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ORIGINAL RESEARCH

Development and Validation of a Risk Mortality Prediction Model for Patients with Pulmonary Tuberculosis Complicated by Severe Community-Acquired Pneumonia in the Intensive Care Unit

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Purpose: The mortality rate from pulmonary tuberculosis (PTB) complicated by severe community-acquired pneumonia (SCAP) in the intensive care unit (ICU) remains high. We aimed to develop a rapid and simple model for the early assessment and stratification of prognosis in these patients.

Patients and Methods: All adult patients with PTB complicated by SCAP admitted to the ICU of a tertiary hospital in Chengdu, Sichuan, China between 2019 and 2021 (development cohort) and 2022 (validation cohort) were retrospectively included. Data on demographics, comorbidities, laboratory values, and interventions were collected. The outcome was the 28-day mortality. Stepwise backward multivariate Cox analysis was used to develop a mortality risk prediction score model. Receiver operating characteristic (ROC) and calibration curves were used to evaluate the model's predictive efficiency. Decision curve analysis (DCA) was used to validate the model's clinical value and impact on decision making.

Results: Overall, 357 and 168 patients were included in the development and validation cohorts, respectively. The Pulmonary Tuberculosis Severity Index (PTSI) score included long-term use of glucocorticoid, body mass index (BMI) <18.5 kg/m^2, diabetes, blood urea nitrogen (BUN) ≥7.14 mmol/L, PO_2/FiO_2 <150 mmHg, and vasopressor use. The area under the ROC curve (AUC) values were 0.817 (95% CI: 0.772–0.863) and 0.814 for the development and validation cohorts, respectively. The PTSI score had a higher AUC than the APACHE II, SOFA, and CURB-65 score. The calibration curves indicated good calibration in both cohorts. The DCA of the PTSI score indicated the high clinical application of the model compared with the APACHE II and SOFA scores.

Conclusion: This prognostic tool was designed to rapidly evaluate the 28-day mortality risk in individuals with PTB complicated by SCAP. It can stratify this patient group into relevant risk categories, guide targeted interventions, and enhance clinical decision making, thereby optimizing patient care and improving outcomes.

Keywords: pulmonary tuberculosis, severe community-acquired pneumonia, mortality risk prediction, intensive care unit

Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, with PTB accounting for 83% of cases.[1] In 2022, the estimated global incidence of TB was 10.6 million, up from 10 million in 2020 and 10.3 million in 2021. Approximately 410,000 patients worldwide developed multidrug-resistant tuberculosis (MDR-TB) or rifampicin-resistant tuberculosis (RR-TB) in 2022. Approximately 3.3% of patients with newly diagnosed TB and 17% of previously treated patients worldwide had MDR-TB or RR-TB. Meanwhile, 1.3 million patients died from TB worldwide

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in 2022.[1] Additionally, the average mortality rate in patients with TB admitted to the ICU reached 52.9%.[2,3] TB remains the second leading cause of death from a single infectious disease worldwide, after coronavirus disease 2019. As a severe stage of pneumonia, SCAP is often associated with serious complications, such as respiratory failure, hemodynamic disturbances, and multiple organ dysfunction. The short- and long-term mortality rates range from 27% to 50%, posing a significant management challenge in the ICU.[4,5] Although PTB and SCAP are caused by different pathogens, their sites of infection are similar. When these two diseases coexist in the same patient, the disease progresses rapidly, treatment becomes significantly more difficult, and the prognosis worsens. Clinical observations suggest that PTB complicated by SCAP is often not fully recognized or effectively managed at an early stage, further increasing the risk of mortality. Therefore, an in-depth investigation and identification of the risk factors that influence the prognosis of patients with PTB complicated by SCAP are crucial.

With the development of critical care medicine, many prognostic models have been developed and applied to critically ill patients. These models play an important role in early clinical prognostic assessment, risk stratification, and clinical intervention. However, these prognostic models have their limitations and may not fully reflect the internal mechanisms of specific diseases. For example, although the Acute Physiology and Chronic Health Evaluation (APACHE) II score can reflect a patient's condition, it has many parameters, is complex and inconvenient to use, and has a limited ability to predict disease outcomes within 24 h of onset.[6] The Sequential Organ Failure Assessment (SOFA) score is specifically used to assess the evolution of patients with sepsis or organ dysfunction, but is less effective in assessing the prognosis of other critically ill patients.[7,8] The confusion, urea >7 mmol/L, respiratory rate >30/min, low blood pressure: diastolic blood pressure <60 mm Hg or systolic blood pressure <90 mmHg, and age >65 years (CURB-65) score is widely used owing to its simplicity, but is mainly suitable for a simple preliminary assessment of pneumonia in outpatient or emergency departments. However, it does not fully reflect the complexity and individual differences of the disease.[9,10] Previous studies have recognized that the APACHE II and SOFA scoring systems tend to underestimate the true risk of mortality in ICU patients with TB.[5] Although some researchers have attempted to develop predictive models for death in ICU patients with TB, the reliability and efficacy of these models have been questioned owing to the small sample sizes, wide variations in results, and the lack of further stratified analysis in some patients with SCAP.[11,12] Risk prediction models for mortality in PTB complicated by SCAP are rare. Therefore, the construction of a risk prediction model for mortality in PTB complicated by SCAP has significant clinical value for early prognostic evaluation, guiding clinical decision making and optimizing medical resource allocation.

Materials and Methods

Study Design and Data Sources

This retrospective observational study was conducted using data from the Public Health Clinical Center of Chengdu, a 1500-bed tertiary infectious disease hospital in Chengdu, southwest China. Data on patients with PTB complicated by SCAP who were admitted to the ICU between 2019 and 2021 (development cohort) and 2022 (validation cohort) were obtained through the electronic medical record management system. The study was conducted in accordance with the tenets of the Declaration of Helsinki (Brazilian Revision 2013) and was approved by the Ethics Committee of the Chengdu Public Health Clinical Center (approval number: YJ-K2022-16-01). As this study was retrospective in nature, did not involve interventional treatment, and used anonymous patient data, the Ethics Committee of the Public Health Clinical Center of Chengdu waived the requirement for obtaining informed patient consent.

