Infection and Drug Resistance

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ORIGINAL RESEARCH

Prognostic Factors and Nomogram for *Klebsiella pneumoniae* Infections in Intensive Care Unit

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Purpose: *Klebsiella pneumoniae* infections pose a significant threat to public health with high morbidity and mortality rates. The early identification of risk factors for mortality and accurate prognostic evaluation are important. Therefore, we aimed to identify the risk factors for mortality in patients with *K. pneumoniae* infections and develop a nomogram model for prognosis.

Methods: Patients diagnosed with *K. pneumoniae* infection were recruited from the intensive care unit of Peking University Third Hospital. The enrolled patients were categorized into survivor and non-survivor groups. Univariate and multivariate regression analyses were performed to identify independent risk factors for 30-day mortality, and a nomogram was constructed and validated.

Results: A total of 408 patients infected with *K. pneumoniae* at different sites were included in this study. PO_2, lactate, respiratory failure, urinary tract infection, heart rate, 24h-urineoutput, neutrophil count, alkaline phosphatase, and vasoactive drug use were significant risk factors and were integrated into a nomogram to predict the risk of 7-day, 14-day, 21-day, and 28-day mortality. The nomogram demonstrated superior prognostic ability, achieving higher area under the receiver operating characteristic curve (AUC) (>0.8) and concordance index (C-index) (>0.8) values than the Pitt bacteremia, sequential organ failure assessment (SOFA), and acute physiology and chronic health evaluation (APACHE) II scores (all AUC and C-index < 0.75). Cross-validation of the nomogram confirmed its consistent performance, with both AUC and C-index values exceeding 0.75. The nomogram demonstrated a strong Hosmer-Leme-show goodness-of-fit and good calibration ($p > 0.05$). Additionally, decision curve analysis revealed that the nomogram provided significant clinical utility for prognostic prediction.

Conclusion: The 30-day mortality risk factors for *K. pneumoniae* infections were identified, and a predictive nomogram model was developed. The nomogram demonstrated good accuracy and predictive efficiency, providing a practical tool for short-term risk assessment and potentially improving clinical outcomes by providing early intervention and personalized patient management.

Keywords: *Klebsiella pneumoniae*, infection, prognosis, mortality, risk factor

Introduction

Klebsiella pneumoniae is a gram-negative bacterium that is commonly found in the environment and widely colonizes the human mucous membranes.[1,2] It is estimated that as many as 35% of humans are colonized by *K. pneumoniae* in their gastrointestinal tract.[3] Although *K. pneumoniae* does not commonly cause gastrointestinal diseases, it possesses the capacity to disseminate from this niche and cause a variety of infections, including pneumonia, urinary tract infections, hepatic abscess, bloodstream infections, and soft tissue infections.[4–7] Research has revealed that *K. pneumoniae* strains

Received: 13 October 2024
Accepted: 18 January 2025
Published: 1 March 2025

account for >90,000 infections and >7,000 deaths annually in Europe alone, thereby posing a significant threat to public health.[8] Early intervention correlates with improved prognosis, making it essential to promptly identify patients at high risk of mortality to ensure that these patients receive timely and appropriate treatment.[9] Thus, there is a pressing need to identify risk factors and develop reliable clinical tools to accurately predict the poor outcomes of *K. pneumoniae* infections. This will provide essential guidance for clinical management and decrease the disease burden.

Accurate prognostic evaluation is fundamental for prevention and treatment strategies in which clinical prognostic factors must be clearly illustrated.[10,11] The acute physiology and chronic health evaluation (APACHE) II scoring system and the Sequential Organ Failure Assessment (SOFA) are widely used in intensive care unit (ICU).[12,13] However, both the APACHE II and SOFA score systems require the collection of numerous physiological parameters, making them complex to calculate and time-consuming.[14] The Pitt bacteremia score uses a simple scoring method that has been used to predict mortality in patients infected with gram-positive or gram-negative bacteria; however, it primarily concentrates on the severity of patients with bacteremia rather than prognosis.[15] In recent years, many risk factors related to *K. pneumoniae* patients with poor outcomes have been found.[16,17] Indeed, there is a paucity of research on risk prediction tools that can effectively integrate various risk factors. The nomogram is a convenient tool that has been widely used in predicting the risk or prognosis of various diseases.[9,18–20] By integrating multiple predictive factors into a visual map, it delineates the probability of risk prediction. This makes the nomogram invaluable for clinical decision-making and for enhancing the management of high-risk populations in advance.[21,22]

This study analyzed the factors affecting 30-day mortality of *K. pneumoniae* infections and constructed a nomogram prediction model that effectively predicted the mortality probability at 7-day, 14-day, 21-day and 28-day intervals, to identify high-risk patients and monitor disease progression.

Methods

Study Participants

Patients were enrolled from the medical and surgical intensive care units of Peking University Third Hospital, a national tertiary-level medical center, between January 2017 and April 2023. All enrolled patients underwent microbial culture testing of specimens from sputum, throat swabs, bronchoalveolar lavage fluid, blood, urine, bile, ascitic fluid, abscesses, or tissue. We enrolled patients with the following inclusion criteria: (i) age ≥18 years; (ii) positive microbial culture results for *K. pneumoniae* for patients who stayed in the ICU within 14 days; and (iii) a confirmed diagnosis of infection, including the presence of clinical signs and symptoms accompanied by positive results in radiography or purulent material microscopic examinations. Exclusion criteria were as follows: (i) ICU stay of less than 24h; (ii) multiple sites of infections; (iii) colonized patients without confirmed infections, and (iv) missing proportion of the corresponding variables greater than 20% (details of the missing proportion were presented in Figure S1). For patients who were admitted more than once, only the first ICU stay was eligible for inclusion. All patients were followed up for 30 days, and only those with definite outcomes were included. This study was approved by the Institutional Review Board of the Peking University Third Hospital (IRB00006761-m2021545), and the requirement for informed patient consent was waived owing to its retrospective nature. All patient data were anonymized and handled with strict confidentiality to ensure compliance with the Declaration of Helsinki. A detailed screening flowchart is provided in Figure S1.

