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ORIGINAL RESEARCH

A Mortality Prediction Nomogram for *Stenotrophomonas maltophilia* Bloodstream Infection

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Background: The World Health Organization classifies *Stenotrophomonas maltophilia* (*S. maltophilia*) as one of the most overlooked and difficult-to-treat multidrug-resistant pathogens. It mainly causes pneumonia and bloodstream infections (BSIs). Therefore, the aim of this study was to investigate the risk factors for mortality in patients with *S. maltophilia* BSIs and to construct a predictive nomogram model.

Methods: Clinical data were collected from patients with *S. maltophilia* BSIs who were admitted to the First Affiliated Hospital of Sun Yat-sen University from January 2013 to December 2023. Prognostic risk factors were identified using Cox regression and LASSO analysis. A nomogram was developed based on a multivariate analysis and validated using bootstrap resampling, receiver operating characteristic curve analysis, and calibration plots.

Results: The mortality rate was 20.0% among 85 patients with *S. maltophilia* BSIs. Multivariable analysis identified septic shock (hazard ratio [HR] = 7.859, 95% confidence interval (CI): 1.569–79.607; P = 0.009) and respiratory diseases (HR = 7.602, 95% CI: 2.269–39.202; $P < 0.001$) as independent risk factors for mortality. A predictive nomogram model incorporating these factors demonstrated excellent discrimination, with a C-index of 0.872 and high area under the curve values for 14-day (0.922) and 28-day (0.882) mortality. Calibration analysis showed precise agreement between predicted and observed outcomes.

Conclusion: Septic shock and respiratory diseases were independent risk factors for mortality in patients with *S. maltophilia* BSIs. The nomogram model developed in this study showed good predictive value for the survival rates of patients with *S. maltophilia* BSIs, thus facilitating clinical prevention and treatment.

Keywords: *Stenotrophomonas maltophilia*, bloodstream infections, risk factors for mortality, nomogram

Introduction

Stenotrophomonas maltophilia (*S. maltophilia*) is a non-fermenting, gram-negative, opportunistic pathogen that has demonstrated an increasing prevalence in clinical settings in recent years.[1–3] The World Health Organization classifies *S. maltophilia* as one of the most overlooked and difficult-to-treat multidrug-resistant pathogens.[3,4] Recent epidemiological data indicate an increasing incidence of *S. maltophilia* infections in healthcare settings, with a global pooled rate of 4.2 cases per 10,000 patient-days, increasing to 12.7 cases per 10,000 patient-days in intensive care units (ICUs).[5] According to the 2023 CHINET China Antimicrobial Resistance Surveillance data, *S. maltophilia* ranks third among non-fermenting bacteria, accounting for 11.6%.[6] *S. maltophilia* is the sixth most common pathogen causing pneumonia in ICUs in the United States,[7] and is one of the top ten pathogens responsible for pneumonia in medical centers in Latin America.[8] *S. maltophilia* mainly causes pneumonia[9] and bloodstream infections (BSIs),[10] the overall mortality rate

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associated with *S. maltophilia* infections is as high as 75% in severely ill, and immunocompromised hospitalized patients.[2,4,11,12]

S. maltophilia is intrinsically resistant to several antibiotics, including β-lactams and aminoglycosides. The bacteria form biofilms that firmly adhere to the surfaces of various medical devices, such as dialysis equipment, blood pressure monitors, sphygmomanometers, and ventilators.[13] A previous meta-analysis demonstrated that the biofilm formation mechanism of *S. maltophilia* involves: (1) extracellular polymeric substance production, (2) quorum-sensing-regulated adhesion, and (3) upregulated efflux pumps, which collectively enhance antimicrobial resistance and surface persistence on both biotic and abiotic substrates.[13] *S. maltophilia* invades the host and can evade the host's immune system through different virulence exoenzymes.[14] Additionally, under antibiotic selection pressure, *S. maltophilia* can acquire resistance genes such as *sul1, sul2*, *qac*, and *smr*, posing significant challenges to effectively treating these infections.[15]

Despite its clinical urgency, risk stratification tools for *S. maltophilia* BSIs remain underdeveloped. Previous studies lacked mortality prediction models, and regional data from China are scarce. We analyzed 11-year data (2013–2023) from a tertiary hospital to identify mortality risk factors and develop a nomogram for clinical risk stratification. This work addresses a critical gap in *S. maltophilia* BSIs.