Participants

Adult ICU inpatients who met the diagnostic criteria for PTB and SCAP were included. PTB was diagnosed according to the standards of "Tuberculosis Diagnosis WS288-2017" from China, published in 2017. The diagnosis was based on the results of a comprehensive assessment including etiological investigation (such as bacteriology and molecular biology), epidemiological history, evaluation of clinical presentation, imaging examinations, ancillary tests, and differential diagnosis. This comprehensive diagnosis was made by more than two clinicians. This study included patients with

both drug-sensitive and drug-resistant tuberculosis. PTB treatment was based on the World Health Organization standards for initial or continuous treatment.

Following the 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association,[13] SCAP was defined as the fulfillment of 1 primary diagnostic criterion or ≥3 minor diagnostic criteria. The primary diagnostic criteria included (1) requirement for tracheal intubation and mechanical ventilation and (2) occurrence of septic shock requiring vasopressors even after fluid resuscitation. The minor diagnostic criteria included (1) Respiratory rate > 30/min, (2) partial pressure of oxygen in arterial blood/fraction of inspiratory oxygen (PO_2/FiO_2) < 250 mmHg (1 mmHg = 0.133 kPa), (3) presence of infiltrates in multiple lung lobes, (4) consciousness impairment and/or orientation disorders, (5) BUN ≥ 7.14 mmol/L, and (6) hypotension (systolic blood pressure < 90 mmHg, requiring active fluid resuscitation). SCAP was treated in accordance with the 2016 clinical practice guidelines.[13]

Patients (1) with a history of lung cancer, (2) pregnant patients, (3) with an ICU stay of less than 24 hours, and (5) with incomplete clinical data were excluded.

Data Collection

The study retrospectively collected the following data: (1) demographic information (including gender, age, BMI, smoking, alcohol abuse, and long-term use of glucocorticoids), (2) severity of illness (including the APACHE II, SOFA, and CURB-65 scores within 24 h of ICU admission), (3) epidemiology of tuberculosis (including previous tuberculosis infection and drug-resistant tuberculosis), (4) comorbidities (including chronic obstructive pulmonary disease (COPD), diabetes, and human immunodeficiency virus (HIV) infection), (5) laboratory data within 24 h of ICU admission (including white blood cell count, red blood cell count, hemoglobin level, platelet count, alanine aminotransferase level, aspartate aminotransferase level, total bilirubin level, albumin level, BUN level, serum creatinine level, procalcitonin level, C-reactive protein level, lactic acid level, PO_2/FiO_2 ratio, cluster of differentiation (CD)3+ T cells, CD4+ T cells, and CD8+ T cells), and (6) interventions (including invasive mechanical ventilation and vasopressor use). If laboratory data were recorded more than once, the first values were used.

The outcome was all-cause mortality within 28 days. The length of hospital stay and the outcomes of each patient were documented. Patients with a hospital stay <28 days were followed up by telephone to determine their survival status if they failed to attend outpatient clinic appointments.

Statistical Analysis

Descriptive statistics were performed for both cohorts, and the differences were compared. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data were expressed as the mean ± standard deviation and analyzed using an independent *t*-test, while non-normally distributed data were expressed as the median (interquartile range (IQR)) and analyzed using the Mann–Whitney *U*-test. Categorical variables were analyzed using either the chi-square test or Yates' corrected χ^2 test.

The developmental cohort was further divided into survival and non-survival groups based on the 28-day prognosis as the outcome variable. Variables with a P-value of <0.05 were included in the stepwise backward multivariate Cox analysis to identify the independent risk factors for 28-day mortality. Results were presented as hazard ratios (HRs) and 95% confidence intervals (CIs).

The scores for each independent risk predictor were assigned as integer values relative to the regression coefficient (β value). A Pulmonary Tuberculosis Severity Index (PTSI) scoring system was developed based on the independent risk factors of the development cohort to predict the probability of death. The cut-off points were determined using Youden's receiver operating characteristic (ROC) index. Kaplan-Meier analysis was performed to compare the survival between the low- and high-risk groups according to the cutoff value.

In both development and validation cohorts, predictive models were evaluated using the AUC, calibration curve analysis, and DCA.

Statistical analyses were performed using SPSS (version 23.0; IBM, Armonk, New York, USA) and R software (version 4.3.2; http://CRAN.R-project.org; R Foundation, Vienna, Austria). All tests were two-sided, and a P-value of <0.05 was considered significant.

Results

Baseline Demographic Characteristics

Between January 2019 and December 2022, 600 consecutive patients with PTB complicated by SCAP were enrolled in this study. After excluding 75 patients based on the exclusion criteria, only 525 patients were analyzed (Figure 1).

The median age of the patients with PTB complicated by SCAP was 63.0 years (48.0–72.0 years), and 77.5% were men. The median BMI was 19.0 (18.2–21.0) Kg/m^2. Approximately 20.1% of the patients had a previous tuberculosis infection, while 16.6% had drug-resistant tuberculosis. The most prevalent comorbidity was COPD (20.2%), followed by diabetes (19.0%). Of the total patients, 23.0% and 18.3% required vasopressors and invasive mechanical ventilation, respectively. The 28-day mortality rate in this study was 45.14% (Table 1).

The development cohort comprised 357 patients diagnosed with PTB complicated by SCAP between January 2019 and December 2021. Of them, 276 (77.3%) were men, with a median BMI of 19.0 (18.6–20.0) Kg/m^2 and a median age of 62.0 (47.0–72.0) years. The validation cohort comprised 168 patients diagnosed with PTB complicated by SCAP between January and December 2022. Of them, 131 (78.0%) patients were men, with a median BMI of 20.0 (18.0–23.5) Kg/m^2 and a median age of 65.0 (53.5–73.0) years.

Although no significant difference was found between the development and validation cohorts except for albumin, BUN, serum creatinine, C-reactive protein, and lactic acid levels, a significant decrease was observed in the CD3, CD4 and CD8+T cell count (Table 1, $P < 0.05$). In this study, patients with PTB complicated by SCAP exhibited severe malnutrition and decreased immune function.

