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Incidence and risk factor of sepsis in patients with severe community-acquired pneumonia: a Chinese, single-center, retrospective study

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Abstract

Background Sepsis represents a high-risk mortality cohort among patients with severe community-acquired pneumonia (SCAP). Rapid and precise identification along with prompt decision-making, serves as a practical approach to improve patient prognosis.

Methods This retrospective observational study enrolled adult patients with severe community-acquired pneumonia (SCAP) who were continuously hospitalized in the intensive care unit (ICU) of West China Hospital, Sichuan University, from September 2011 to September 2019. Univariate and multivariate logistic regression analyses were employed to identify independent risk factors for co-sepsis, followed by the utilization of LASSO regression to filter features to establish a nomogram. Model robustness was evaluated via the C index, receiver operating characteristic (ROC) analysis, and calculation of the area under the curve (AUC). Furthermore, its predictive accuracy was assessed via decision curve analysis (DCA).

Results In total, 5855 SCAP patients were included in the present study, of whom 654 developed sepsis. Patients with sepsis exhibited a prolonged length of stay in the ICU and higher mortality rates, indicating a worse prognosis than those without sepsis. We identified 15 independent risk factors associated with the development of sepsis in SCAP patients. Further analysis incorporating 9 of these features to construct a nomogram demonstrated a C index of 0.722 (95%CI 0.702–0.742), including lactate, D-dimer, respiratory rate, heart rate, albumin, hemoglobin, activated partial thromboplastin time (APTT), glucose, and C-reactive protein (CRP) levels. The AUC values and DCA curves demonstrated that the model exhibited superior accuracy and overall net benefit in predicting co-sepsis development compared with the qSOFA, CURB-65, SOFA, and APACHE II scores. Additionally, the calibration curve confirmed good concordance between the predicted probabilities of the model.

Conclusions This study investigated the risk factors for co-sepsis in SCAP patients and constructed an expedited, cost-effective and personalized model for predicting the probability of co-sepsis.

Keywords Severe community-acquired pneumonia, Sepsis, Clinical characteristics, Risk factors, Nomogram, Mortality

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Introduction

Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma acquired in the community (outside the hospital setting) and remains a major public health concern [1]. With approximately 6 million cases reported annually in the United States and over 1.5 million individuals requiring hospitalization [2], CAP is considered the leading cause of approximately 61.3 deaths per 100,000 individuals [3]. Severe community-acquired pneumonia (SCAP) is the most common cause of acute respiratory failure leading to intensive care unit (ICU) admission, with an in-hospital mortality rate of 17% and a 1-year mortality rate approaching 50% [4]. Even though patients with SCAP can survive until discharge, the long-term disease caused by pneumonia and the relatively high mortality rate still persist [5].Thus, it is vital to formulate a scientific and reasonable early assessment strategy, that enables clinicians to implement effective interventions in a timely manner and prevent further deterioration of the condition.

Sepsis, a type of life-threatening organ dysfunction induced by a dysregulated host response consequent to infection, can be diagnosed when the Sequential Organ Failure Assessment (SOFA) score is ≥ 2 points [6]. The concurrent occurrence of sepsis and SCAP generally indicates a more unfavorable prognosis than other patient cohorts do, particularly among patients with one or multiple comorbidities as well as those who are immunocompromised [7, 8]. Pneumonia remains one of the most prevalent sites of infection in sepsis patients, yet sepsis frequently also arises as an adverse outcome of SCAP due to compromised host defense failure [9, 10]. According to the literature, the incidence of sepsis among CAP patients in China is approximately 40%—50% [11, 12]. The earlier identification of sepsis assists in optimizing the time-window for timely empiric antimicrobial therapy, intravenous fluid resuscitation, and the recognition of potential microbial-resistance [13].

Both the pneumonia severity index (PSI) and the CURB-65 score are designed to assess CAP severity and prognosis estimation, and demonstrate similar performance in terms of mortality prediction capability [14]. However, these scores lack further risk identification and stratification for SCAP patients, such as the occurrence of sepsis. [15]. The SOFA score, a widely recognized diagnostic criterion, performs well in both the diagnosis and prognosis prediction of sepsis; it requires complex laboratory test results for support and is mostly used for retrospective diagnosis, which is not conducive to the early identification of sepsis [16]. While the Acute Physiology and Chronic Health Evaluation II (APACHE II) score is an important tool for classifying conditions and predicting the prognosis of critically ill patients, it is was not specifically designed to emphasize early sepsis recognition [17]. Like the other scores mentioned above, they seem to fail to reflect the interaction between the source of pulmonary infection and organ dysfunction. The quick SOFA (qSOFA) score simplifies bedside screening (based on three non-laboratory indicators: respiration, consciousness, and blood pressure), but its sensitivity is insufficient, making it prone to missing early sepsis [18]. This type of rapid illness assessment tool may be more appropriate for pre-hospital settings or emergency departments, where opportunities for laboratory testing are limited. However, for patients who have already been hospitalized, direct application of this tool could overlook various valuable test results, potentially leading to unreliable assessment outcomes. There is still a lack of a rapid but reliable and effective evaluation system to identify sepsis in patients with SCAP [19].

The present study aimed to explore the association between sepsis and SCAP, identify risk factors for sepsis in SCAP patients, and develop a novel predictive model to assess the probability of co-sepsis development in SCAP patients. Our objective is to provide a superior variable selection and scoring system for clinical decision-making.

Methods

Study design and population

All consecutive patients diagnosed with SCAP from September 2011 to September 2019 at the 172-bed medical ICU of West China Hospital, a large tertiary-care teaching hospital in Chengdu, Sichuan Province, China, were enrolled in the present study. This study was approved by the West China Hospital of Sichuan University Biomedical Research Ethics Committee (No. 2021–828) and was conducted in accordance with the amended Declaration of Helsinki. Given the retrospective non-interventional design of this study, the requirement for informed consent was waived.

The"rms"R package was utilized for the development and validation of the nomogram. Selecting the"pmsampsize"package, a minimum clinic sample size of 1701 for developing the model was estimated on the basis of the outcome incidence in the study population, the number of candidate predictive parameters, and the expected predictive performance of the current model [20].