Data Collection and Study Outcome

All clinical data were extracted from the medical record database by two independent reviewers (YZ and HWZ). Any controversies were resolved by a third reviewer (CD). Data within the first 24h of ICU admission on patients' demographics, underlying comorbidities, and hematological parameters (eg, blood routine, coagulation profile, blood gas, liver, and renal function) were recorded. Treatments before or after 72h of ICU admission, including the use of mechanical ventilation, peripherally inserted central catheter, urinary catheter, nasogastric tube, vasoactive drugs, and antibiotic treatment, were collected. Other information regarding the bacteria isolated and the site of infection during the ICU stay was also collected. Vital signs, APACHE II, SOFA, and Pitt bacteria scores were based on the worst values during the first 24h of ICU admission. Respiratory infection indicated pneumonia or ventilator-associated pneumonia,

which was defined as lower respiratory tract symptoms (eg, fever or chills, cough, or shortness of breath) and new focal chest signs coinciding with the onset or progressive pulmonary infiltrates on chest radiography. Respiratory failure was defined as the presence of clinical signs (eg, dyspnea, tachypnea, cyanosis, or altered mental status) accompanied by hypoxemia (PaO_2 < 60 mm Hg) and/or hypercapnia ($PaCO_2$ > 50 mmHg).[23] The survival time was defined as the time from ICU admission to death or discharge. The endpoint was all-cause mortality, defined as death from any cause within 7, 14, 21, and 28 days of ICU admission.

Statistical Analysis

Continuous variables were presented as medians with interquartile ranges or means with standard deviations, and their statistical significance was assessed using the *t*-test or Wilcoxon rank-sum test. Categorical variables were reported as frequencies and percentages, and their statistical significance was analyzed using chi-square ($\chi 2$) or Fisher's exact test. Univariate Cox regression was performed to explore risk factors for 30-day mortality. Factors with a value of p <0.2 were entered into the multivariate Cox regression model.[24] A nomogram was used to visualize the model. The discrimination and calibration abilities of the prediction model were assessed using the concordance index (C-index), receiver operating characteristic curve (ROC), area under the ROC curve (AUC), and a calibration plot. The significant 7-day, 14-day, 21-day and 28-day ROC curves and calibration curves were plotted to verify the performance of the model. Internal cross-validation was applied to validate the stability of the model by randomly splitting the patients in the training cohort into five equal samples. Four of these samples were used to construct Cox regression models, and the model coefficients were applied to the remaining samples. This process was repeated five times, and the mean AUC and C-statistics corresponding to each iteration were calculated.[19] The clinical utility of the model was evaluated using the Log rank test to determine whether the survival distributions differed among the low-, median-, and high-risk groups. Decision curve analysis (DCA) was conducted to evaluate the clinical benefits of the nomogram by assessing net benefits at different threshold probabilities. All statistical analyses were performed using Stata (v. 17.0) or R (v. 4.2.2). The "survival" package and "rms" package of R software were used to plot the nomogram and calculate the AUC and C-index. The "PredictABEL" package and "survminer" package were used to plot calibration curves and Kaplan–Meier survival curve. The "pROC" and "stdca" package were used to plot ROC curves and decision curves. A 2-sided *p*-values <0.05 were considered statistically significant.

Results

Patient Characteristics

A total of 408 participants were enrolled in this study, including 320 survivors (78.43%) and 88 dead people (21.57%). There were 269 male patients (65.93%), with a mean age of 77 years, and most participants were from the medical ICU (92.89%). The demographic characteristics of the survivors were as follows: mean age, 76 years (range, 64–84 years); 212 (66.25%) male, and 294 (91.88%) from the medical ICU. The demographic characteristics of the dead group were as follows: mean age 79.5 years (range, 69–85 years), 57 (64.77%) male, and 85 (96.59%) were from the medical ICU. Detailed patient characteristics are summarized in Tables 1 and S1.

Risk Factors and Model Construction

Univariate Cox regression analysis was used to screen for potential risk factors of 30-day mortality. Potential prognostic factors, including patient information, infection site, comorbidities, vital signs, arterial blood gas, laboratory tests, treatments, and three existing critical care score scales (Pitt, SOFA, and APACHE II), were integrated (Table 2). Variables with p values less than 0.2 were subsequently included in the multivariate Cox regression analysis. As shown in Table 3, nine variables were identified and incorporated into the model, named Prediction of *K. pneumoniae* Infections (POKPI). The POKPI model includes respiratory infection, respiratory failure, heart rate (HR), 24h-urinary output, PaO_2, lactic acid (Lac), neutrophils, alkaline phosphatase (ALP), and vasoactive drugs. As shown in Figure 1, the prognostic model is presented as a nomogram to predict the risk of 7-, 14-, 21-, and 28-day mortality. Each predictor

Table 1 Baseline Characteristics of Patients in Survivors and Non-Survivors

Variable	Survivors	Non-survivors	*p* value
No. of patients, n (%)	320 (78.43)	88 (21.57)	
Age (years)	76 (64, 84)	79.5 (69, 85)	0.104
Male, n (%)	212(66.25)	57(64.77)	0.796
Type of ICU, n (%)			0.127
Medical	294(91.88)	85(96.59)	
Surgical	26(8.12)	3(3.41)	
Infection site, n (%)			
Blood infection	28(8.75)	10(11.36)	0.455
Urinary infection	36(11.25)	4(4.55)	0.061
Respiratory infection	228(71.25)	70(79.55)	0.120
Wound/Tissue infection	17(5.31)	2(2.27)	0.361
Abdominal infection	11(3.44)	2(2.27)	0.835
Co-morbidities, n (%)			
Hypertension	197(61.56)	53(60.23)	0.820
Diabetes	111(34.69)	38(43.18)	0.143
Chronic pulmonary disease	35(10.94)	9(10.23)	0.849
Respiratory failure	165 (51.56)	66 (75)	<0.001
Coronary heart disease	85(26.56)	28(31.82)	0.329
AKI	24 (7.5)	17 (19.32)	0.001
Chronic renal failure	44(13.75)	21(23.86)	0.022
Liver cirrhosis/hepatic failure	1(0.31)	2(2.27)	0.119
Malignancy	17(5.31)	7(7.95)	0.351
Leukemia	1(0.31)	0 (0)	1.000
Immunosuppression	2 (0.62)	0 (0)	1.000
Elective surgery	98 (30.63)	19 (21.59)	0.097
Sudden cardiac arrest	5(1.56)	0 (0)	0.527
Vital signs			
Temperature (°C)	36.50 (36.10, 37.00)	36.75 (36.20, 37.42)	0.039
RR (cpm)	20 (16, 22)	20.5 (18.0, 26.0)	0.003
HR (bpm)	88.00 (75.75, 102.00)	96.00(84.00,112.00)	0.001
MAP (mmHg)	114.73(19.66)	109.72(23.59)	0.070
SBP (mmHg)	129.00 (114.75, 145.00)	127.00 (107, 146)	0.274
24h-urinary output (mL)	1700 (1200.00, 2452.50)	1375 (787.50, 1862.50)	<0.001
Arterial blood gas			
PH	7.40 (7.36, 7.45)	7.41 (7.33, 7.45)	0.733
PaO_2 (mmHg)	90.35(63.98,113.59)	75.90(51.85,103.98)	0.007
$PaCO_2$ (mmHg)	44.08(36.00,58.15)	44.75(35.02,68.05)	0.643
HCO_3- (mmol/L)	24.70(22.00,28.14)	24.11(19.50,28.74)	0.291
Lac (mmol/L)	1.7(1.1,2.5)	2.30(1.27,3.70)	0.001
Laboratory tests			
WBC (10^9/L)	9.81(6.93,13.36)	11.33(8.37,15.06)	0.008
Neutrophil (10^9/L)	84.50(77.07,90.05)	87.45(82.97,91.05)	0.004
Lymphocyte (10^9/L)	9.30 (5.18,14.80)	7.50(4.92,10.00)	0.012
Neutrophil (%)	8.20(5.38,11.57)	9.72(7.42,13.33)	0.002
Lymphocyte (%)	0.86(0.52,1.29)	0.84(0.53,1.12)	0.330
Platelet (10^9/L)	178.50 (127.00, 229.00)	162.00 (102.75, 238.50)	0.202
NLR (%)	8.92 (5.40, 17.40)	11.60(8.21,18.45)	0.007
PLR (%)	190.22 (125.00, 327.90)	201.74(115.51,312.90)	0.814
RBC (10^{12}/L)	3.56 (2.95, 4.21)	3.27 (2.79, 4.04)	0.160
Hemoglobin (g/dl)	11.00 (8.90, 12.80)	9.80 (8.40, 12.20)	0.064
HCT	33.00 (27.00,39.00)	31.00 (26.00,37.25)	0.105