Development of the Risk Prediction Score Model

The Results of the development cohort are presented in Table 2, with a detailed summary of the statistical and P-values. Fourteen statistically significant ($P < 0.05$) and clinically significant variables were identified. These included age; BMI; long-term use of glucocorticoids; diabetes; albumin level; BUN level; procalcitonin level; lactic acid level; PO_2/FiO_2 ratio; CD3+ T, CD4+ T, and CD8+ T cell counts; invasive mechanical ventilation; and vasopressor use (Supplementary Table 1). Further

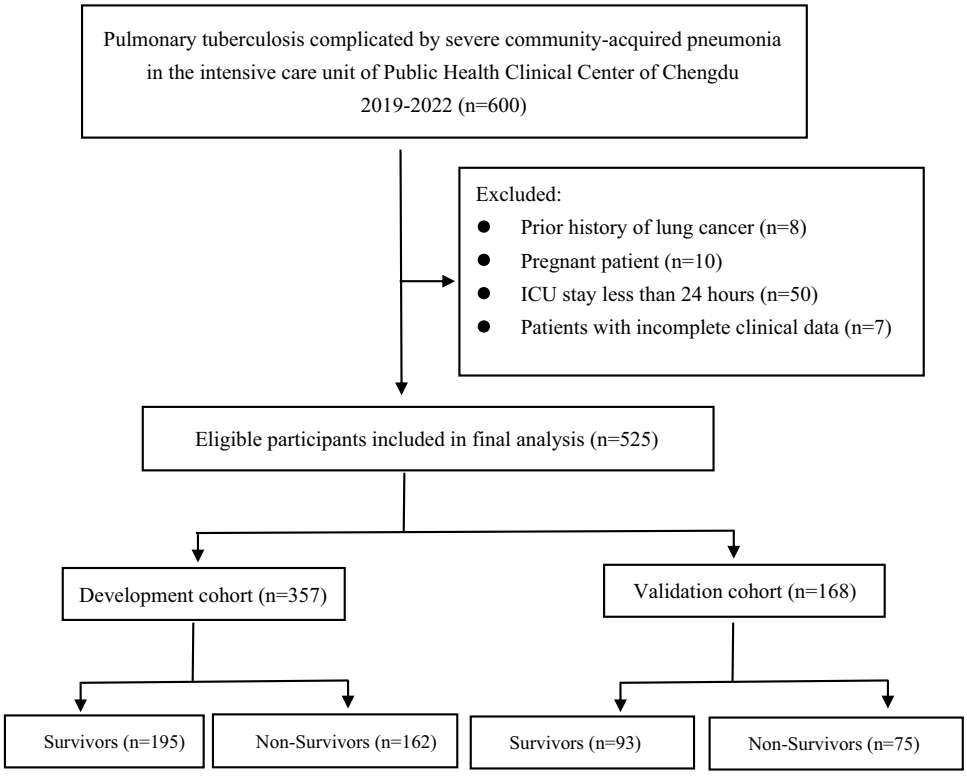

Figure 1 Flow chart of Participants included in this analysis.

Table 1 Comparison of Clinical Statistics Between the Development Cohort and the Validation Cohort

Variables	Total (N=525)	Development Cohort (N=357)	Validation Cohort (N=168)	Statistical Values	*P*-value
Gender (Male)	407(77.5)	276(77.3)	131(78.0)	0.029[a]	0.865
Age (years)	63.0(48.0,72.0)	62.0(47.0,72.0)	65.0(53.5,73.0)	−1.602[b]	0.109
BMI (kg/m^2)	19.0(18.2,21.0)	19.0(18.6,20.0)	20.0(18.0,23.5)	−1.613[b]	0.107
Smoking (yes)	307(58.5)	212(59.4)	95(56.5)	0.378[a]	0.538
Alcohol abuse (yes)	207(39.4)	135(37.8)	72(42.9)	1.216[a]	0.270
CURB-65 score	2.0(1.0,3.0)	2.0(1.0,3.0)	2.0(1.0,3.0)	−1.005[b]	0.315
APACHE II score	**17.0(13.0,21.0)**	**16.0(13.0,21.0)**	**18.0(14.0,22.5)**	**−2.095[b]**	**0.036**
SOFA score	4.0(3.0,6.0)	3.0(3.0,6.0)	4.0(3.0,6.0)	−0.791[b]	0.429
Long-term use of glucocorticoid (yes)	33(6.3)	19(5.3)	14(8.3)	1.758[a]	0.185
History of tuberculosis (yes)	107(20.4)	74(20.7)	33(19.6)	0.083[a]	0.773
Drug-resistant tuberculosis (yes)	87(16.6)	64(17.9)	23(13.7)	1.483[a]	0.223
Chronic obstructive pulmonary disease (yes)	106(20.2)	66(18.5)	40(23.8)	2.008[a]	0.156
Diabetes (yes)	100(19.0)	66(18.5)	34(20.2)	0.227[a]	0.634
HIV infection (yes)	12(2.3)	9(2.5)	3(1.8)	0.045[d]	0.831
White blood cell (10^9/L)	8.52(6.19,11.72)	8.44(6.19,12.01)	8.66(6.15,11.37)	−0.199[b]	0.843
Red blood cell (10^{12}/L)	3.85(3.23,4.45)	3.81(3.23,4.36)	3.98(3.20,4.70)	−1.639[b]	0.101
Hemoglobin (g/L)	107.81±26.49	107.06±25.698	109.38±28.111	−0.935[c]	0.350
Platelet (10^9/L)	211.0(134.0,290.0)	215.0(133.0,301.0)	207.5(137.5,279.0)	−1.033[b]	0.301
Alanine aminotransferase (U/L)	22.0(12.0,39.0)	21.0(12.0,40.0)	23.5(13.0,38.0)	−0.694[b]	0.488
Aspartate aminotransferase (U/L)	33.0(22.0,63.0)	34.0(22.0,63.0)	32.0(21.0,64.0)	−0.387[b]	0.699
Total Bilirubin (umol/L)	9.8(6.6,15.6)	10.0(6.60,16.30)	9.75(6.55,14.05)	−0.472[b]	0.637
Albumin (g/L)	**27.6(24.0,31.0)**	**27.3(23.7,30.5)**	**28.4(24.9,31.5)**	**−2.334[b]**	**0.020**
Blood urea nitrogen (mmol/L)	**5.87(4.11,8.85)**	**5.59(3.80,8.80)**	**6.32(4.57,9.92)**	**−2.354[b]**	**0.019**
Serum creatinine (umol/L)	**56.0(44.7,79.4)**	**54.7(43.4,77.3)**	**60.9(45.6,84.8)**	**−2.379[b]**	**0.017**
Procalcitonin (ng/mL)	0.47(0.17,1.58)	0.52(0.17,1.50)	0.40(0.18,1.85)	−0.433[b]	0.665
C-reactive protein (mg/L)	**95.0(60.6,138.5)**	**101.0(67.7,155.5)**	**71.9(43.6,115.3)**	**−5.708[b]**	**<0.001**
Lactic acid (mmol/L)	**2.01(1.52,2.80)**	**2.12(1.62,2.97)**	**1.82(1.36,2.46)**	**−3.738[b]**	**<0.001**
PO_2/FiO_2 (mmHg)	165.7(129.3,200.3)	166.0(134.0,199.0)	161.9(120.1,207.4)	−0.168[b]	0.867
CD3+ T cells (cells/ul)	329.0(191.0,519.0)	312.0(173.0,516.0)	358.5(211.0,532.5)	−1.615[b]	0.106
CD4+ T cells (cells/ul)	177.0(86.0,287.0)	158.0(84.0,282.0)	199.5(97.0,311.0)	−1.826[b]	0.068
CD8+ T cells (cells/ul)	123.0(64.0,213.0)	118.0(60.0,208.0)	130.0(74.0,216.0)	−1.344[b]	0.179
Invasive mechanical ventilation (yes)	96(18.3)	73(20.4)	23(13.7)	3.491[a]	0.062
Vasopressor use (yes)	121(23.0)	84(23.5)	37(22.0)	0.146[a]	0.702

