositions, to enhance the nomogram's predictive accuracy and precision. The decision curve analysis further underscores the nomogram's clinical utilization by demonstrating its net benefit across a range of threshold probabilities. This suggests that the nomogram could be used to make more nuanced decisions regarding patient care, such as the need for intensive care admission or the initiation of advanced therapeutic interventions.

Although our study has made significant advances to the understanding of the risk factors for in-hospital mortality in patients with sCAP and respiratory failure, it is important to acknowledge some limitations that should be taken into account when interpreting the results. The retrospective nature of our analysis may have caused selection bias, as the inclusion of patients was based on historical medical records, determined by past medical records, which may not correctly represent the full range of disease severity or treatment approaches [41]. Additionally, the use of a single-center dataset limits the external validity and generalizability of our findings to other populations or healthcare settings. Also, the stepwise method used in the logistic regression analysis for variable selection is known to have limitations, including the potential

for overfitting and the introduction of bias, which may affect the stability and reproducibility of the model.

The predictive factors identified may not be the most concise group of variables for mortality risk prediction. Additionally, while the nomogram shows good predictive accuracy, external validation in a broader population is necessary to confirm its applicability across different contexts. Future research should investigate additional potential predictors, such as genetic factors, immune status, and the impact of timely and appropriate antimicrobial therapy, *etc.*, which could further refine the risk stratification provided by the nomogram.

5. Conclusions

In conclusion, our study presents a practical tool for predicting in-hospital mortality among patients with respiratory failure caused by severe community-acquired pneumonia (CAP). The nomogram developed in this study has the potential to assist clinicians in identifying high-risk patients who may benefit from more aggressive management strategies, thus potentially improving outcomes in severe community-acquired pneumonia patients. Additional clinical trials would be necessary to validate the nomogram.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

BX and QH—designed the research study; wrote the manuscript. QH—performed the research. QH and PP—analyzed the data. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was reviewed and approved by the Ethical Committee of the West China Hospital, Approval number: 493 in 2022. All experiments were performed in accordance with relevant guidelines and regulations. Written informed consent was obtained from all patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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