Materials and Methods

Study Design and Patients

This study was conducted at the First Affiliated Hospital of Sun Yat-sen University, a national tertiary care hospital with over 3,000 inpatient beds in China. A total of 85 patients with *S. maltophilia* BSIs at the First Affiliated Hospital of Sun Yat-sen University from January 2013 to December 2023 were included in this study. The inclusion criteria were (1) age ≥ 18 years, (2) definitive *S. maltophilia* BSIs, defined as monomicrobial isolation from ≥ one blood culture accompanied by one or more clinical signs of a systemic inflammatory response (temperature ≥ 38°C or < 36°C, chills, a decrease in systolic blood pressure of < 90 mmHg or > 40 mmHg from baseline, heart rate > 90 beats/min, respiratory rate > 20 breaths/min, or altered mental status),[16] (3) positive blood culture, with *S. maltophilia* as the sole isolate, and (4) complete clinical documentation. The exclusion criteria were (1) hospitalization duration < 48 hours, and (2) polymicrobial BSIs. Data on demographics, clinical characteristics, therapeutic interventions, and patient outcomes were collected.

Definitions

Hospital-acquired infection refers to a new infection that occurs during hospitalization (usually 48 hours after admission) and the patient has no history of hospitalization within 90 days prior to the infection. Septic shock is a life-threatening condition characterized by an infection-induced systemic inflammatory response, hemodynamic instability, and multiple organ dysfunction. Respiratory diseases were clinically defined by the presence of respiratory-related symptoms accompanied by objective evidence of structural or functional abnormalities in the respiratory system. Hematologic tumors were defined as malignant disorders originating from the hematopoietic or lymphoid systems, primarily characterized by the clonal proliferation of abnormal cells in the bone marrow, blood, lymph nodes, and lymphoid tissues. In this study, kidney diseases referred to a spectrum of disorders that impair the structure and/or function of the kidneys.

Microbiological Methods

Blood cultures were analyzed using the automated BacT/ALERT® 3D microbial detection system (bioMérieux, France) with continuous monitoring for microbial growth. The strains were identified and tested for antimicrobial susceptibility using the VITEK 2 automated microbial identification and susceptibility testing system developed by bioMérieux in France. The antimicrobial susceptibility testing standards adhered to the current Clinical and Laboratory Standards Institute M100 guidelines. *Pseudomonas aeruginosa* ATCC 27853 was used as the quality control strain for the tests.

Statistical Analysis

Categorical variables were presented as n (%), and compared using the chi-square test. All statistical analyses were performed using R software (version 4.4.0). Univariate Cox regression analysis was initially performed to identify the variables associated with mortality risk in *S. maltophilia* BSIs. Subsequently, least absolute shrinkage and selection operator (LASSO) regression was applied to further refine the variable selection. The final independent risk factors were determined using a multivariate Cox model with Firth's penalized partial likelihood correction to construct a nomogram. A prognostic nomogram was constructed based on the independent risk factors identified for *S. maltophilia* BSIs-related mortality. The model's discriminative ability was assessed using the concordance index (C-index). Internal validation was performed using bootstrap resampling (B = 1000 iterations). Model performance was further evaluated using receiver operating characteristic (ROC) curve analysis and calibration plots.