Notes: [a]χ^2; [b]Z; [c]t; [d]continuity correction χ^2. Values are presented as mean ± SD or median (IQR) for continuous variables and number (percentage) for categorical variables. Variables in bold have p-value < 0.05.

Abbreviations: BMI, Body mass index; APACHE II, Acute physiology and chronic health evaluation; SOFA, Sequential organ failure assessment; PO_2/FiO_2, Partial pressure of oxygen in arterial blood/fraction of inspiratory oxygen.

Table 2 Univariable Analysis Between Survivors and Nonsurvivors in the Development Cohort

Variables	Total (N=357)	Survivors (N=195)	Non-survivors (N=162)	Statistical Values	*P*-value
Gender (Male)	276(77.3)	151(77.4)	125(77.2)	0.004[a]	0.951
Age (years)	**59.0(44.5, 69.0)**	**59.0(44.0,69.0)**	**64(50.1,75.2)**	**−3.115[b]**	**0.002**
BMI (kg/m^2)	**19.0(18.6,20.0)**	**19.1(18.7,20.3)**	**18.9(17.9,20.0)**	**−3.709[b]**	**<0.001**
Smoking (yes)(yes)	212(59.4)	111(56.9)	101(62.3)	1.079[a]	0.299
Alcohol abuse (yes)	135(37.8)	72(36.9)	63(38.9)	0.145[a]	0.703
Long-term use of glucocorticoid (yes)	**19(5.3)**	**5(2.6)**	**14(8.6)**	**6.487[a]**	**0.011**
CURB-65 score	**2(1,3)**	**1(1,2)**	**2(1,3)**	**−5.063[b]**	**<0.001**
APACHE II score	**16(13,21)**	**15(12,18)**	**18(15,24)**	**−6.682[b]**	**<0.001**
SOFA score	**3(3,6)**	**3(3,4)**	**5(3,7)**	**−7.464[b]**	**<0.001**
History of tuberculosis (yes)	74(20.7)	42(21.5)	32(19.8)	0.172[a]	0.679
Drug-resistant tuberculosis (yes)	64(17.9)	37(19.0)	27(16.7)	0.320[a]	0.571
Chronic respiratory disease (yes)	66(18.5)	39(20.0)	27(16.7)	0.652[a]	0.419

(*Continued*)

Table 2 (Continued).

Variables	Total (N=357)	Survivors (N=195)	Non-survivors (N=162)	Statistical Values	*P*-value
Diabetes (yes)	**66(18.5)**	**28(13.8)**	**39(24.1)**	**6.143[a]**	**0.013**
HIV infection (yes)	9(2.5)	7(3.6)	2(1.2)	1.154[d]	0.283
White blood cell (10^9/L)	8.44(6.17,12.03)	8.68(6.36,12.27)	8.09(6.04,11.87)	−1.022[b]	0.307
Red blood cell (10^{12}/L)	3.81(3.23,4.37)	3.85(3.31,4.33)	3.77(3.112,4.39)	−0.724[b]	0.469
Hemoglobin (g/L)	227.8±127.2	108.4±25.8	105.4±25.5	1.090[c]	0.276
Platelet (10^9/L)	**215.0 (132.5, 301.5)**	**243 (154,315)**	**183 (109,259)**	**−3.880[b]**	**<0.001**
Alanine aminotransferase (U/L)	21.0(12.0,40.5)	22.0(13.0,42.0)	20.0(11.0,39.0)	−0.755[b]	0.450
Aspartate aminotransferase (U/L)	34.0(22.0,63.0)	34.0(22.0,62.0)	34.5(22.5,64.3)	−0.362[b]	0.717
Total Bilirubin (umol/L)	10.0(6.6,16.3)	9.9(6.7,16.0)	10.2(6.6,16.4)	−0.038[b]	0.970
Albumin (g/L)	**27.3(23.7,30.6)**	**28.2(24.8,31.3)**	**26.2(22.6,29.3)**	**−3.969[b]**	**<0.001**
Blood urea nitrogen (mmol/L)	**5.6(3.8,8.8)**	**4.6(3.5,6.5)**	**7.2(4.7,10.9)**	**−5.960[b]**	**<0.001**
Serum creatinine (umol/L)	**54.7(43.4,77.4)**	**51.4(40.1,65.9)**	**59.0(47.0,91.2)**	**−3.558[b]**	**<0.001**
Procalcitonin (ng/mL)	**0.52(0.16,1.51)**	**0.37(0.13,1.10)**	**0.81(0.26,2.6)**	**−4.301[b]**	**<0.001**
C-reactive protein (mg/L)	101.0(67.7,155.8)	95.6 (68.0,147.7)	112.4 (67.5,160.)	−1.157[b]	0.247
Lactic acid (mmol/L)	**2.1(1.6,2.9)**	**2.0(1.6,2.6)**	**2.2(1.7,3.3)**	**−2.742[b]**	**0.006**
PO_2/FiO_2 (mmHg)	**163.1±44.7**	**172.6±40.4**	**151.5±47.0**	**4.496[e]**	**<0.001**
CD3+ T cells (cells/ul)	**312.0(173.0,517.5)**	**356.0(196.0,561.0)**	**262.5(141.0,439.5)**	**−3.453[b]**	**0.001**
CD4+ T cells (cells/ul)	**158.0(82.0,282.0)**	**181.0(97.0,325.0)**	**145.5(65.8, 247.3)**	**−2.972[b]**	**0.003**
CD8+ T cells (cells/ul)	**118.0(59.5,209.0)**	**141.0(73.0,233.0)**	**98.5(52.5,189.0)**	**−3.127[b]**	**0.002**
Invasive mechanical ventilation (yes)	**73(20.4)**	**13(6.7)**	**60(37.0)**	**50.174[a]**	**<0.001**
Vasopressor use (yes)	**84(23.5)**	**12(6.0)**	**72(44.4)**	**72.104[a]**	**<0.001**