(*Continued*)

Table 1 (Continued).

Variable	Survivors	Non-survivors	*p* value
ALT (U/L)	24.00 (16.82, 37.00)	22.00 (14.75, 42.75)	0.353
ALP (U/L)	74.00 (57.00, 97.00)	88.00 (69.00, 132.25)	<0.001
AST (U/L)	29.00 (22.00, 43.25)	31.00 (23.00, 46.25)	0.255
TBIL (μmol/L)	14.40(10.57,21.60)	14.65(10.88,24.28)	0.282
BUN (mmol/L)	7.73(5.41,12,47)	11.05(7.00,18.72)	0.001
Cr (mg/dL)	77.00(57.00,110.00)	89.5(72.5,194.5)	<0.001
INR	1.16 (1.06, 1.30)	1.17 (1.05, 1.33)	0.986
PT (s)	12.50 (11.40, 14.00)	12.60 (11.25, 14.35)	0.850
PTT (s)	29.10 (24.15, 33.02)	30.15 (27.50, 34.78)	0.019
Treatment, n (%)			
MV	179(55.94)	55(62.50)	0.270
PICC	172(53.75)	54(61.36)	0.203
Urinary catheter	299(93.44)	85(96.59)	0.266
Nasogastric tube	247(77.19)	83(94.32)	<0.001
Vasoactive drugs	162(50.62)	82(93.18)	
Dopamine	76(23.75)	51(57.95)	
Dobutamine	4(1.25)	5(5.68)	
Epinephrine	63(19.69)	58(65.91)	
Norepinephrine	118(36.88)	74(84.09)	
Metaraminol	50(15.63)	27(39.68)	
Antibiotic treatment	169(67.87)	108(67.92)	0.991
Penicillins only	14(5.62)	3(1.89)	
Cephalosporins only	28(11.25)	4(2.52)	
Carbapenems only	3(1.20)	4(2.52)	
Fluoroquinolones only	2(0.80)	0	
Glycopeptides	4(1.61)	0	
Combination of two kinds of antibiotics	43(17.27)	21(13.21)	
Combination of three or more kinds of antibiotics	75(30.12)	76(47.80)	
Pitt score	5.0 (4.0, 7.25)	4.0 (2.0, 6.25)	0.001
SOFA score	9.00 (7.00, 11.00)	11.00 (9.00, 14.00)	<0.001
APACHE II score	19.00 (14.00, 24.00)	22.00 (18.00, 28.25)	<0.001

Abbreviations: AKI, acute kidney injury; APACHE, acute physiology and chronic health evaluation; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; HCT, hematocrit; HR, heart rate; INR, international normalized ratio; Lac, lactate; MAP, mean arterial pressure; MV, mechanical ventilation; NLR, neutrophil lymphocyte ratio; PICC, peripherally inserted central catheter; PLR, platelet lymphocyte ratio; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cell; RR, respiratory rate; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; TBIL, total bilirubin; WBC, white blood cell.

corresponds to a score by drawing a point line. The sum of the nine predictors was located on the total point line, and a vertical line was drawn downwards from the total point axis to the risk of mortality.

Performance and Validation of the Nomogram Model

Based on the model prediction value and patient survival data, the ROC and calibration curves of these models (POKPI model, Pitt, SOFA, and APACHE II) for predicting 7-day, 14-day, 21-day and 28-day mortality were drawn. As shown in Figure 2 and Table 4–5, the POKPI model had a higher AUC (0.833, 0.840, 0.834, 0.851 for predicting 7-day, 14-day, 21-day and 28-day mortality respectively) and C-index (0.820, 0.822, 0.808, 0.814 for predicting 7-day, 14-day, 21-day and 28-day mortality respectively) than those of the Pitt, SOFA, and APACHE II scores (all AUC and C-index < 0.75). Meanwhile, the average AUC and C-index of the POKPI model calculated in internal cross validation were both higher than 0.75 (Table S2). Moreover, the calibration curves of the POKPI model performed favorable consistency between prediction and observation, and the Hosmer-Leme-show tests conducted to predicting 7-day, 14-day, 21-day, and 28-day survival showed non-significant p-values ($p > 0.05$) (Figures 3, S2–S4 and Tables S3–S6).

