Clinical features and risk factors analysis for poor outcomes of severe community-acquired pneumonia (SCAP) in children: a nomogram prediction model

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Research Article

Keywords: Severe Community-Acquired Pneumonia, Children, Risk factor, Nomogram, Predictive model

Posted Date: May 4th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1538033/v1

Abstract

Background: Early prediction of poor outcomes (PO) is of great significance to the improvement of the longterm prognosis of children with a diagnosis of severe community-acquired pneumonia (SCAP).The study aimed to explore the risk factors for PO of SCAP in children. We further aimed to develop and validate a PO-predictive nomogram model for SCAP in children.

Methods: A population-based, retrospective case-control study was conducted in children with a diagnosis of SCAP who were hospitalized in our hospital from August 1, 2018 to October 31, 2021. Based on the occurrence of poor outcomes (PO), children were divided into PO and the non-PO groups. The multivariate logistic regression model was used to construct the nomogram model.

Results: A total of 300 children with a diagnosis of SCAP were included, and 56 children had PO. The results of multivariate logistic regression analysis revealed that the possible independent risk factors for PO were comorbidity and invasive mechanical ventilation (IMV). In internal validation, the model displayed good discrimination with a C-index of 0.866 (95% CI: 0.772~0.960) and high quality of calibration plots in the nomogram model was noted.

Conclusions: The nomogram model presented good discrimination and calibration in estimating the risk of PO among pediatric patients with a diagnosis of SCAP.

Background

Community-acquired pneumonia (CAP) is a common infectious disease during childhood, especially in infants and young children, and it is the most common reason for hospitalization of children. According to the statistics of the World Health Organization (WHO) in 2016, pneumonia was the leading cause of death in children aged from 1 month to 5 years from 2000 to 2015. Among children younger than 5 years, there were about 156 million cases of pneumonia every year in the world, of which as many as half of the children with CAP needed hospitalization, and as many as 20 million children were seriously ill every year[1−2]. Early prediction of poor outcomes (PO) is of great significance to the improvement of the longterm prognosis of children with a diagnosis of SCAP. A few studies have devised predictive statistical models based on clinical features to predict the severity of disease and the need for more refined respiratory care, which plays a crucial role in optimizing clinical treatment and management of adults with CAP[3−5]. Derek J. Williams et al. developed a predictive statistical model in American children with SCAP[6]; however, no validated models exist to predict clinical outcomes among children with pneumonia in the developing countries.

Of all the predictive statistical models, nomograms can provide highly accurate risk estimation and allow the clinicians to standardize clinical decision making using evidence-based and fully individualized tools[7−8]. However,to our knowledge, there is lack of a nomogram model to predict the risk of poor outcomes in children with SCAP; hence, we established a nomogram based on a multivariate logistic

regression analysis,with the hope to provide ideas for the early diagnosis of SCAP and the timing of intervention.

Methods

Study subjects

This was a population-based, retrospective case-control study of hospitalizations among children aged from > 28 days to 18 years with a diagnosis of SCAP, which was conducted between August 1, 2018 and October 31, 2021 at the Department of Pediatrics of Affiliated Hospital of Southwest Medical University. The clinical data of the included patients were obtained from the hospital's medical records.

Pneumonia was diagnosed by the presence of signs or symptoms of acute infection (e.g., fever), acute respiratory illness (e.g., cough), and radiographic evidence of pneumonia[9–10]. The diagnostic criteria of severe pneumonia fulfilled the criteria for"severe or very severe pneumonia" according to the WHO guidelines(11). CAP was defined as pneumonia diagnosed within 48h of hospital admission; whereas, HAP was defined as pneumonia developing 48h after hospital admission(12).Predictors were pre-determined by clinical expertise and literature review.A pre-determined data collection form was developed to collect the clinical data, such as clinical (history, vital signs, and physical examination findings), laboratory,IMV,and radiological data, which may affect the prognosis of patients(Table 1).All predictors were assessed at the time of admission.The study excluded patients with recent hospitalization, severe immunosuppression, cystic fibrosis, tracheostomy, or a clear alternative diagnosis.