Notes: [a]χ^2; [b]Z; [c]*t*. Values are presented as mean ± SD or median (IQR) for continuous variables and number (percentage) for categorical variables. Variables in bold have p-value < 0.05.

Abbreviations: BMI, Body mass index; APACHE II, Acute physiology and chronic health evaluation; SOFA, Sequential organ failure assessment; PO_2/FiO_2, Ratio of partial pressure of arterial oxygen to fraction of inspired oxygen.

stepwise backward multivariate Cox analysis of the 14 variables showed that long-term use of glucocorticoid, a BMI of <18.5 kg/m², diabetes, a BUN level of ≥ 7.14 mmol/L, a PO_2/FiO_2 ratio of <150 mmHg, and vasopressor use were independent risk factors for mortality in ICU patients with PTB complicated by SCAP in the development cohort.

In order to develop a simple and useful clinical prediction tool (PTSI score), relative weights were assigned according to the regression coefficient of each categorical variable (β). Figure 2 shows the β; HR; 95% CI; and calculation of the long-term use of glucocorticoids, a BMI of <18.5 kg/m², diabetes, a BUN of ≥ 7.14 mmol/L, a PO_2/FiO_2 ratio of <150 mmHg, and vasopressor use scores.

Assessment of the PTSI Score Model

ROC curves were used to compare the PTSI model with the three classical scoring systems (APACHE II, SOFA, and CURB-65). Figure 3A shows the ROC curve of the development cohort. The AUC values were 0.817 for the PTSI score model (95% CI: 0.772–0.863), 0.705 for the APACHE II score (95% CI: 0.651–0.759), 0.721 for the SOFA score (95% CI: 0.667–0.774), and 0.647 for the CURB-65 score (95% CI: 0.590–0.705). The ROC curve of the validation cohort is shown in Figure 3B. The AUC values were 0.814 for the PTSI score model (95% CI: 0.750–0.878), 0.716 for the APACHE II score (95% CI 0.638–0.793), 0.716 for the SOFA score (95% CI: 0.637–0.794), and 0.683 for the CURB-65 score (95% CI: 0.603–0.764). The results indicated the good predictive power and accuracy of the PTSI score model for mortality associated with PTB complicated by SCAP. It outperformed the traditional APACHE II, SOFA, and CURB-65 scoring systems.

Table 3 shows the upward trend in patient mortality with increasing PTSI score in the development and validation cohort. A cut-off point of 3 is determined based on Youden's ROC index, and patients were divided into low-risk (<3 score) and high-risk (≥3 score) groups. The Kaplan-Meier survival curves for the low- and high-risk groups of the development and validation cohort are shown in Figure 4A and B for the development and validation cohorts (log-rank P < 0.0001).

Variable	β	SE	Wals	HR(95%CI)	P-value	Score
Long−term use of glucocorticoid	0.836	0.285	8.606	2.307(1.320−4.032)	0.003	2
BMI<18.5kg/m^2	0.558	0.170	10.753	1.747(1.252−2.438)	0.001	1
Diabetes	0.430	0.189	5.177	1.538(1.061−2.228)	0.023	1
Blood urea nitrogen ⩾7.14mmol/L	0.778	0.161	23.422	2.178(1.589−2.985)	<0.001	2
PO_2/FiO_2<150 mmHg	0.599	0.162	13.725	1.820(1.326−2.499)	<0.001	1
Vasopressor use	1.276	0.168	57.691	3.582(2.577−4.979)	<0.001	3

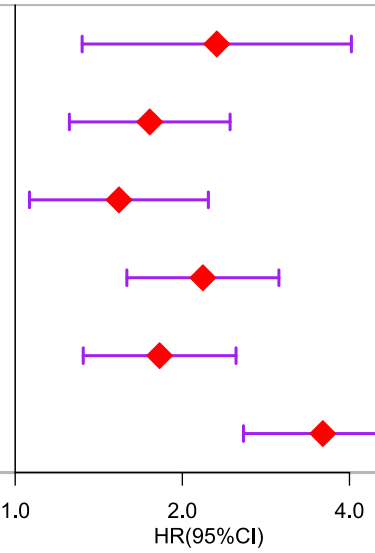

Figure 2 The Multivariate Cox regression analysis associated with 28-day mortality in PTB patients complicated by SCAP.