Table 2 Univariate Analysis of Risk Factors Associated with 30-Day Mortality

Classification	Variables	Univariate Cox Regression	
		HR (95%)	*p* value
Patient information	Age (years)	1.02(1.00,1.03)	0.034
	Male, n (%)	1.04(0.67,1.61)	0.855
Infection site	Blood infection	1.32(0.68,2.55)	0.406
	Urinary infection	0.42(0.15,1.14)	0.090
	Respiratory infection	1.45(0.87,2.44)	0.157
	Wound/Tissue infection	0.46(0.11,1.89)	0.283
	Abdominal infection	0.66(0.16,2.68)	0.561
Co-morbidities	Hypertension	0.94(0.61,1.44)	0.777
	Diabetes	1.39(0.91,2.12)	0.125
	Chronic pulmonary disease	0.92(0.46,1.83)	0.807
	Coronary heart disease	1.27(0.81,1.99)	0.300
	Malignancy	1.60(0.74,3.46)	0.234
	Liver cirrhosis/hepatic failure	3.76(0.92,15.31)	0.064
	Chronic renal failure	1.74(1.07,2.85)	0.026
	Respiratory failure	2.54(1.57,4.11)	<0.001
	AKI	2.37(1.40,4.02)	0.001
	Leukemia	0(0, Inf)	0.995
	Immunosuppression	0(0, Inf)	0.995
	Elective surgery	0.64(0.39,1.07)	0.090
	Sudden cardiac arrest	0(0, Inf)	0.995
Vital signs	Temperature (°C)	1.38(1.09,1.74)	0.007
	RR (cpm)	1.05(1.02,1.09)	0.003
	HR (bpm)	1.01(1.01,1.02)	0.002
	MAP (mmHg)	0.99(0.98,1.00)	0.028
	SBP (mmHg)	0.99(0.98,1.00)	0.117
	24h-urinary output (mL)	1.00(1.00,1.00)	0.002
Arterial blood gas	PH	0.09(0.01,0.65)	0.017
	PaO_2 (mmHg)	1.00(0.99,1.00)	0.126
	$PaCO_2$ (mmHg)	1.01(1.00,1.01)	0.143
	HCO_3^- (mmol/L)	0.99(0.96,1.03)	0.632
	Lac (mmol/L)	1.09(1.04,1.14)	<0.001
Laboratory tests	WBC (10^9/L)	1.05(1.01,1.08)	0.006
	Neutrophil (10^9/L)	1.05(1.02,1.09)	0.004
	Lymphocyte (10^9/L)	0.91(0.67,1.22)	0.527
	Neutrophil (%)	1.03(1.00,1.05)	0.021
	Lymphocyte (%)	0.97(0.95,1.00)	0.062
	Platelet (10^9/L)	1.00(1.00,1.00)	0.502
	NLR	1.01(1.00,1.03)	0.073
	PLR	1.00(1.00,1.00)	0.993
	RBC (10^{12}/L)	0.88(0.70,1.11)	0.289
	Hemoglobin (g/dl)	0.95(0.88,1.02)	0.160
	HCT	0.98(0.95,1.01)	0.142
	ALT (U/L)	1.00(1.00,1.00)	0.381
	ALP (U/L)	1.00(1.00,1.01)	<0.001
	AST (U/L)	1.00(1.00,1.00)	0.836
	TBIL (μmol/L)	1.00(0.99,1.01)	0.478
	BUN (mmol/L)	1.02(1.00,1.03)	0.014
	Cr (mg/dL)	1.00(1.00,1.00)	0.004
	INR	0.84(0.48,1.46)	0.530

(*Continued*)

Table 2 (Continued).

Classification	Variables	Univariate Cox Regression	
		HR (95%)	***p* value**
	PT (s)	0.98(0.93,1.03)	0.466
	PTT (s)	1.02(1.01,1.03)	0.003
Treatment, n (%)	MV	1.26(0.82,1.94)	0.293
	PICC	1.33(0.87,2.04)	0.192
	Urinary catheter	1.88(0.59,5.93)	0.284
	Nasogastric tube	4.29(1.74,10.58)	0.002
	Vasoactive drugs	11.01(4.80,25.22)	<0.0001
	Antibiotic treatment	1.384(0.86,2.23)	0.181
Severity score	Pitt score	1.14(1.05,1.23)	0.001
	SOFA score	1.19(1.11,1.27)	<0.001
	APACHE II score	1.07(1.04,1.10)	<0.001

Abbreviations: AKI, acute kidney injury; APACHE, acute physiology and chronic health evaluation; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; HCT, hematocrit; HR, heart rate; INR, international normalized ratio; Lac, lactate; MAP, mean arterial pressure; MV, mechanical ventilation; NLR, neutrophil lymphocyte ratio; PICC, peripherally inserted central catheter; PLR, platelet lymphocyte ratio; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cell; RR, respiratory rate; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; TBIL, total bilirubin; WBC, white blood cell.

Table 3 Multivariate Cox Analysis of Risk Factors Associated with 30-Day Mortality

Classification	Variables	Multivariate Cox regression	
		HR	***p* value**
Infection site, n (%)	Respiratory infection	1.79(1.01,3.16)	0.046
Co-morbidities, n (%)	Respiratory failure	2.18(1.28,3.69)	0.004
Vital signs	HR (bpm)	1.01(1.00,1.02)	0.022
	24h-urinary output (mL)	1.00(1.00,1.00)	<0.001
Arterial blood gas	PaO_2 (mmHg)	1.00(0.99,1.00)	0.024
	Lac (mmol/L)	1.09(1.03,1.16)	0.002
Laboratory tests	Neutrophil (10^9/L)	1.06(1.01,1.12)	0.017
	ALP (U/L)	1.00(1.00,1.01)	0.016
Treatment, n (%)	Vasoactive drugs	11.91(5.12,27.72)	<0.001

Abbreviations: ALP, alkaline phosphatase; HR, heart rate; Lac, lactate; MAP, mean arterial pressure; NLR, neutrophil lymphocyte ratio; SBP, systolic blood pressure.

Clinical Utility of the POKPI Nomogram

The clinical validity of the POKPI model was evaluated using DCA. DCA curves revealed that the POKPI model had greater net benefits than the conventional Pitt, SOFA, and APACHE II scoring systems (Figures 4, and S5–S7). Compared with the Pitt, SOFA, and APACHE II scoring systems, the POKPI model had a higher net benefit when the risk threshold ranged from 0 to 0.78, while the risk threshold of the Pitt scoring system ranged from 0.12 to 0.29, that of the SOFA scoring system ranged from 0.15 to 0.44, and that of the APACHE II scoring system ranged from 0.10 to 0.52 (Figure 4). To further substantiate the discriminative power of the model, enrolled patients were stratified into three distinct risk categories based on the quantile probability value of the nomogram model: low-, medium-, and high-risk.