In accordance with the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) CAP severity criteria, SCAP was defined as present in patients with one major criterion: (1) septic shock with the need for vasopressors; (2) respiratory failure requiring mechanical ventilation; or three or more minor criteria: (1) respiratory rate ≥ 30 breaths/min; (2) PaO2/FiO2

ratio ≤250; (3) multilobar infiltrates; (4) confusion/disorientation; (5) blood urea nitrogen level ≥20 mg/dL; (6) white blood cell count <4,000 cells/μL; (7) platelet count <100,000/μL; (8) core temperature <36 °C; and (9) hypotension requiring aggressive fluid resuscitation [10]. The exclusion criteria were as follows: (1) under 18 years old; (2) pregnant or perinatal; (3) severe immunosuppression: active solid or hematological malignancy, human immunodeficiency virus infection, transplantation, autoimmune diseases, cancer chemotherapy, biological immune modulators, or other immunosuppressive therapy; (4) repeated admission; (5) hospital acquired pneumonia; (6) discharged within 24 h of admission; and (7) incomplete data.

The diagnosis of sepsis relied on the Sepsis-3 criteria which was mainly based on screening at the bedside with the qSOFA score and the detection of organ dysfunction via the SOFA score [16]. The occurrence of septic shock was determined by the physician in charge on the basis of the presence of persisting hypotension, requiring vasopressor support to maintain a mean arterial pressure (MAP) ≥65 mm Hg as well as an elevated serum lactate level >2 mmol/L (18 mg/dL) despite adequate fluid resuscitation [16]. Standard care and antibiotic therapy were administered to all patients based on the discretion of the ICU attending physician, in accordance with the CAP guidelines. The study only considered the initial admission if patients were admitted multiple times during the study period. The detailed selection process is visually represented in Fig. 1 through a comprehensive flowchart.

Clinical outcomes and data collection

The following demographic and clinical variables were anonymously collected from electronic medical records within 24 h of admission to the ICU: age; sex; vital signs on the day of SCAP diagnosis; laboratory examinations (hematological indicators, coagulation indicators, biochemical parameters, inflammatory markers, etc.); and the comorbidities (cancer, coma, diabetes mellitus, chronic hepatic diseases, cerebrovascular diseases, chronic renal diseases, etc.). The qSOFA score, CURB-65 score, SOFA score and APACHE II score were assessed through the data of patients on the day of SCAP diagnosis. The worst value was extracted for analysis if any laboratory examination was repeated more than once within 24 h of admission. Two experienced respiratory clinicians independently reviewed the medical records and conducted data collection with a standardized data collection form. In cases of disagreement, a third reviewer reached a consensus. The follow-up of patients continued until they were discharged from the hospital. The primary outcome was the incidence of sepsis, and the secondary outcomes included in-hospital mortality, ICU mortality, length of stay (LOS) in the hospital, and LOS in the ICU, as well as 7-day, 14-day, 28-day, and 90-day mortality after diagnosis with the SCAP.

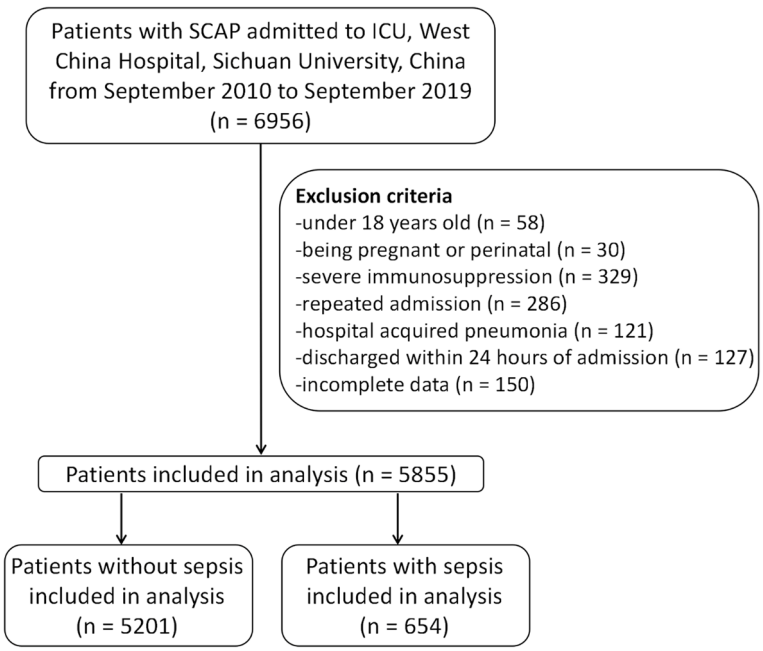

Fig. 1 Flow diagram of SCAP patients with or without sepsis selection

Statistical analysis

Statistical analyses and graphs were generated via IBM SPSS Statistical version 25.0 (SPSS, Chicago, IL, USA) and R software (version 4.2.3, https://www.R-project.org/). Continuous variables are presented as medians (interquartile ranges (IQRs), 25–75%), and categorical variables are presented as numbers (percentages) as appropriate. The demographic and clinical characteristics of the patients were compared between the SCAP patients with or without sepsis via the nonparametric Mann–Whitney U test or Pearson's chi-square test as appropriate. The missing data were addressed using multiple imputation (MI) if the proportion of missing values was less than 20%, whereas variables with a missing date rate exceeding 20% were excluded from the analysis. MI was conducted utilizing Bayesian methods in SPSS.

Univariate logistic regression analysis was initially performed to identify the potential variables ($p < 0.1$) associated with the incidence of sepsis among SCAP patients. The aforementioned variables were included in the subsequent multivariate logistic regression analysis to determine a more crucial and comprehensible set of risk factors. Then, by selecting the appropriate lambda in the logistic least absolute shrinkage and selection operator (LASSO) model, the variables with non-zero coefficients were collected to identify the optimal features for the present study. The features described above were subsequently introduced to construct a nomogram, which serves as a prognostic model for the risk of sepsis among SCAP patients.

In addition, the robustness of the model was visually evaluated through the concordance index (C-index) and area under the receiver operating characteristic curve (ROC and AUC). Additionally, calibration curves and decision curve analysis (DCA) were employed to assess the predictive accuracy for clinical application. A two-tailed p-value of ≤ 0.05 was adopted for statistical inference.

Results

Clinical characteristics of SCAP in adults.