Results

Characteristics of Patients with *S. maltophilia* BSIs

Among the 85 patients with *S. maltophilia* BSIs, 71.8% were male and 18.8% were ≥ 65 years old. Among them, 31.8% were admitted to the ICU, and 34.1% had septic shock. The most common underlying disease among patients was hematological tumors (45.9%), followed by respiratory diseases (36.5%). The invasive procedure performed most frequently was arteriovenous cannulation (74.1%), followed by the placement of a drainage tube (42.4%) or urinary catheters (36.5%). Prior to the onset of BSIs, 81.2% of the patients had received carbapenems, while 30.6% were treated with tigecycline and 12.9% with levofloxacin. After adjusting the antimicrobial regimen according to blood culture susceptibility results, the treatment distribution was levofloxacin in 41.2% of the patients, tigecycline in 41.2%, trimethoprim/sulfamethoxazole in 5.9%, and minocycline in 7.1% (Table 1). Regarding the recommended first-line antibiotics, antimicrobial susceptibility testing revealed that the resistance rates were generally low. Specifically, 12.4% of the isolates showed levofloxacin resistance, 2.6% showed trimethoprim-sulfamethoxazole resistance, and 0.9% showed minocycline resistance.

Risk Factors for Mortality in Patients with *S. maltophilia* BSIs

Seventeen patients died and 68 survived, for a mortality rate of 20.0% (Table 1). The results of the univariate Cox regression analysis indicated that ICU admission, septic shock, respiratory diseases, kidney diseases, endotracheal intubation, and a nasogastric tube were potential risk factors for mortality in patients with *S. maltophilia* BSIs ($P < 0.05$, Table 2). The potential predictors were subjected to LASSO-Cox regression analysis, with variable coefficient shrinkage paths shown in Figure 1A. The optimal penalty parameter ($\lambda = 0.104$) was determined through tenfold cross-validation using the one-standard-error rule, resulting in the most parsimonious set of predictive variables while preserving model performance (Figure 1B). Sensitivity analysis confirmed the robustness of this variable selection, as the core prognostic factors (ICU admission, septic shock, and respiratory diseases) were consistently selected under both the optimal (λ.min = 0.045) and conservative (λ.1se = 0.104) criteria. The variable kidney diseases, while selected in the optimal model, was excluded by the more stringent 1-SE rule due to its relatively weaker effect, demonstrating the method's ability to distinguish stable predictors from context-sensitive ones. Selected variables (ICU admission, septic shock, and respiratory diseases) were subsequently analyzed using the multivariable Cox model with Firth's penalized partial likelihood correction. The final analysis identified both septic shock (hazard ratio [HR] = 7.859, 95% confidence interval (CI): 1.569–79.607; $P = 0.009$) and respiratory diseases (HR = 7.602, 95% CI: 2.269–39.202; $P < 0.001$) as independent risk factors for mortality in patients with *S. maltophilia* BSIs (Table 2).

Predictive Nomogram Model for the Probability of Survival in Patients with *S. maltophilia* BSIs

A nomogram was constructed based on the two independent risk factors for mortality, septic shock and respiratory diseases, to predict the probability of the survival of patients with *S. maltophilia* BSIs (Figure 2). In practical applications, the corresponding score for each predictive factor was indicated in the nomogram, and a total score was