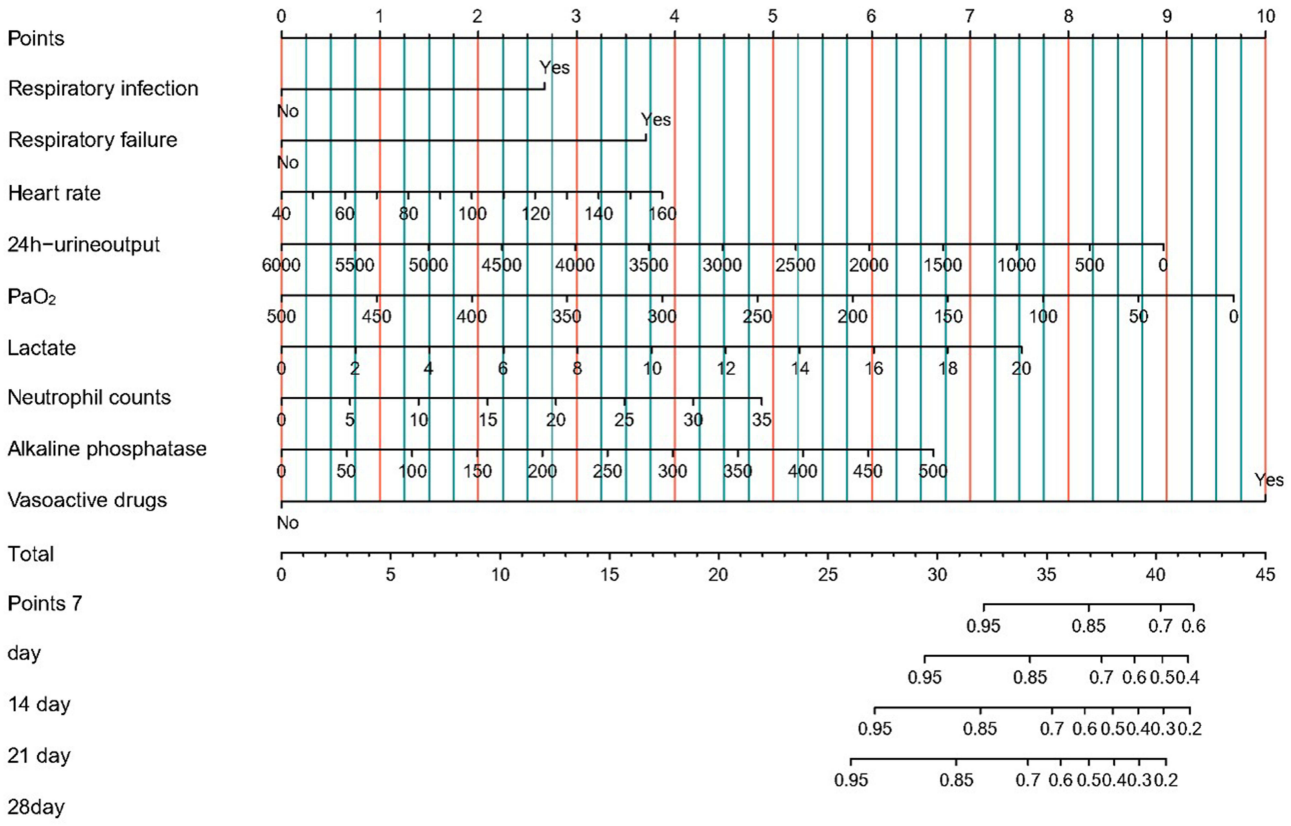

Figure 1 Nomogram prognostic model of *K. pneumoniae* infections.

Kaplan–Meier analysis was used to compare the survival of patients in these groups. As shown in Figure 5, the POKPI nomogram model effectively differentiated high-risk patients from low- and median-risk patients based on their varying survival probabilities.

Discussion

K. pneumoniae infections pose a great challenge to clinicians owing to their high morbidity and mortality rates.[25] The increasing trends in antimicrobial resistance, particularly carbapenem-resistant *K. pneumoniae* and hypervirulent strain, highlight the broader challenges faced in managing these infections.[26,27] Recognizing prognostic factors and establishing an efficient model for prognosis are essential for guiding clinical management and reducing the disease burden. This study demonstrated that PO_2, lactate, respiratory failure, respiratory tract infection, HR, 24h-urineoutput, neutrophil count, ALP, and of vasoactive drug use represent significant risk factors for the 30-day mortality of *K. pneumoniae* infections. Using these straightforward and readily available clinical indicators, a visualized nomogram model was developed and validated to predict the 7-day, 14-day, 21-day, and 28-day mortality rates of *K. pneumoniae* infection. This model provides a practical tool for clinicians for short-term risk assessment as well as a theoretical reference for planning treatment strategies.

Traditional scoring systems, such as the APACHE II, SOFA, and Pitt bacteremia scores, can be employed to predict outcomes in patients infected with *K. pneumoniae*.[12,13,15] However, compared to these traditional scoring systems, the nomogram model developed in this study presents several advantages for assessment. First, the nomogram model demonstrated superior discriminatory ability and predictive accuracy compared to the Pitt, SOFA, and APACHE II scores, indicating its effectiveness in accurate prediction. Second, the nomogram model incorporated 9 simple and clinically relevant indicators. By inputting a patient's clinical data into the model, an immediate estimation of the