The present study ultimately enrolled a total of 5855 patients who fulfilled the inclusion and exclusion criteria and received a diagnosis of SCAP; these patients were divided into two cohorts (SCAP patients without sepsis and SCAP patients with sepsis). Among them, 654 patients were afflicted with sepsis (11.2%), of whom 343 progressed to a state of septic shock (5.9%) (Fig. 1, Table 1). The utilization rate of vasopressors was greater (62.8% vs 57.9%, $p = 0.015$) in patients with sepsis than in those without sepsis, whereas the demographic characteristics and the rate of invasive mechanical ventilation remained unchanged. The presence of chronic renal diseases (8.6% vs 5.9%, $p = 0.007$), and chronic cerebrovascular diseases (30.9% vs 27.1%, $p = 0.040$) was greater among sepsis patients. A comparison of vital signs on admission, was revealed that patients with sepsis had an elevated respiratory rate (21.00 vs 18.00 breaths/min, $p < 0.001$), heart rate (105.50 vs 94.00 beats/min, $p < 0.001$), incidence of coma (20.6% vs 16.6%, $p = 0.009$), and temperature (36.80 vs 36.70 °C, $p < 0.001$). However, these patients presented exhibited lower systolic blood pressure (SBP) (123.50 vs 129.00 mmHg, $p < 0.001$), diastolic blood pressure (DBP) (71.00 vs 73.00 mmHg, $p < 0.001$), mean arterial pressure (MAP) (89.67 vs 91.30 mmHg, $p < 0.001$), PaO_2 levels (83.75 vs 89.57%, $p < 0.001$), and PaO_2/FIO_2 ratios (192.00 vs 237.50, $p < 0.001$).

When comparing the laboratory examination data, patients with sepsis demonstrated elevated levels of white blood cell (10.38 vs 9.44 $\times 10^9$/L $p < 0.001$), neutrophil (8.19 vs 7.64 $\times 10^9$/L, $p = 0.003$), neutrophil/lymphocyte ratio (10.16 vs 8.03, $p < 0.001$), methemoglobin [121.30 (80.54, 400.75) vs 121.30 (76.62, 179.90) g/L, $p < 0.001$], alanine aminotransferase (ALT) (25.00 vs 22.00 IU/L, $p = 0.001$), aspartate aminotransferase (AST) (39.00 vs 28.00 IU/L, $p < 0.001$), activated partial thromboplastin time (APTT) (35.20 vs 31.00 s, $p < 0.001$), prothrombin time (PT) (13.90 vs 12.70 s, $p < 0.001$), d-dimer (6.00 vs 4.00 mg/L, $p < 0.001$), creatinine (75.00 vs 71.00 μmol/L, $p = 0.001$), lactate (1.70 vs 1.50 mmol/L, $p < 0.001$), troponin T (33.00 vs 27.00 ng/mL, $p < 0.001$), brain natriuretic peptide (BNP) (1322.00 vs 926.00 pg/mL, $p < 0.001$), blood urea nitrogen (BUN) (8.00 vs 6.00 mg/dL, $p < 0.001$), glucose (8.00 vs 7.06 mmol/L, $p < 0.001$), c-reactive protein (CRP) (89.63 vs 65.61 mg/L, $p < 0.001$), procalcitonin (PCT) (0.65 vs 0.31 ng/mL, $p < 0.001$) and interleukin 6 (IL-6) [46.23 (34.54, 179.10) vs 46.23 (29.23, 68.53) pg/mL, $p < 0.001$] but lower levels of monocyte (0.37 vs 0.44 $\times 10^9$/L, $p < 0.001$), lymphocyte (0.80 vs 0.97 $\times 10^9$/L, $p < 0.001$), platelet (158.00 vs 185.00 $\times 10^9$/L, $p < 0.001$), hemoglobin (101.00 vs 114.00 g/L, $p < 0.001$), albumin (29.90 vs 33.40 g/L, $p < 0.001$), ang globulin (24.30 vs 25.40 g/L, $p < 0.001$) in their biological samples.

Notably, significant disparities in prognosis were observed between the two groups except for in-hospital length of stay (LOS), which suggested that comorbid sepsis had adverse impacts on the prognosis of SCAP patients. Patients in the sepsis group exhibited a prolonged LOS in ICU (13.86 vs 11.00 days, $p < 0.001$) and higher rates of in-hospital mortality (41.4% vs 26.6%, $p < 0.001$), ICU mortality (36.1% vs 23.0%, $p < 0.001$), 7-day mortality (8.1% vs 4.4%, $p < 0.001$), 14-day mortality (17.3% vs 10.0%, $p < 0.001$), 28-day mortality (30.0% vs 18.9%, $p < 0.001$), and 90-day mortality (40.2% vs 26.0%, $p < 0.001$), than did those in the non-sepsis group (Table 1).