Table 1 Comparison of Clinical Data Between Patients with *S. maltophilia* BSIs

Variable	Total, N (%)	Survivors, N (%)	Death, N (%)	χ^2	*P* value
	(N=85)	(N=68)	(N=17)		
Male	61 (71.8)	47 (69.1)	14 (82.4)	0.613	0.434
Age≥65y	16 (18.8)	12 (17.6)	4 (23.5)	0.043	0.835
Hospital-acquired infections	5 (5.9)	3 (4.4)	2 (11.8)	0.332	0.564
ICU admission	27 (31.8)	13 (19.1)	14 (82.4)	25.090	<0.001
Septic shock	29 (34.1)	13 (19.1)	16 (94.1)	34.034	<0.001
Comorbidities					
Respiratory diseases	31 (36.5)	16 (23.5)	15 (88.2)	24.576	<0.001
Hematological tumors	39 (45.9)	36 (52.9)	3 (17.6)	6.823	0.009
Kidney Diseases	18 (21.2)	12 (17.6)	6 (35.3)	1.590	0.207
Co-morbidities ≥ 3	32 (37.6)	22 (32.4)	10 (58.8)	4.060	0.044
Invasive operation					
Endotracheal intubation	25 (29.4)	14 (20.6)	11 (64.7)	12.750	<0.001
Arteriovenous cannulation	63 (74.1)	46 (67.6)	17 (100.0)	5.830	0.016
Urinary catheters	31 (36.5)	20 (29.4)	11 (64.7)	7.312	0.007
Drainage tube	36 (42.4)	27 (39.7)	9 (52.9)	0.976	0.323
Nasogastric tube	24 (28.2)	14 (20.6)	10 (58.8)	8.016	0.005
Previous antimicrobial exposure					
Carbopenems	69 (81.2)	53 (77.9)	16 (94.1)	1.391	0.238
Levofloxacin	11 (12.9)	9 (13.2)	2 (11.8)	<0.001	1.000
Tigecycline	26 (30.6)	21 (30.9)	5 (29.4)	0.014	0.906
Targeted antimicrobial medication					
Levofloxacin	35 (41.2)	28 (41.2)	7 (41.2)	<0.001	1.000
Sulfamethoxazole/trimethoprim	5 (5.9)	3 (4.4)	2 (11.8)	0.332	0.564
Minocycline	6 (7.1)	5 (7.4)	1 (5.9)	<0.001	1.000
Tigecycline	35 (41.2)	26 (38.2)	9 (52.9)	1.214	0.270

Table 2 Identification of Risk Factors for Mortality in Patients with *S. maltophilia* BSIs Through Univariate Cox Regression-LASSO Regression-Multivariate Cox Regression

Variable	Univariate Cox		LASSO		Multivariate Cox	
	HR(95% CI)	*P* value	Coef	HR	HR(95% CI)	*P* value
ICU admission	10.517 (3.014–36.698)	<0.001	0.267	1.306	2.259 (0.713–9.686)	0.177
Septic shock	14.419 (4.562–59.662)	0.001	0.742	2.099	7.859 (1.569–79.607)	0.009
Respiratory diseases	8.091 (2.674–24.477)	<0.001	0.738	2.092	7.602 (2.269–39.202)	<0.001
Kidney Diseases	2.789 (1.022–7.615)	0.046	0.029	1.029		
Endotracheal intubation	3.578 (1.317–9.723)	0.012				
Nasogastric tube	2.751 (1.043–7.260)	0.041				

obtained by summing the scores of all predictive factors. The total score on the risk axis represented the survival probability of the patient with *S. maltophilia* BSIs. The higher the total score, the lower the survival probability of the patient with *S. maltophilia* BSIs.

Evaluation of the Nomogram Prediction Model

The developed nomogram demonstrated robust discriminative capacity, with a C-index value of 0.872 (95% CI: 0.803–0.940) in the derivation cohort and a bootstrap-validated C-index value of 0.882 (95% CI: 0.765–0.919). The model showed superior predictive performance in *S. maltophilia* BSIs mortality risk stratification; the time-dependent ROC analysis yielded AUC values of 0.922 (95% CI: 0.813–0.970; sensitivity 85.7%, specificity 93.0%) for 14-day