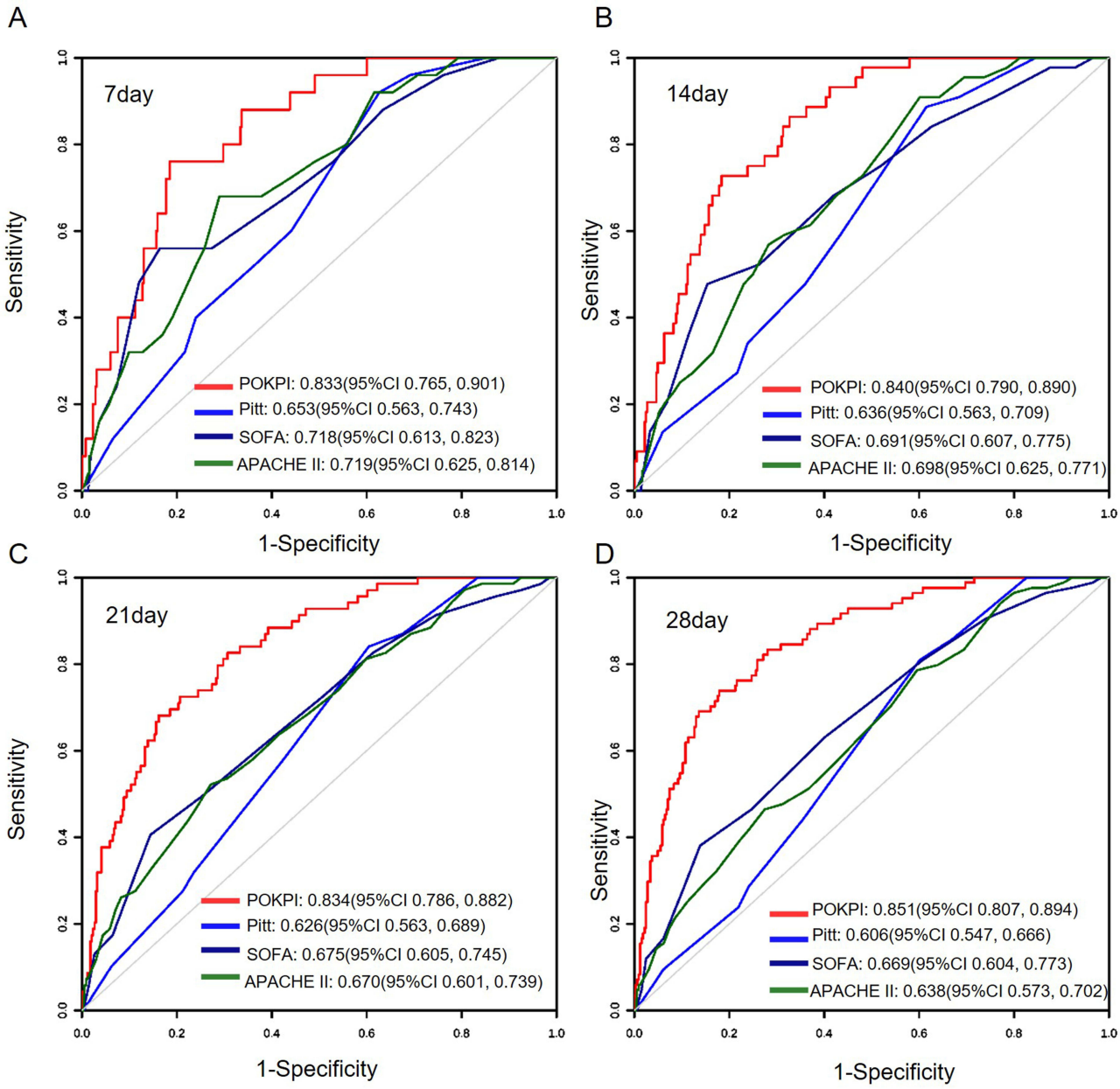

Figure 2 The ROC curves of each model for predicting 7-day, 14-day, 21-day, and 28-day mortality. The ROC curves of POKPI, Pitt, SOFA and APACHE II for predicting (**A**) 7-day mortality, (**B**) 14-day mortality, (**C**) 21-day mortality, and (**D**) 28-day mortality.
Abbreviations: AUC, area under the ROC curve; POKPI, prognostic model of *K. pneumoniae* infections; ROC, receiver operating characteristic.

likelihood of mortality risk was generated, empowering clinicians to identify critical cases and initiate prompt intervention. Finally, the nomogram model provides a practical instrument to predict mortality at critical time points (7, 14, 21, and 28-day admitted to the ICU), covering a spectrum from acute to subacute or later stages. This comprehensive temporal assessment is an exceptionally tailored tool for clinicians engaged in risk stratification and decision-making.

Previous studies have identified multiple risk factors related to the mortality of patients infected with *K. pneumoniae*, including lactic acid, respiratory infection and respiratory failure.[28–30] These factors were considered in this study. In addition, our nomogram showed that vasoactive drug use was the largest contributor to patient mortality, followed by PO_2 and lactate levels. This implies that decreased PaO_2, high lactate levels, and vasopressor requirement are strong indicators of severe disease progression, reflecting a state of septic shock or profound cardiovascular instability in

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Table 4 The AUC of Overall Mortality in Each Model Score

Models	AUC (95% CI)			
	7-day	14-day	21-day	28-day
POKPI	0.833(0.765, 0.901)	0.840(0.790, 0.890)	0.834(0.786, 0.882)	0.851(0.807, 0.894)
Pitt	0.653(0.563, 0.743)	0.636(0.562, 0.709)	0.626(0.563, 0.689)	0.606(0.547, 0.666)
SOFA	0.718(0.613, 0.823)	0.691(0.607, 0.775)	0.675(0.605, 0.745)	0.669(0.604, 0.733)
APACHE II	0.719(0.625, 0.814)	0.698(0.625,0.771)	0.670(0.601, 0.739)	0.638(0.573, 0.702)

Abbreviations: AUC, area under the ROC curve; CI, Confidence Interval; ROC, receiver operating characteristic; POKPI, prognostic model of *K. pneumoniae* infections.

Table 5 The C-Index of Overall Mortality in Each Model Score

Models	C-index (95% CI)			
	7-day	14-day	21-day	28-day
POKPI	0.820(0.767, 0.891)	0.822(0.784, 0.873)	0.808(0.775, 0.846)	0.814(0.787, 0.853)
Pitt	0.649(0.546, 0.720)	0.630(0.576, 0.701)	0.617(0.562, 0.677)	0.601(0.553, 0.655)
SOFA	0.711(0.602, 0.800)	0.683(0.604, 0.760)	0.664(0.603, 0.726)	0.656(0.602, 0.714)
APACHE II	0.713(0.622, 0.798)	0.690(0.630, 0.757)	0.660(0.606,0.721)	0.633(0.577, 0.691)

Abbreviations: APACHE, the acute physiology and chronic health evaluation; SOFA, the Sequential Organ Failure Assessment; Pitt, Pitt bacteremia score; POKPI, prognostic model of *K. pneumoniae* infections.

response to *K. pneumoniae* infection. Decreased PaO_2, rising lactate concentration, and vasopressor requirement should be considered crucial predictors for the recognition of impending critical illness.

Respiratory infection and failure are significant predictors of mortality risk. *K. pneumoniae* commonly colonizes the lower respiratory tract and frequently causes pulmonary infections, particularly in severely ill patients. This study revealed that 73.08% of the enrolled patients with *K. pneumoniae* infections had their primary site of infection originating from the respiratory tract, indicating lung involvement in most cases. The presence of respiratory failure not only reflects the severity of lung injury but also indicates a higher likelihood of multiorgan dysfunction.[31] The inability of the respiratory system to sustain adequate gas exchange results in a chain reaction that may impair the perfusion and function of other vital organs, potentially increasing the risk of systemic collapse.[32] Therefore, the early identification, prompt treatment, and effective management of respiratory infections caused by *K. pneumoniae* are imperative. This highlights the urgency of aggressive interventions to counteract the imminent threat to the overall organ functionality and survival in infected patients.

Neutrophils are the most abundant cells of the innate immune system, play crucial roles in the body's immune response to bacterial infections, and have significant implications for the outcome of *K. pneumoniae* infections.[33,34] Our findings demonstrate that neutrophil count at the time of admission to the ICU is a significant risk factor for 30-day mortality in patients with *K. pneumoniae* infection. This observation is consistent with a previous study that investigated 103 patients co-infected with carbapenem-resistant *Acinetobacter baumannii* and carbapenem-resistant *K. pneumoniae*, which proposed that neutrophils, along with C-reactive protein, could serve as predictors of 30-day mortality.[35] As a readily available laboratory parameter, neutrophil count offers a practical and objective way to assess the likelihood of adverse outcomes in infected individuals.