Table 1
Characteristics of the study population, overall

Factors	n(%)	Factors	n(%)
Age<1year	193(64.33)	Grunting	46(15.33)
Male sex	181(60.33)	Nodal breathing	132(44)
Cyanosis	124(41.33)	Nasal flaring	79(26.33)
Septic shock	20(6.67)	Hydrothorax	40(13.33)
Temperature[a]	38(12.67)	Hemoglobin<90 g/L	39(13)
pH<7.35	44(14.67)	WBC<4 or>$10*10^9$	182(60.67)
Malnutrition	37(12.33)	CRP>20 mg/L	83(27.67)
RF	79(26.33)	PCT>0.3 ng/mL	117(39)
Unawareness	38(12.67)	CK-MB>4.87 μg/L	129(43)
Altered mental status	127(42.33)	ALB<35 g/L	37(12.33)
Co-morbidity	102(34)	ALT>40 U/L	66(22)
Tachypnea	54(18)	IMV	42(14)
Wheezing	147(49)	Chest indrawing	256(85.33)

a :Temperature>41℃ or temperature greater than 39℃ for more than 5 days; RF:respiratory failure; WBC:white blood cell count; CRP:high-sensitivity C-reactive protein; PCT:procalcitonin; CK-MB:Creatine kinase isoenzyme; ALB:albumin;ALT:Alanine transaminase; IMV:invasive mechanical ventilation; pH:blood pH.

For the PO group, the following criteria needed to be met:(1)Children with SCAP were diagnosed; (2)Children who died or whose symptoms and signs did not improve at the time of discharge, but their parents discontinued treatment;(3)Patients with complete medical records.

The study was approved by the Ethics Committee of The Affiliated Hospital of Southwest Medical University(No.KY2022004).At least one guardian of all participants signed written informed consent before entering the study.

Statistical analysis

Categorical data were presented as frequency with corresponding percentages, and continuous data were presented as medians with interquartile ranges (IQR). The association between categorical variables was tested using the χ2 test or Fisher exact test, while continuous variables were tested using the Mann-Whitney U test. Univariate and multivariate logistic regression analysis was performed to determine the risk factors related to the occurrence of PO in SCAP patients.And a nomogram was constructed based on

the results of previous multivariate analysis.The effect of individual predictors on the outcome was reported by using the odds ratios (OR) and corresponding 95% confidence intervals (95%CIs). We assessed the ability of our model to differentiate between children with and without the outcome (discrimination) using the concordance index (c-index), which is analogous to the commonly reported area under the receiver operating characteristic (ROC) curve. A c-index of 1 indicated perfect concordance;The c-index of most models is 0.7-0.85[7]. Finally, we graphically assessed the agreement between the predicted and observed outcome frequencies (calibration) by using an internal bootstrap validation (1000 replications with replacement). Analyses were conducted by using SPSS-22 and R-4.1.2. A twotailed $p < 0.05$ was considered statistically significant.

Results

Characteristics of the study population

A total of 300 patients who met the inclusion criteria were enrolled in the study.Among the 300 cases of SCAP patients, PO occurred in 56 patients with RMPP.Median age of the 300 included children was 6.83 months (interquartile range [IQR], 2.1–19);60.33%were boys;34% of children had ≥ 1 co-morbidity (Table 1),and the congenital heart disease was the most common co-morbidity, followed by pulmonary disease,21.67% of children had congenital heart disease;14% of children had IMV during hospitalization.