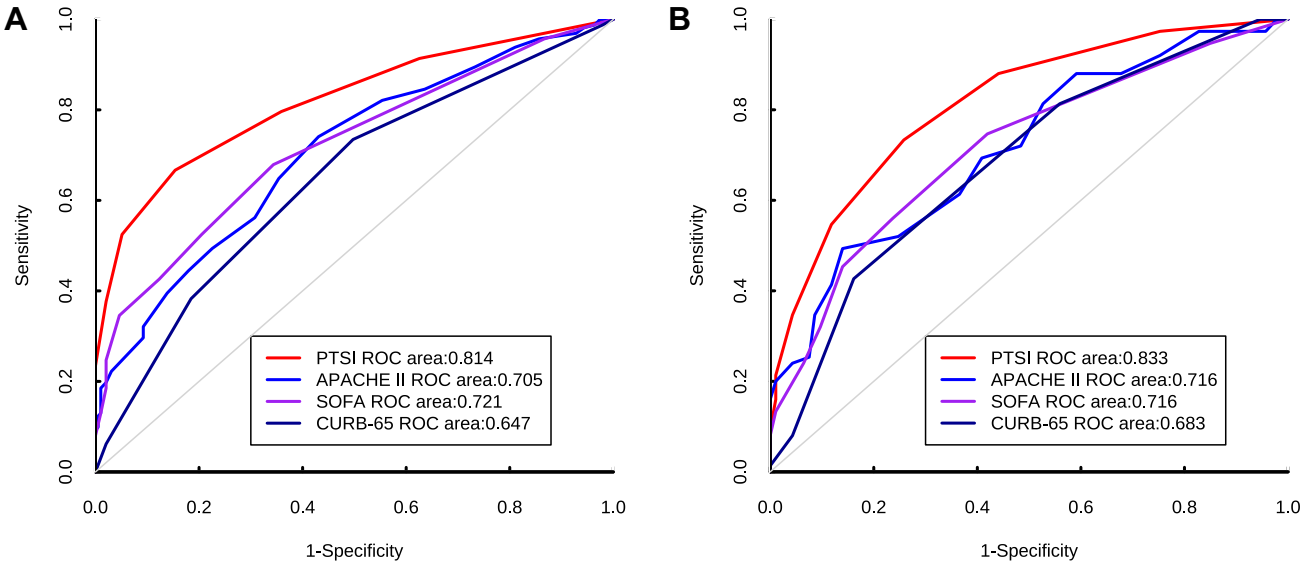

Figure 3 (**A**) The receiver operating characteristic (ROC) curve of the PTSI, APACHE II, SOFA and CURB-65 scores in predicting ICU mortality in the development cohort. (**B**) The receiver operating characteristic (ROC) curve of the PTSI, APACHE II, SOFA and CURB-65 scores in predicting ICU mortality in the validation cohort.

In addition, the accuracy of the PTSI score in the development and validation cohorts was evaluated using calibration curves (Figure 5A and B). The bias-corrected curve generated using a bootstrap method showed a slight deviation from the reference line; however, the predicted 28-day mortality remained in good agreement with the actual 28-day mortality in patients with PTB complicated by SCAP. The DCA of the PTSI score demonstrated a significant net benefit across different threshold probabilities in both cohorts compared with the APACHE II and SOFA scores (Figure 6A and B).

Table 3 Mortality Rates According to the PTSI Score

Score	Development Cohort			Validation Cohort		
	Survivors (N=195)	Non-survivors (N=162)	Mortality (%)	Survivors (N=93)	Non-survivors (N=75)	Mortality (%)
0	73	14	16.1	23	2	8
1	52	19	26.8	29	7	19.4
2	40	21	34.4	17	11	39.3
3	20	23	53.5	13	14	51.9
≥4	10	85	89.4	11	41	78.8
<3	165	54	24.6	69	24	30.4
≥3	30	108	78.2	20	55	69.6

Discussion

Outcome prediction systems for PTB complicated by SCAP are rarely explored. Therefore, we developed a simple PTSI score model using simple clinical data, including long-term glucocorticoid use, a BMI of <18.5 kg/m^2, diabetes, a BUN level ≥7.14 mmol/L, a PO_2/FiO_2 ratio of <150 mmHg, and vasopressor use. This PTSI score model was assessed using the AUC, calibration curve analysis, and DCA, demonstrating robust performance and accuracy in predicting the 28-day mortality risk of patients with PTB complicated by SCAP.

Previous studies have developed prediction models to help clinicians identify patients with TB admitted to the ICU who have a high mortality risk. A study based on 83 ICU patients with TB in South Africa developed a SCCOR-TB model using six factors, including septic shock, HIV with CD4 count (<140 μmol/L in men or <120 μmol/L in women), a PO_2/FiO_2 ratio of <200 mmHg, chest radiograph showing diffuse parenchymal infiltrates/miliary pattern, and the absence of TB treatment upon admission.[11] To improve the clinical applicability and accuracy of the model, this team conducted conducted a prospective study involving 78 patients treated between February 2015 and July 2018. The revised model was streamlined to four parameters: septic shock, immunosuppression, acute kidney injury, and lack of

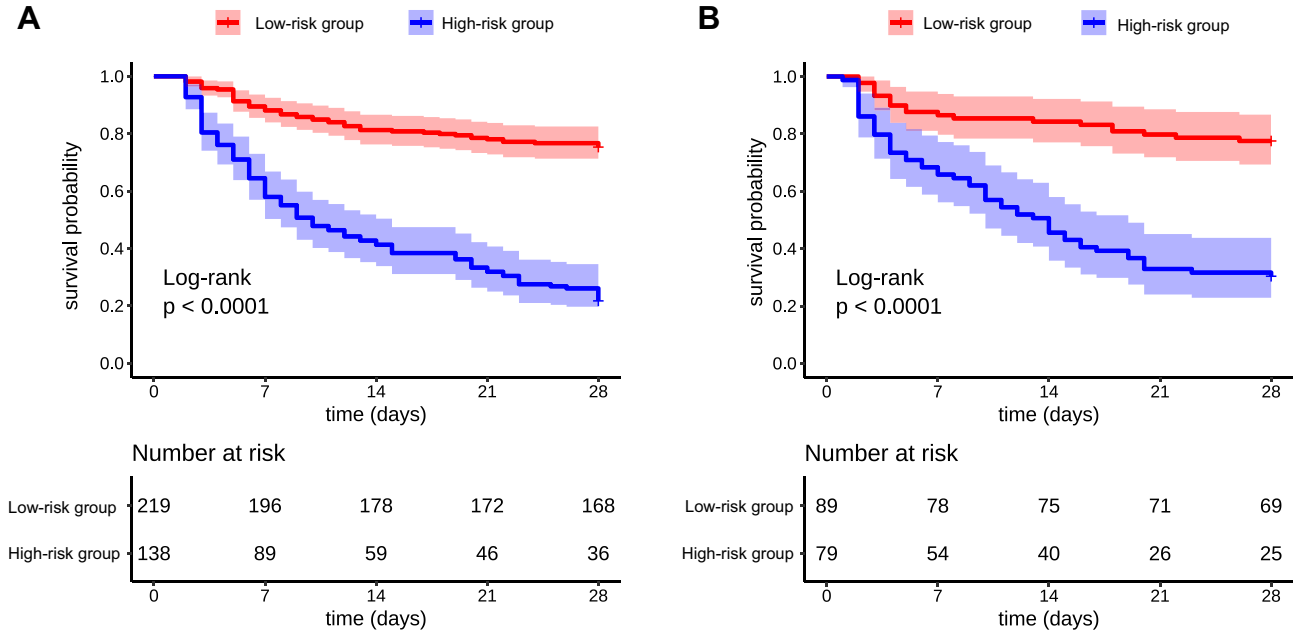

Figure 4 (**A**) The Kaplan-Meier survival analysis of the low-risk and high-risk groups in PTB patients complicated by SCAP in the development cohort. (**B**) The Kaplan-Meier survival analysis of the low-risk and high-risk groups in PTB patients complicated by SCAP in the validation cohort.
Note: Low-risk group: PTSI score <3; High- risk group: ≥3.