Table 1 Baseline characteristics of SCAP individuals with or without sepsis

Variables	Overall ($n=5855$)	SCAP patients without Sepsis ($n=5201$)	SCAP patients with Sepsis ($n=654$)	$P^{\dagger}$ value
Demographic characteristics				
Age, median (IQR), y	63.00 (49.00, 74.00)	63.00 (49.00, 74.00)	63.00 (48.00, 73.00)	*0.819*
Sex: male, n (%)	3762 (64.3%)	3330 (64.0%)	432 (66.1%)	*0.308*
Treatment, n (%)				
IMV[‡]	5792 (98.9%)	5144 (98.9%)	648 (99.1%)	*0.677*
Vasopressor	3422 (58.4%)	3011 (57.9%)	411 (62.8%)	***0.015***
Direct ICU	2155 (36.8%)	1757 (33.8%)	398 (60.9%)	***< 0.001***
Comorbidities, n (%)				
Cancer	1090 (18.6%)	982 (18.9%)	108 (16.5%)	*0.143*
Chronic hepatic diseases	158 (2.7%)	133 (2.6%)	25 (3.8%)	*0.060*
Chronic renal diseases	362 (6.2%)	306 (5.9%)	56 (8.6%)	***0.007***
Chronic pulmonary diseases	1434 (24.5%)	1256 (24.1%)	178 (27.2%)	*0.086*
Chronic cardiac diseases	984 (16.8%)	875 (16.8%)	109 (16.7%)	*0.919*
Chronic cerebrovascular diseases	1611 (27.5%)	1409 (27.1%)	202 (30.9%)	***0.040***
Diabetes mellitus	949 (16.2%)	855 (16.4%)	94 (14.4%)	*0.177*
Vital signs on admission, median (IQR)				
Respiratory rate, breath/min	18.57 (14.00, 23.00)	18.00 (14.00, 22.49)	21.00 (16.00, 25.00)	***< 0.001***
Heart rate, beat/min	96.00 (80.85, 111.00)	94.00 (80.00, 109.75)	105.50 (90.00, 124.00)	***< 0.001***
Systolic blood pressure, mmHg	128.34 (110.94, 145.61)	129.00 (111.09, 146.00)	123.50 (104.36, 141.00)	***< 0.001***
Diastolic blood pressure, mmHg	73.00 (63.00, 84.00)	73.00 (63.00, 84.00)	71.00 (60.75, 82.00)	***< 0.001***
Mean arterial pressure, mmHg	91.00 (82.30, 100.00)	91.30 (82.33, 100.11)	89.67 (80.66, 98.33)	***0.007***
Temperature, °C	36.70 (36.30, 37.19)	36.70 (36.30, 37.10)	36.80 (36.40, 37.50)	***< 0.001***
PaO_2, (%)	88.70 (70.50, 116.40)	89.57 (71.00, 117.80)	83.75 (67.70, 108.07)	***< 0.001***
PaO_2/FIO_2[‡]	230.00 (165.00, 250.00)	237.50 (166.67, 250.00)	192.00 (117.50, 247.50)	***< 0.001***
Coma	996 (17.0%)	861 (16.6%)	135 (20.6%)	***0.009***
Laboratory examinations, median (IQR)				
White blood cell, ($\times 10^9$/L)	9.53 (6.70, 13.16)	9.44 (6.69, 13.01)	10.38 (6.97, 14.98)	***< 0.001***
Monocyte, ($\times 10^9$/L)	0.43 (0.28, 0.62)	0.44 (0.28, 0.63)	0.37 (0.20, 0.61)	***< 0.001***
Neutrophil, ($\times 10^9$/L)	7.70 (4.94, 11.25)	7.64 (4.94, 11.08)	8.19 (5.04, 12.54)	***0.003***
Lymphocyte, ($\times 10^9$/L)	0.95 (0.61, 1.36)	0.97 (0.63, 1.38)	0.80 (0.49, 1.23)	***< 0.001***
Neutrophil/Lymphocyte ratio	8.20 (4.43, 15.34)	8.03 (4.36, 14.91)	10.16 (5.31, 20.29)	***< 0.001***
Platelet, ($\times 10^9$/L)	182.89 (120.00, 259.85)	185.00 (125.00, 261.82)	158.00 (89.75, 249.00)	***< 0.001***
Hemoglobin, g/L	113.00 (93.00, 131.00)	114.00 (94.00, 132.00)	101.00 (84.00, 122.00)	***< 0.001***
Methemoglobin, g/L	121.30 (77.45, 198.60)	121.30 (76.62, 179.90)	121.30 (80.54, 400.75)	***< 0.001***
Albumin, g/L	32.90 (28.50, 38.47)	33.40 (28.90, 38.80)	29.90 (26.70, 33.90)	***< 0.001***
Globulin, g/L	25.30 (22.00, 28.80)	25.40 (22.10, 28.90)	24.30 (20.50, 27.90)	***< 0.001***
ALT[‡], IU/L	23.00 (14.00, 45.00)	22.00 (14.00, 44.00)	25.00 (15.00, 50.25)	***0.001***
AST[‡], IU/L	28.00 (19.00, 53.00)	28.00 (19.00, 49.37)	39.00 (23.00, 75.00)	***< 0.001***
Total bilirubin, μmol/L	12.00 (8.00, 18.00)	12.00 (8.00, 18.00)	13.00 (8.00, 21.00)	*0.057*
Direct bilirubin, μmol/L	5.40 (3.50, 9.40)	5.40 (3.50, 9.40)	5.20 (3.40, 9.21)	*0.354*
APTT[‡], s	31.40 (27.20, 37.50)	31.00 (26.90, 36.95)	35.20 (29.30, 43.13)	***< 0.001***
PT[‡], s	12.80 (11.70, 14.40)	12.70 (11.60, 14.20)	13.90 (12.40, 15.70)	***< 0.001***
Fibrinogen, g/L	3.58 (2.66, 4.69)	3.58 (2.66, 4.64)	3.75 (2.65, 4.96)	*0.094*
D-dimer, mg/L	5.00 (2.00, 9.00)	4.00 (2.00, 9.00)	6.00 (3.00, 12.00)	***< 0.001***
Creatinine, μmol/L	71.00 (54.00, 100.60)	71.00 (54.00, 98.00)	75.00 (53,00, 130.00)	***0.001***
Uric acid, μmol/L	235.00 (149.00, 335.00)	237.00 (151.00, 335.00)	219.85 (140.60, 339.50)	*0.164*
Lactate, mmol/L	1.50 (1.10, 2.20)	1.50 (1.00, 2.10)	1.70 (1.30, 2.50)	***< 0.001***
Troponin T, ng/mL	27.00 (17.70, 43.50)	27.00 (17.10, 38.95)	33.00 (22.25, 88.45)	***< 0.001***
BNP[‡], pg/mL	926.00 (429.00, 1983.00)	926.00 (398.00, 1642.50)	1322.00 (670.25, 5357.50)	***< 0.001***

Table 1 (continued)

Variables	Overall ($n=5855$)	SCAP patients without Sepsis ($n=5201$)	SCAP patients with Sepsis ($n=654$)	$P^{\dagger}$ value
BUN[‡], mg/dL	7.00 (5.00, 10.00)	6.00 (5.00, 10.00)	8.00 (5.00, 13.00)	***<0.001***
Glucose, mmol/L	7.15 (5.59, 0.40)	7.06 (5.54, 9.21)	8.00 (6.03, 10.51)	***<0.001***
CRP[‡], mg/L	67.90 (23.30, 114.00)	65.61 (22.30, 109.38)	89.63 (35.70, 150.25)	***<0.001***
PCT[‡], ng/mL	0.31 (0.14, 0.80)	0.31 (0.14, 0.65)	0.65 (0.20, 2.72)	***<0.001***
PH value	7.41 (7.37, 7.45)	7.41 (7.37, 7.45)	7.40 (7.36, 7.45)	*0.067*
IL-6[‡], pg/mL	46.23 (29.81, 76.87)	46.23 (29.23, 68.53)	46.23 (34.54, 179.10)	***<0.001***
Prognosis				
LOS[‡] in Hospital, median (IQR), d	21.00 (13.00, 32.00)	21.00 (13.00, 32.00)	21.00 (11.00, 34.00)	*0.557*
LOS[‡] in ICU, median (IQR), d	11.00 (5.00, 21.00)	11.00 (5.00, 20.00)	13.86 (7.00, 26.00)	***<0.001***
In-hospital mortality, n (%)	1656 (28.3%)	1385 (26.6%)	271 (41.4%)	***<0.001***
ICU mortality, n (%)	1430 (24.4%)	1194 (23.0%)	236 (36.1%)	***<0.001***
7-day mortality, n (%)	282 (4.8%)	229 (4.4%)	53 (8.1%)	***<0.001***
14-day mortality, n (%)	632 (10.8%)	519 (10.0%)	113 (17.3%)	***<0.001***
28-day mortality, n (%)	1179 (20.1%)	983 (18.9%)	196 (30.0%)	***<0.001***
90-day mortality, n (%)	1616 (27.6%)	1353 (26.0%)	263 (40.2%)	***<0.001***

Data are presented as the median with interquartile range (IQR) for continuous variables, and as counts with percentages for categorical variables

[†] A *p* value of ≤0.05 was deemed to possess statistical significance and highlighted in bold