Univariate regression analysis of the occurrence of PO in patients due to SCAP

All variables listed in Table 1 were used for univariate logistic regression analysis. The univariate analysis results showed that there were no significant difference in age<1year, gender,temperature,tachypnea,wheezing,chest indrawing,grunting,nodal breathing and nasal flaring between the PO group and non-PO group (Table 2).However,compared with non-PO patients,patients with PO had a higher risk of cyanosis, septic shock, malnutrition, unawareness, altered mental status, co-morbidity, respiratory failure and IMV (p<0.05). The comparison of laboratory data found that there was no statistically significant difference in procalcitonin (PCT),C-reaction protein (CRP),WBC count,creatine kinase-MB (CK-MB) and alanine aminotransferase (ALT) levels between the two groups (Table 2).The Hemoglobin,albumin (ALB)and pH levels were significantly lower than those of non-PO group (p<0.05). There was no significant difference in the proportion of patients with hydrothorax between the two groups ($p > 0.05$).

Table 2
Results of univariate analysis

Factors	PO, n(%) ,T = 56	Non-PO, n(%),T = 244	χ2	*P* value
Cyanosis [b]	34(60.71)	90(36.89)	10.67	0.002
Septic shock [b]	11(19.64)	9(3.69)	16.16	<0.0001
Temperature [a]	11(19.64)	27(11.07)	2.30	0.129
PCT>0.3 ng/mL	27(48.21)	110(45.08)	0.08	0.783
CRP>20 mg/dl	17(30.36)	66(27.05)	0.11	0.739
Age<1year	32(57.14)	161(65.98)	1.19	0.275
Male sex	28(50)	153(62.7)	2.56	0.109
Malnutrition [b]	18(32.14)	19(7.79)	22.79	<0.0001
Unawareness [b]	20(35.71)	18(7.38)	30.55	<0.0001
Altered mental status [b]	40(71.43)	87(35.66)	22.43	<0.0001
Co-morbidity [b]	43(76.79)	59(24.18)	53.85	<0.0001
Tachypnea	15(26.79)	39(15.98)	2.91	0.088
Wheezing	17(30.36)	130(53.28)	2.680	0.208
Chest indrawing	45(80.36)	211(86.48)	0.913	0.338
Grunting	12(21.43)	34(13.93)	1.435	0.231
Nodal breathing	21(37.5)	111(45.49)	0.879	0.349
Nasal flaring	11(19.64)	68(27.87)	1.193	0.273
RF [b]	30(53.57)	49(20.08)	24.64	<0.0001
Hemoglobin<90 g/L [b]	14(25)	25(10.25)	7.510	0.006
WBC<4 or>10	38(67.86)	145(59.43)	1.030	0.310
CK-MB>4.87 μg/L	28(50)	101(41.39)	1.048	0.306

a:Temperature>41℃ or temperature greater than 39℃ for more than 5 days

RF:respiratory failure; WBC:white blood cell count; CRP:high-sensitivity C-reactive protein; PCT:procalcitonin; CK-MB:Creatine kinase isoenzyme; ALB:albumin; ALT:Alanine transaminase; IMV:invasive mechanical ventilation; pH:blood pH.

b: $P<0.05$

Factors	PO, n(%) ,T = 56	Non-PO, n(%),T = 244	χ2	*P* value
ALB<35 g/L [b]	17(30.36)	20(8.2)	18.69	<0.0001
ALT>40 U/L	18(32.14)	51(20.9)	2.646	0.104
pH<7.35 [b]	23(41.07)	21(8.61)	35.81	<0.0001
Hydrothorax	11(19.64)	29(11.89)	1.748	0.186
IMV [b]	25(44.64)	17(6.97)	50.61	<0.0001
a:Temperature>41℃ or temperature greater than 39℃ for more than 5 days				
RF:respiratory failure; WBC:white blood cell count; CRP:high-sensitivity C-reactive protein; PCT:procalcitonin; CK-MB:Creatine kinase isoenzyme; ALB:albumin; ALT:Alanine transaminase; IMV:invasive mechanical ventilation; pH:blood pH.				
b: *P*<0.05				

Multivariate regression analysis of the occurrence of PO in patients due to SCAP

The above significant factors on univariate analysis were considered as independent variables,and whether PO occurred was considered as dependent variables, then they were included in the multivariate logistic regression analysis (Table 3). The multivariate analysis showed that co-morbidity (*OR*: 8.649,95% *CI*:3.928 ~ 20.402, *P* < 0.0001) and IMV (*OR*:5.850, 95%*CI*:1.742 ~ 20.816, *P* = 0.0049) were the independent risk factors influencing the occurrence of BO in patients due to SCAP.