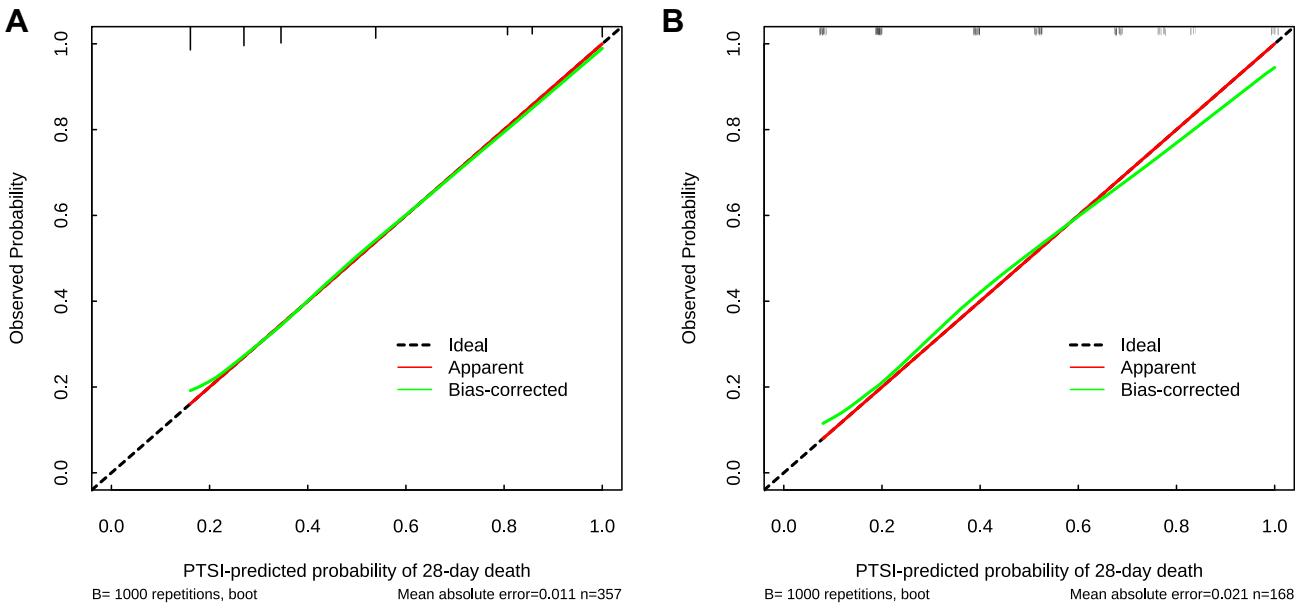

Figure 5 (**A**) The calibration curve of PTSI score constructed through the bootstrap approach in the development cohort. (**B**) The calibration curve of PTSI score constructed through the bootstrap approach in the validation cohort.
Notes: The horizontal axis was the predicted probability of 28-days death by the PTSI score, and the vertical axis was the actual probability. The dashed line indicates the predicted probability completely fits the actual probability.

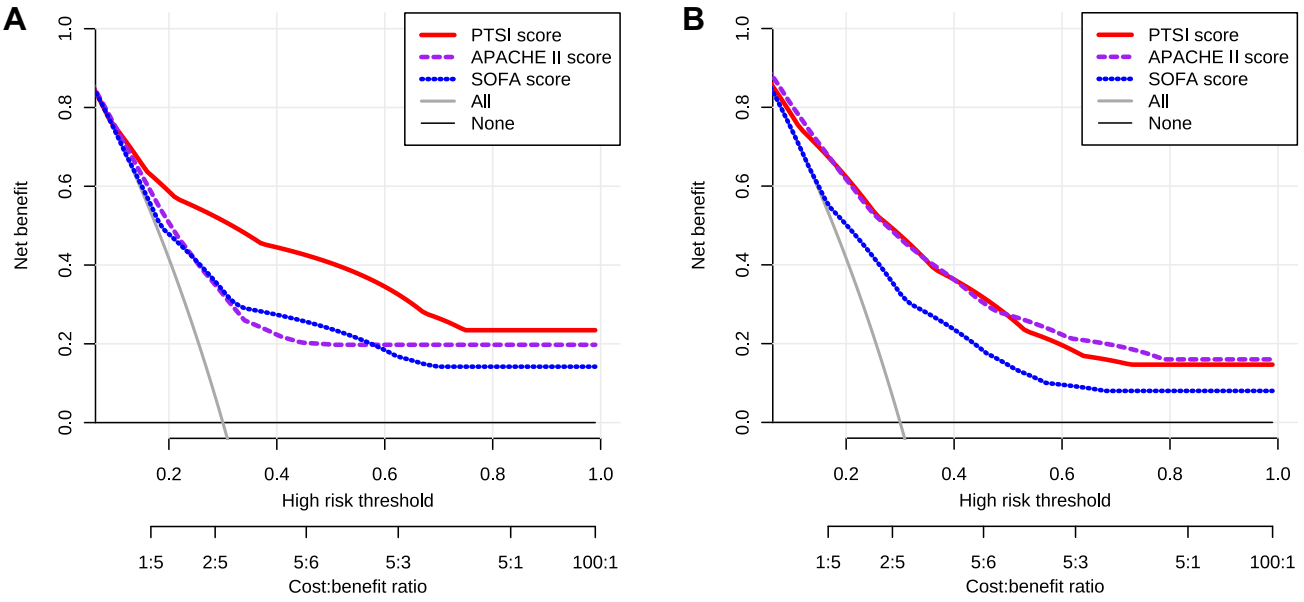

Figure 6 (**A**) The decision curve analysis of of the PTSI, APACHE II, and SOFA scores in predicting ICU mortality in the development cohort. (**B**) The decision curve analysis of of the PTSI, APACHE II, and SOFA scores in predicting ICU mortality in validation cohort.
Notes: The y-axis measures the standardized net benefit. The red line represents the PTSI score. The purple line represents the APACHE II score. The blue line represents the SOFA score. The gray dotted line represents the assumption that all patients dead. The black dotted line represents the assumption that no patients dead.
Abbreviation: DCA, Decision curve analysis.

lobar consolidation.[12] However, both the development and validation sample sizes were small, and the model was not well-validated, further limiting its clinical application.