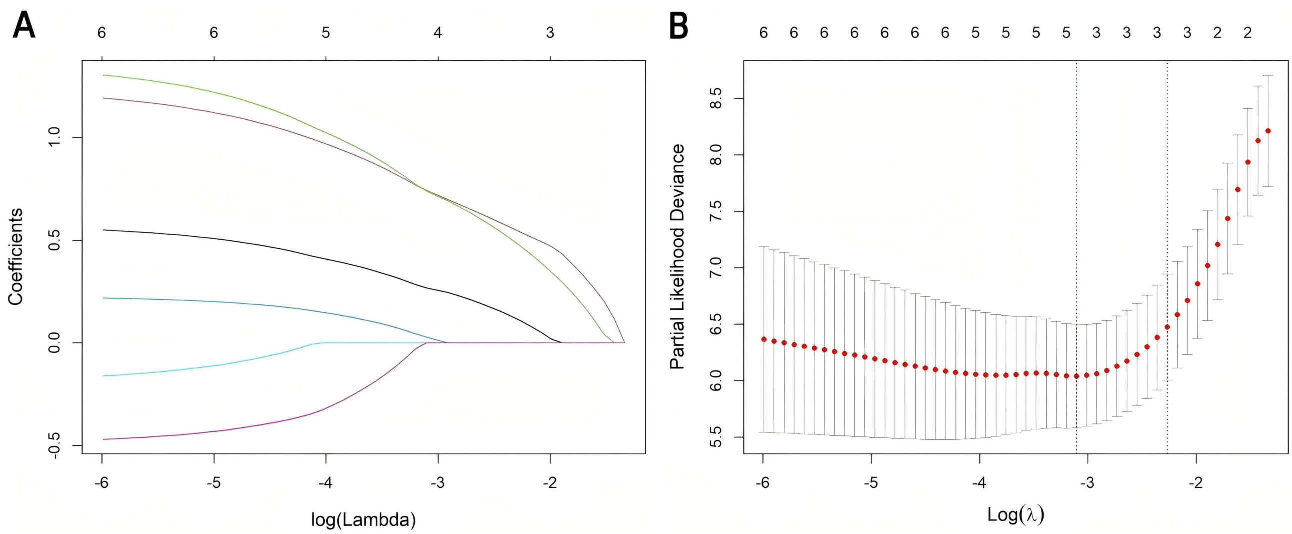

Figure 1 LASSO-Cox regression analysis for factor selection in patients with *S. maltophilia* BSIs. (**A**) Coefficients profiles of the radiomic features. (**B**) Optimal parameter (lambda) selection in the LASSO model used tenfold cross-validation. The partial likelihood deviance curve was plotted versus log (lambda).