[‡] *Abbreviations*: *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *APTT* activated partial thromboplastin time, *BNP* brain natriuretic peptide, *BUN* blood urea nitrogen, *CRP* C-reactive protein, FIO_2 fraction of inspiration oxygen *ICU* intensive care unit *IL-6* interleukin 6, *IMV* invasive mechanical ventilation, *LOS* Length of stay, PaO_2 partial arterial oxygen pressure, *PCT* procalcitonin, *PT* prothrombin time

Additionally, our findings indicate that over half of SCAP and co-sepsis patients (52.4%) progress to septic shock. The survival probabilities at 28-day and 90-day intervals were depicted using survival curves for each group of patients in the three groups (those with only sepsis, without sepsis, and with sepsis shock), emphasizing the detrimental outcomes associated with severe sepsisemic events (Fig. 2). Kaplan–Meier analysis revealed that the 28-day survival rate of SCAP patients with sepsis was significantly lower than that of the non-sepsis patients ($P<0.001$, HR =0.58, 95%CI 0.50–0.68) (Fig. 2A). Further stratification revealed that the survival rate of patients with only sepsis was significantly lower than that of patients without sepsis ($P<0.001$, hazard ratio (HR) =0.78, 95%CI 0.595–1.013), whereas the survival rate of patients with sepsis shock was markedly lower ($P<0.001$, HR =2.14, 95%CI 1.653–2.769). Moreover, the HR indicated a significantly higher risk of mortality in the sepsis shock group than in the only sepsis group ($P<0.001$, HR =1.65, 95%CI 1.250–2.189). The 90-day survival curve confirmed that the mortality risk in the sepsis group was significantly elevated than that in the without sepsis group ($P<0.001$, HR =0.58, 95%CI 0.51–0.66). Specifically, the survival rate of patients with only sepsis was significantly lower than that of patients without sepsis ($P<0.001$, HR =0.75, 95%CI 0.595–0.938), and the survival rate of patients with sepsis shock further decreased ($P<0.001$, HR =2.11, 95%CI 1.683–2.638), indicating a significant difference from that of patients with only sepsis ($P<0.001$, HR =1.57, 95%CI 1.232–1.999). Notably, the survival curve of the without sepsis group plateaued within 90 days, whereas the curve for the sepsis group continued to decline, indicating a persistent risk of infection-related death during long-term follow-up.

Construction of the nomogram

A total of 31 variables (with a p-value <0.1) were identified in the univariate logistic regression model. Variables were subsequently included in the multivariate analysis, which preliminarily revealed that 15 independent clinical risk factors contributed to the development of sepsis in SCAP patients, including the presence of chronic hepatic diseases, chronic renal diseases, and chronic cerebrovascular diseases; decreased levels of SBP, globulin, hemoglobin, and albumin; and increase respiratory rates; heart rates, and incidences of coma, APTT, D-dimer, glucose, CRP, and lactate (Table 2). The corresponding odds ratios (ORs) and their 95% confidence intervals (CIs) are presented in Table 2. The variables were subsequently subjected to logistic LASSO regression analysis, resulting in the identification of only 9 independent prognostic factors for constructing the succeeding predictive model, including lactate, D-dimer, respiratory rate, heart rate, albumin, hemoglobin, APTT, glucose, and CRP (Fig. 3, Fig. S1).

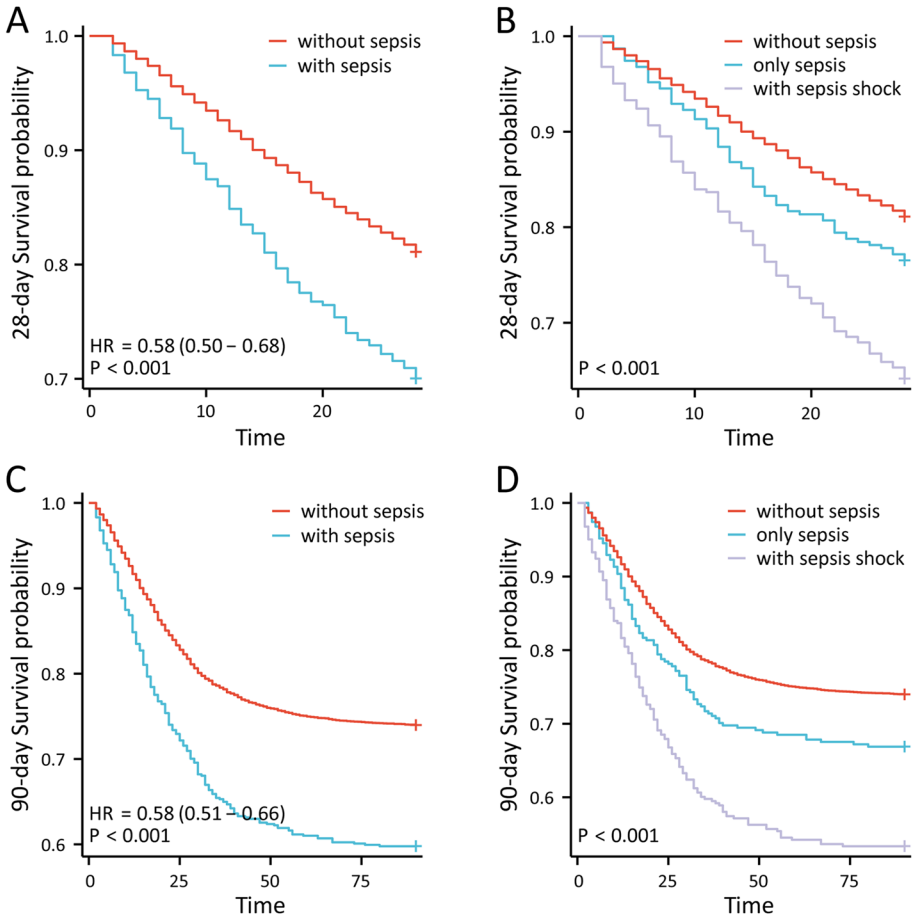

Fig. 2 The 28-day (**A**) and 90-day (**B**) survival curves of SCAP patients with or without sepsis. The 28-day (**C**) and 90-day (**D**) survival curves of SCAP patients with or without sepsis or with sepsis shock

Therefore, the above nine risk factors were utilized to construct an intuitive nomogram for predicting co-sepsis risk among sepsis patients. As depicted in Fig. 3, each predictor was assigned a corresponding point whose score was visually represented on the top line of our nomogram. The total points were calculated by summing the scores of seven predictors for each patient, and then projected vertically onto the predictor axis to obtain an individualized risk probability of developing sepsis in SCAP patients with sepsis.