In current clinical practice, scoring systems such as APACHE II, SOFA, and CURB-65 are commonly used to assess the prognosis of patients with TB admitted to the ICU.[5] However, our study showed that these scoring systems have certain limitations in their application, especially for PTB complicated by SCAP. The APACHE II model was only

moderately effective in predicting the prognosis of patients with PTB complicated by SCAP, which was mainly attributed to its failure to adequately incorporate pathophysiological characteristics specific to these patients, such as severe malnutrition and immune dysfunction.[6,14,15] By contrast, the SOFA scoring system, which focuses on the assessment of organ dysfunction, is more sensitive to hemodynamic changes and therefore plays a key role in the diagnosis and prognostic assessment of sepsis or septic shock.[7,8] However, as only some patients with PTB complicated by SCAP exhibit symptoms of septic shock, the scope of application of the SOFA score in this patient population is somewhat limited. The CURB-65 scoring system, a straightforward tool for assessing prognosis based on the patient's level of consciousness, urea, respiratory rate, blood pressure and age, provides a convenient method for the rapid screening and prognostic assessment of patients with pneumonia.[9] However, in the prognostic assessment of patients with PTB complicated by SCAP, the CURB-65 scoring system demonstrates limited applicability. This scoring system does not adequately consider chronic nutrient depletion, a pathophysiological feature of PTB. Based on the limitations of the existing scoring systems for the prognostic assessment of critically ill patients, some scholars have suggested the development of a severity-of-illness model for ICU patients based on different population characteristics.[16] Our PTSI score model comprehensively considered the immune and nutritional status of patients with PTB complicated by SCAP and integrated key indicators from the APACHE II, SOFA, and CURB-65 scoring systems. This model was validated and showed significantly higher efficacy compared with other scoring systems in the prognostic assessment of PTB complicated by SCAP.

In our study, the mortality risk in patients with long-term glucocorticoid use was 1.307 times higher than that in patients without glucocorticoid use. This higher risk may be due to the glucocorticoids' suppression of type 1 helper T cells (Th1), CD8+ T cells, and natural killer cells and the induction of apoptosis of T and B lymphocytes, thus weakening the body's defense against infections and increasing the risk of recurrent infections and opportunistic infections.[17–19] Additionally, patients with PTB complicated by SCAP demonstrated below-normal levels of CD3+, CD4+, and CD8+ T cells. Detailed analyses showed that patients in the non-survivor group had significantly lower levels of these T lymphocyte subsets. These findings suggest that immune function plays an important role in patient prognosis. A series of studies have reported that diabetes is not only an important risk factor for the development of PTB and infection but also exacerbates the risk of poor prognosis.[20–22] An animal study[23] showed that diabetic guinea pigs with PTB had a more intense pro-inflammatory response with granulocyte inflammation and significantly higher gene expression levels of interferon-γ, interleukin (IL)-17A, IL-8, and IL-10 in their lungs compared with non-diabetic guinea pigs. These findings support the notion that diabetes influences the immune-inflammatory response in PTB, potentially impacting its prognostic course.[24]

In this study, the mortality rate of patients with PTB complicated by SCAP reached 59.3% when the PO_2/FiO_2 ratio was <150 mmHg; this may be because hypoxia can inhibit the signal transduction of type I interferon in the bone marrow, resulting in the reduction of monocyte-derived macrophages and enhanced neutrophil infiltration, promoting pulmonary vascular injury, protein leakage, and alveolar epithelial injury.[25–27] Furthermore, with the decrease in PO_2/FiO_2 ratio in patients with acute respiratory distress syndrome, the severity of lung injury increases, along with the mortality rate.[28] In a study involving 428 critically ill patients in India, vasopressor use was independently associated with patient mortality.[29] This association is likely due to the release of large amounts of inflammatory mediators from the organism triggered by severe infections, causing capillary endothelial damage, tissue microcirculation ischemia, and hypoxia. This process results in vascular paralysis, reduced vascular tone, and organ dysfunction. This dysfunction persists even after fluid resuscitation, vasopressor administration, and hemodynamic therapy for infection.[30,31] Similarly, our study confirmed that vasopressor use is an important factor affecting patient prognosis.

The PTSI score model combines the four core dimensions (patients' nutritional status, immune status, respiratory function, and organ perfusion) and reflects the pathophysiological mechanisms of PTB and SCAP. This model provides clinicians with a scientific basis for assessing prognosis and accurately determining disease progression and mortality risk in patients with PTB complicated by SCAP. Based on the PTSI score model, we implemented early nutritional and immune support therapy for patients, aiming to enhance their nutritional status and strengthen their immune function to effectively control the infection and promote recovery from the disease. Simultaneously, attention should be paid to the importance of early respiratory support therapy, which improves the respiratory function of patients and increases the

level of oxygenation to alleviate the damage caused by hypoxia. In addition, we actively implemented the necessary organ support therapy, including hemodynamic management, renal function protection, and other measures, to prevent multiorgan damage and further improve the overall prognosis of the disease.

Our study has several limitations. First, the study population included only patients from the Public Health Clinical Center of Chengdu (southwest region). Second, the sample size was relatively small. Third, some patients with PTB complicated by SCAP were not admitted to the ICU due to inadequate recognition of disease severity or financial constraints, introducing bias in the study population. Fourth, the PTSI score model has a retrospective design. Therefore, the uncertainty of bias may have inevitably affected our evaluation. Future prospective, multicenter, large patient studies may help update and validate the PTSI score model to further improve the early identification of patients at high risk of mortality from PTB complicated by SCAP.

Conclusion

A PTSI score model was developed to predict the 28-day mortality risk in patients with PTB complicated by SCAP, demonstrating good discrimination and calibration. Our model can help clinicians accurately assess prognosis and manage patients with PTB complicated by SCAP.

Data Sharing Statement

The data supporting the findings of this study are available from the first author, Kunping Cui, upon reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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