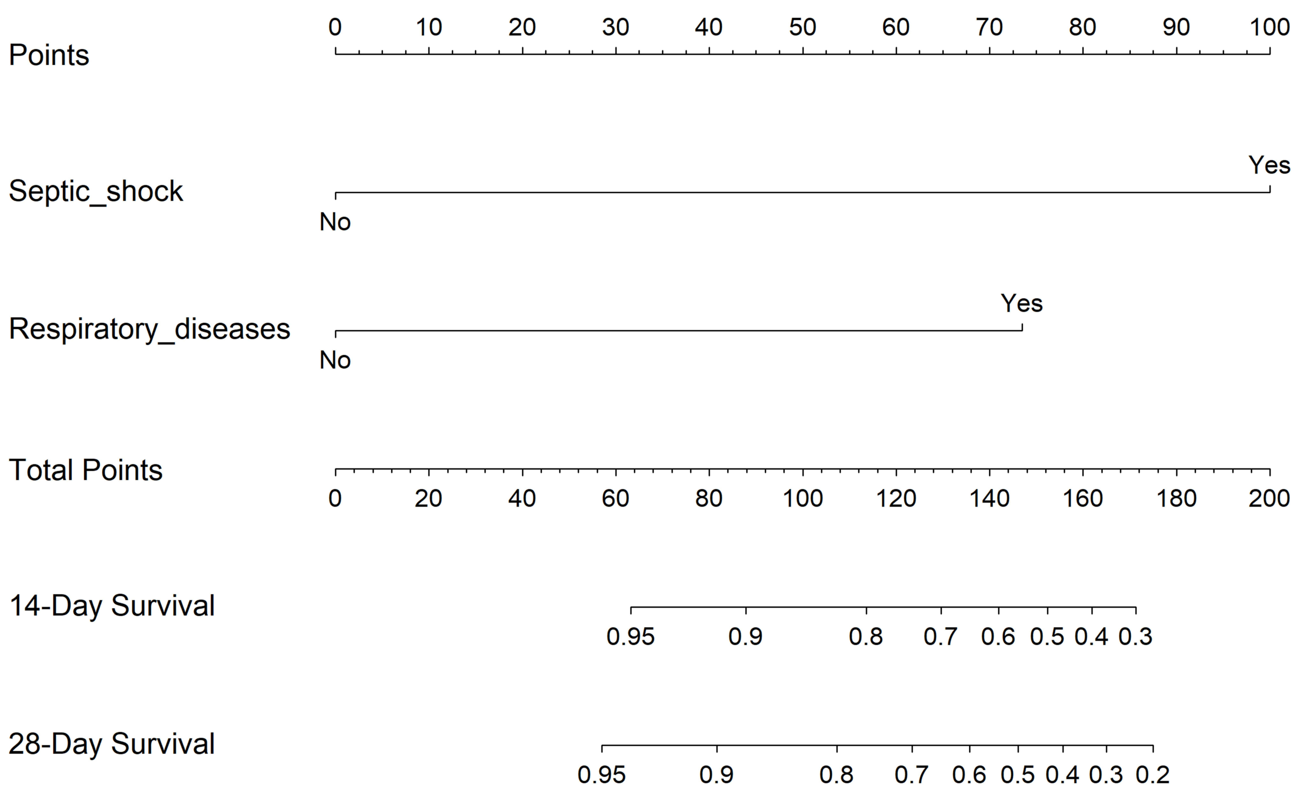

Figure 2 Nomogram model predicting 14-Day and 28-Day survival in patients with *S. maltophilia* BSIs.

mortality and 0.882 (95% CI: 0.703–0.959; sensitivity 80.0%, specificity 92.9%) for 28-day mortality prediction (Figure 3). Calibration analysis revealed precise agreement between the predicted and observed outcomes across both timepoints (Figure 4). The Hosmer–Lemeshow goodness-of-fit test confirmed model calibration (14-day: $\chi^2 = 0.992$, $P = 0.803$; 28-day: $\chi^2 = 0.328$, P = 0.567), with non-significant *P*-values indicating appropriate fit. The combined evidence of strong discrimination and precise calibration suggests that this nomogram meets rigorous standards for clinical implementation in predicting *S. maltophilia* BSIs prognosis.

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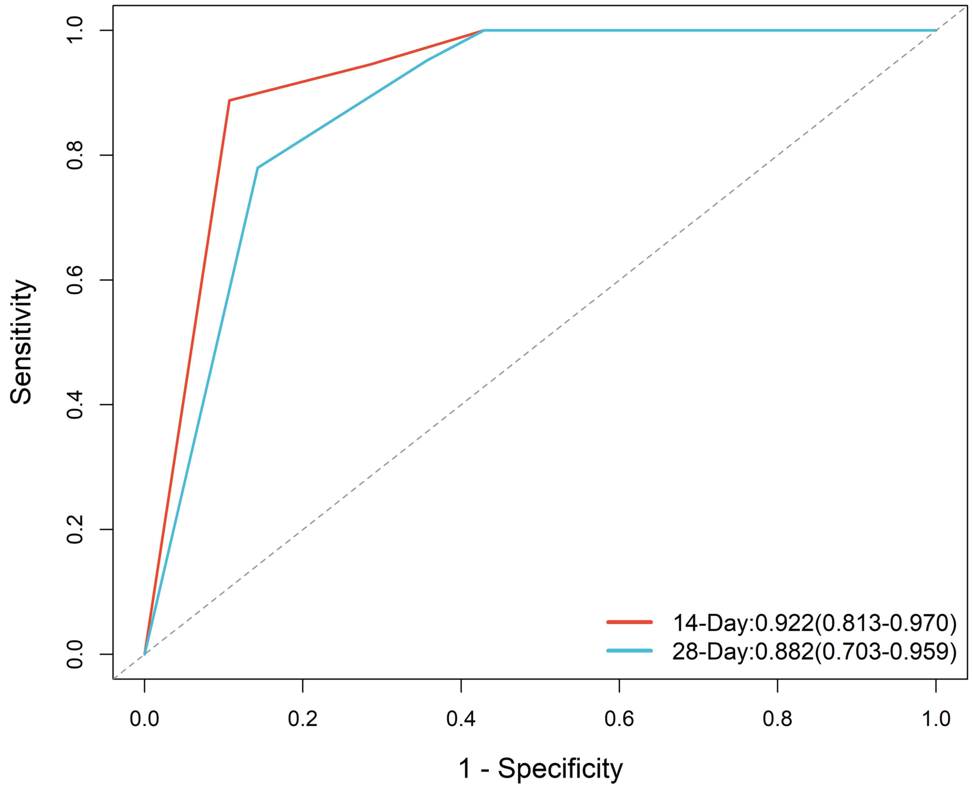