Assessment and validation of the nomogram

The C-index of the developed prediction model was 0.722 (95% CI 0.702–0.742). To validate this result, bootstrapping analysis was performed, yielding a consistent value of 0.711 and indicating that the risk of overfitting for the nomogram is relatively low. The model's differentiation capability for co-sepsis risk among patients with SCAP exceeds that of both the qSOFA (AUC = 0.610; 95% CI 0.588–0.631), CURB-65 (AUC = 0.419; 95% CI 0.397–0.441), SOFA (AUC = 0.620; 95% CI 0.598–0.643), and APACHE II scores (AUC = 0.658; 95% CI 0.635–0.679), as validated and demonstrated by ROC curve analysis. The ROC curve of the Nomogram rose rapidly in the early stage (characterized by high true positive rate at a low false positive rate), indicating that its ability to identify early sepsis is superior to that of traditional scores (Fig. 4A).

The calibration plots in Fig. S2 demonstrate good concordance between the predicted probabilities of the model and the observed actual probabilities, as evidenced by the close alignment of the calibration curve with the reference line. Compared with the qSOFA, CURB-56, SOFA, and APACHE II scores, our nomogram demonstrated better overall net benefits within the clinical decision threshold range of 10%−50%. across a wide range of threshold probabilities, highlighting the advantage of the nomogram in predicting sepsis in patients with SCAP. (Fig. 4B).

Table 2 Risk factors for developing sepsis among patients hospitalized for SCAP

Risk factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	$P^{\dagger}$	OR (95% CI)	$P^{\dagger}$
Treatment				
Vasopressor	1.230 (1.040, 1.455)	*0.016*		
Comorbidities				
Chronic hepatic diseases	1.515 (0.980, 2.340)	*0.062*	1.683 (1.067, 2.653)	*0.025*
Chronic renal diseases	1.498 (1.113, 2.017)	*0.008*	1.387 (1.011, 1.904)	*0.043*
Chronic cerebrovascular diseases	1.203 (1.008, 1.435)	*0.041*	1.242 (1.013, 1.522)	*0.037*
Chronic pulmonary diseases	1.175 (0.978, 1.411)	0.086		
Vital signs				
Respiratory rate (breath/min)	1.059 (1.046, 1.072)	*< 0.001*	1.020 (1.005, 1.035)	*0.008*
Heart rate (beat/min)	1.021 (1.017, 1.024)	*< 0.001*	1.011 (1.007, 1.015)	*< 0.001*
Temperature (°C)	1.288 (1.170, 1.419)	*< 0.001*		
Systolic blood pressure (mmHg)	0.996 (0.994, 0.999)	*0.004*	0.995 (0.991, 1.000)	*0.041*
Diastolic blood pressure (mmHg)	0.996 (0.992, 1.000)	0.05		
PaO2/FiO_2	0.995 (0.994, 0.997)	*< 0.001*		
Coma	1.311 (1.070, 1.606)	*0.009*	1.303 (1.028, 1.636)	*0.022*
Laboratory examinations				
Neutrophil/Lymphocyte ratio	1.012 (1.007, 1.016)	*< 0.001*		
Monocyte (× 10^9/L)	0.617 (0.462, 0.825)	*0.001*		
Globulin (g/L)	0.966 (0.951, 0.980)	*< 0.001*	0.982 (0.967, 0.997)	*0.016*
Hemoglobin (g/L)	0.986 (0.983, 0.989)	*< 0.001*	0.993 (0.989, 0.997)	*< 0.001*
Platelet (× 10^9/L)	0.998 (0.997, 0.999)	*< 0.001*		
APTT‡ (s)	1.020 (1.016, 1.025)	*< 0.001*	1.009 (1.003, 1.015)	*0.002*
PT‡ (s)	1.026 (1.017, 1.036)	*< 0.001*		
Fibrinogen (g/L)	1.057 (1.004, 1.113)	*0.034*		
D-dimer (mg/L)	1.031 (1.022, 1.041)	*< 0.001*	1.015 (1.004, 1.026)	*0.008*
Albumin (g/L)	0.931 (0.919, 0.943)	*< 0.001*	0.983 (0.967, 0.999)	*0.035*
Total bilirubin (μmol/L)	1.003 (1.001, 1.005)	*< 0.001*		
ALT‡ (IU/L)	1.001 (1.000, 1.001)	*0.001*		
Creatinine (μmol/L)	1.001 (1.001, 1.002)	*< 0.001*		
Myoglobin (ng/mL)	1.000 (1.000, 1.001)	*< 0.001*		
BUN‡ (mg/dL)	1.035 (1.026, 1.045)	*< 0.001*		
Glucose (mmol/L)	1.071 (1.050, 1.092)	*< 0.001*	1.027 (1.005, 1.050)	*0.016*
CRP‡ (mg/L)	1.004 (1.003, 1.005)	*< 0.001*	1.002 (1.001, 1.003)	*0.001*
Lactate (mmol/L)	1.144 (1.104, 1.185)	*< 0.001*	1.066 (1.025, 1.109)	*0.001*
PCT‡ (ng/mL)	1.022 (1.016, 1.028)	*< 0.001*		

† A p value of ≤ 0.05 was deemed to possess statistical significance and highlighted in bold

‡ *Abbreviations*: *ALT* alanine aminotransferase, *APTT* activated partial thromboplastin time, *BUN* blood urea nitrogen, *CRP* C-reactive protein, FIO_2 fraction of inspiration oxygen, PaO_2 partial arterial oxygen pressure, *PCT* procalcitonin, *PT* prothrombin time

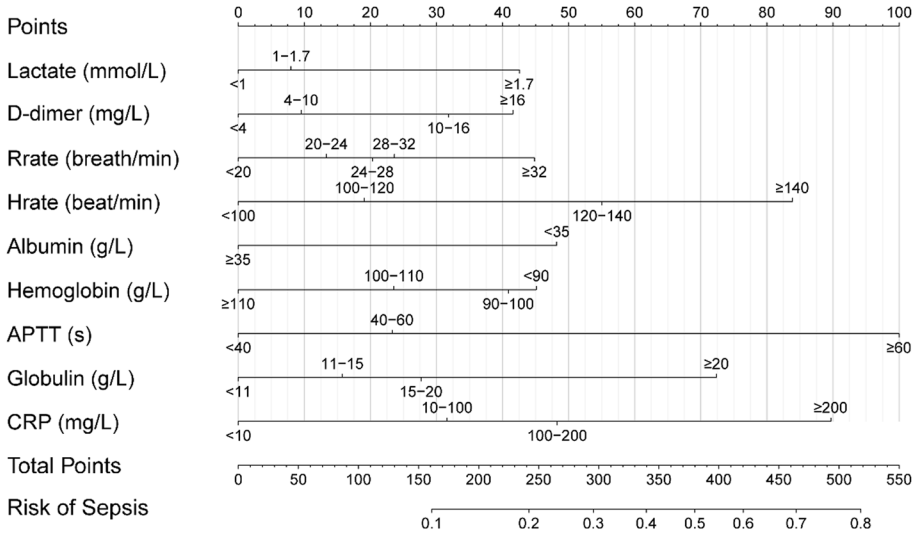

Fig. 3 Nomogram for co-sepsis risk in SCAP patients. SCAP, severe community-acquired pneumonia; Rrate, respiratory rate; Hrate, heart rate; APTT, activated partial thromboplastin time; CRP, C-reactive protein