Table 3
The results of Multivariate logistic regression analysis

Factors	*P* value	OR	OR(95%CI)	
			Lower limit	Upper limit
Cyanosis	0.657	0.831	0.358	1.863
Septic shock	0.946	1.045	0.274	4.010
Malnutrition	0.173	1.892	0.750	4.730
Unawareness	0.795	1.186	0.315	4.235
Altered mental status	0.193	1.811	0.732	4.436
Co-morbidity [b]	< 0.0001	8.649	3.928	20.402
RF	0.712	0.828	0.293	2.196
Hemoglobin<90 g/L	0.922	0.952	0.341	2.493
ALB<35 g/L	0.610	1.243	0.528	2.837
pH<7.35	0.097	2.275	0.854	6.028
IMV [b]	0.005	5.850	1.742	20.816
RF:respiratory failure; ALB:albumin; IMV:invasive mechanical ventilation; pH:blood pH.				
[b]:*P*<0.05				

The nomogram of PO occurrence and the performance evaluation of the nomogram

Factors, such as cyanosis, RF, and hemoglobin<90 g/L, whose OR were less than 1, were inconsistent with clinical practice; hence, they were not included in the prediction model. The rest of variables obtained from multivariate logistical regression analysis established a nomogram of the risk of PO (Fig. 1). The nomogram was generated by assigning a weighted score to each influencing factor.The highest score is 300 points, and the range of PO incidence is 0.05 to 0.9.A higher score calculated from the sum of the distribution points of each high-risk factor in the nomogram corresponds to a higher risk of occurrence of PO.

The resulting model was internally validated using the Bootstrap validation method. The nomogram demonstrated good accuracy in estimating the risk of occurrence of PO, with an unadjusted C-index of 0.866 (95% CI, 0.772–0.96). And the area under ROC curve was 0.866 (Fig. 2). In addition, The calibration chart showed that the nomogram had a sufficient degree of fit for predicting the incidence of PO in SCAP patients (Fig. 3).

Discussion

CAP is the most common infectious disease during childhood,Nevertheless, no validated nomogram models exist to predict the risk of PO caused by SCAP.Although vaccination has significantly reduced the incidence and mortality of severe pneumonia in children in recent years, this initiative is yet to become universal, and pneumonia remains the leading cause of death among children aged between 1 month and 5 years [11–12]. There are limitations in the evaluation and prognosis of children's condition relying on a single symptom and sign, but there is no precise and practical comprehensive evaluation standard at present and there are no adequate tools to predict their outcomes[13]. Therefore, in this study, univariate analysis and multivariate logistic regression analysis were used to identify the risk factors for PO, and a PO-predictive nomogram was constructed to comprehensively and accurately estimate the risk of PO for each patient with SCAP.

This study showed that SCAP mainly occurred in infancy, and Walker CLF et al. have also shown that the occurrence of and death from SCAP in children were most common in children aged less than 1 year [12]. This is related to the imperfect anatomical and physiological characteristics and functional development of the respiratory system in this age group, which leads to easy invasion by pathogens. The results of this study showed that the gender composition of children had a preponderance for males than females, with a male:female ratio of 1.5:1, and previous studies have shown similar results[12, 14].