Figure 3 ROC curves of the nomogram model for predicting 14-Day and 28-Day survival in patients with *S. maltophilia* BSIs.

Discussion

BSIs are some of the most severe infections commonly occurring in clinical practice and are the leading cause of death in elderly patients,[17] most of which are caused by *S. maltophilia* (13.7%), ranking only second after *Escherichia coli* (17.3%).[10] Consistent with prior findings,[18] our study observed a male predominance among *S. maltophilia* BSIs cases. This gender disparity may stem from stronger innate and adaptive immune responses in women, as well as behavioral factors (eg, lifestyle, environmental exposure, and healthcare access).[19] Approximately one-fifth of patients in this study were aged ≥ 65 years, whose infections might be related to declining immune function, high hospitalization rates, and the presence of multiple underlying diseases.[20,21]

S. maltophilia is commonly found in healthcare settings, and the risk of infection increases in patients who undergo invasive procedures, including endotracheal intubation.[1] ICU patients are particularly vulnerable due to comorbidities, critical illnesses, frequent broad-spectrum antibiotic exposure, and invasive interventions.[22,23] A previous study reported that the mortality rate in patients with *S. maltophilia* BSIs[24] ranged from 14% to 69%, underscoring the need for vigilance in these populations. In this study, the mortality rate of patients with *S. maltophilia* BSIs was 20%, with septic shock and respiratory diseases as independent risk factors for mortality in these patients.

We developed and validated a nomogram for predicting the survival of patients with *S. maltophilia* BSIs, which demonstrated robust discriminative power (C-index: 0.872–0.882) and calibration accuracy. The model incorporates two easily assessable predictors, septic shock and respiratory diseases, enabling straightforward bedside risk stratification. Clinicians can calculate individual scores, sum them, and map the total to a survival probability, where higher scores correlate with poorer outcomes. This tool addresses a critical gap in managing *S. maltophilia* BSIs, particularly in immunocompromised patients.

The main challenge of *S. maltophilia* infections in clinical practice is the significant increase in its antibiotic resistance, which is primarily attributed to the production of inducible β-lactamase,[25] which confers resistance to β-lactams and carbapenems.[26,27] A total of 68.2% of the patients who received an empirical combination of antibiotics after BSI onset,