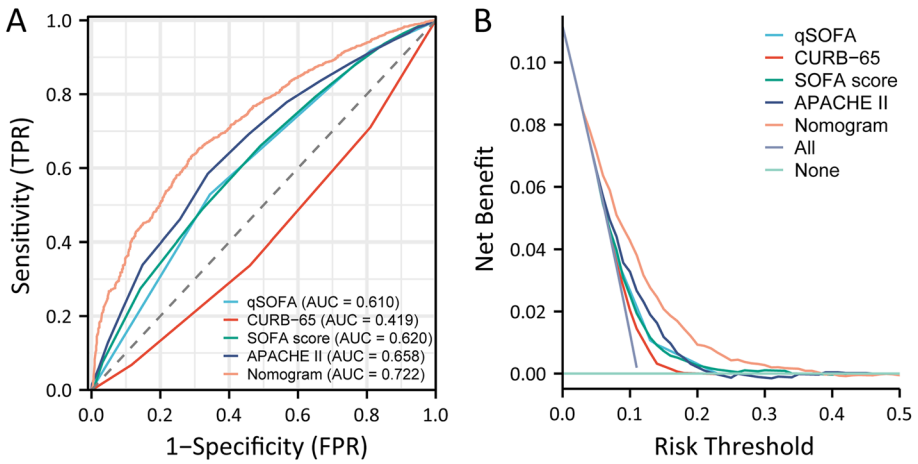

Fig. 4 **A** ROC curve of the nomogram for co-sepsis risk in SCAP patients. **B** DCA of the nomogram. ROC, receiver operating characteristic curve; DCA, decision curve analysis

Discussion

In accordance with the severity criteria for CAP from the IDSA/ATS, a total of 6956 SCAP patients admitted to the medical ICU over a 9-year period were included in the present study. Following the exclusion criteria screening, 5855 patients were ultimately categorized into two groups on the basis of the presence or absence of sepsis according to the sepsis 3.0 diagnosis. Univariate and multivariate logistic regression analyses were employed to identify independent risk factors associated with sepsis in patients diagnosed with SCAP. Ultimately, a risk prediction model for sepsis in SCAP patients was established based on the outcomes of LASSO logistic regression analysis. The internal verification results demonstrated superior DCA curves, C-indexes and AUROC values compared with commonly used clinical scores for sepsis and SCAP, indicating its relatively favorable performance in co-sepsis prediction. Therefore, based on several routine laboratory test results and basic signs available within 24 h, the probability of sepsis in patients with SCAP can be obtained through simple calculations, making it a rapid and economical tool with certain clinical practicability.

SCAP continues to be a prominent etiology for intensive care unit admissions, imposing substantial resource burdens and increasing global mortality rates [21].

Without prompt diagnosis, prognosis assessment, and appropriate treatment initiation for SCAP, overall mortality increases by 20% when the patient progresses to shock (22% higher), necessitates invasive mechanical ventilation (25% higher), or experiences both conditions simultaneously (30% higher) [9]. A recent extensive study, which included a cohort of 10,000 individuals from 730 ICUs, reported that the incidence of sepsis is as high as 30%. [22]. Pneumonia accounts for approximately half of all sepsis cases in high-income countries [23]. The results of our multifactor analysis revealed 15 clinical risk factors leading to the development of sepsis in SCAP patients, including chronic hepatic diseases; chronic renal diseases; chronic cerebrovascular diseases; decreased levels of SBP, globulin, hemoglobin, and albumin; and increased respiratory rates, heart rates, incidences of coma, APTT, D-dimer, glucose, CRP, and lactate. Albumin (ALB) levels were reduced in the hypervirulent klebsiella pneumoniae patient cohort (OR =0.867; 95% CI, 0.758–0.990), and diabetes mellitus (OR =9.591; 95%CI, 1.766–52.075) was reported as an independent risk factor for sepsis shock [24]. Consistent with our findings, the premortem spectrum independently associated with mortality in SCAP patients with or without sepsis also included cerebrovascular diseases, renal diseases, and hepatic diseases [25–27]. The analysis of blood transcriptome data from patients with sepsis caused by community-acquired pneumonia revealed that the dysregulation of mRNA levels in red blood cells and platelets, along with subsequent coagulopathy, was directly correlated with the severity of sepsis and the 28-day survival rate [28]. Przybilla et al. proposed a continuous-time Markov 28-day mortality risk model based on SOFA score intervals, emphasizing the feasibility of updating the risk assessment for CAP patients daily. However, both the reliability of the model validation design and the predictive performance of model fitting when there is a sudden change in individual disease state are unsatisfactory [29]. Personalized anticipation of the progression of SCAP patients has always been an important fulcrum for clinical decision making.

In this cohort, patients with SCAP-related sepsis had significantly higher mortality rates of all types than patients without sepsis did ($p < 0.001$), which may be attributed to the fact that the development of sepsis is crucial for adverse outcomes. When sepsis shock occurs in SCAP patients, they are confronted with a more formidable challenge in terms of survival, as demonstrated by the 28-day and 90-day survival curves ($p < 0.001$). The high mortality rates reported here are close to those reported in other cohorts. A contemporary cohort (GenOSept) of patients admitted to ICUs across Europe with SCAP reported an ICU mortality rate, as well as 28-day mortality rates of 19% and 17%, respectively [24]. Furthermore, as one of the most severe complications of SCAP, the mortality rate among patients subsequent to sepsis shock can reach 50% [30]. However, relevant epidemiological data vary widely across cohorts, potentially because of fluctuations in the sensitivity and specificity of diagnostic criteria for sepsis and sepsis shock. For example, according to the International Consensus Criteria for Sepsis published in 2003, 573 patients (49%) met the criteria for sepsis shock in the GenOSept cohort, whereas in another cohort of Spanish multicenter CAP patients, 1529 patients (37.6%) were defined as having severe sepsis [24, 25]. The literature has focused predominantly on mortality-related risk factors or prognostic models, but few studies have investigated the risk factors and corresponding probability of sepsis in patients with SCAP. However, the early and timely identification of sepsis during the course of SCAP appears to be beneficial for selecting the most appropriate mode of care and empiric antibiotic therapy, shortening the duration of clinical stabilization and length of hospital stay, enhancing pulmonary physiology, and diminishing mortality rates [7, 31–35]. As of June 2024, the present study represents the first study on this specific subject in China. The primary aim of our study was to develop an initial practical and rapid predictive model for assessing the risk of sepsis in patients with SCAP.