This study showed that comorbidity and IMV were independent risk factors for PO in children with SCAP. Congenital heart disease has been found to be the most common co-morbidity in children with SCAP, and children with congenital heart disease may have an increase in pulmonary blood volume, which can lead to repeated infection of respiratory tract[15], hospitalization, and repeated antimicrobial application, which leads to infection with multiple drug-resistant bacteria, and all of these factors may be contribute to a reduction in treatment efficacy. Previous studies have confirmed that basic cardiopulmonary diseases and other systemic diseases, including congenital heart disease, bronchopulmonary dysplasia, cystic fibrosis, and asthma, can induce and aggravate pneumonia[16–17]. Koh JWJC et al. have also shown that co-morbidity was an independent risk factor for PO in patients with SCAP(14). On the other hand, children who require IMV often develop severe hypoxia and illness, while children with SCAP undergoing IMV may experience some complications, such as ventilator-associated pneumonia (VAP), pulmonary barotrauma, laryngeal edema, airway injury, and pneumothorax[18], and these complications can affect the prognosis in severe cases.

In conclusion, our study suggested that active treatment of the co-morbidity in children with SCAP should be carried out to reduce its impact on the course of pneumonia and the prognosis of children. In children requiring IMV, great attention should be paid to the prevention of the above-mentioned complications. For example, the movement of endotracheal intubation should be as gentle as possible, and the assistance of experienced physicians should be requested whenever necessary. In children who have received IMV treatment, more careful care, such as manual lung inflation, vibration expectoration and early functional exercise[19], should be given to prevent the occurrence of IMV complications.

In order to accurately predict the risk of PO in children with SCAP, the study visualized the results of multivariate logistic regression analysis in a simplified and convenient nomogram model, which is convenient for clinical workers to comprehensively evaluate the disease of the children according to various clinical indicators in the treatment process. Based on AUC and calibration curve evaluation,the nomogram model showed good accuracy and consistency, which can effectively help predict the development of PO in children due to SCAP as early as possible and take strong preventive or therapeutic measures, which can improve the outcomes of patients due to SCAP to a certain extent.

However, our study still had some limitations. First, this retrospective study was based on reviewing medical records data from a single institution and with a small simple size. Second, bootstrap repeated sampling was used to verify the model in the study, and thus, it is necessary to validate the results from other centers. In addition, a prospective multi-center in-sample study is required to further confirm the reliability of the nomogram.

Conclusions

In summary,a prognostic model and nomogram for predicting the risk of poor outcomes in children due to SCAP was built and demonstrated good discrimination and calibration in our study. It allowed prediction of outcomes as early as at the time of admission and could help the clinical management of SCAP.

Abbreviations

SCAP: severe community-acquired pneumonia; PO: poor outcomes; IMV: invasive mechanical ventilation; CAP: Community-acquired pneumonia; RF: respiratory failure; WBC: white blood cells count; CRP: high-sensitivity C-reactive protein; PCT: procalcitonin; CK-MB: Creatine kinase isoenzyme; ALB: albumin; ALT: Alanine transaminase; PH: blood pH.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The Affiliated Hospital of Southwest Medical University (No.KY2022004). At least one guardian of all participants signed written informed consent before entering the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declared that they had no conflict of interest.

Funding

This work was supported by research funding from Science and Technology Planning Project of Sichuan Province (No 2019YFS0180). Doctoral Research Initiation Found of Affiliated Hospital of Southwest Medical University (No 21032).

Authors' Contributions

CX and YH conceived and designed this study. JZ,YL and CH conceptualized and supervised this study. CX,XT and WZ collected clinical data and completed statistical analysis. CX and LF curated and drafted the original manuscript. XY and YH reviewed and edited the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We would like to thank all the participants and their families who encouraged the production of this study.