ALP is an enzyme found in various tissues including the liver, kidneys, and bones.[36] Research has shown that elevated ALP levels are correlated with poor outcomes in critically ill patients, especially in infectious diseases involving the liver.[37] In this study, ALP level was found to be a significant predictor of mortality risk. In the context of *K. pneumoniae* infections, higher ALP concentrations may suggest more extensive organ involvement or a greater degree of organ failure, both of which increase the likelihood of death. However, whether ALP had a prognostic

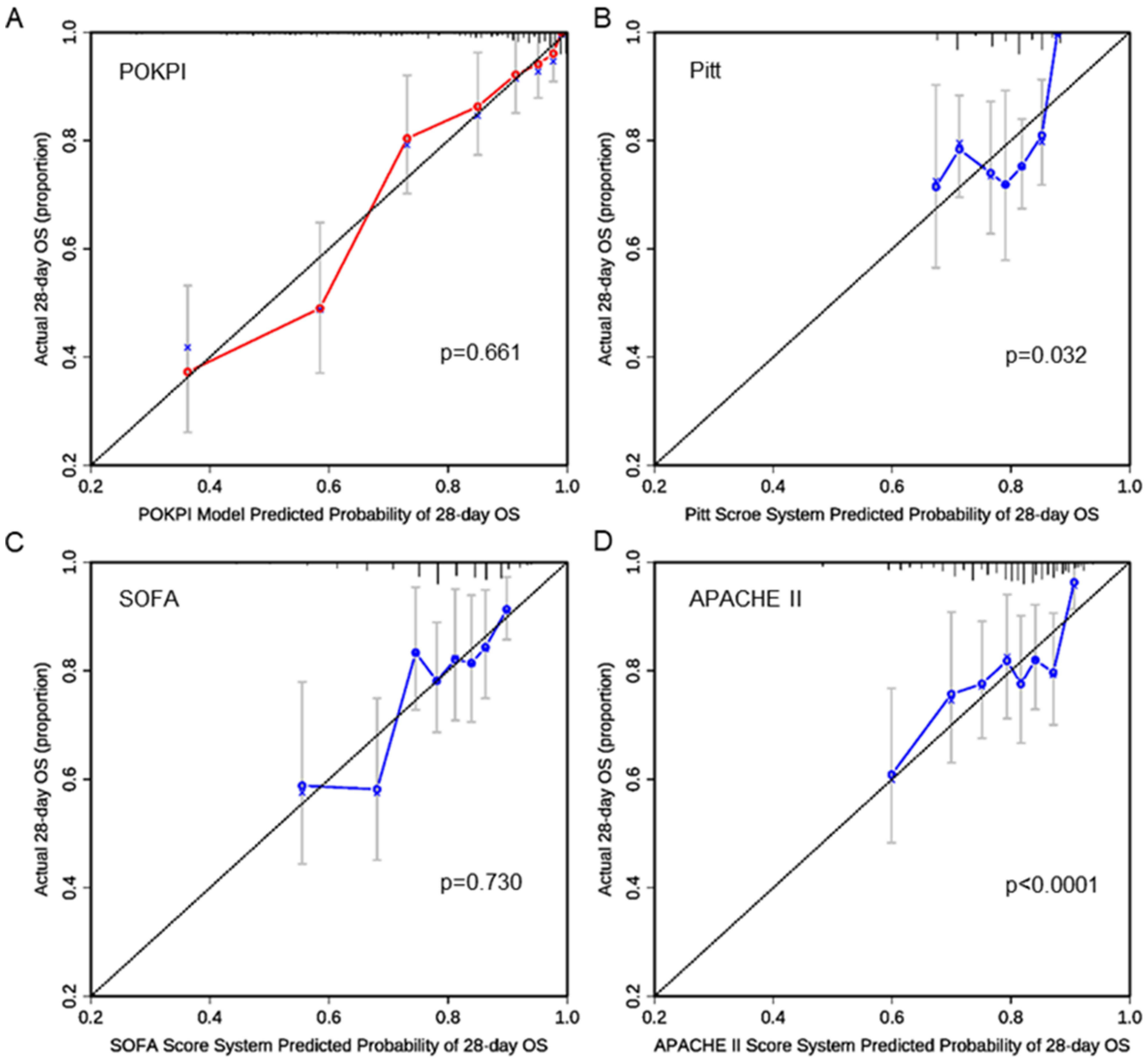

Figure 3 Calibration curves of each model for predicting 28-day mortality. Calibration curves of (**A**) POKPI model, (**B**) Pitt bacteremia score, (**C**) SOFA score, and (**D**) APACHE II score for predicting 28-day mortality. Each model predicted probability of 28-day mortality is shown on the x-axis, and actual rate of 28-day mortality is shown on the y-axis.

Abbreviations: APACHE, the acute physiology and chronic health evaluation; SOFA, the Sequential Organ Failure Assessment; POKPI, prognostic model of *K. pneumoniae* infections.

significance remains uncertain.[36,38,39] This variability could stem from differences in study populations, sample sizes, and methodologies used, as well as the multifactorial nature of host-pathogen interactions and diverse pathophysiological pathways involved in *K. pneumoniae* infections.

Compared to traditional prediction models or scoring systems, this model offers several advantages. First, as a visual assessment tool, the nomogram enables users to through simple addition and subtraction to quickly obtain the occurring probability of predicted results. Second, the predictors incorporated into this nomogram are readily assessable, and the nomogram has demonstrated good discriminatory ability, calibration, and clinical utility across both the development and validation cohorts. This indicates that the nomogram possesses strong transferability and generalizability. Although our study has strengths, there are also limitations to consider. First, although the nomogram model performed well in internal cross-validation, external validation through multicenter studies may