We constructed a predictive nomogram to estimate the likelihood of sepsis within SCAP. Our nomogram composed of 9 variables, which was derived from routine blood tests and basic vital signs available within 24 h, including lactate, D-dimer, respiratory rate, heart rate, ALB, hemoglobin, APTT, glucose, and CRP, can avoid the delay defect of traditional scoring. In patients who develop severe sepsis or SCAP, low serum ALB levels during the acute phase indicate increased risks of severity and death [36]. Previous studies have shown that patients with hypoalbuminemia exhibit elevated levels of D-dimer and high-sensitivity CRP [37, 38], indicating that the combination of albumin with other clinical parameters/markers (such as blood glucose, D-dimer, lactate, CRP, MAP, and temperature, etc.) has greater predictive value [39–41]. In a multi-center prospective cohort study in the United States, persistent coagulation abnormalities, particularly D-dimer (> 80.6%), were common in CAP patients and increased with disease severity and adverse outcomes. The findings of another multicenter nested case–control study revealed a significant increase in the levels of the proinflammatory cytokines IL-6, CRP, and fibrinogen α, β, and γ chains among young sepsis patients (< 65 years old). These indicators were also selected as the components in our model, which focused on the median age group below 65 years. Collectively, our nine selected variables encompass a multidimensional evaluation of

the inflammatory burden, organ functional reserve, and systemic immune status, demonstrating the capacity of the nomogram to capture early-stage characteristics of the transition from pneumonia to sepsis. Meanwhile, the nomogram can provide continuous probabilistic output and support threshold adjustment, making it possible to provide personalized prediction of the occurrence of severe comorbidities sepsis in SCAP patients.

The nomogram visualizes and accurately quantifies the probability of sepsis occurrence, and then the model was assessed from four perspectives: the C-index, ROC curve, calibration curve, and decision analysis curve. Our nomogram demonstrated a promising C-index of 0.722 (95% CI 0.702–0.742) and a corrected C-index of 0.711 by bootstrapping validation. Compared with the ROC curves of the qSOFA, CURB-65, SOFA, and APACHE II scores, the present model had a good validation effect. This finding also indirectly confirms that individual disease assessment scores or prognostic scores specifically for CAP patients or sepsis patients do not necessarily have an advantage in the early identification of pulmonary sepsis. While rapid clinical assessment scores may demonstrate advantages in pre-hospital settings or emergency departments, their direct application in hospitalized patients could overlook various valuable test results, potentially leading to unreliable assessment outcomes. In contrast, our nomogram model, which integrates readily obtainable laboratory parameters and vital signs within 24 h, effectively addresses this limitation by providing targeted guidance for clinicians to monitor relevant clinical indicators. Since the patients were screened according to the diagnostic criteria of SCAP and sepsis, compared with the model established according to the International Classification of Diseases code, our nomogram avoids the degradation of model fit due to code iteration of the International Classification of Diseases (ICD) and facilitates the comparison and reference of other researchers.

Despite the commendable practicality and robustness of our model, several limitations inevitably exist in our research. First, it is important to note that this study was conducted solely at a single-center retrospectively, albeit with a substantial volume of data obtained from a large tertiary hospital in China. Second, although it has undergone internal validation, a wider range of data collection is needed for external validation to extend its applicability to more areas or populations. Additionally, our research findings may be influenced by confounding factors such as the type of pathogen, antibiotic usage, different stages of sepsis, and social support. Finally, we must also consider the cost and complexity involved in implementing intervention measures as well as their availability and the level of professional knowledge needed. Given that we have collected data on long-term outcomes including 90-day mortality, we plan to focus on three aspects in subsequent research: external validation of the model in the context of pulmonary infection (Collecting data from other large medical centers in China), prediction of long-term outcomes, and improvement of the model by integrating existing assessment scores.

Conclusion

In conclusion, we reported 15 independent risk factors and proposed a prediction nomogram for the development of sepsis in patients with SCAP. The internal verification results demonstrated that these nine risk predictors exhibit ideal predictive accuracy, robustness, and clinical relevance, emphasizing the necessity and feasibility of rapid updates for individual estimation of sepsis risk. We expect to extend its applicability through more external evaluation.

Abbreviations

ALT	Alanine aminotransferase
APTT	Activated partial thromboplastin time
AST	Aspartate aminotransferase
AUC	Area under the receiver operating characteristic curve
BNP	Brain natriuretic peptide
BUN	Blood urea nitrogen
CAP	Community-acquired pneumonia
CRP	C-reactive protein
DBP	Diastolic blood pressure
DCA	Decision curve analysis
FIO_2	Fraction of inspiration oxygen
ICU	Intensive care unit
IDSA/ATS	Infectious Diseases Society of America/American Thoracic Society
IL-6	Interleukin 6
IMV	Invasive mechanical ventilation
IQR	Interquartile range
LASSO	Logistic least absolute shrinkage and selection operator
LOS	Length of stay
MAP	Mean arterial pressure
MI	Multiple imputation
PaO_2	Partial arterial oxygen pressure
PCT	Procalcitonin
PSI	Pneumonia Severity Index
PT	Prothrombin time
ROC	Receiver operating characteristic curve
SBP	Systolic blood pressure
SCAP	Severe community-acquired pneumonia
SOFA	Sequential Organ Failure Assessment

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-11027-w.

Supplementary Material 1.

Supplementary Material 2.

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Not applicable.

Authors' contributions

XYW, CW, and DXHe gave the study concept and design; all authors acquired, analyzed, and interpreted the data, and critically revised the manuscript for

important intellectual content; XYW, CW and DH drafted the manuscript; YAZ, XYW and LYR carried out the statistical analysis; LJG, HY and ZAL supervised the study; All authors read and approved the final manuscript.

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Data availability
The datasets utilized and/or analyzed in the present study can be obtained from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval was obtained from biomedical research ethic committee of the West China Hospital of Sichuan University (No. 2021–828). The retrospective noninterventional design led to the waiver of written informed consent, and study conduction was in accordance with the Helsinki Declaration. The confidentiality of all patient data was strictly maintained.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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