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Figures

Fig.1

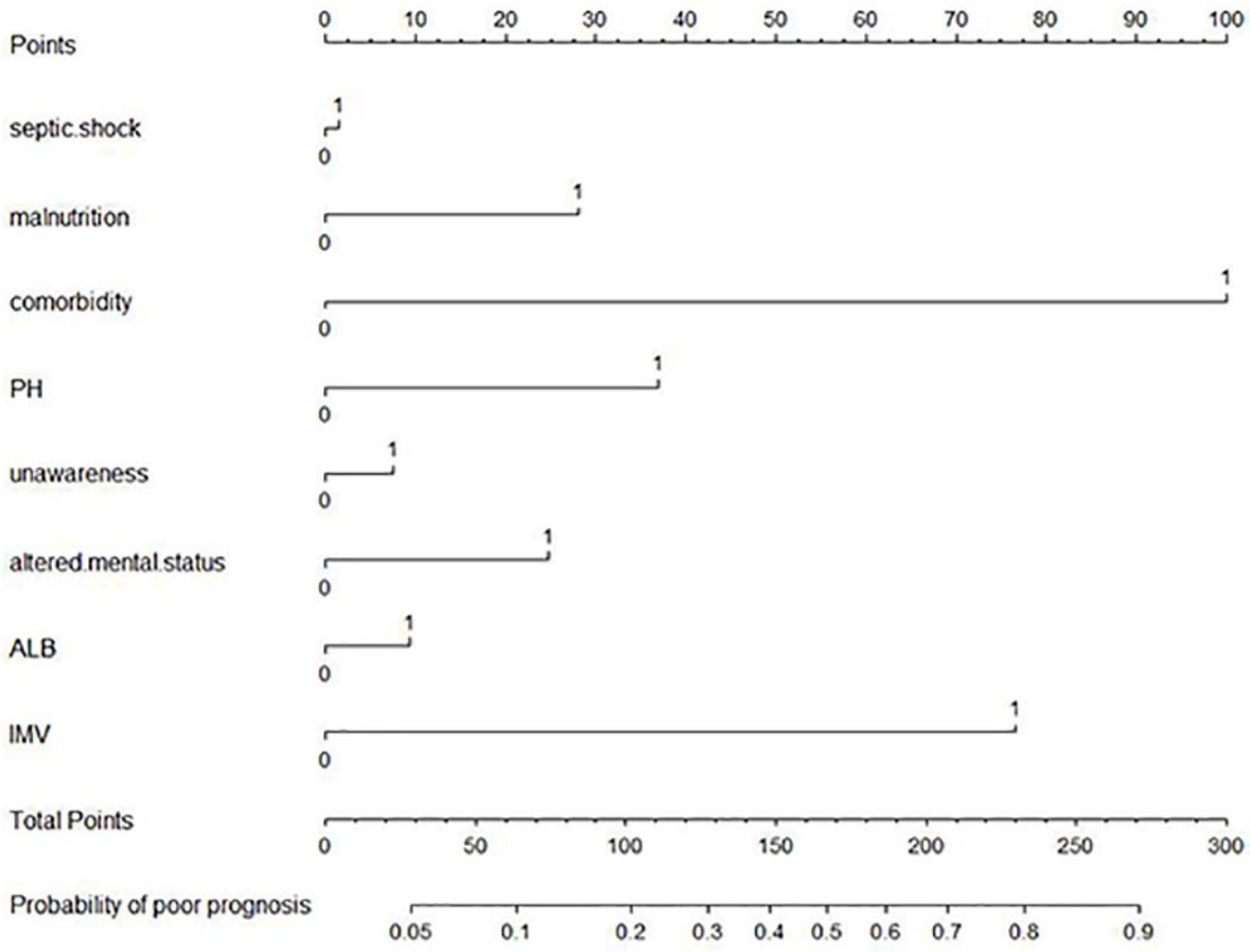

Figure 1

The nomogram for calculating the risk score and predicting the risk of PO in SCAP patients. PH:blood pH;ALB:albumin; IMV:invasive mechanical ventilation.