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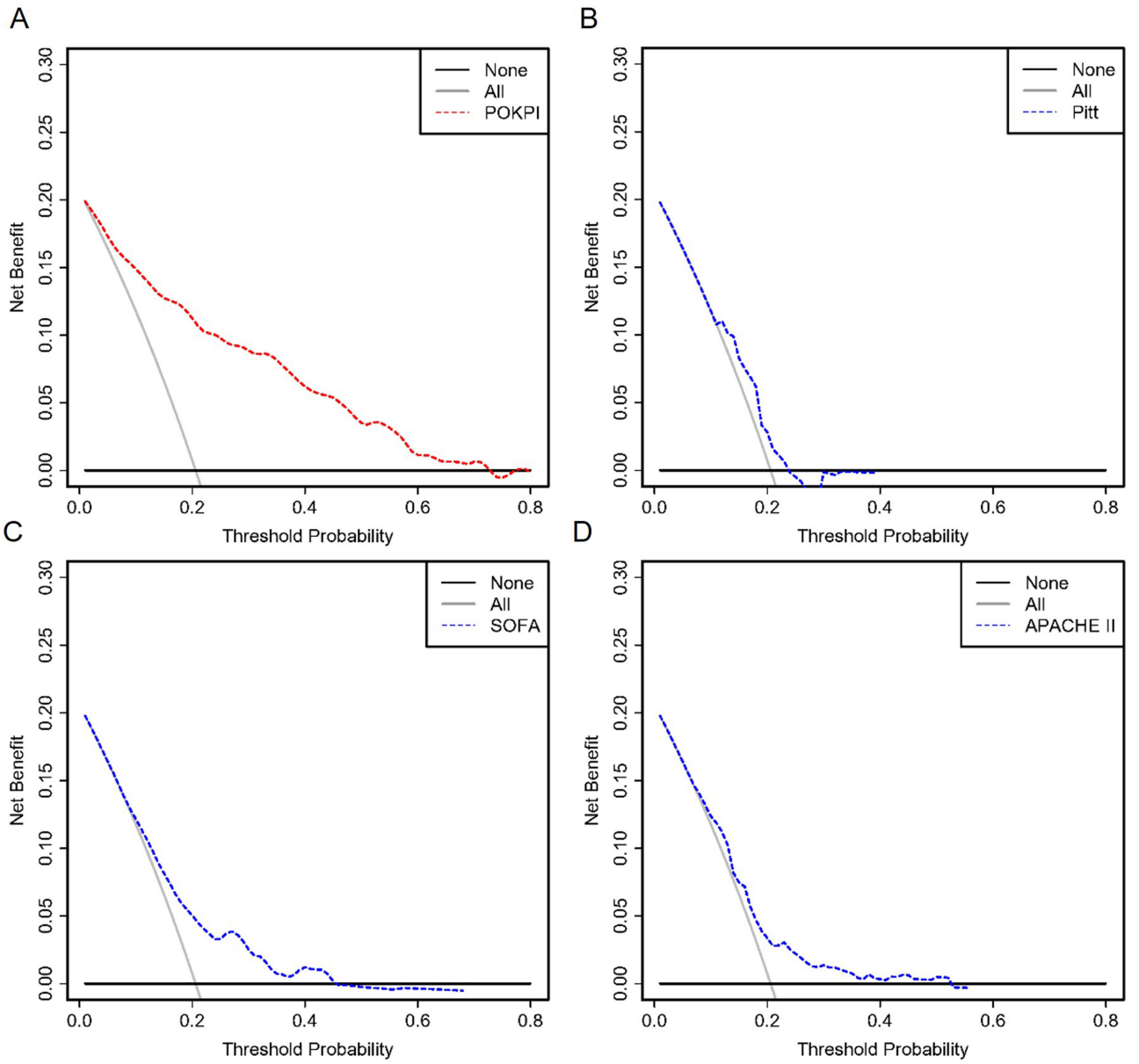

Figure 4 Decision curves analysis of each model for predicting 28-day survival. Decision curves analysis of (**A**) POKPI model, (**B**) Pitt bacteremia score, (**C**) SOFA score, and (**D**) APACHE II score for predicting 28-day mortality.

Abbreviations: APACHE, the acute physiology and chronic health evaluation; SOFA, the Sequential Organ Failure Assessment; POKPI, prognostic model of *K. pneumoniae* infections.

be required. Second, we selected cases with confirmed *K. pneumoniae*-positive microbial cultures, without considering multiple infections. Future studies should take this into consideration. Finally, while ALP and neutrophil counts in this study can provide valuable insights into risk prediction, further research is essential to fully understand their specific mechanisms. This understanding could pave the way for exploring new classes of antibiotics, providing a promising avenue for combating diseases caused by *K. pneumoniae*.[40,41]

In summary, nine clinical prognostic factors were identified, and a nomogram was constructed to predict the 7-day, 14-day, 21-day, 28-day mortality rates of *K. pneumoniae* infections. The nomogram model showed good predictive value, implying its potential as a clinical instrument for early identification of high-risk patients and monitoring disease progression.

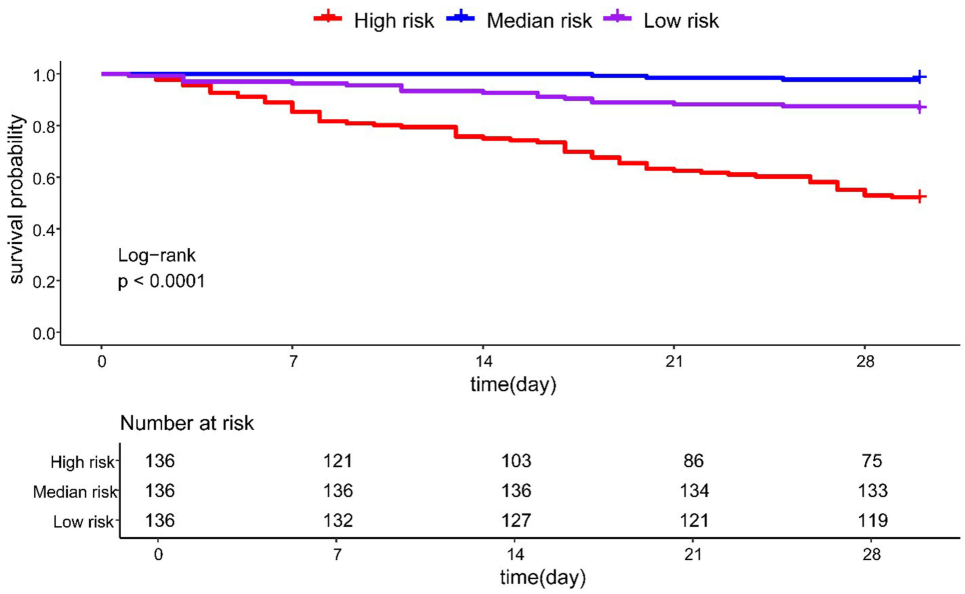

Figure 5 Kaplan-Meier survival curve of the POKPI. Abbreviations: POKPI, prognostic model of *K. pneumoniae* infections.

Abbreviations

AKI, acute kidney injury; APACHE, acute physiology and chronic health evaluation; ALP, alkaline phosphatase; ALT, alanine transaminase; AUC, area under the receiver operating characteristic curve; AST, aspartate aminotransferase; BUN, blood urea nitrogen; C-index, concordance index; Cr, creatinine; DCA, decision curves analysis; ESBL, extended-spectrum β-lactam; HCT, hematocrit; HR, heart rate; ICU, intensive care unit; INR, international normalized ratio; Lac, lactate; MAP, mean arterial pressure; MV, mechanical ventilation; NLR, neutrophil lymphocyte ratio; PICC, peripherally inserted central catheter; PLR, platelet lymphocyte ratio; POKPI, prediction of *K. pneumoniae* infections; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cell; ROC, receiver operating characteristic curve; RR, respiratory rate; SBP, systolic blood pressure; SOFA, sequential organ failure assessment; TBIL, total bilirubin; WBC, white blood cell.

Data Sharing Statement

Data for this study are available upon request from the author.

Acknowledgments

We thank Peking University Third Hospital for providing open data resources and all investigators who participated in the study.

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.

Funding

This work was supported by grants from the National Key Research and Development Program of China (2022YFC2303200) and Beijing Key Clinical Specialty Funding (No. 010071).

Disclosure

The authors declare no conflicts of interest.

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