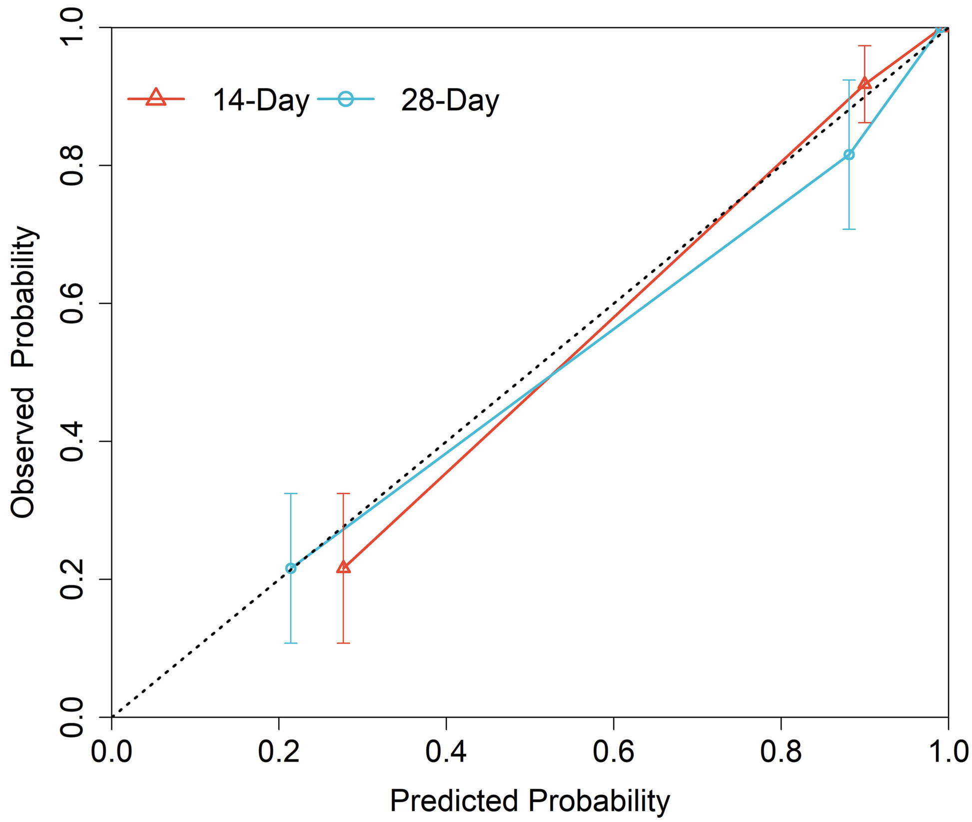

Figure 4 Calibration curves of the nomogram model for predicting 14-Day and 28-Day survival in patients with *S. maltophilia* BSIs.

with carbapenems being the most commonly used drug, showed poor therapeutic outcomes.[18] The Infectious Diseases Society of America guidelines recommend trimethoprim-sulfamethoxazole for *S. maltophilia* mild infections and combination therapy for severe cases;[28,29] however, its use was limited in our hematologic malignancy cohort due to myelosuppression risks, leading to preferential levofloxacin use. Levofloxacin was also preferred to prevent infections during stem cell transplantation or chemotherapy.[30] This study has several limitations. First, genotyping analysis was not performed to confirm clonality. Second, this was a single-center, retrospective analysis with a relatively small cohort. Although stringent statistical methods were applied, the limited sample size may compromise the stability of the predictive model. Future multicenter studies incorporating molecular profiling and machine learning could enhance the predictive robustness of the nomogram.

Conclusion

In summary, this study systematically validated septic shock and respiratory diseases as effective predictors of mortality in patients with *S. maltophilia* BSIs and developed a time-dependent dynamic prediction model, which demonstrated high discriminative performance. The model exhibited good discrimination and calibration, outperforming conventional static scoring systems. Although limited by its single-center retrospective design, this tool addresses a critical gap in managing *S. maltophili*a BSIs, particularly in immunocompromised patients.

Data Sharing Statement

Data will be available upon reasonable request from the corresponding author (Liubing Li, Email: lilb8@mail.sysu.edu.cn).

Ethics Approval and Consent to Participate

This study complies with the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University (Approved No. of ethics committee: 2025503). The requirement for written informed consent was waived because of the retrospective analysis of anonymized data.

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Disclosure

The authors report no conflicts of interest in this work.

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