Fig.2

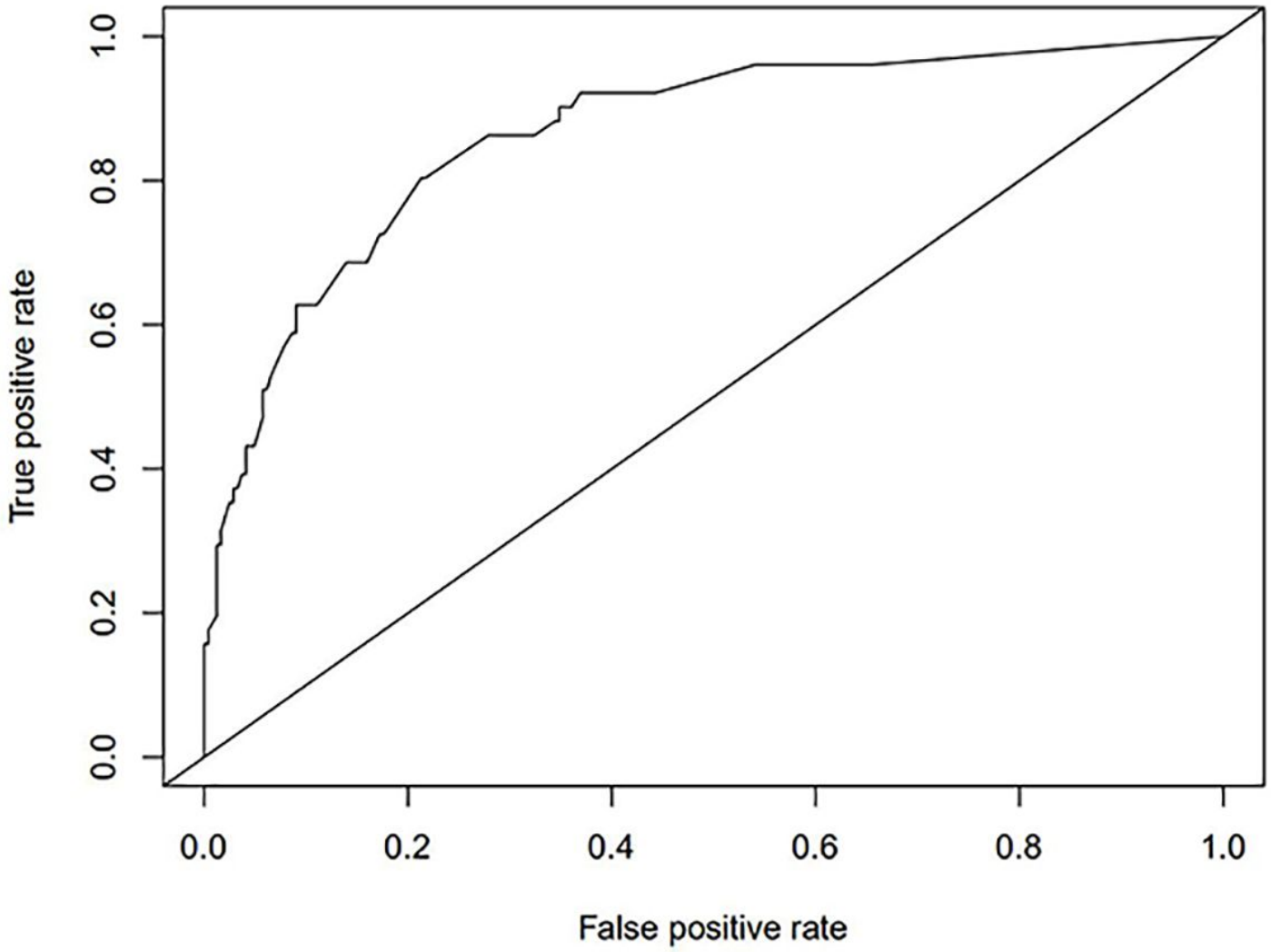

Figure 2

Receiver operating characteristic (ROC) curve and AUC of the nomogram, AUC=0.866(95% CI: 0.772~0.960).

Fig.3

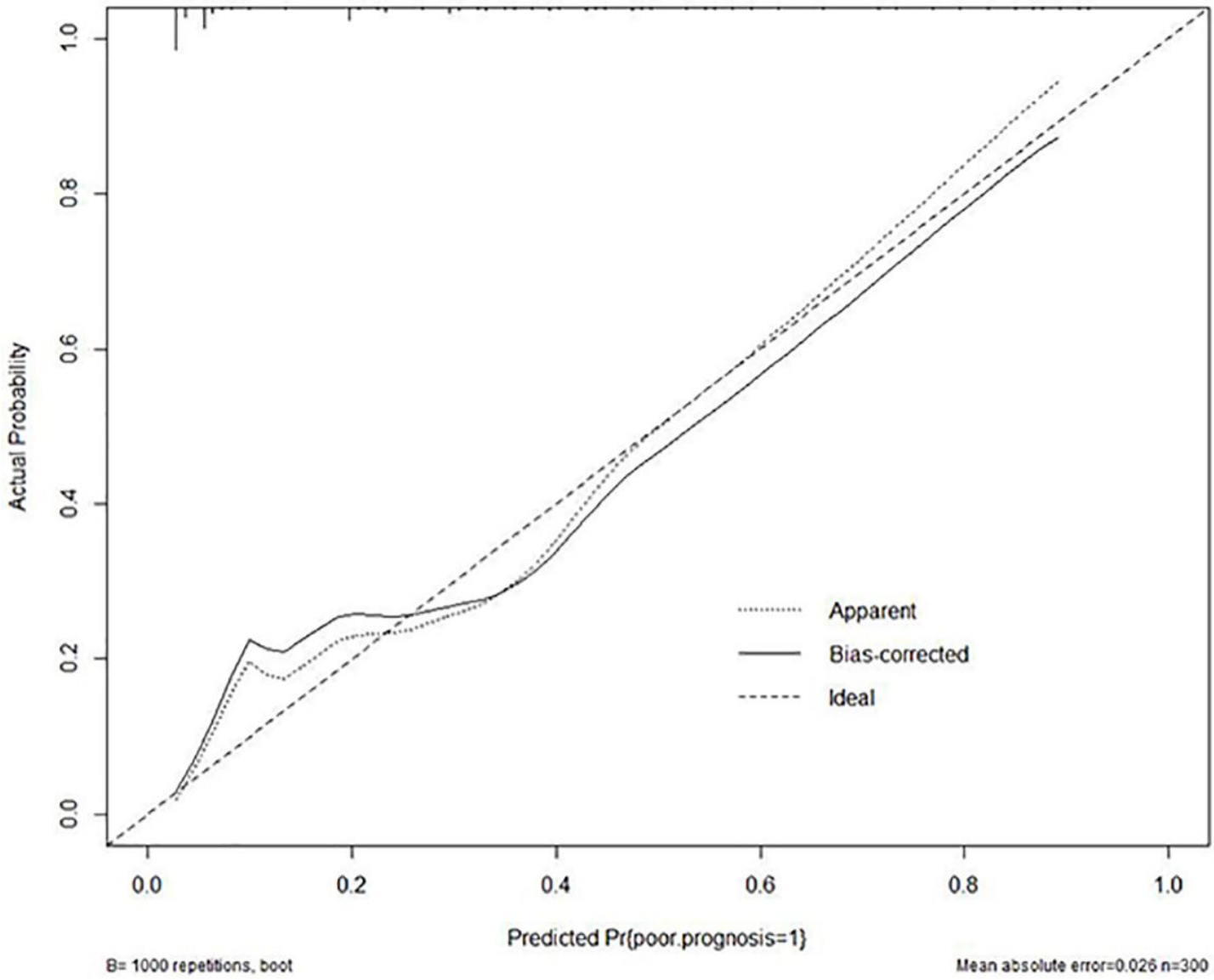

Figure 3

The calibration plot of the nomogram.The horizontal axis indicates the risk of PO occurrence predicted by the nomogram, and the vertical axis represents the actual observed risk of PO occurrence.